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# New Functionalized Grignard Reagents and their Applications in Amination Reactions

von

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aus

Pforzheim

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**Erklärung**

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**Ehrenwörtliche Versicherung**

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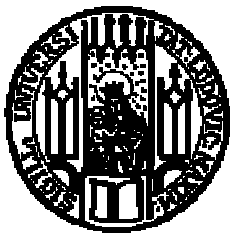

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1.) A. Eeg Jensen, W. Dohle, I. Sapountzis, D. M. Lindsay, V. Anh Vu, P. Knochel "Practical Synthetic Procedures: Preparation and Reactions of Functionalized Arylmagnesium Reagents" *Synthesis*, **2002**, 565-569.

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4.) I. Sapountzis, P. Knochel, "A New General Preparation of Polyfunctional Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Nitroarenes" *J. Am. Chem. Soc.* **2002**, *124*, 9390-9391.

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7.) I. Sapountzis, P. Knochel "New General Amination Method Using the Addition of Polyfunctional Arylmagnesium Reagents to Functionalized Arylazo Tosylates" *Angew. Chem.* **2004**, *116*, 915-918; *Angew. Chem. Int. Ed.* **2004**, *43*, 897-900.

8.) I. Sapountzis, H. Dube, P. Knochel "Synthesis of Nitro-Substituted Polyfunctional Biphenyls by Negishi Cross-Coupling of *o*-Nitroarylzinc Reagents" *Adv. Synth. Catal.*, in press.

9.) C. Duplais, F. Bures, I. Sapountzis, T. J. Korn, G. Cahiez, P. Knochel "A New Iron-Catalyzed Arylation of Aroyl Cyanides - An Efficient Preparation of Polyfunctionalized Diaryl Ketones" *Angew. Chem.* **2004**, *116*, 3028-3030; *Angew. Chem. Int. Ed.* **2004**, *43*, 2968-2970.

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11.) P. Knochel, W. Dohle, N. Gommermann, F. F. Kneisel, F. Kopp, T. Korn, I. Sapountzis and V. A. Vu "Highly Functionalized Magnesium Organometallics Prepared via a Halogen-Metal Exchange" *Angew. Chem.* **2003**, *115*, 4438-4456; *Angew. Chem. Int. Ed.* **2003**, *42*, 4302-4320.

**To Chris, with love.**

## Abbreviations

| | |
|---|---|
| Ac | acetyl |
| AcOH | acetic acid |
| approx. | approximately |
| Bn | benzyl |
| Boc | *tert*-butoxycarbonyl |
| br | broad |
| Bu | butyl |
| c | concentration |
| cat | Catalytic |
| $CH_2Cl_2$ | dichloromethane |
| *c*Hex | *cyclo*-hexyl |
| d | doublet |
| dba | *trans*, *trans*-dibenzylideneacetone |
| decomp. | decomposition |
| DIC | *N,N*-diisopropylcarbodiimide |
| DMAP | 4-dimethylaminopyridine |
| DMF | dimethylformamide |
| DMSO | dimethyl sulfoxide |
| equiv | equivalent |
| $E^+$ | electrophile |
| EI | electron ionisation |
| EN | electronegativity |
| EOM | ethoxy methyl |
| Et | ethyl |
| EtOAc | ethyl acetate |
| FAB | fast atom bombardment |
| FG | functional group |
| GC | gas chromatography |
| h | hour |
| HOMO | highest occupied molecular orbital |
| HPLC | high performance liquid chromatography |
| HRMS | high resolution mass spectroscopy |
| *i*Pr | isopropyl |
| IR | infra-red |
| *J* | coupling constant |
| LUMO | lowest unoccupied molecular orbital |
| *m* | meta |
| m | multiplett |
| M | molar |
| Me | methyl |
| Met | metall |
| min | minute |
| mp. | melting point |
| Ms | methanesulfonyl |
| MS | mass spectroscopy |
| NBA | 2-nitrobenzyl alcohol |
| NMP | *N*-methyl-pyrrolidone |
| NMR | nuclear magnetic resonance |
| Nu | nucleophile |
| *o* | ortho |
| *p* | para |
| Pent | pentyl |
| PG | protecting group |
| Ph | phenyl |
| Piv | pivaloyl |
| q | quartet |
| quant. | quantitative |
| quint | quintett |
| R | organic substituent |
| rt | room temperature |
| s | singlet |
| sec | seconds |
| t | triplet |
| *t*Bu | *tert*-butyl |
| TEA | triethyl amine |
| Tf | trifluoromethanesulfonyl |
| TFA | trifluoroacetic acid |
| TLC | thin layer chromatography |
| tfp | *tris*-2-furylphosphine |
| THF | tetrahydrofuran |
| Ts | 4-toluenesulfonyl |
| TP | typical procedure |
| $t_R$ | retention time |
| UV | ultra-violet |

# THEORETICAL PART

# 1. Overview

The continuous search for biologically active molecules for the pharmaceutical and agrochemical industries is probably one of the largest areas of research in which synthetic organic chemistry plays a fundamental role. Since most biologically active molecules are synthesized in chemical laboratories, there is a constant need for the development of new methods for selective carbon-carbon and carbon-heteroatom bond formation. Such procedures should ideally be mild and highly tolerant towards a wide range of functional groups. In most biologically interesting molecules, heteroatoms play a fundamental role for binding and activity, due to their ability to interact through H-bonding or lone pair donation with enzymes and receptor systems. Nitrogen has probably the most prominent position, interacting either as part of a heterocycle or as a substituent attached to the molecule's backbone.

Frankland set the stage for modern organometallic chemistry already in 1849 with the synthesis of diethylzinc.[1] However, it was Victor Grignard and his synthesis of organomagnesium reagents who has paved the way for the outstanding track record of organometallic chemistry.[2] Today, almost every metal in the periodic table has found an application in organic chemistry and, frequently, new organometallic reagents are added to the repertoire of synthetic chemists. As illustrated in Figure 1, the reactivity of an organometallic species increases with the ionic character of the carbon-metal bond. The use of highly reactive species, such as organolithium reagents, often compromises selectivity. Furthermore, a reduced tolerance towards sensitive functional groups is observed. On the other hand, the less reactive organometallic species, such as organo zinc, -tin or -boron compounds, require transition metal catalysts, such as palladium or nickel complexes, to promote the reaction of these nucleophiles, giving access to the broad field of transition metal catalyzed transformations.[3]

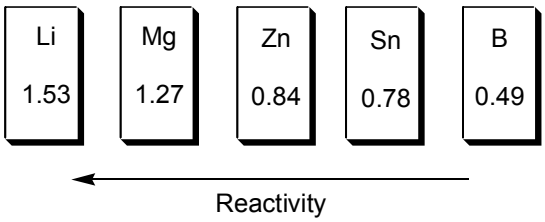


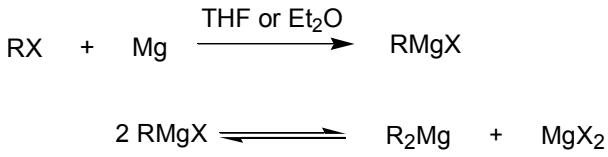

**Figure 1:** Electronegativity difference of some metals relative to carbon.[4]

Organomagnesium reagents display a less reactive polar carbon-metal bond than in the corresponding lithium compounds. They still have a high reactivity towards many electrophiles combined with a remarkable functional group tolerance at low temperatures.[5]

## 1.1 Preparation of Organomagnesium Compounds

### 1.1.1 Properties and Conventional Preparation Methods

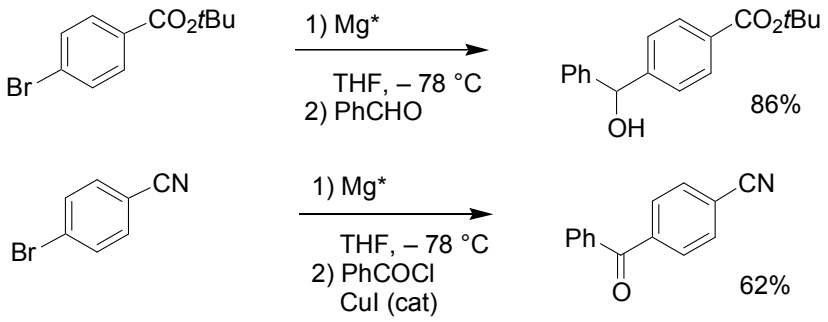
By far the most commonly used method to prepare organomagnesium reagents is the reaction of organic halides with magnesium metal in a polar, aprotic solvent like THF or diethyl ether (Scheme 1), allowing the preparation of Grignard reagents even on a "fine chemical" scale. Most commercially available Grignard reagents are prepared by this direct oxidative addition of Mg metal to organic halides.




**Scheme 1:** Synthesis of Grignard reagents by oxidative addition and Schlenk equilibrium.

The mechanism of this reaction is not yet fully clarified, but radical intermediates are commonly assumed.[6] In solution, a Grignard reagent (RMgX) is in equilibrium (the so called Schlenk equilibrium, Scheme 1) with $R_2Mg$ and $MgX_2$, depending on temperature, solvent and the anion X. Magnesium is most commonly four-coordinated in solids but might have even higher coordination numbers. All experimental evidence indicates similar coordination numbers in solution as well. The additional bonds to magnesium result from some combination of association by bridging of the X-anion or the R-group between two magnesium atoms and/or coordination by donor molecules, usually the solvent. This coordination can result from donor groups in the substrates as well, playing an important role in directed reactions of magnesium compounds or for the stabilization of reaction intermediates.

The increasing complexity of target molecules and the need of highly functionalized building-blocks led to the development of functionalized organometallics, which considerably increased the scope of these nucleophilic reagents in organic synthesis. The presence of sensitive functional groups makes their preparation more complicated and the above mentioned, conventional method is here neither appropriate nor general, precluding the presence of many functional groups in the same molecule. If, however, the direct oxidative addition is conducted at low temperatures with activated metals, like Rieke magnesium ($Mg^*$), the preparation of functionalized Grignard reagents is possible, but generally shows limitations in the tolerance of functional groups (Scheme 2).[7]

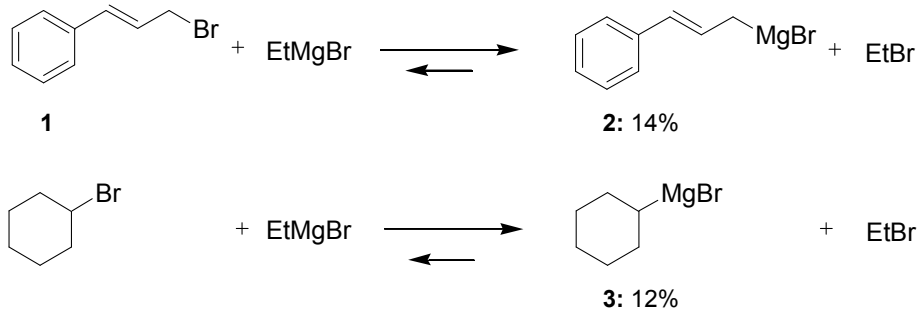



**Scheme 2:** Preparation of functionalized Grignard reagents using Rieke Magnesium ($Mg^*$).

Several other methods are known for the synthesis of organomagnesium halides, like the transmetalation of lithium or mercury compounds,[6h] the sulfoxide-magnesium exchange,[8] the hydromagnesiation reaction[9] or the direct metalation with magnesium amides.[10] Again, however, all these methods lack a good functional group tolerance.

### 1.1.2 Halogen-Magnesium Exchange Reaction

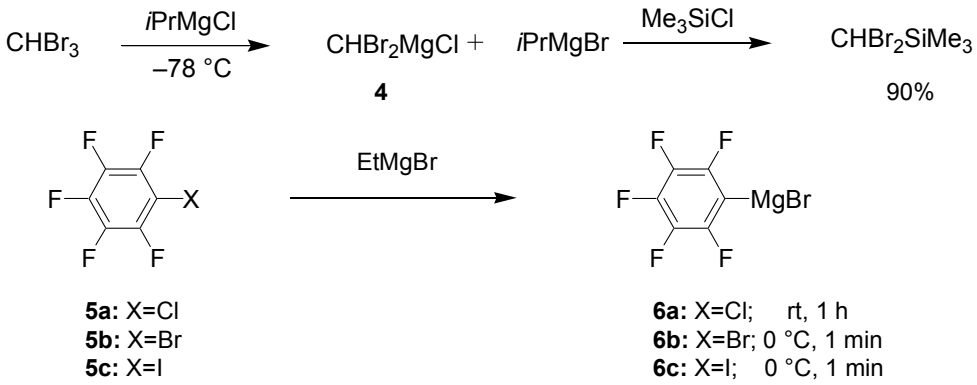
In contrast, the halogen-magnesium exchange has been found to be the method of choice for preparing new functionalized organomagnesium reagents of considerable synthetic utility.
The first example of a bromine-magnesium exchange reaction was briefly reported in 1931 by C. Prévost.[11] Thus, the reaction of cinnamyl bromide **1** with EtMgBr furnished cinnamylmagnesium bromide **2** although only in modest yield (Scheme 3). Similarly, E. Urion reported the preparation of cyclohexylmagnesium bromide **3** *via* a Br/Mg exchange.[12]




**Scheme 3:** First examples of a bromine-magnesium exchange.

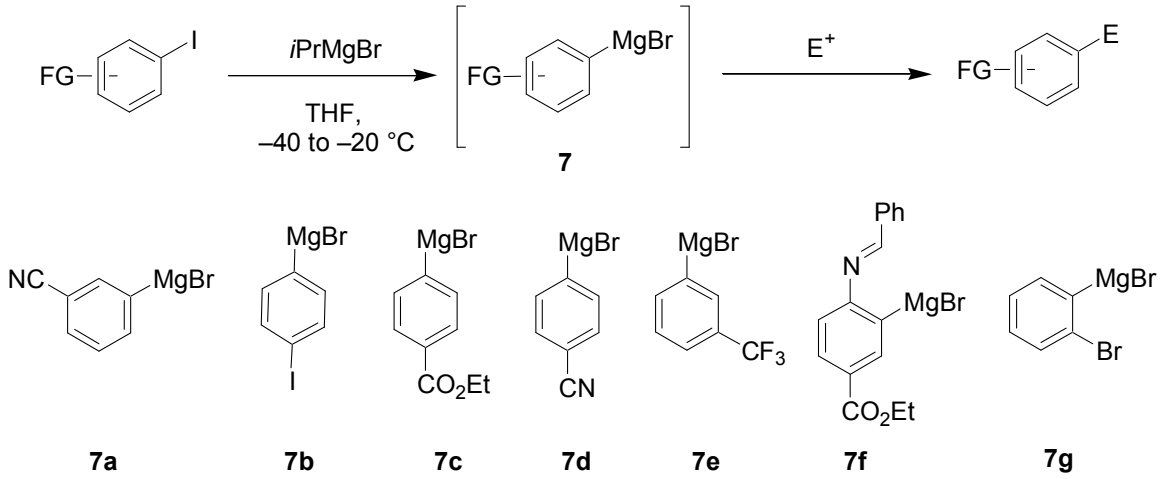
To shift the equilibrium of these exchange reactions to the desired side, the resulting organomagnesium species has to be more stable than the Grignard reagent used for the exchange reaction. Although the mechanism is not clear, a halogen ate complex is believed to be an intermediate, as proposed for the halogen-lithium exchange.[13]
The halogen-magnesium exchange reaction was used later by Villiéras and co-workers to generate magnesium carbenoids **4** which could be trapped with chlorotrimethylsilane (Scheme 4).[14] These early studies as well as later ones including the pioneering work of Tamborski, who studied the exchange reaction of polyhalogenated arenes **5a-c** with

EtMgBr, furnishing compounds of type **6,**[15] showed the potential of this reaction (Scheme 4).



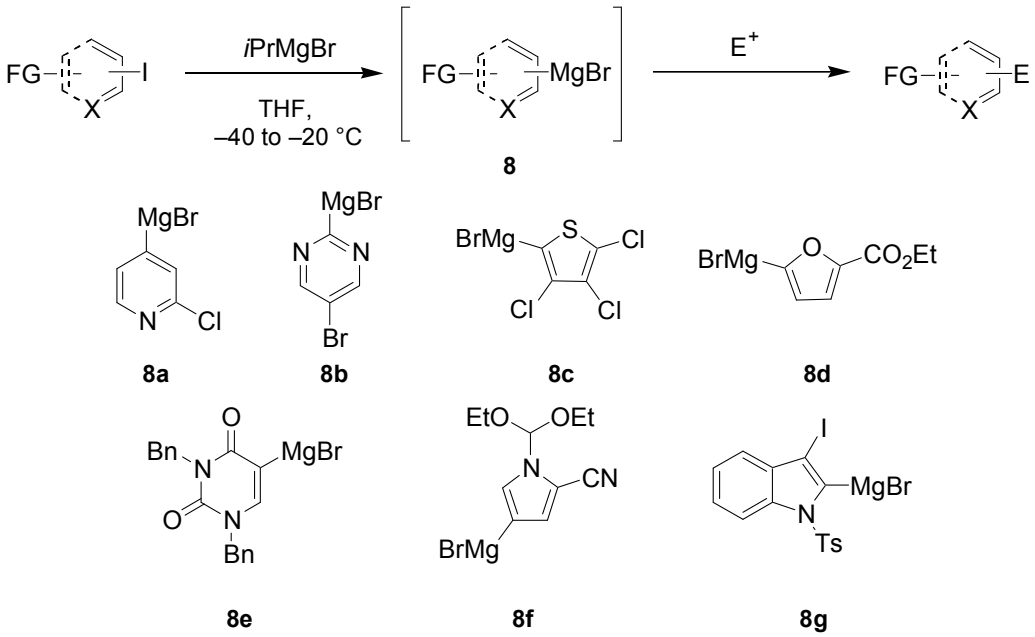

**Scheme 4:** Preparation of polyhalogenated Grignard reagents **4** and **6**.

In 1998, P. Knochel and co-workers showed for the first time, the excellent functional group tolerance of this method, using a low-temperature I/Mg exchange for the preparation of various functionalized Grignard reagents of type **7**. Since then, the scope of this reaction has been considerably extended to encompass a variety of substrates (Scheme 5).[16] They were able to show that functional groups that normally react at ambient temperature with organomagnesium halides are well tolerated at lower temperatures.



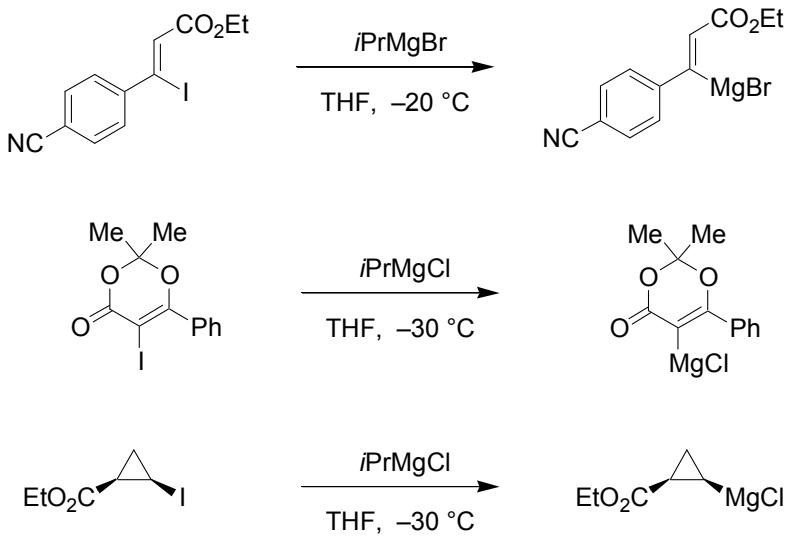

**Scheme 5:** Synthesis of various functionalized aromatic Grignard reagents.

As well as aryl halides, many functionalized magnesiated heterocycles of type **8** were prepared using this method, in particular, pyridines (**8a**), pyrimidines (**8b**), thiophenes (**8c**), furans (**8d**), uracils (**8e**), pyrroles (**8f**), indoles (**8g**) and many others (Scheme 6).[17]




**Scheme 6:** Functionalized heterocycles of type **8** prepared *via* halogen-magnesium exchange.

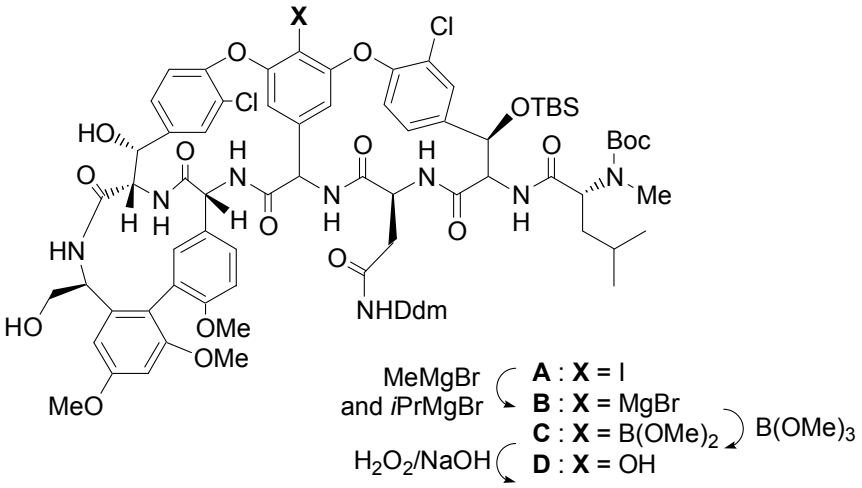
In addition, functionalized alkenyl- and cyclopropyl Grignard reagents were also prepared (Scheme 7).[18]




**Scheme 7:** Synthesis of alkenyl- and alkylmagnesium reagents.

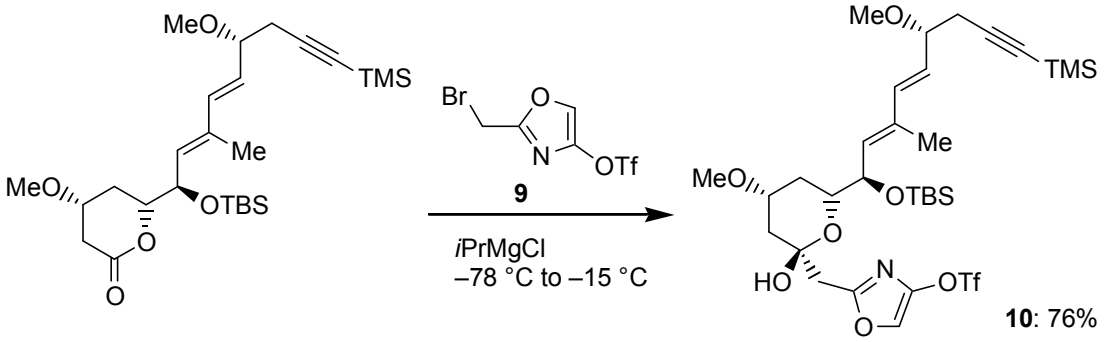
The halogen-magnesium exchange reaction could be applied to solid phase supported derivatives as well, opening up applications in the field of combinatorial chemistry.[19] More recently, P. Knochel and co-workers showed that the halogen-metal exchange reaction can be extended to other metals like copper[20] or zinc,[21] allowing the presence of very sensitive functional groups, such as an aldehyde, in the same molecule. Furthermore, an extension of this methodology to aromatic bromides was achieved very recently, by enhancing the reactivity of *i*PrMgCl with Li salts.[22]

In addition to the work in this area by the group of P. Knochel, many other research teams have adopted this methodology. Two outstanding examples, with a focus on applications in natural product synthesis and biologically active molecules are given below, but have been excellently reviewed elsewhere.[5] For example, K. C. Nicolaou and co-workers used this methodology in their total synthesis of Vancomycin (Scheme 8).[23]



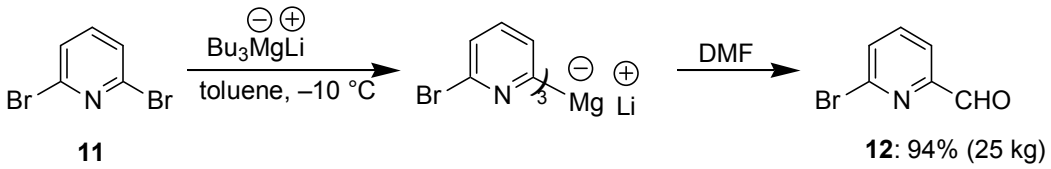

**Scheme 8:** Iodine-magnesium exchange in the synthesis of Vancomycin.

A particularly impressive use of the halogen-magnesium exchange reaction in the total synthesis of (+)-Phorboxazole A was provided by the group of A. B. Smith III. A benzylic Grignard reagent was generated from the corresponding bromo-oxazole **9** at low temperature, furnishing hemiacetal **10** in 76% yield (Scheme 9).[24]




**Scheme 9:** Preparation of intermediate **10** by using a bromine-magnesium exchange.

Finally, K. Oshima and co-workers showed that in addition to alkylmagnesium halides, lithium trialkylmagnesiates ($R_3MgLi$) readily undergo iodine- or bromine-magnesium exchange reactions.[25] An impressive example for this methodology is given in the selective exchange of one bromine in 2,6 dibromopyridine (**11**), developed by T. Mase and I. Houpis at Merck Process Research, who performed this reaction on a kilogram scale in the synthesis of a muscarine receptor antagonist, and trapped the resulting magnesiate with DMF, furnishing compound **12** in 94% yield (Scheme 10).[26]




**Scheme 10:** Br/Mg exchange reaction using a magnesiate ($R_3MgLi$).

## 1.2 Amination Reactions

As already mentioned, nitrogen atoms play an important role in most biologically active compounds. For example the topoisomerase inhibitor Amsacrine,[27] used for the treatment of ovarian carcinomas and leukemia, the Novartis blockbuster Diclophenac (Voltaren™) or the first clinically useful oxazolidinone antibacterial agent Linezolid[28] bear an aniline group (Figure 2).

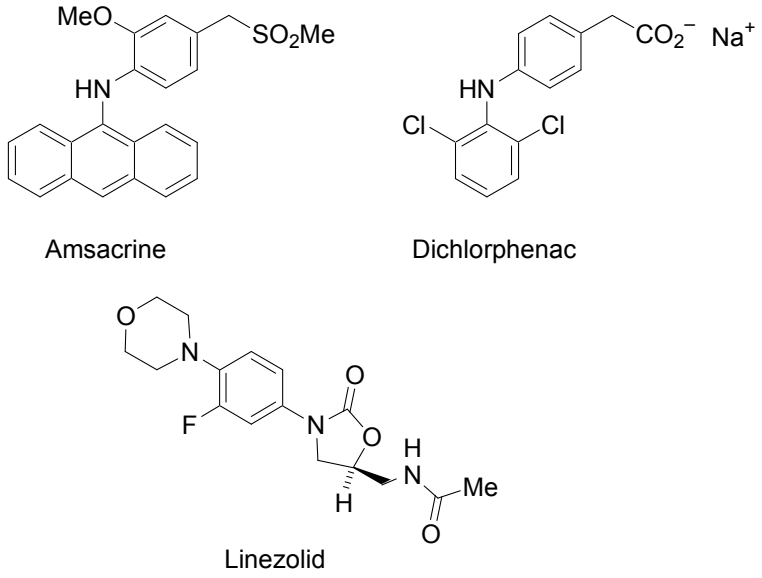
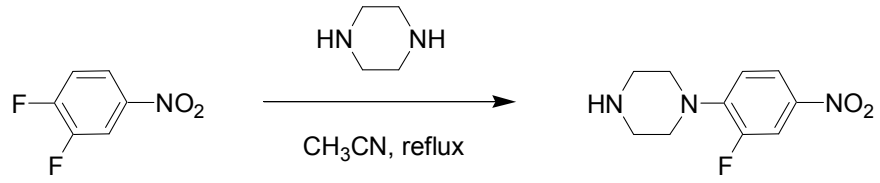



**Figure 2:** Biologically active amine substituted compounds.

This structural motif is found very often in modern pharmaceuticals. The synthesis of aniline derivatives will be briefly highlighted.[29]

### 1.2.1 Nucleophilic Aromatic Substitutions

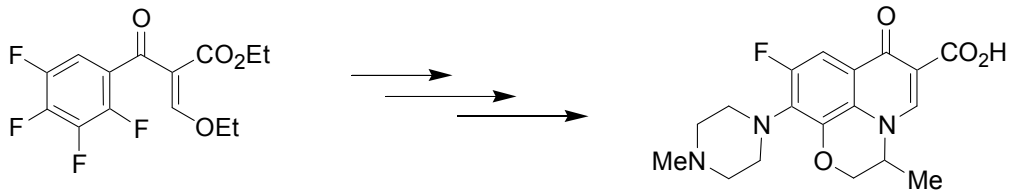
The amination of aromatic compounds is often carried out as a nucleophilic substitution ($S_NAr$). Nitrogen acts as a nucleophile, and typically a halide (F>>Cl>Br>I) acts as a leaving group, whereas a carbonyl, cyanide or a nitro group *ortho*- or *para*- to the leaving group facilitates this substitution through delocalization of the negative charge. This method works very well, as indicated below in the selective substitution of the *para*-fluorine in compound **13** with piperazine, furnishing **14** in 81% yield (Scheme 11).[28]




**13** **14**: 81%

**Scheme 11:** Selective nucleophilic aromatic substitution of fluorine in compound **13**.

However, electron-rich arenes cannot be used, and the introduction of an appropriate leaving group can be difficult. *Meta*-substituents do not activate the ring and are, therefore, regarded as problematic. The removal of the activating groups by additional reaction steps renders this method less efficient. Despite these limitations, this method is still very popular and can be used for the synthesis of complex molecules as well, as shown in Scheme 12. Here, three fluorine atoms in starting material **15** are selectively substituted by different nucleophiles in the synthesis of the antibiotic ofloxacin **16**.[30]




**15** **16**

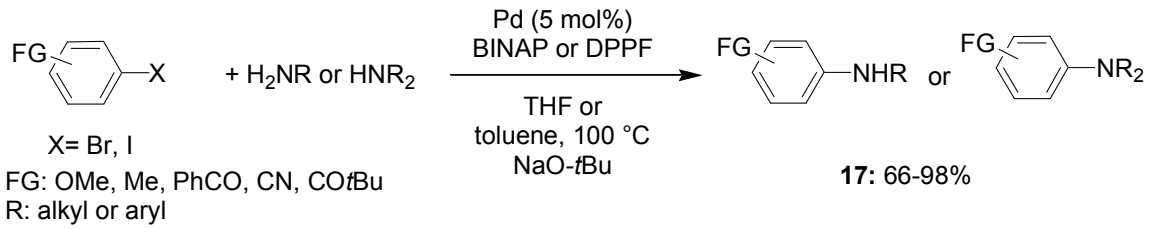
**Scheme 12:** Synthesis of ofloxacin **16**.

### 1.2.2 Transition Metal-Catalyzed Amination Reactions

The recent development of transition metal catalyzed C(aryl)-N-bond forming reactions has been a significant discovery.

#### 1.2.2.1 Palladium-Mediated Strategies

The groups of S. L. Buchwald and J. F. Hartwig developed the palladium-mediated C(aryl)-N bond formation with their pioneering work using *bis*-phosphine palladium complexes in 1996.[31] Both groups independently discovered that aryl bromides or iodides could be transformed to the corresponding arylamines **17** in the presence of a *bis*(phosphine) ligand like BINAP or DPPF and a base, typically NaO-*t*Bu, in good to excellent yields (Scheme 13).

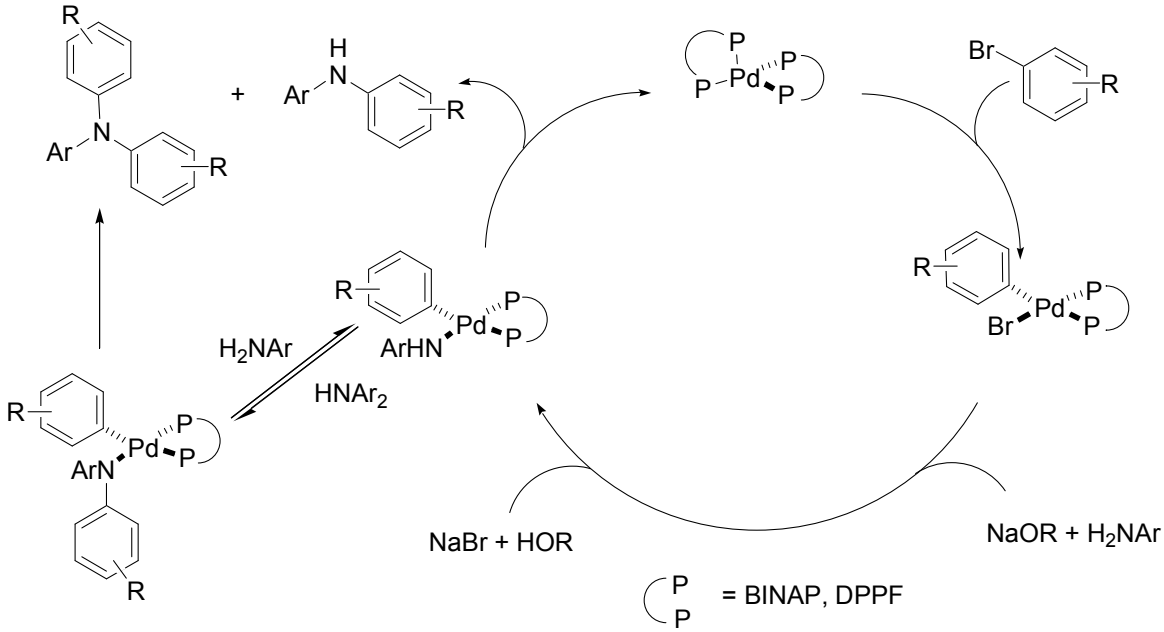



**Scheme 13:** Palladium catalyzed arylamination or aryl bromides and iodides.

The generality of this reaction has led to a toolbox of tuneable reaction conditions whose scope should allow access to many target molecules bearing an arylamine. Furthermore, aromatic chlorides, tosylates or triflates have been shown to convert to arylamines by this method as well as to the synthesis of heterocycles.[32] This is in accordance with the vast amount of published material available, describing ligand, solvent, temperature and substrate testing.[33] These research groups, among others, provided important new advances in this methodology through iterative development of new catalytic methods and have extended this to C(aryl)-O bond formation reactions.[32,33]

However, the method has some drawbacks, in particular the time consuming solvent, ligand and base testing for a specific target. Some functional groups are still incompatible or troublesome with these amination methodology, most importantly bromides, iodides and sulfonates. The use of polyhalogenated substrates or diamines usually leads to further substitution and polymers, but does not allow a selective mono-substitution.[34] Another very important drawback is the price of palladium and the ligands, making this method less cost effective.

Though very well applicable to the formation of triarylamines, the synthesis of diarylamines sometimes causes problems, since the products can participate further in the catalytic cycle, leading to mixtures of di- and trisubstituted products (Scheme 14).

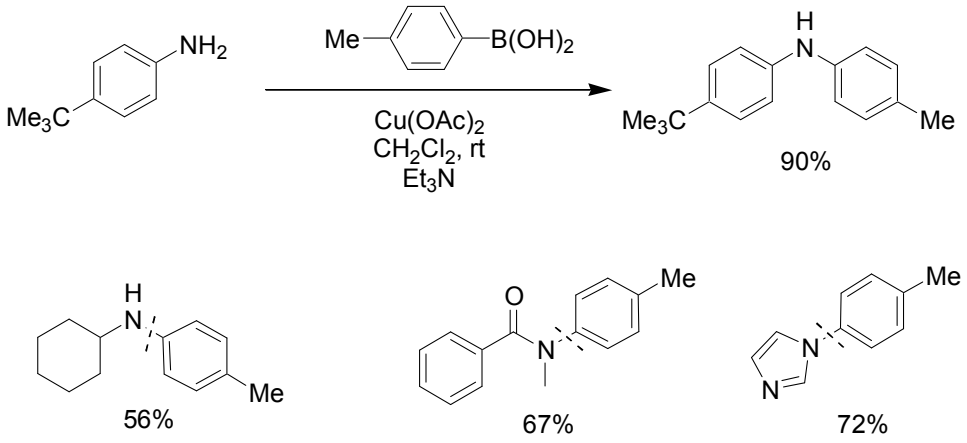



**Scheme 14:** Catalytic cycle for the palladium catalyzed amination.[33c]

Besides this very powerful method, several other transition metals have found applications in C-N bond formations.

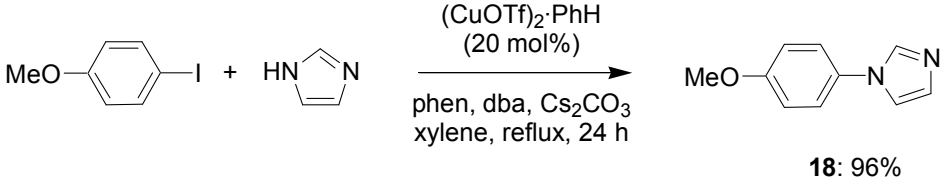
### 1.2.2.2 Copper- and Nickel-Mediated Strategies

Pioneering work in the field of copper-catalyzed arylation of amines was carried out by Ullmann at the beginning of the last century.[35] However, the initial work on modern copper-catalyzed aminations, published simultaneously by D. Chan and co-workers and by P. Lam and co-workers, had a significant impact on the cross coupling of boronic acids and nitrogen nucleophiles (Scheme 15) roughly 100 years after the initial disclosure.[36] A variety of substrates including amines, anilines, amides, imides, ureas, carbamates, sulfonamides and several aromatic heterocycles were applied, showing the broad scope of this reaction (Scheme 15).




**Scheme 15:** Copper mediated cross-coupling of boronic acids with amines.

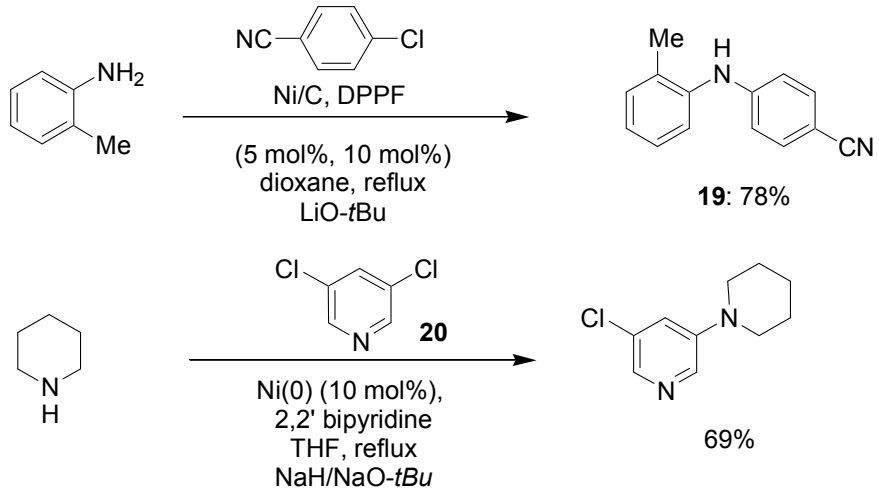
A variety of modified procedures have been published since this initial report, and have recently been excellently reviewed elsewhere.[37] Even catalytic amounts of copper salts have proved to be sufficient.[38] A seminal contribution in modern copper-catalyzed formation of diarylamines was again made by the group of Buchwald, showing that $(CuOTf)_2$ can efficiently catalyze the reaction between imidazoles and aryl halides, leading to compound **18** in excellent yield (Scheme 16).[39]




**Scheme 16:** First copper-catalyzed amination using $(CuOTf)_2$.

This new example initiated the drive to discover new catalytic systems, being today a complementary method to the palladium-catalyzed amination. However, the drawback that halides and sulfonates are not tolerated also holds true for the copper-catalyzed procedure.

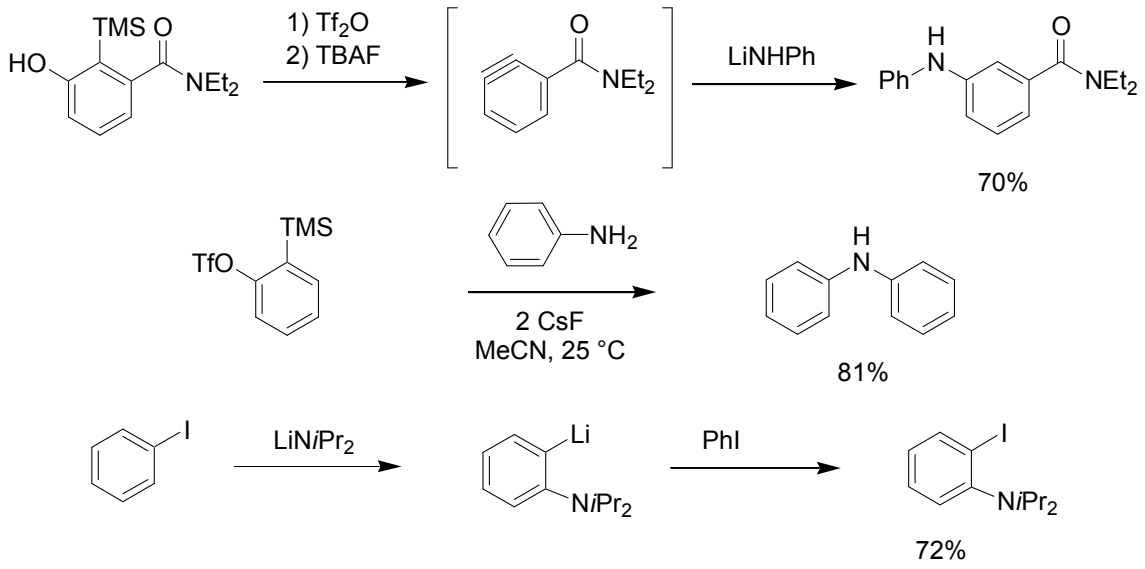
The nickel-catalyzed amination, initially developed by the groups of Lipshutz and Fort, found significantly fewer applications, although chlorides can be cross-coupled under these conditions, leading to compound **19**. Even chloropyridines **20**, which proved to be difficult substrates in palladium-catalyzed amination reactions, gave satisfactory yields (Scheme 17).[40]




**Scheme 17:** Nickel-catalyzed amination of chloro-arenes.

### 1.2.3 Benzynes in Aromatic Aminations

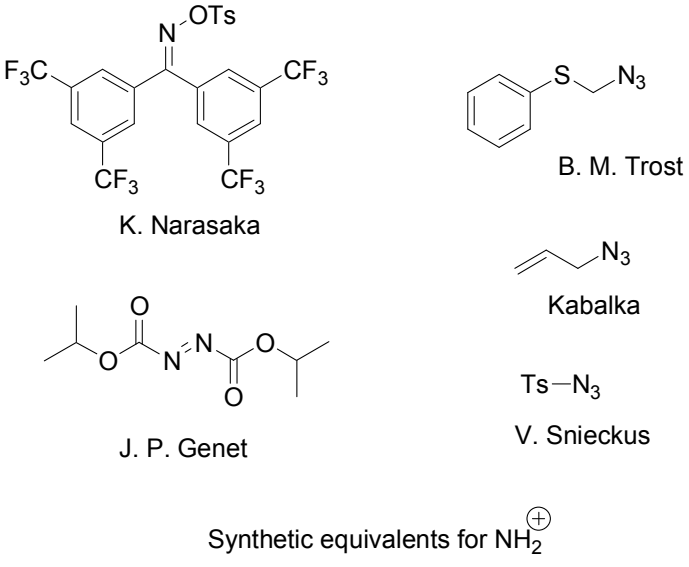
Benzyne and its derivatives are important reactive intermediates and many studies on their generation were undertaken.[41] Many applications in organic synthesis were therefore reported. The first example of benzyne formation was reported by Roberts during an amination of chlorobenzene with $KNH_2$.[42] However, the harsh reaction conditions usually applied for the formation of benzyne made this transformation less attractive for a long time. Novel methodologies for the generation of benzyne derivatives making use of advances in organometallic chemistry and the easy access to TMS phenols,[43] aryl triflates[44] and aryl iodides[45] put this method back on the center stage of organic chemist's synthetic tools (Scheme 18).




**Scheme 18:** Amination reactions using benzynes as aromatic acceptors.

### 1.2.4 Electrophilic Aromatic Aminations of Carbanions

All methods mentioned above use nitrogen nucleophiles for the formation of arylamines. Although the electrophilic amination of carbanions was a very active field of research especially in the 1980s,[46] no synthetically valuable diarylamine formation was reported.[47] However, several useful reagents bearing an electrophilic nitrogen were reported by various groups, transforming organometallic nucleophiles into the corresponding anilines (Scheme 19).

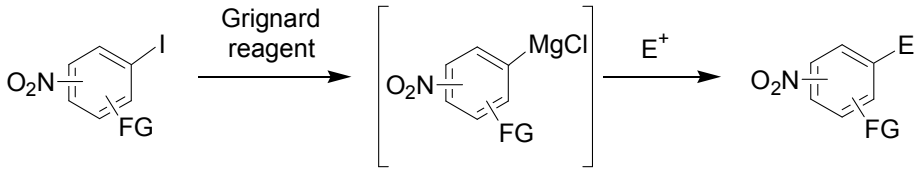



**Scheme 19:** Reagents for the electrophilic amination of carbanions.

## 2. Objectives

After the successful development of a mild and selective I/Mg exchange reaction,[16] it was of interest to further extend this chemistry to substrates bearing very sensitive groups, in particular a nitro group, which was at the time believed to be incompatible with most organometallic reagents (Scheme 20). The objectives were:

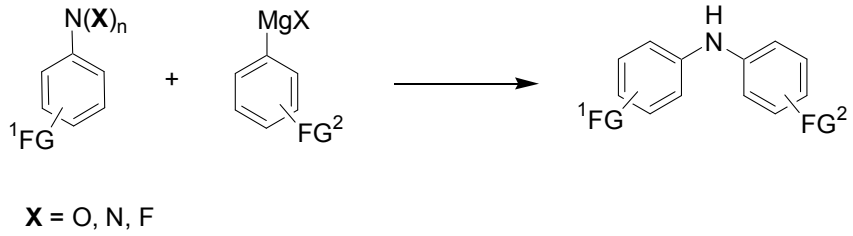
- access to all possible substitution patterns (*ortho*-, *meta*- and *para*-magnesiated nitroarenes),
- extension of this methodology to highly functionalized Grignard reagents,
- application to transition metal catalyzed reactions.




**Scheme 20:** Proposed synthesis of nitro-functionalized Grignard reagents

A second project involved the development of new amination methods, allowing the synthesis of diarylamines starting from organomagnesium compounds (Scheme 21). The objectives for this work were:

- development of a general procedure, allowing the synthesis of diarylamines without time-consuming screening of conditions for every substrate,
- extension to functional groups incompatible with transition metal-catalyzed procedures, in particular the applicability to halogen- and sulfonate-substituted arylamines and arylmagnesium halides.



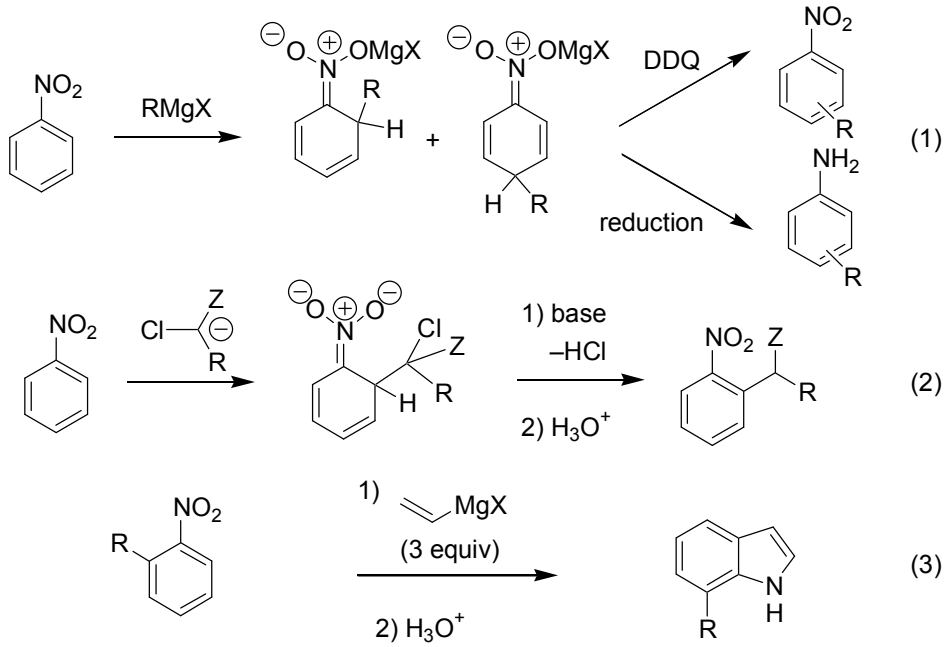

**Scheme 21:** Development of new electrophilic amination reactions using Grignard reagents to produce diarylamines.

# 3. Preparation of Functionalized Nitroarylmagnesium Halides *via* an Iodine-Magnesium Exchange

## 3.1 Introduction

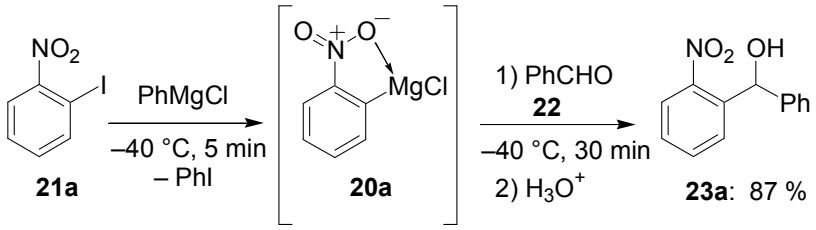
Nitro compounds are key intermediates in organic synthesis. They are found in numerous fine chemicals, dyes, high-energy materials and biologically active substances, and many nitrogen substituents in an aromatic molecule are initially introduced by nitration.[48] Their easy transformation to a plethora of derivatives allows the application of nitro chemistry to numerous total syntheses,[49] and the reduction to an amino function is possible using a variety of catalysts and reagents.[50]

This enormous significance of the nitro group has made it an attractive target for organometallic chemists, but only a few successful attempts to prepare organometallic nitro compounds have been reported.[51] Most often, the metal of choice was lithium, precluding many functional groups and requiring very low reaction temperatures (typically −100 °C) for the preparation. Great efforts were undertaken to produce this substance class by the oxidative addition of metals, in particular Mg and Zn, into a carbon-halogen bond without reducing the nitro group, but all were in vain.[52] The nitro group, like many oxygen containing functional groups, prevents the oxidative addition by coordinating to the metal surface.[6d-f] Despite these unsuccessful attempts to generate nitro functionalized organometallics, nitro compounds have found numerous applications in organometallic chemistry as electrophiles. Several synthetically useful procedures have been reported, through reaction of a Grignard reagent with an aromatic nitro compound. Important examples include the 1,4- or 1,6-addition of alkylmagnesium halides (eq. 1, Scheme 22),[53] the vicarious nucleophilic substitution of stabilized α-chlorocarbanions (eq. 2),[54] or, most prominently, the synthesis of indoles through the Bartoli indole synthesis[55] *via* a reaction cascade (eq. 3).[56]




**Scheme 22:** Selected reactions of aromatic nitro compounds.

Further applications are found in the selective 1,4 addition of carbanions to nitroalkenes.
As shown in the general introduction, the preparation of functionalized Grignard reagents through a halogen-magnesium exchange reaction enables the formation of a variety of functionalized organometallic compounds that were not accessible before. Functional groups, which reacted with other organomagnesium reagents were tolerated at low temperatures. We found that the halogen-magnesium exchange reaction could help solve the long-standing problem of the selective formation of nitro functionalized organometallics. Therefore, we attempted the preparation of 2-magnesiated nitrobenzene **20a**. Chelation should lead to a stabilized species (Scheme 23).[57]




**Scheme 23:** Iodine-magnesium exchange on 2-iodonitrobenzene (**21a**).

As shown in Scheme 23, a very fast iodine-magnesium exchange is possible, using phenylmagnesium chloride as the magnesium source, at low temperatures (−40 °C). Thus, 2-iodonitrobenzene (**21a**) was converted to the corresponding Grignard reagent **20a** which furnished after reaction with benzaldehyde (**22**) benzylic alcohol **23a** in 87% yield. While *iso*propylmagnesium chloride or bromide is the reagent of choice for most substrates, we discovered that the use of phenylmagnesium chloride was crucial for this venture. Unselective reactions were observed when alkyl- or alkenylmagnesium reagents were used in this exchange reaction. With these pleasing results in hand, we were encouraged to examine the functional group tolerance of this methodology and to extend the scope to *meta*- and *para*- substituted nitrophenylmagnesium halides.

## 3.2 Preparation of Functionalized *o*-Nitroarylmagnesium Halides of Type 20 *via* an Iodine-Magnesium Exchange

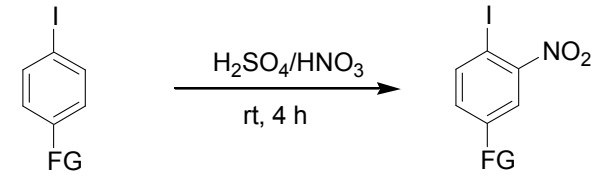
### 3.2.1 Preparation of Functionalized 2-Iodonitrobenzenes 21

Only a few functionalized 2-iodonitrobenzenes of type **21** are commercially available, in particular 2-iodonitrobenzene (**21a**) itself, 2,4-dinitroiodobenzene (**21b**) and 3-iodo-4-nitroanisole (**21c**). All the other derivatives had to be prepared from various precursors.
Several different routes were envisioned:

1. Oxidation of the corresponding functionalized aniline derivatives,
2. iodination of the corresponding functionalized nitrobenzenes,
3. selective nitration of the corresponding functionalized iodobenzene, or
4. conversion of the corresponding 2-amino-1-nitrobenzene to the iodo compound *via* a Sandmeyer reaction.

The first two approaches seemed less suitable for this problem, because oxidation of 2-iodoanilines gave very low yields of the desired nitro compound.[57] The selective iodination

appeared even less promising, since a nitro group should direct in the *meta*- and not in the required *ortho*-position. The strong electron-withdrawing effect should prevent an iodination even with such strong iodinating reagents like I-Py-$BF_4$,[58] ICl,[59] NIS[60] and $Ag_2SO_4/I_2$.[61] However, in some cases this method proved to be advantageous.
The most general approach seemed to be the nitration of iodobenzenes, since most aromatic compounds can be nitrated, because of a wide variety of available nitrating agents.[48,62] In the case of an electron-withdrawing group attached to the arene, like an ester **24**, a cyano function **25** or an amide **26,** the nitration occurred at ambient temperature under standard reaction conditions using a mixture of concentrated nitric acid and sulfuric acid (Scheme 24), leading to compounds **21d-f** in good yields.

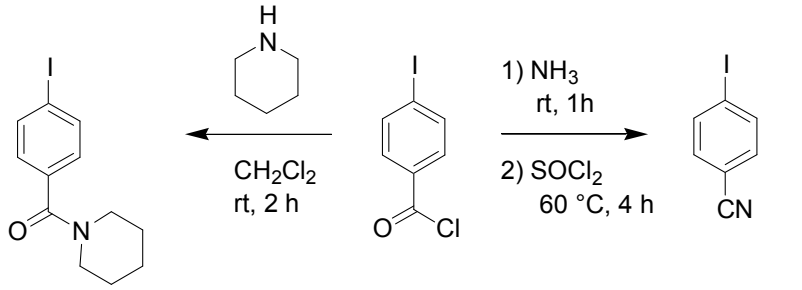



**24**: FG = $CO_2Et$
**25**: FG = CN
**26:** FG = $CONC_5H_{10}$

**21d**: FG = $CO_2Et$; 86%
**21e**: FG = CN; 67%
**21f:** FG = $CONC_5H_{10}$; 83%

**Scheme 24:** Nitration of electron poor 1,4-functionalized iodobenzenes **24-26**.

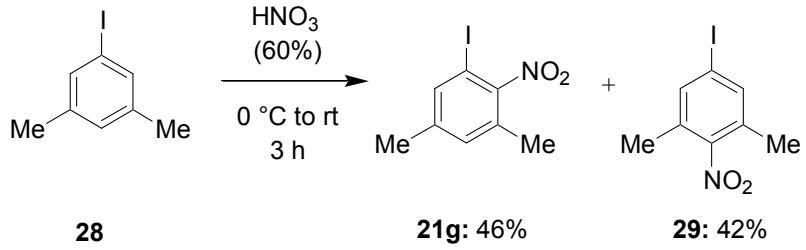
The preparation of iodobenzenes **25** and **26** is outlined in Scheme 25. The synthesis commenced with the commercially available 4-iodobenzoyl chloride (**27)**, which was reacted with ammonia yielding the corresponding amide. The crude reaction mixture was dehydrated to 4-iodobenzonitrile (**25**) with an excess of thionyl chloride ($SOCl_2$). Amide **26** was prepared by reacting 4-iodobenzoyl chloride (**27**) with piperidine.




**26**: 94% **27** **25**: 84%

**Scheme 25:** Synthesis of the functionalized aryl iodides **25** and **26**.

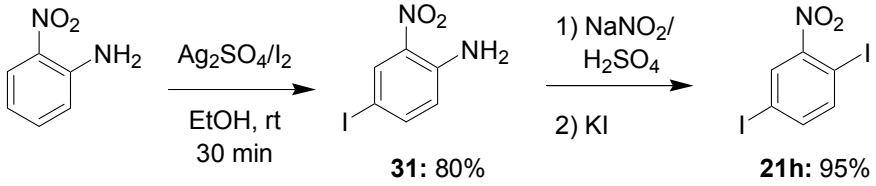
For the preparation of less electron-poor nitrobenzenes, milder conditions were necessary since the above-mentioned conditions oxidized these substrates. Thus, the nitration of 3,5-dimethyliodobenzene (**28**) with nitric acid (60%) gave both possible regioisomers **21g** and **29** in 46% and 42% isolated yield (Scheme 26).




**28** **21g:** 46% **29:** 42%

**Scheme 26:** Synthesis of functionalized iodides **21g** and **29**.

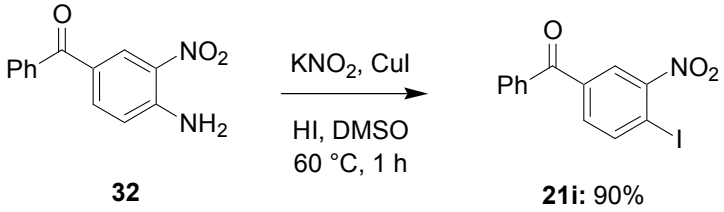
Unfortunately, the nitration of commercially available 1,4-diiodobenzene (**30**) was not possible. Therefore, a combined approach of iodination and Sandmeyer reaction was used to synthesize compound **21h**, as lined out in Scheme 27. First, a selective iodination of 2-nitroaniline at the 4-position was carried out with $Ag_2SO_4/I_2$, leading to compound **31**, which was converted subsequently to 2,5-diiodonitrobenzene (**21h**) in a second step by diazotisation and subsequent replacement of the diazonium group with iodine, using KI.




**31:** 80% **21h:** 95%

**Scheme 27:** Synthesis of 2,5-diiodonitrobenzene (**21h**).

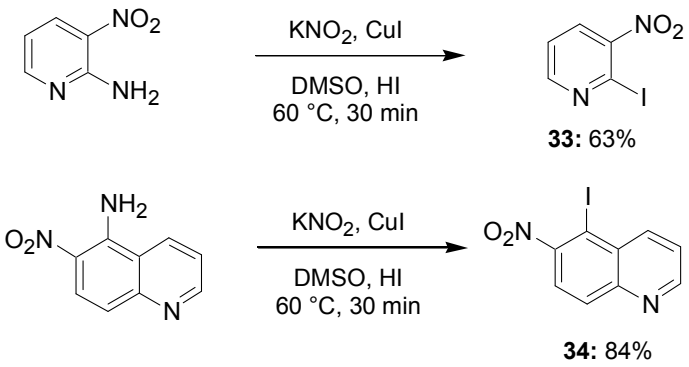
Finally, a modified Sandmeyer reaction developed by Baik and Wong was found to allow the selective conversion of 4-amino-3-nitrobenzophenone (**32**) to the corresponding iodide **21i**, as outlined in Scheme 28.[63] Standard diazotization and subsequent reaction with KI led to lower yields.




**32** **21i:** 90%

**Scheme 28:** Synthesis of 4-iodo-3-nitrobenzophenone (**21i**).

The synthesis of the following two nitro functionalized heterocyclic iodides was troublesome, since all routes mentioned above failed. The only method leading to appreciable amounts of iodo compounds **33** and **34** was the modified Sandmeyer reaction described by Wong (Scheme 29).[63]

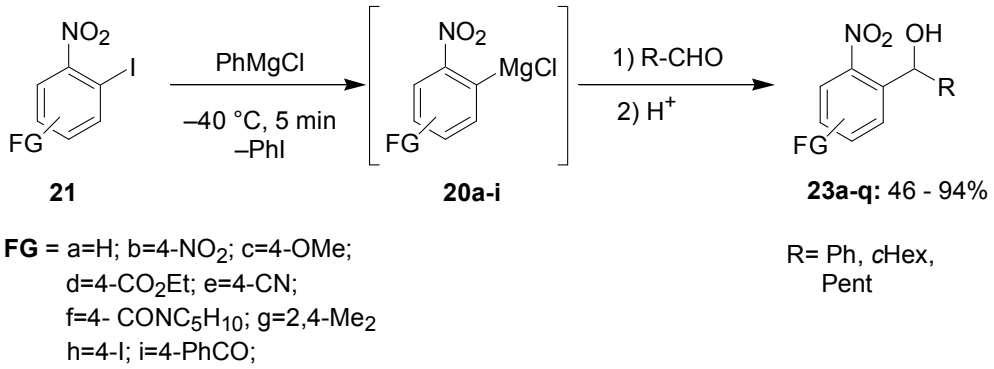



**Scheme 29:** Preparation of compounds **33** and **34**.

### 3.2.2 Preparation of Functionalized *o*-Nitroarylmagnesium Halides 20 *via* an Iodine-Magnesium Exchange Reaction

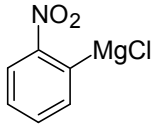
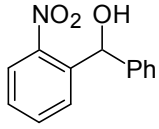
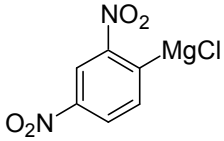
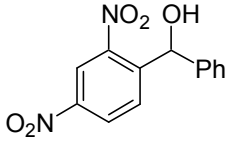
#### 3.2.2.1 Reactions with Aldehydes

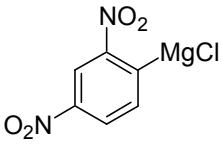
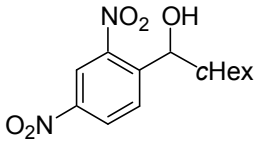
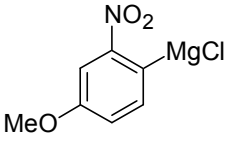
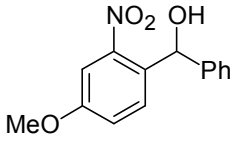
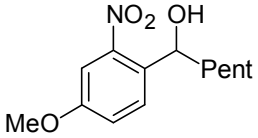
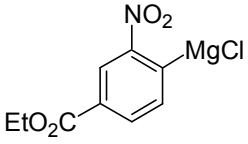
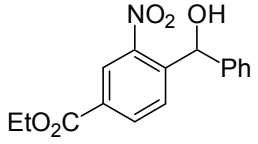
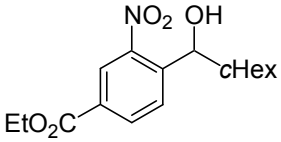
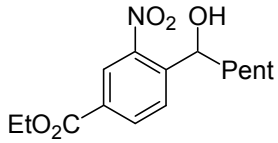
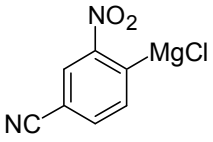
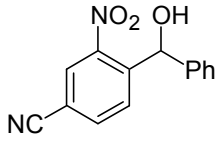
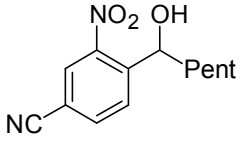
In a preliminary experiment, shown in Scheme 23, 2-iodonitrobenzene (**21a**) was treated with phenylmagnesium chloride (1.1 equiv) in THF at −40 °C. Within 5 min a complete iodine-magnesium exchange was observed, as indicated by GC analysis of the reaction mixture. The resulting nitro-substituted Grignard reagent **20a** reacted with benzaldehyde (**22**) (1.5 equiv) within 30 min at −40 °C, leading to the expected benzhydryl alcohol **23a** in 87% isolated yield (Scheme 23). A variety of functional groups including ester, amide, cyano and methoxy, as well as additional nitro or iodo functionalities, were tolerated, allowing the synthesis of a broad range of functionalized *ortho*-nitro-substituted arylmagnesium species (**20b-i**). These compounds reacted in good to excellent yields with aliphatic and aromatic aldehydes (Scheme 30, Table 1).

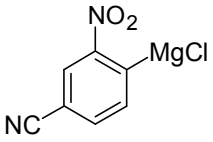
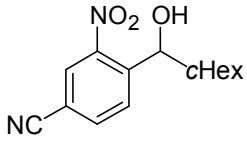
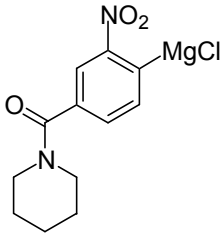
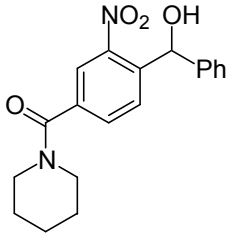
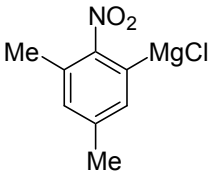
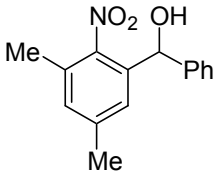
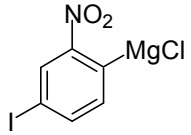
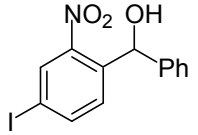
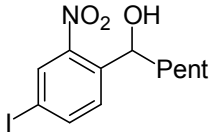
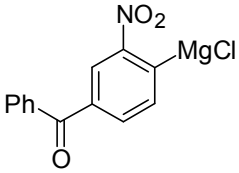
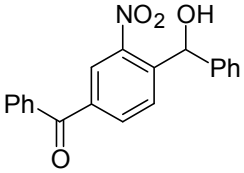



**Scheme 30:** Reaction of *o*-nitro Grignard reagents **20** with aldehydes.

**Table 1:** Products **23a-q** obtained by the reaction of functionalized *o*-nitro-substituted arylmagnesium compounds **20** with aldehydes.

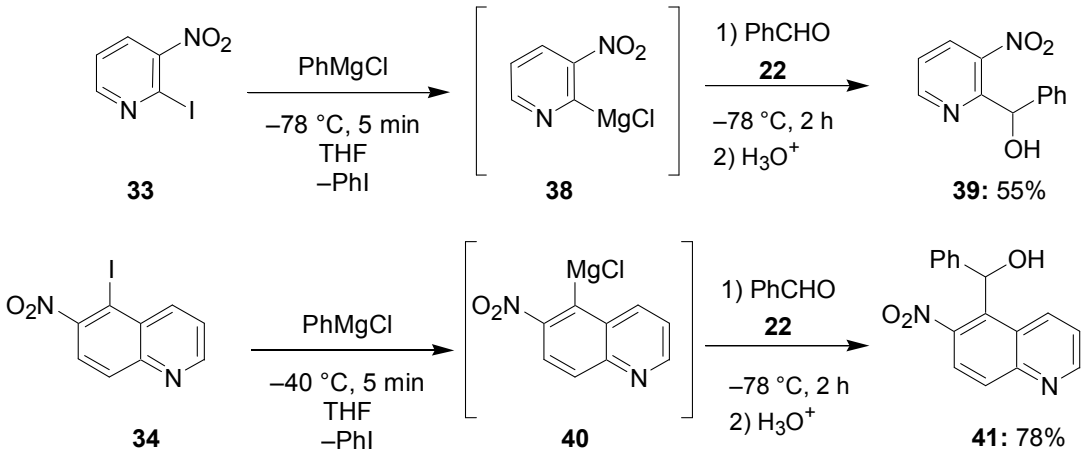
| Entry | Arylmagnesium Reagent **20** | Aldehyde | Product **23** | Isolated yield (%) |
|---|---|---|---|---|
| 1 |  **20a** | PhCHO **22** |  **23a** | 87 |
| 2 |  **20b** | PhCHO **22** |  **23b** | 81 |

| Entry | Arylmagnesium Reagent **20** | Aldehyde | Product **23** | Isolated yield (%) |
|---|---|---|---|---|
| 3 |  **20b** | *c*HexCHO **35** |  **23c** | 74 |
| 4 |  **20c** | PhCHO **22** |  **23d** | 72 |
| 5 | **20c** | PentCHO **36** |  **23e** | 71 |
| 6 |  **20d** | PhCHO **22** |  **23f** | 94 |
| 7 | **20d** | *c*HexCHO **35** |  **23g** | 64 |
| 8 | **20d** | PentCHO **36** |  **23h** | 87 |
| 9 |  **20e** | PhCHO **22** |  **23i** | 94 |
| 10 | **20e** | PentCHO **36** |  **23j** | 63 |

| Entry | Arylmagnesium Reagent **20** | Aldehyde | Product **23** | Isolated yield (%) |
|---|---|---|---|---|
| 11 |  **20e** | *c*HexCHO **35** |  **23k** | 46 |
| 12 |  **20f** | PhCHO **22** |  **23l** | 84 |
| 13 |  **20g** | PhCHO **22** |  **23m** | 74 |
| 14 |  **20h** | PhCHO **22** |  **23n** | 89 |
| 15 | **20h** | PentCHO **36** |  **23o** | 86 |
| 16 |  **20i** | PhCHO **22** |  **23p** | 93 |

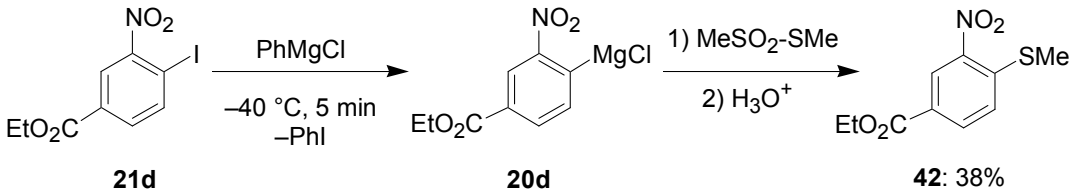
As shown in Table 1 a variety of benzylic alcohols was accessible with this method. Amazingly, a fast iodine-magnesium exchange was observed for 2,5-dinitroiodobenzene (**21b**). Here, the iodine-magnesium exchange was complete within 30 s at −40 °C. A smooth reaction was observed with aldehydes, despite the presence of two nitro groups in the Grignard reagent, leading to alcohols **23b** and **23c** in 81% and 74% yield, respectively (entries 2 and 3, Table 1). Substrates with strongly electron-donating functional groups, like a methoxy group **21c** or the two methyl substituents in compound **21g** underwent a fast exchange reaction (<15 min for the exchange reaction), and the magnesiated products **20c**

and **20g** were trapped with benzaldehyde in good yields (entries 4 and 13). The electron withdrawing substituents like an ester **20d**, an amide **20f** and a cyano group **20e** proved well tolerated under reaction conditions, furnishing the addition products in good to excellent yields (entries 6-12). Remarkably, on 2,5-diiodonitrobenzene (**21h**), only the *ortho*-iodine atom underwent an iodine-magnesium exchange, furnishing, after reaction with benzaldehyde **22,** or hexanal **36** the corresponding alcohols **23n** and **23o** in 89% and 86% yield (entry 14 and 15). This selectivity can be explained by a chelation of the nitro functionality to magnesium. Its electronic effect should also favor the *ortho*-iodine-magnesium exchange. By using phenylmagnesium chloride for the I/Mg exchange reaction, sensitive functional groups such as a ketone were tolerated (entry 16), leading at lower temperatures (−78 °C) to the magnesiated species **20i** and, after addition to benzaldehyde **22**, to product **23p** in an excellent yield of 93%.
The iodine-magnesium exchange reaction was also found to be applicable to heteroaromatic *ortho*-iodonitro compounds **33** and **34**, as shown in Scheme 31.




**Scheme 31:** I/Mg exchange on nitro functionalized heterocycles **33** and **34**.

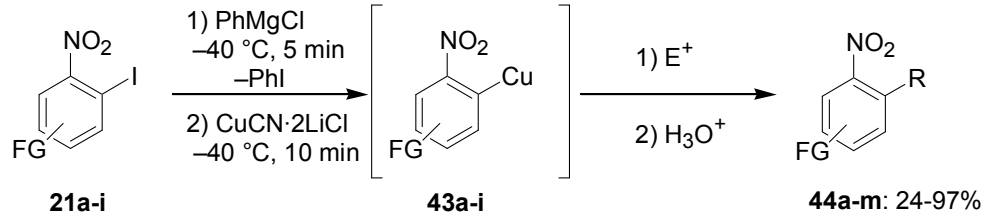
Therefore, the reaction of 2-iodo-3-nitropyridine (**33**) at −78 °C led to magnesiated heterocycle **38** within 5 min, and subsequent reaction with benzaldehyde **22** furnished alcohol **39** in 55% yield. Similarly, the formation of magnesiated quinoline **40** proceeded under mild conditions (−40 °C, 5 min) from the corresponding iodide **34** and reaction with benzaldehyde again led to product **41** in 78% yield.
Reactions with other electrophiles gave significantly lower yields, for example the reaction of Grignard reagent **20d** with methyl methanethiosulfonate furnished product **42** in only 38% yield (Scheme 32).




**Scheme 32:** Synthesis of compound **42**.

### 3.2.2.2 Transmetalation to Copper Reagents 43 and Further Reactions

The reactivity and selectivity of the Grignard reagents **20** was not appropriate for reactions with some electrophiles. Here, transmetalation to a transition metal was advantageous. Thus, for the reaction with allylic halides or acid halides the intermediate *o*-nitroarylmagnesium reagents **20** were treated with CuCN·2LiCl[64] (1 equiv, −40 °C, 5 min), resulting in the *in situ* formation of arylcopper species **43a-i**, which smoothly reacted with a variety of electrophiles (Scheme 33 and Table 2).

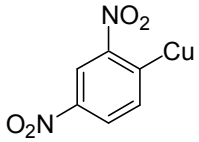
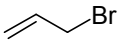
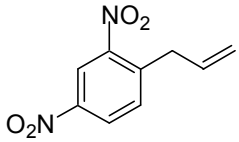
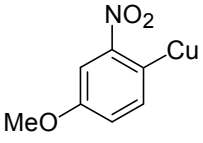
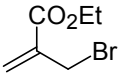
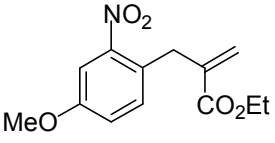
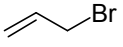
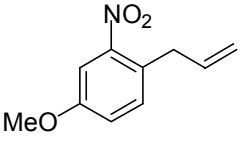


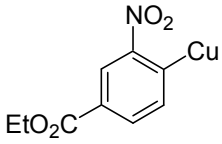
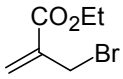
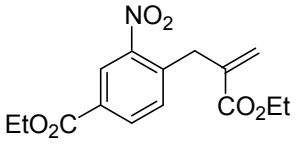
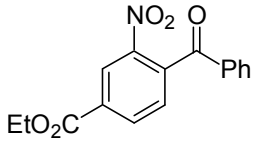
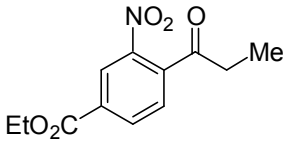
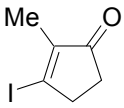
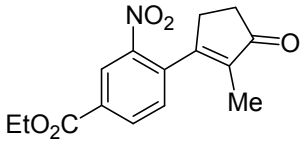
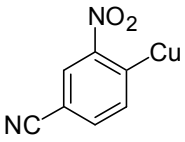
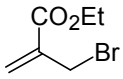
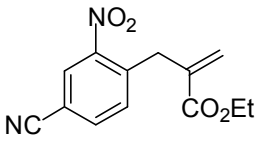
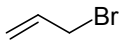
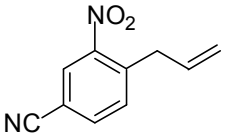
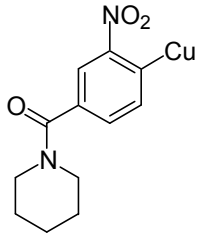
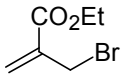
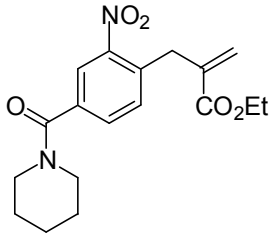
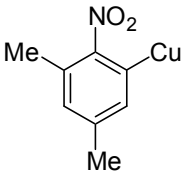
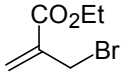
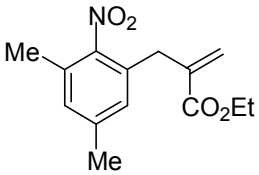

**21a-i** **43a-i** **44a-m**: 24-97%

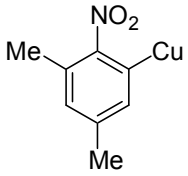
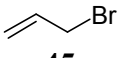
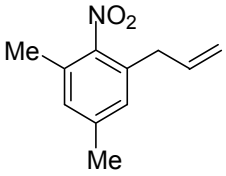
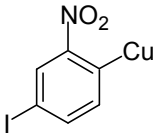
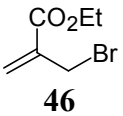
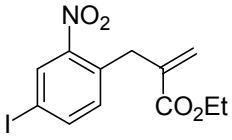
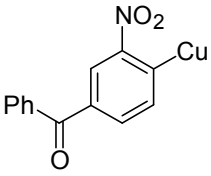
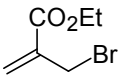
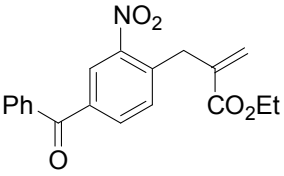
**FG** = a=H; b=4-$NO_2$; c= 4-OMe;
d=4-$CO_2$Et; e=4-CN;
f=4- $CONC_5H_{10}$; g=2,4-$Me_2$
h=4-I; i=4-PhCO;

**Scheme 33:** Transmetalation of Grignard reagents **20** to copper derivatives **43** and further reactions.

**Table 2:** Products **44** obtained by the reaction of the functionalized nitro-substituted arylcopper reagents **43** with different electrophiles.

| Entry | Arylcopper Reagent **43** | Electrophile | Product **44** | Isolated yield (%) |
|---|---|---|---|---|
| 1 |  **43b** |  **45** |  **44a** | 24[a] |
| 2 |  **43c** |  **46** |  **44b** | 72 |
| 3 | **43c** |  **45** |  **44c** | 55 |

| Entry | Arylcopper Reagent **43** | Electrophile | Product **44** | Isolated yield (%) |
|---|---|---|---|---|
| 4 |  **43d** |  **46** |  **44d** | 75 |
| 5 | **43d** | PhCOBr **47** |  **44e** | 76 |
| 6 | **43d** | EtCOCl **48** |  **44f** | 61 |
| 7 | **43d** |  **49** |  **44g** | 61 |
| 8 |  **43e** |  **46** |  **44h** | 58 |
| 9 | **43e** |  **45** |  **44i** | 53 |
| 10 |  **43f** |  **46** |  **44j** | 78 |
| 11 |  **43g** |  **46** |  **44k** | 76 |

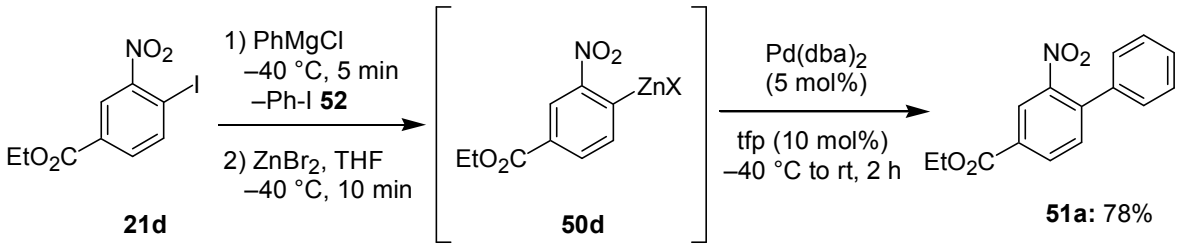
| Entry | Arylcopper Reagent **43** | Electrophile | Product **44** | Isolated yield (%) |
|---|---|---|---|---|
| 12 |  **43g** |  **45** |  **44l** | 78 |
| 13 |  **43h** |  **46** |  **44m** | 74 |
| 14 |  **43i** |  **46** |  **44n** | 97 |

[a] GC-conversion; Product **44a** was not isolated from the reaction mixture

As shown in Table 2, the transmetalation to copper opens a wide new field of application for these functionalized Grignard reagents. Thus, an allylation was possible with either allyl bromide (**45**) (entries 1, 3, 9, 12) or with the more reactive ethyl (2-bromomethyl) acrylate (**46**)[65] (entries 2, 4, 8, 10, 11, 13, 14) furnishing the corresponding products in good to excellent yields. The transmetalation of Grignard reagent **20b,** bearing two nitro groups, led to a copper species, which was no longer as stable as the corresponding Grignard reagent, showing the limitations of this methodology and allowing the conversion to the allylated compound **44a** in only 24% GC-yield (entry 1). Furthermore, these copper reagents underwent acylation reactions with benzoyl bromide (**47**), leading to highly functionalized ketone **44e** in good yield (entry 5). The use of the less reactive benzoyl chloride furnished product **44e** in only 45% yield, whereas the more reactive aliphatic propionyl chloride (**48**) delivered product **44f** in moderate 61% yield (entry 6). Remarkably, copper derivative **43d** participated in an addition-elimination reaction as well, leading to product **44g** upon reaction with 3-iodo-2-methyl-2-cyclopentenone (**49**) in 65% yield (entry 7).

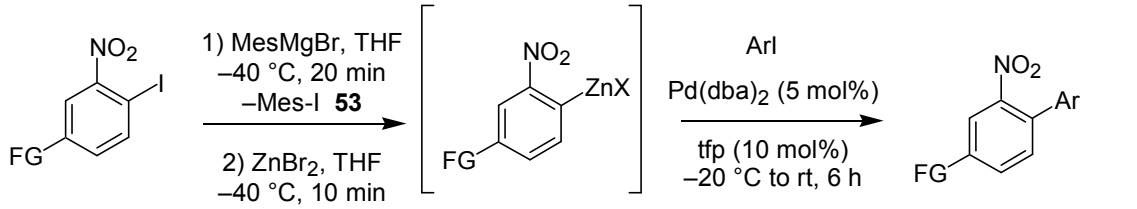
### 3.2.2.3 Palladium Catalyzed Cross-Coupling Reactions of *o*-Nitroarylzinc Halides 50

Transition-metal catalyzed cross-coupling reactions between $Csp^2$-centers are extensively used for preparing pharmaceuticals and agrochemical intermediates.[3] In particular, the Suzuki cross-coupling reaction has found many applications due to the high functional group compatibility of boronic acids and esters.[66] The Negishi cross-coupling reaction,[67] involving the reaction of organozinc reagents with organic halides in the presence of a palladium catalyst, has understandably been less well-utilized due to the water and air sensitivity of organozinc species. However, the excellent ability of organozinc species to undergo transmetalation reactions often allows Negishi cross-coupling reactions to be performed under exceedingly mild reaction conditions.[68] Since polyfunctionalized organozinc reagents can readily be prepared by direct insertion of zinc,[69] I/Zn exchange[21] or by transmetalation reactions,[51] a number of polyfunctionalized organozinc reagents are readily available for cross-coupling reactions. As mentioned in the introduction to this chapter, this direct insertion of zinc is not possible when nitro groups are present.[52]
However, similarly to the above-mentioned transmetalation to copper with a soluble copper salt, organomagnesium reagents can be transformed to the corresponding zinc species **50** by addition of $ZnBr_2$, allowing a palladium catalyzed Negishi cross-coupling reaction. As shown in Scheme 34, cross-coupling product **51** was isolated in 78% within 2 h upon addition of $Pd(dba)_2$ (5 mol%) and tfp (10 mol%) at ambient temperature yield, when the initially formed iodobenzene (**52**) reacted as an electrophile,.




**Scheme 34:** Negishi cross-coupling of zinc reagent **50d** with iodobenzene (**52**) formed during the I/Mg exchange.

Therefore, a more sterically hindered Grignard reagent was required, which would still allow a fast exchange reaction, but would be less reactive in the Negishi cross-coupling reaction. It turned out that for performing these cross-coupling reactions, mesitylmagnesium bromide[70] was advantageous for the preparation of the starting organomagnesium species **20** (Scheme 35).



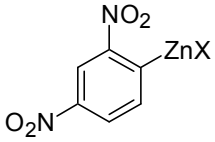
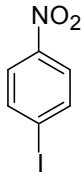
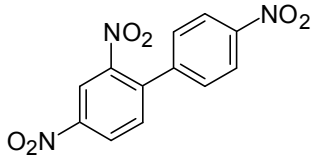
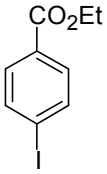
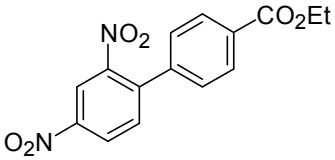
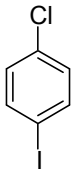
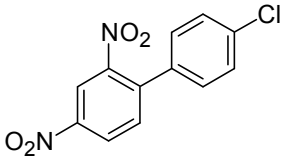
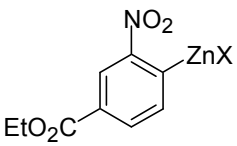
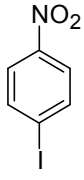
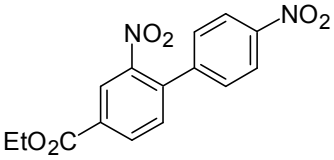

**21** **50b, d-f** **51b-n**: 48 - 85%

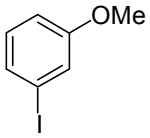
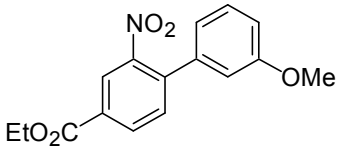
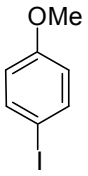
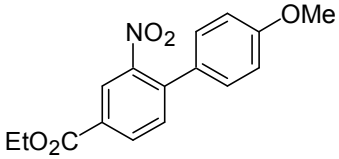
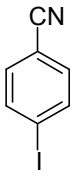
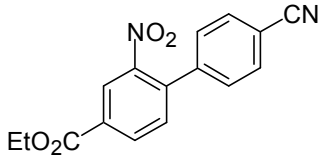
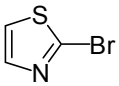
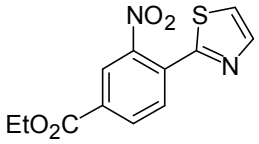
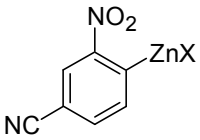
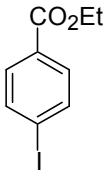
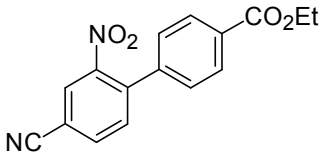
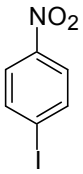
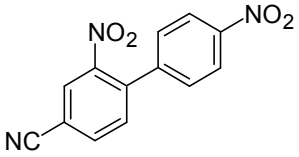
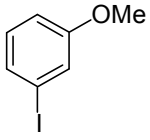
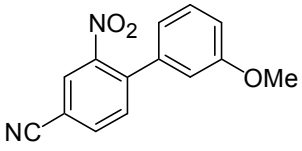
**FG** = b=4-$NO_2$; d=4-$CO_2Et$;
e=4-CN; f=4-$CONC_5H_{10}$;

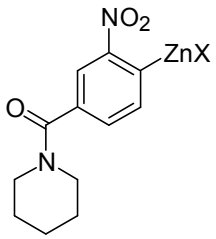
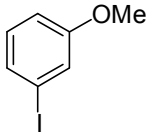
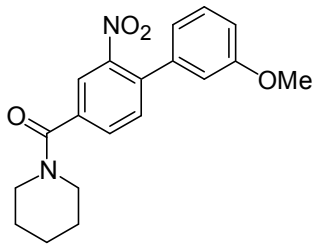
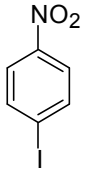
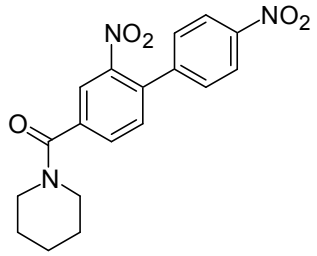
**Scheme 35:** Negishi cross-coupling of *o*-nitro-arylzinc halides **50** with aryl iodides.

For mesitylmagnesium bromide, the iodine-magnesium exchange reaction produced mesityl iodide (**53**), which underwent only reluctantly an insertion of palladium due to the steric hindrance and the electron donating effects of the methyl substituents. A variety of different iodo arenes and 2-bromothiazole (**58**) were substituted under these conditions, as shown in Table 3.

**Table 3:** Polyfunctional biphenyls **51**, obtained by Pd-catalyzed cross-couplings of nitro-substituted arylzinc compounds **50**.

| Entry | Arylzinc reagent **50** | Aryl iodide | Biphenyl **51** | Isolated yield (%) |
|---|---|---|---|---|
| 1 |  **50b** |  **54** |  **51b** | 55 |
| 2 | **50b** |  **24** |  **51c** | 68 |
| 3 | **50b** |  **55** |  **51d** | 55 |
| 4 |  **50d** |  **54** |  **51e** | 85 |

| Entry | Arylzinc reagent **50** | Aryl iodide | Biphenyl **51** | Isolated yield (%) |
|---|---|---|---|---|
| 5 | **50d** |  **56** |  **51f** | 80 |
| 6 | **50d** |  **57** |  **51g** | 53 |
| 7 | **50d** |  **25** |  **51h** | 53 |
| 8 | **50d** |  **58** |  **51i** | 48 |
| 9 |  **50e** |  **24** |  **51j** | 73 |
| 10 | **50e** |  **54** |  **51k** | 68 |
| 11 | **50e** |  **56** |  **51l** | 75 |

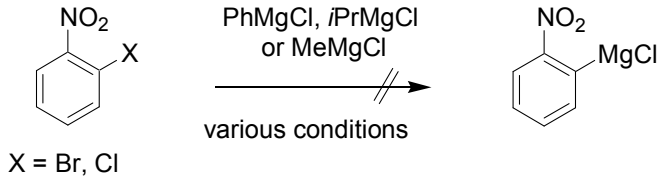
| Entry | Arylzinc reagent **50** | Aryl iodide | Biphenyl **51** | Isolated yield (%) |
|---|---|---|---|---|
| 12 |  **50f** |  **56** |  **51m** | 67 |
| 13 | **50f** |  **54** |  **51n** | 74 |

To our delight, the 2,4-dinitro-substituted arylzinc compound **50b** which was prepared according to our method using mesitylmagnesium bromide, showed a good thermal stability under the reaction conditions. The exchange reaction was again very fast, furnishing Grignard reagent **20b** within 1 min at −40 °C. After transmetalation with zinc bromide to zinc reagent **50b**, its cross-coupling with the functionalized aryl iodides **54, 24** and **55** furnished the expected biphenyls **51b-d** in 55-68% yield (entries 1-3, Table 3). Especially interesting was the synthesis of biphenyl **51b**, which bears three nitro groups but did not undergo any electron-transfer processes under the reaction conditions, showing that Negishi cross-coupling reactions are compatible with the presence of reagents bearing several nitro functionalities. The reaction of ethyl 4-iodo-3-nitrobenzoate (**21d**) with mesitylmagnesium bromide (1.05 equiv) in THF at −40 °C furnished within 15 min the desired arylmagnesium species **20d**, which was immediately transmetalated to the corresponding zinc derivative **50d** by reaction with zinc bromide at −40 °C (10 min). The resulting organozinc species **50d** was perfectly stable at 20 °C and reacted with a broad range of aryl iodides in the presence of $Pd(dba)_2$ (5 mol%) and tfp (10 mol%) within 6 h at 20 °C. Aromatic halides like 4-nitro-1-iodobenzene (**54**) reacted especially well, furnishing the desired biphenyl **51e** in 85% yield (entry 4). An aryl iodide bearing an electron-withdrawing group, like 3-methoxy-1-iodobenzene (**56**), reacted similarly with **50d** affording the corresponding biphenyl **51f** in 80% yield (entry 5). Interestingly, 4-iodobenzonitrile (**25**) gave biphenyl **51g** only in 53% yield (entry 7). A heterocyclic bromide such as 2-bromothiazole (**58**) provided the desired cross-coupling product **51i** in 48 % yield (entry 8). Similarly, the cyano-substituted zinc reagent **50e** reacted with aryl iodides **24, 54, 56** as expected leading to polyfunctional biphenyls **51j-l** in 68-75% yield (entries 9-11). The amide substituted organozinc compound **50f** led to the Negishi cross-coupling products **51m** and **51n** in 67 and 74%, respectively (entries 12 and 13).

One major drawback of the sterically hindered mesitylmagnesium bromide was the reduced reactivity in the I/Mg exchange reaction. Therefore, only sufficiently electron-poor arenes underwent a clean I/Mg exchange reaction. Electron-donating substituents like in compounds **21a**, **21c** and **21g** gave mixtures of the exchange product and products generated through addition to the nitro group when mesitylmagnesium bromide was used for the I/Mg exchange.

### 3.2.2.4 Preparation of Functionalized *o*-Nitroarylmagnesium Halides *via* a Bromine- or Chlorine-Magnesium Exchange

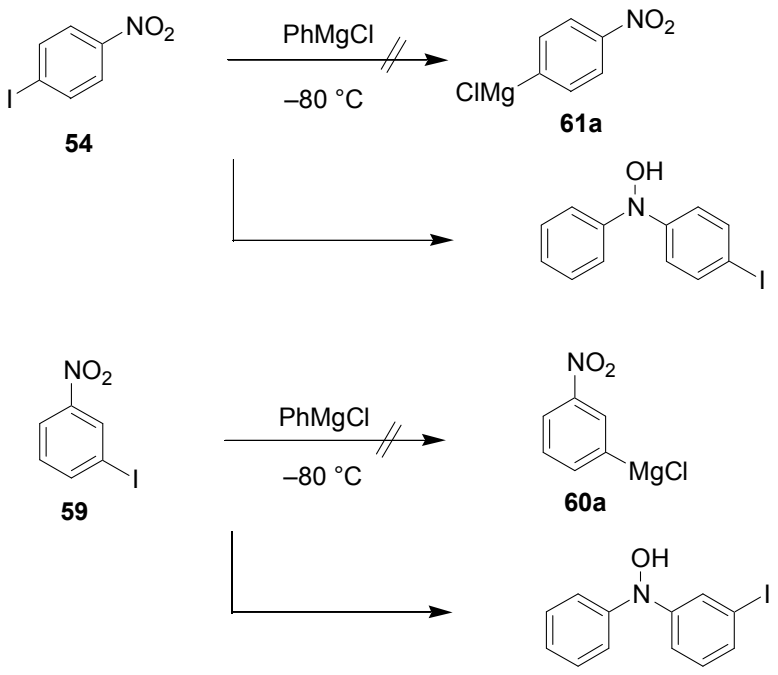
Although the formation of Grignard reagents **20** proceeded very well, starting from functionalized iodides **21**, the application to bromides and even chlorides was desirable. However, all attempts to extend this methodology to the corresponding 2-bromo or 2-chloronitrobenzenes were unsuccessful and with the less reactive exchange reagent phenylmagnesium chloride no conversion was observed. Our endeavors to achieve this exchange reaction with more powerful reagents like *i*PrMgCl or MeMgCl were without success either, leading only to complicated product mixtures (Scheme 36).




**Scheme 36:** Attempts to achieve a Br/ or Cl/Mg exchange reaction.

## 3.3 Preparation of Functionalized *m*- and *p*-Nitroarylmagnesium Halides of Type 60 and 61 *via* an Iodine-Magnesium Exchange

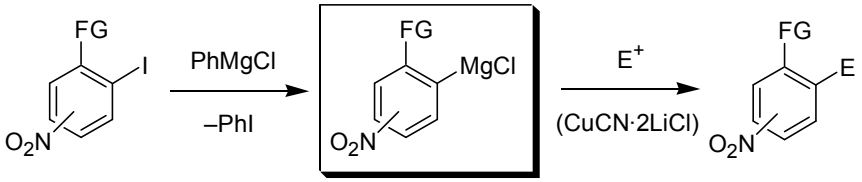
While the preparation of *o*-nitroarylmagnesium halides **20** was possible, the formation of arylmagnesium halides bearing a nitro group in *m*- and *p*-position turned out to be much more difficult. The chelation of the nitro group reduces the reactivity of the formed Grignard reagent significantly and therefore no intermolecular addition to the nitro group is possible. Both *m*- and *p*-nitroarylmagnesium halides lack this stabilization and could therefore, even if the halogen-magnesium exchange reaction were fast enough, react with themselves. Side reactions could then take place during the transformation. These side reactions led to new applications, which will be discussed in chapter 4 in detail.
As shown in Scheme 37, the addition of phenylmagnesium chloride to 3- and 4-iodonitrobenzene (**59** and **54**) did not lead to any exchange product like **60a** or **61a**, but instead led only to reduction of the nitro group, resulting in the formation of 3- and 4-iododiphenylhydroxylamine as indicated by GC-MS analysis, which will be discussed later in chapter 4.




**Scheme 37:** Attempted formation of 3- and 4-magnesiated nitrobenzenes **60a** and **61a**.

As well as different solvents, different reaction temperatures were screened without any improvement in the formation of the desired Grignard reagents. Even at very low temperatures (as low as −100 °C) the addition to the nitro group could not be prevented.

We envisioned that the introduction of either another chelating group or steric hindrance could protect the nitro group from an attack of the Grignard reagent (Scheme 38).




**Scheme 38:** Preparation of 3- and 4-magnesiated nitrobenzenes **60** and **61** bearing a chelating group in the *o*-position.

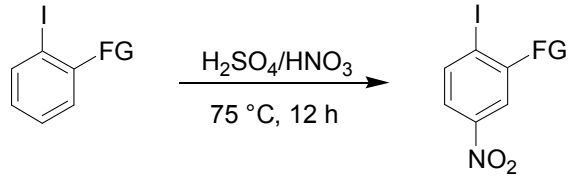
As mentioned above, the synthesis of starting materials was again crucial, since most of the iodides were not commercially available.

### 3.3.1 Preparation of Functionalized 3- and 4-Iodonitrobenzenes of type 72 and 65

While for 2-iodonitrobenzenes **20**, the *meta*-directing effects of the nitro group hampered the direct iodination or nitration, in case of functionalized *m*- and *p*-iodobenzenes this effect was beneficial. Therefore, only the following approaches were used:

1. iodination of the corresponding functionalized nitrobenzene,
2. selective nitration of the corresponding functionalized iodobenzenes, or
3. the Sandmeyer reaction.

Again, the nitration of functionalized iodobenzenes **62-64** proved to be a powerful method for the introduction of a nitro group (Scheme 39).[62]

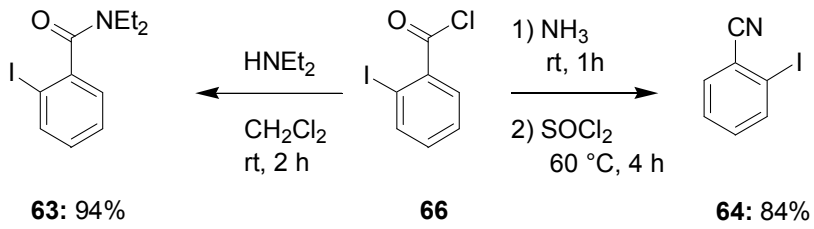



**62:** FG = $CO_2Et$;
**63:** FG = $CONEt_2$;
**64:** FG = CN;

**65a**: FG = $CO_2Et$; 84%
**65b:** FG = $CONEt_2$; 60%
**65c**: FG = CN; 62%

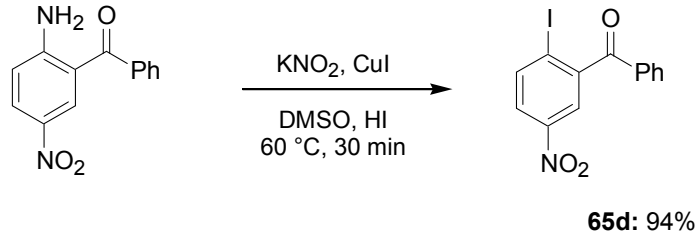
**Scheme 39:** Nitration of 2-iodofunctionalized aromatic compounds **62-64**.

Thus, the nitration of ethyl 2-iodobenzoate (**62**) proceeded at elevated temperatures (75 °C) within 12 h leading to ethyl 4-nitro-2-iodobenzoate (**65a**) in 84% yield. Similarly, iodides **63** and **64** were transformed into the corresponding nitro compounds **65b** and **65c** in good yields. Formation of the non-commercially available iodides **63** and **64** commenced again with the transformation of 2-iodobenzoyl choride (**66**) into 2-iodobenzamide with ammonia, which was straightforwardly dehydrated with thionyl chloride to compound **64** in excellent yield. Amide **63** was prepared by reacting **66** with diethylamine (Scheme 40).



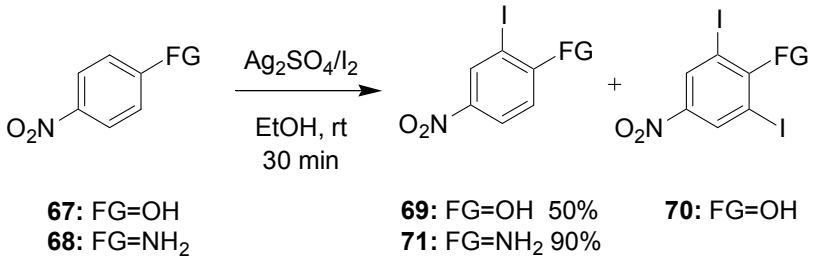

**Scheme 40:** Synthesis of starting materials **63** and **64**.

The modified Sandmeyer reaction of Baik and co-workers[63] turned out to be very useful for the synthesis of the keto-substituted derivative **65d**, starting from commercially available 2-amino-5-nitrobenzophenone (Scheme 41).



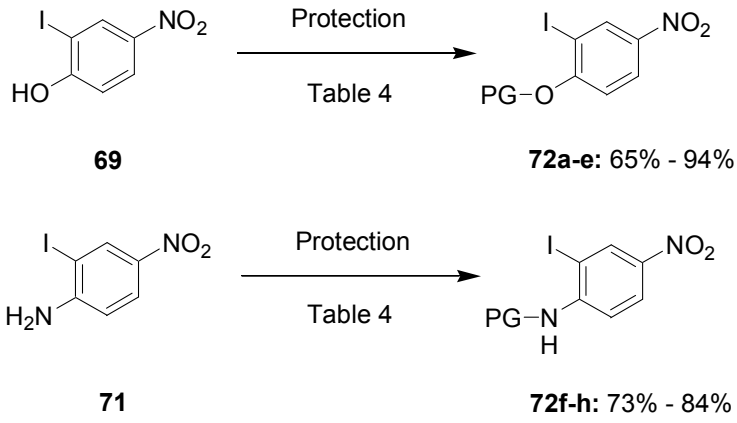

**Scheme 41:** Preparation of 2-iodo-5-nitro-benzophenone (**65d**).

For substrates bearing electron-donating substituents, iodination with strong iodinating reagents like $Ag_2SO_4/I_2$ led to satisfactory results (Scheme 42).



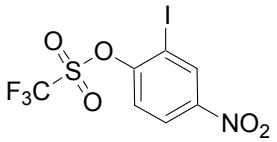
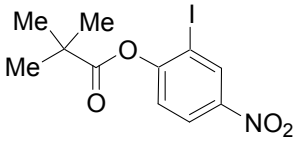
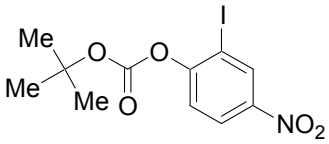
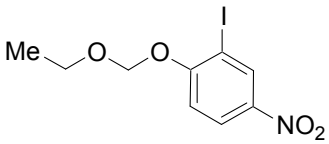
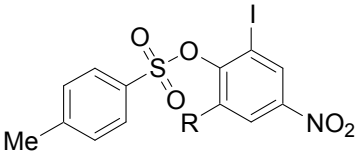

**Scheme 42:** Iodination of 4-nitrophenol **67** and 4-nitroaniline **68**.

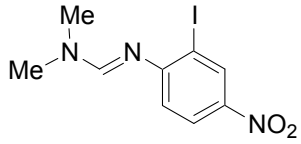
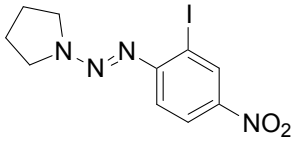
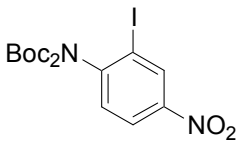
Selective mono-iodination was usually not possible, but the two products were easily separated by column chromatography. Furthermore, the quest for a suitable protecting group for these functional groups appeared more difficult than it seemed at first glance. Several different protecting groups showing different chelating properties were introduced subsequent to iodination (Scheme 43, Table 4).



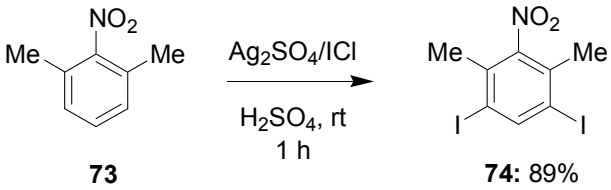

**Scheme 43:** Preparation of protected phenol and aniline derivatives **72**.

**Table 4:** Synthesis of *O*- and *N*-protected derivatives **72**

| Entry | Reagents and Conditions | Aromatic compounds **72** | Isolated yield (%) |
|---|---|---|---|
| 1 | $Tf_2O$, pyridine<br>0 °C, 15 h |  **72a** | 84 |
| 2 | Piv-Cl, $NEt_3$,<br>DCM, rt, 48 h |  **72b** | 65 |
| 3 | $Boc_2O$, DMAP,<br>DCM, rt, 24 h |  **72c** | 78 |
| 4 | NaH, EOM-Cl,<br>DMF, rt, 3 h |  **72d** | 92 |
| 5 | TsCl, pyridine,<br>0 °C, 12 h |  R=H: **72e** | 94 |
| 6 | TsCl, pyridine,<br>0 °C, 12 h | R=I: **72f** | 93 |

| Entry | Reagents and Conditions | Aromatic compounds **72** | Isolated yield (%) |
|---|---|---|---|
| 7 | DMF-DMA, toluene, reflux, 12 h |  **72g** | 84 |
| 8 | 1) $NaNO_2$, HCl, 0 °C, 30 min 2) pyrrolidine, $K_2CO_3$ rt, 1 h |  **72h** | 78 |
| 9 | $Boc_2O$, DMAP, MeCN, 60 °C, 12 h |  **72i** | 73 |

Finally, the iodination of 1,3-dimethyl-2-nitrobenzene (**73**) furnished diiodo compound **74** with the very active electrophilic iodination reagent, prepared *in situ* from ICl and $Ag_2SO_4$, in excellent yield (Scheme 44).[71]

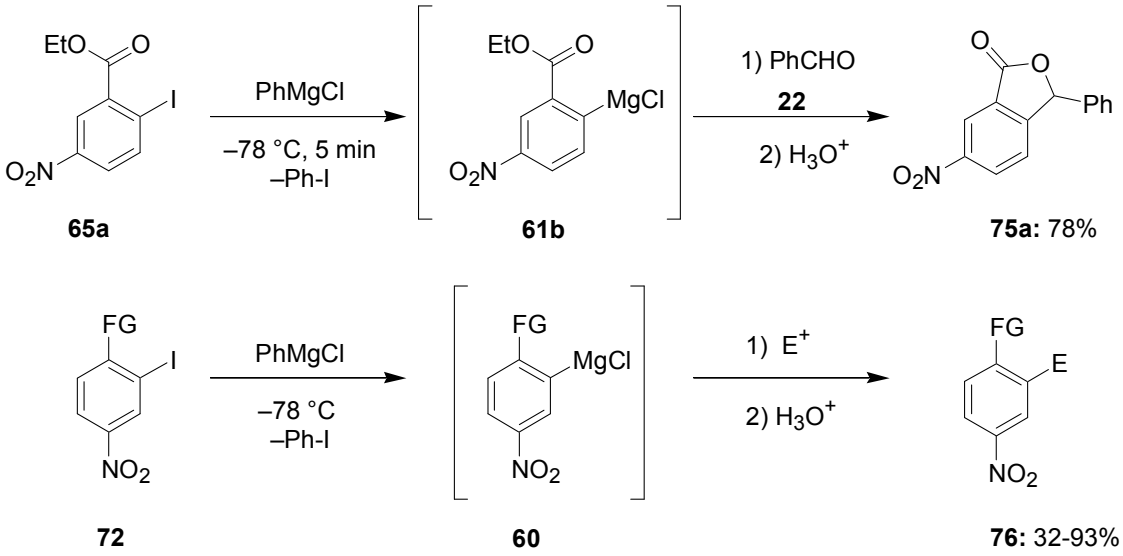



**73** **74:** 89%

**Scheme 44:** Synthesis of compound **74**.

### 3.3.2 Preparation of Functionalized *m*- and *p*-Nitroarylmagnesium Halides 60 and 61 *via* an Iodine-Magnesium Exchange Reaction

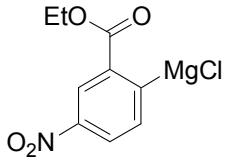
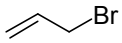
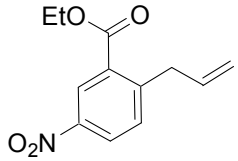
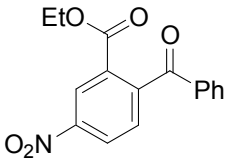
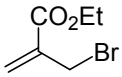
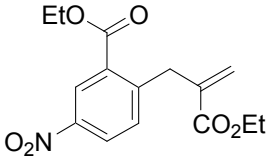
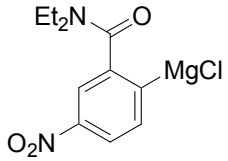
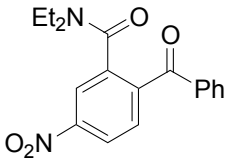
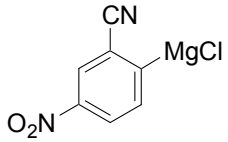
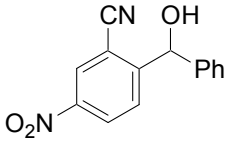
The initial concept of adding an additional chelating group on the aromatic ring proved successful, as shown in Scheme 45. Treatment of ethyl 2-iodo-4-nitrobenzoate (**65a**) with phenylmagnesium chloride (1.1 equiv) in THF at −78 °C, led to a fast exchange reaction (10 min), as indicated by gas-chromatographical analysis of reaction aliquots. The resulting nitro-substituted Grignard reagent **61b** was reacted subsequently with benzaldehyde (1.5 equiv), furnishing lactone **75a** in 78% isolated yield (Scheme 45 and Table 5).




**Scheme 45:** Preparation of *meta*- and *para*-nitro functionalized Grignard reagent **60** and **61**.

Similarly, compounds of type **72** were transformable into the corresponding Grignard reagents **60** using phenylmagnesium chloride (Scheme 45 and Table 6).
Depending on the nature of the group *ortho* to the iodide, different reactivities were observed, showing that these Grignard reagents represent clearly the limits of our approach. Tables 5 and 6 display the products of type **75** and **76**, prepared by directly reacting the Grignard reagent or after subsequent transmetalation to copper.

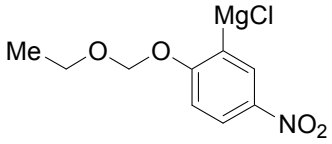
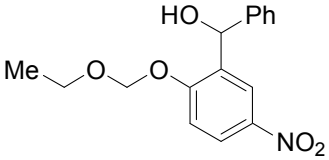
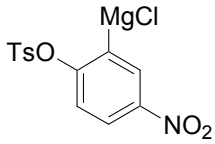
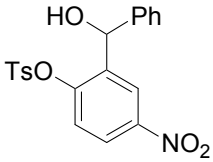
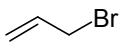
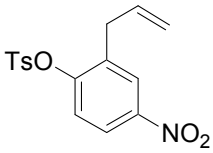
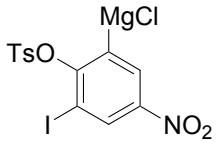
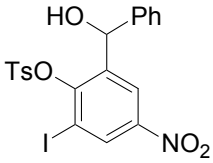
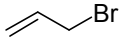
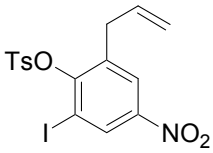
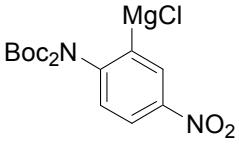
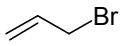
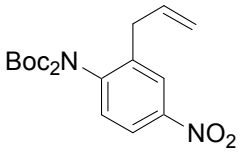
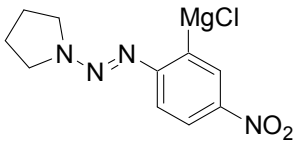
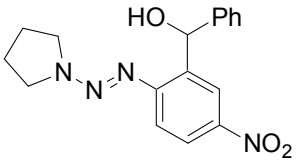
**Table 5:** *para*-Nitro functionalized aromatic compounds **75**, obtained by reaction of *para*-nitro-substituted arylmagnesium reagents **61**.

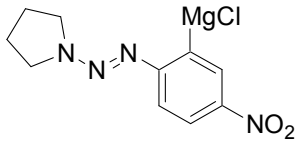
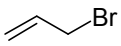
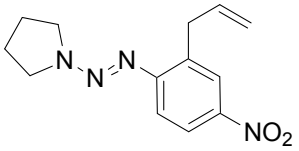
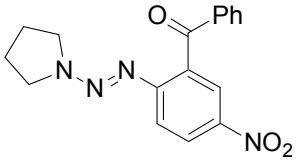
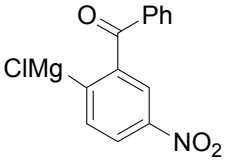
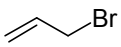
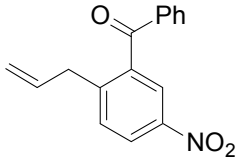
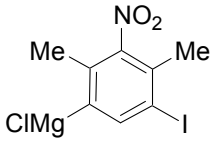
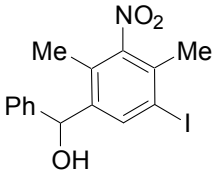
| Entry | Arylmagnesium Reagent **61** | Electrophile | Product **75** | Isolated yield (%) |
|---|---|---|---|---|
| 1 |  **61b** |  **45** |  **75b** | 87[a] |
| 2 | **61b** | PhCOBr **47** |  **75c** | 94[a] |
| 3 | **61b** |  **46** |  **75d** | 67[a] |
| 4 |  **61c** | PhCOBr **47** |  **75e** | 68[a] |
| 5 |  **61d** | PhCHO **22** |  | --- |

[a] The Grignard reagent was transmetalated with CuCN·2LiCl to the corresponding copper reagent before reaction with the electrophile

The carbonyl group stabilized the Grignard reagent **61b** well, leading to a clean and fast reaction with phenylmagnesium chloride even at low reaction temperatures (−78 °C). Transmetalation to copper with the soluble copper source CuCN·2LiCl allowed reactions with allyl bromide (**45**), ethyl (2-bromomethyl) acrylate (**46**) and benzoyl bromide (**47**) (entries 1, 2 and 3, Table 5) in good to excellent yields. The same was true for the amido function in compound **65b** and the corresponding Grignard reagent **61c** was after transmetalation to copper reacted with benzoyl bromide (**47**), delivering compound **75e** in 68% yield (entry 4). The highly electron-withdrawing cyano group in compound **65c** facilitated the exchange reaction, but due to bad chelating properties did not stabilize sufficiently the resulting Grignard reagent **75c**, leading to complicated mixtures.

**Table 6:** *meta*-Nitro functionalized aromatic compounds **76**, obtained by reaction of *meta*-nitro-substituted arylmagnesium reagents **60**.

| Entry | Arylmagnesium Reagent **60** | Electrophile | Product **76** | Isolated yield (%) |
|---|---|---|---|---|
| 1 |  **60b** | PhCHO **22** |  **76a** | 32 |
| 2 |  **60c** | PhCHO **22** |  **76b** | 80 |
| 3 | **60c** |  **45** |  **76c** | 93[a] |
| 4 |  **60d** | PhCHO **22** |  **76d** | 78 |
| 5 | **60d** |  **45** |  **76e** | 87 [a] |
| 6 |  **60e** |  **45** |  **76f** | 64 [a] |
| 7 |  **60f** | PhCHO **22** |  **76g** | 58 |

| Entry | Arylmagnesium Reagent **60** | Electrophile | Product **76** | Isolated yield (%) |
|---|---|---|---|---|
| 8 |  **60f** |  **45** |  **76h** | 61[a] |
| 9 | **60f** | PhCOBr **47** |  **76i** | 75[a] |
| 10 |  **60g** |  **22** |  **76j** | 54 |
| 11 |  **60h** | PhCHO **22** |  **76k** | 71 |

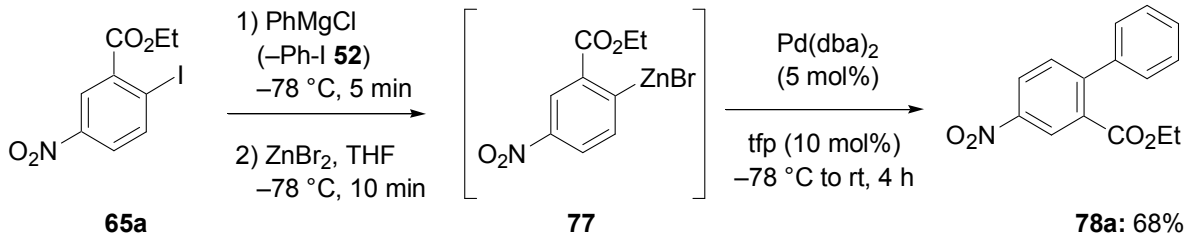
[a] The Grignard reagent was transmetalated with CuCN·2LiCl to the corresponding copper reagent before reaction with the electrophile

For protected phenol derivatives **72a-e** it turned out that good chelating properties but bad leaving abilities were essential for the formation of Grignard reagents **60**. While the trifluoromethylsulfonyl group in **72a** (Table 4) reduced the electron density very much and, therefore, facilitated the exchange reaction, the corresponding Grignard reagent **60** had a strong tendency to eliminate and forms benzyne, even at low temperatures. The same behavior was observed for pivaloate **72b** and carbonate **72c**. These compounds all gave good conversions for the I/Mg exchange, as indicated by formation of 1 equiv of iodobenzene (**52**) after addition of phenylmagnesium chloride, but no iodolysis product was obtained after quenching with $I_2$. Protecting phenol **69** as an ethoxymethyl-ether **72d** led to a very slow I/Mg exchange reaction at −78 °C (4 h) and the isolated yield for the reaction of **60b** with benzaldehyde (**22**) was moderate 32% (entry 1, Table 6). The right balance between good chelating and leaving group abilities was found for tosylates. Thus, the exchange of 2-iodo-4-nitrophenyl tosylate **72e** was complete within 15 min and the Grignard reagent **60c** was reacted subsequently with benzaldehyde, leading to benzhydryl **76b** (entry 2) in good yield. The 2,6-diiodo compound **72f** underwent the mono-exchange reaction even faster, leading to compound **76d** (entry 4) after reaction with benzaldehyde (**22**). Both Grignard reagents **60c** and **60d** could be transmetalated to copper and reaction

with allyl bromide (**45**) furnished compounds **76c** and **76e** in 93% and 87% yield, respectively (entries 3 and 5).
For the protected aniline derivatives **72g-i**, di-Boc protection was most suitable, allowing the I/Mg exchange reaction at −78 °C within 30 min. Subsequent transmetalation of Grignard reagent **60e** to copper and reaction with allyl bromide (**45**) led to compound **76f** in 64% yield (entry 6). Trapping with an aldehyde led to partial transfer of the Boc group from nitrogen to oxygen, which could not be avoided even at low temperatures. In contrast, the formation of triazene-protected Grignard reagent **60f** required elevated temperatures (−55 °C) and a more polar solvent mixture (THF:NMP=3:1) to ensure a better solubility and faster reaction. However, Grignard reagent **60f** reacted with benzaldehyde (**22**), yielding alcohol **76g** in 58% (entry 7). Transmetalation to copper and reaction with allyl bromide (**45**) or benzoyl bromide (**47**) furnished compounds **76h** and **76i** in 61% and 75% yield, respectively (entries 8 and 9). It turned out, that even a keto group was sufficient to stabilize the new organomagnesium compound **60g**, allowing the formation of compound **76j** in 54% yield after transmetalation to copper (entry 10). Finally, the sterical hindrance of two methyl groups in nitro compound **74** allowed the synthesis of Grignard reagent **60h** which was reacted with benzaldehyde (**22**) furnishing compound **76k** in 75% yield (entry 11).

### 3.3.3 Palladium Catalyzed Cross-Coupling Reactions of Magnesiated 4-Nitroarenes 61

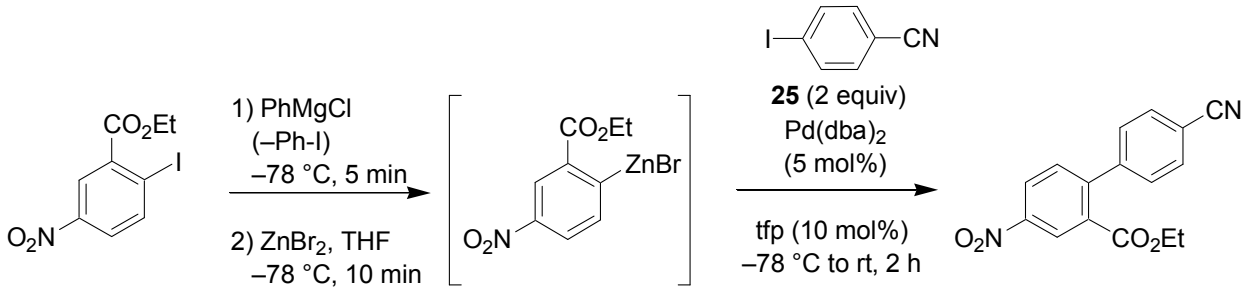
A transmetalation to zinc was also possible, allowing the application of the new Grignard reagents to the wide field of palladium catalyzed cross-coupling reactions. As shown in Scheme 46, the transmetalation to arylzinc reagent **77**, followed by the addition of $Pd(dba)_2$ (5 mol%) and tfp (10 mol%) furnished biphenyl **78a** at ambient temperature within 2 h in 68% yield.




**65a** **77** **78a:** 68%

**Scheme 46:** Negishi cross coupling of arylzinc **77** with iodobenzene (**52**).

Mesitylmagnesium bromide did not lead to the desired Grignard species, but to the reductive addition to the nitro group, hampering further reactions. However, the use of an excess of an electron-poor aryl iodide such as 4-iodobenzonitrile (**25**), allowed the formation of biaryl **78b** in satisfactory 83% isolated yield (Scheme 47).




**65a** **77** **78b:** 83%

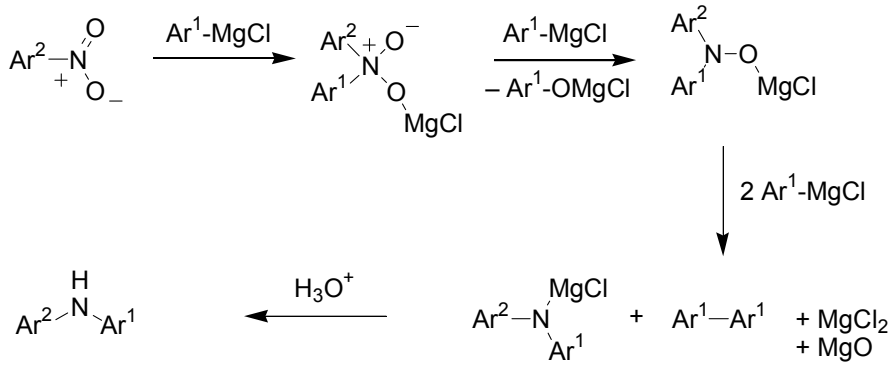
**Scheme 47:** Negishi cross-coupling reaction of compound **77**.

# 4. Preparation of Polyfunctionalized Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Nitroarenes

## 4.1 Introduction

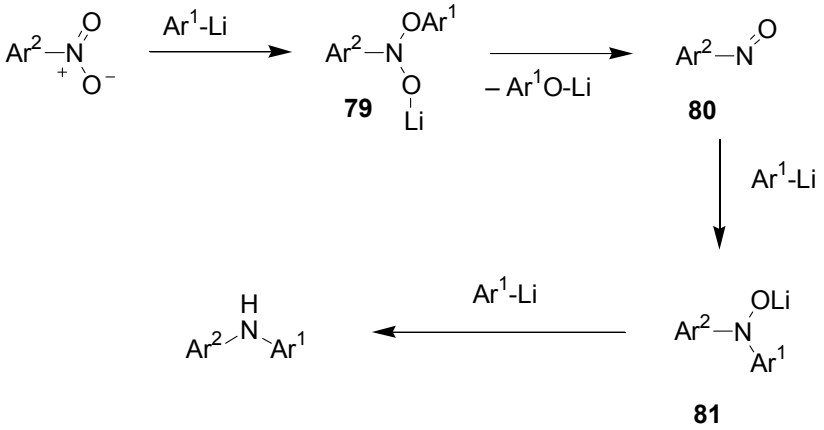
As discussed in the previous chapter, the iodine magnesium exchange reaction on various nitro functionalized iodobenzenes led to the corresponding magnesiated reagents in good to excellent yields. However, despite great efforts, no selective exchange reaction was observed when no chelating functionalities were present *ortho* to the iodine. When aromatic Grignard reagents were used for the exchange reaction, to our surprise, not an unselective reaction but rather a very clean conversion to a single new product was observed. GC-MS analysis of the reaction mixture indicated a reduction of the nitro group to the corresponding diarylamine.

Indeed, the reaction of arylmagnesium halides with nitro- and nitrosoarenes has been studied earlier. H. Wieland and later H. Gilman and R. McCracken reported the formation of diphenylamine in poor yield (42%), along with phenol and biphenyl, when reacting phenylmagnesium bromide with nitrosobenzene (Scheme 48).[72,73] D. Kursanov and P. Solodkov reproduced the results and postulated another mechanism for this reaction, starting from the corresponding nitrobenzene.[74]




**Scheme 48:** Proposed mechanism for the formation of diarylamine from nitrobenzene and phenylmagnesium chloride.[72,74]

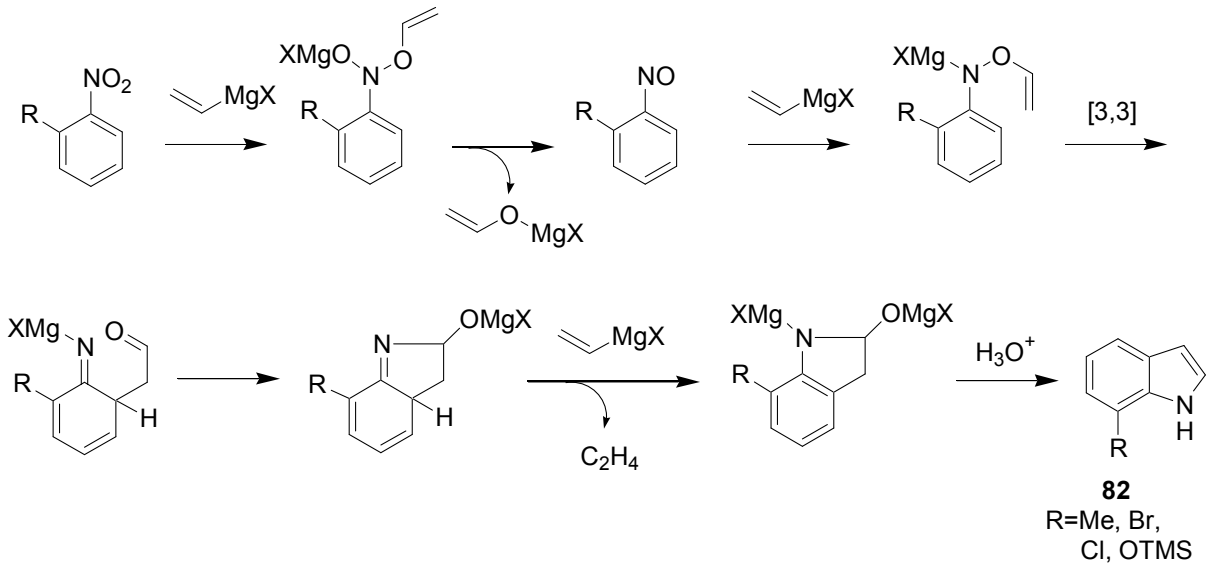
Y. Yost and co-workers confirmed this mechanism in the early 1970s and succeeded in isolating diarylhydroxylamino derivatives from the reaction mixture in appreciable yields.[75] However, the experiments of Y. Yost did not confirm the first step of this reaction which could also be an addition of the arylmagnesium halide to the oxygen of the nitro group. This different initial step was favoured by G. Koebrich, who studied the metalation of nitroarenes with PhLi.[51d,e,76] No metalation of the aromatic ring took place but instead the formation of mainly phenol, azobenzene and diphenylamine was observed, and a mechanistic rationale was given (Scheme 49).




**Scheme 49:** Proposed mechanism for the formation of diarylamine from nitrobenzene and PhLi.[76]

These authors suggested an *O*-arylation as the first step, leading to the formation of intermediate **79**, which can eliminate a phenolate, thereby furnishing a nitroso species **80**. This nitroso species can react subsequently with a second equivalent of phenyllithium, leading to hydroxylamide **81**.

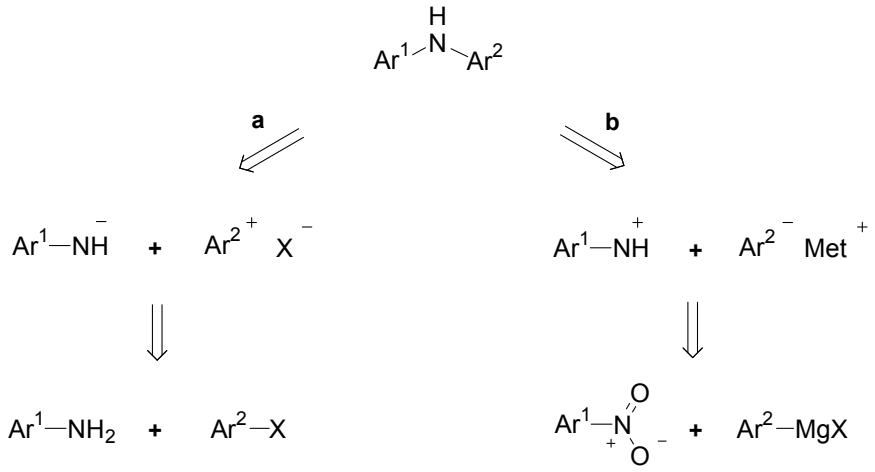
As mentioned in the introduction of chapter 3, a variety of reactions involving Grignard reagents and nitroarenes was reported, mainly by the group of G. Bartoli,[53c] such as the reported, convenient procedure for the preparation of 7-substituted indoles **82** (Scheme 50).[55,56,76c,77]




**Scheme 50:** Mechanism for the Bartoli indole synthesis.[77b]

The proposed mechanism again favours an attack of the Grignard reagent at the oxygen atom as shown in Scheme 50. In the first step, vinylmagnesium bromide adds to the oxygen and eliminates a magnesium enolate. Then a second equivalent adds to the oxygen of the

nitroso function. This intermediate undergoes a [3,3] sigmatropic rearrangement and finally furnishes indole **82** after a third equivalent of vinylmagnesium halide operates as a base.
However, no further investigations were made to turn the initial results of H. Wieland and G. Koebrich into a synthetically valuable procedure. The reason for this might be the very sensitive nature of the resulting diarylhydroxylamines, which readily oxidize in air leading to reactive diarylnitroxyl radicals.
We realized that our methodology for the preparation of functionalized Grignard reagents combined with this interesting result could lead to a new method for the formation of diarylamines, starting from the corresponding nitroarenes. This would be complementary to other methods reported for the preparation of this very popular substance class. Scheme 51 illustrates the two different pathways.




**Scheme 51:** Synthesis of diarylamines using pathway **a** or **b**.

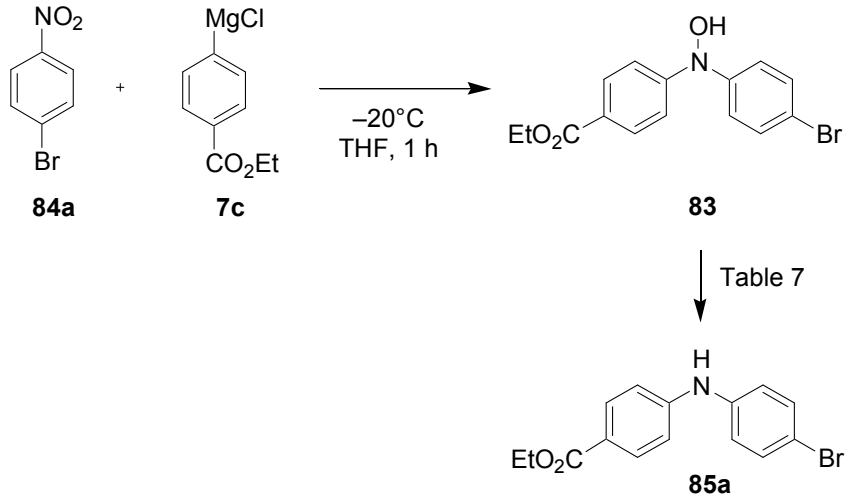
As discussed in the general introduction, usually a nitrogen nucleophile is reacted with an aromatic halide following a $S_NAr$ mechanism, but, generally, activating groups are required together with a good leaving group (pathway a).[78] More recently, various diarylamines were prepared by palladium catalyzed cross-coupling reactions of amines with aryl halides.[32,3379] Other transition metals such as copper[37,80] and nickel[40] have also allowed the performance of C(aryl)-N bond formation reactions. Oxidative coupling procedures between arylboronic acids and aromatic or heterocyclic amines mediated by Cu(II) salts proved to be effective as well.[37] In all these approaches, aromatic amines were used as precursors following pathway a (Scheme 49). In case of aromatic Grignard reagents, nitrogen would have to act as an electrophile, resulting in an "Umpolung" of the reactivity (pathway b).[81] The polarization of the nitro group would in principle permit this retrosynthetic transformation analysis.

## 4.2 Preparation of Polyfunctionalized Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Nitroarenes

### 4.2.1 Optimization of the Reaction Conditions and the Reduction Step

In order to develop this undesired side reaction into an efficient procedure for the synthesis of diarylamines, we had to overcome several obstacles. In particular, the equivalents of Grignard reagent reported previously (4 equiv) needed to be reduced, and side reactions of the hydroxylamine had to be avoided.

Therefore, we carefully examined how many equivalents of Grignard reagent were necessary to quantitatively convert nitrobenzene to the corresponding hydroxylamine derivative. We found that the reduction of nitrobenzene with phenylmagnesium chloride required some excess of Grignard reagent (2.3 equiv) to give full conversion on GC and TLC analysis. However, since the hydroxylamine was found to be very sensitive towards air, a subsequent one-pot reduction seemed advantageous. A major requirement for the reduction was to tolerate as many functional groups as possible. Several different metals were tested, which had been used for the reduction of a nitro group to the corresponding amine[48,82] together with a hydrogen source (Table 7). As a test substrate, a bromo ester-substituted diarylhydroxylamine **83** was chosen, possessing two interesting functional groups. This substrate was freshly synthesized each time, starting from 4-bromonitrobenzene (**84a**) and Grignard reagent **7c** (Scheme 5), easily accessible through an iodine-magnesium exchange reaction on compound **24** (Scheme 52).




**Scheme 52:** Optimization of the reduction conditions of hydroxylamine **83**.

**Table 7:** Isolated yield of diphenylamine **85a** after reduction of hydroxylamine **83** with different reducing agents (Scheme 52).

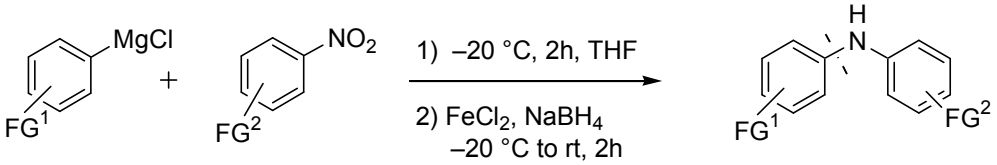
| Entry | Reagents and Conditions | Yield of **85a** (%) |
|---|---|---|
| 1 | 1) solvent evaporation<br>2) Fe (5 equiv)<br>AcOH, reflux | 71 |
| 2 | Pd/C (0.1 equiv)/$NaBH_4$ (1 equiv)<br>EtOH (2 mL), rt<br>THF | --<br>(80)[a] |
| 3 | 1) solvent evaporation<br>2) $SnCl_2$ (5 equiv)/$NaBH_4$ (1 equiv)<br>EtOH, 60 °C | 60 |
| 4 | 1) solvent evaporation<br>2) $CoCl_2$ (5 equiv)/$NaBH_4$ (1 equiv)<br>EtOH, 60 °C | 58 |
| 5 | 1) solvent evaporation<br>2) $FeCl_2$ (5 equiv)/$NaBH_4$ (1 equiv)<br>EtOH, 60 °C | 68 |
| 6 | $NaBH_4$ (1 equiv)<br>EtOH, 60 °C | 0 |
| 7 | $FeCl_2$ (2 equiv)/$NaBH_4$ (1 equiv)<br>EtOH (2 mL), rt<br>THF | 73 |

[a] yield of dehalogenated product

Table 7 gives selected examples of several reducing reagents that led to good yields of diarylamine **85a**. It turned out that standard conditions for the reduction of nitro groups, such as the reduction with iron powder (entry 1, Table 7), led to compound **85a** in good yield. However, they were not convenient for two reasons. First, the step of solvent evaporation was less user-friendly and, second, the reaction conditions were rather harsh. It was found that, for example, a cyano function was not tolerated under these conditions. The use of $NaBH_4$ together with different transition metal salts was reported as very efficient for the reduction of nitro groups.[83] The use of palladium on charcoal resulted in a very clean formation of dehalogenated product, reducing significantly the scope of the reaction (entry 2).[84] Thus, several different transition metal halides were tested, such as $SnCl_2$, $CoCl_2$ and $FeCl_2$ (entries 3-5).[85] All were efficient in MeOH or EtOH solvent, with $FeCl_2$ being the most efficient and least toxic. A control experiment without transition metal led to no formation of diarylamine, showing the importance of the metal activation (entry 6). We were pleased to observe that only a small amount of EtOH was sufficient for the activation of $NaBH_4$ and that the reaction took place in THF solvent as well, leading to the initially desired one-pot synthesis (entry 7).

### 4.2.2 Preparation of Polyfunctionalized Diarylamines 85 by the Addition of Functionalized Arylmagnesium Compounds to Mono-Nitroarenes 84

With these optimized reaction conditions in hand, we started to investigate the functional group tolerance and the applicability of this reaction (Scheme 53 and Table 8).

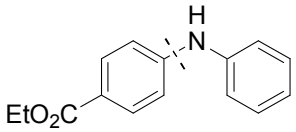
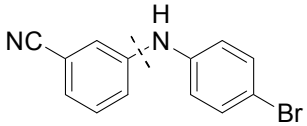
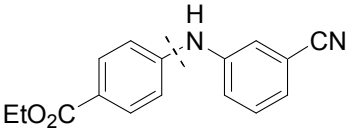
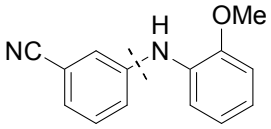
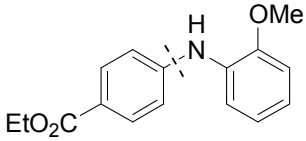
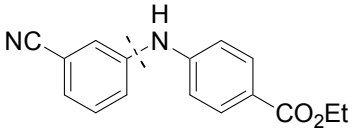
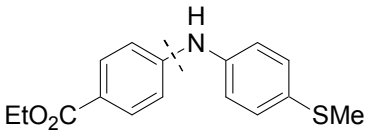
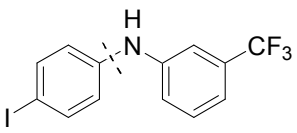


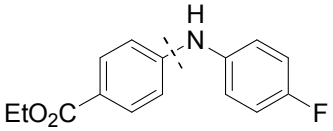
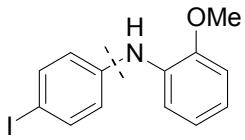
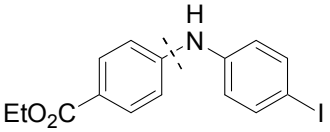
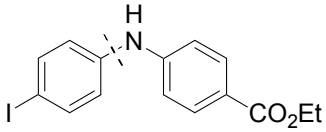
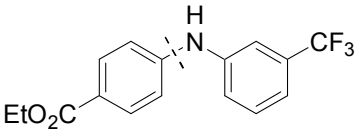
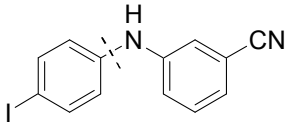
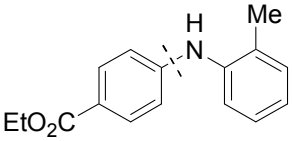
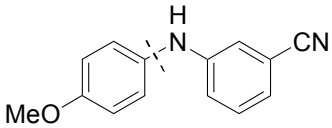
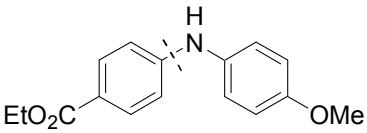
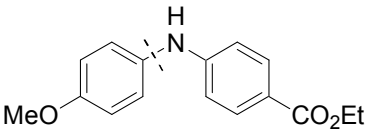
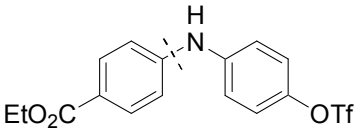
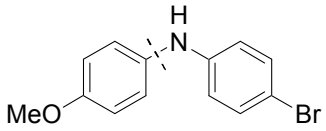
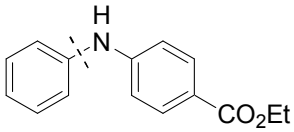
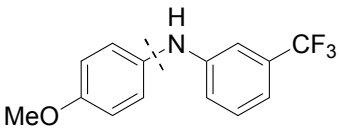
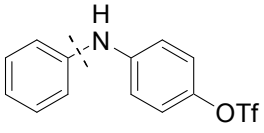
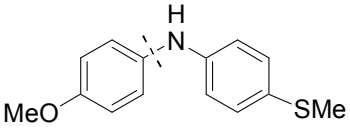

**7**: (2.3 equiv) **84a-l** **85a-x:** 63 - 86%

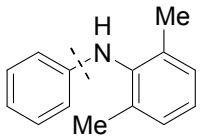
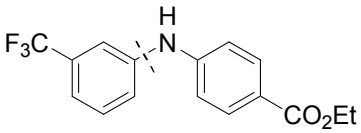
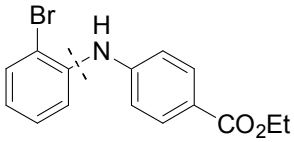
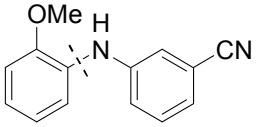
**FG$^1$**: a=3-CN; b=4-I; c=4-$CO_2$Et; e=4-$CF_3$; g=2-Br; h=4-OMe i=2-OMe

**FG$^2$**: a=4-Br; b=H, c=3-CN; d=2-OMe; e=4-SMe; f=4-F; g=3-$CF_3$; h=2-Me; i=4-OMe; j=4-OTf; k=4-$CO_2$Et; l=2,6-$Me_2$

**Scheme 53 and Table 8:** Polyfunctionalized diarylamines **85** obtained by the reaction of arylmagnesium halides **7** with nitroarenes **84.** The dotted lines indicate the new C-N bond formed.

| Entry | Product **85** | Isolated yield (%) | Entry | Product **85** | Isolated yield (%) |
|---|---|---|---|---|---|
| 1 |  **85b** | 77 | 15 |  **85o** | 84 |
| 2 |  **85c** | 75 | 16 |  **85p** | 74 [a] |
| 3 |  **85d** | 85[a] | 17 |  **85c** | 63 |
| 4 |  **85e** | 72 | 18 |  **85q** | 60 |

| Entry | Product **85** | Isolated yield (%) | Entry | Product **85** | Isolated yield (%) |
|---|---|---|---|---|---|
| 5 |  **85f** | 79 | 19 |  **85r** | 86[a] |
| 6 |  **85g** | 64 | 20 |  **85g** | 71 |
| 7 |  **85h** | 71 | 21 |  **85s** | 71 |
| 8 |  **85i** | 67[b] | 22 |  **85t** | 72 |
| 9 |  **85j** | 78 | 23 |  **85j** | 74 |
| 10 |  **85k** | 85 | 24 |  **85v** | 84 |
| 11 |  **85b** | 72 | 25 |  **85u** | 85 |
| 12 |  **85l** | 85 | 26 |  **85v** | 79 |

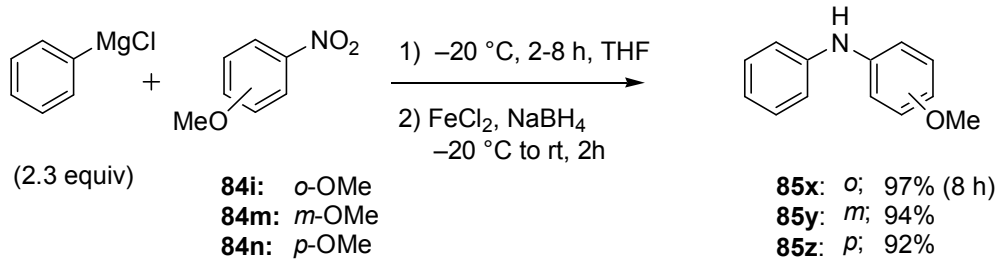
| Entry | Product **85** | Isolated yield (%) | Entry | Product **85** | Isolated yield (%) |
|---|---|---|---|---|---|
| 13 |  **85m** | 76[c] | 27 |  **85h** | 52 |
| 14 |  **85n** | 50[e] | 28 |  **85p** | 95[d] |

[a] reaction time: 8 h at 0 °C; [b] reaction time: 8 h at −5 °C; [c] reaction time: 24 h at −5 °C; [d] reaction time: 12 h at −10 °C; [e] reaction time: 48 h at −5 °C

Thus, 4-carbethoxyphenylmagnesium chloride (**7c**) added to a variety of nitroarenes bearing electron-withdrawing (CN, F, I, $CF_3$, OTf; entries 2, 5, 6, 7, 10, Table 8) or electron-donating substituents (H, OMe, SMe, Me; entries 1, 9, 4, 8) on the aromatic ring. Even *ortho*-substituted nitro compounds participated in this reaction, although longer reaction times were necessary (6-12 h) and, in the case of a smaller group like a methoxy substituent without decrease of yield (entry 3). Remarkably, halogen substituents that were regarded as troublesome in the transition-metal catalyzed aminations were well tolerated and even very electrophilic functionalities, such as a triflate group, did not disturb the reaction, delivering the desired products in yields from 64-85%. A fluorine atom, which is commonly used as a leaving group in nucleophilic substitutions of electron-poor aromatics, was also tolerated (entry 5). Phenylmagnesium chloride reacted equally well under these conditions and, at −5 °C, the addition to 2-nitro-*m*-xylene **84l** led to diarylamine **85m** in 76% yield (entry 13). A variety of other functionalized Grignard reagents **7** were used for the preparation of functionalized diarylamines. *m*-Cyanoarylmagnesium chloride (**7a**) was reacted with several nitroarenes, leading to the desired products **85c**, **85o** and **85p** in good yields (entries 15-17). A selective mono-exchange on 1,4-diiodobenzene (**30**) furnished Grignard reagent **7b** which participated in the amination, furnishing compounds **85g** and **85q-s**, in good yields (entries 18-21). The electron-rich *p*- or *o*-methoxyphenylmagnesium bromides, reacted very well under these conditions (entries 22-26 and 28). The bulky *o*-bromophenylmagnesium bromide (**7g**) led to product **85n** in only 50% yield (entry 14) and a very long reaction time (48 h at −5 °C) was necessary to obtain full conversion. Finally, Grignard reagent **7e**, bearing a $CF_3$-group was used, leading to compound **85h** in 52% yield (entry 27).

This wide range of tolerated functional groups, as well as the compatibility with halogen substituents either on the nucleophile or the electrophile make this reaction a very powerful, complementary tool to the well known procedures for the synthesis of diarylamines.

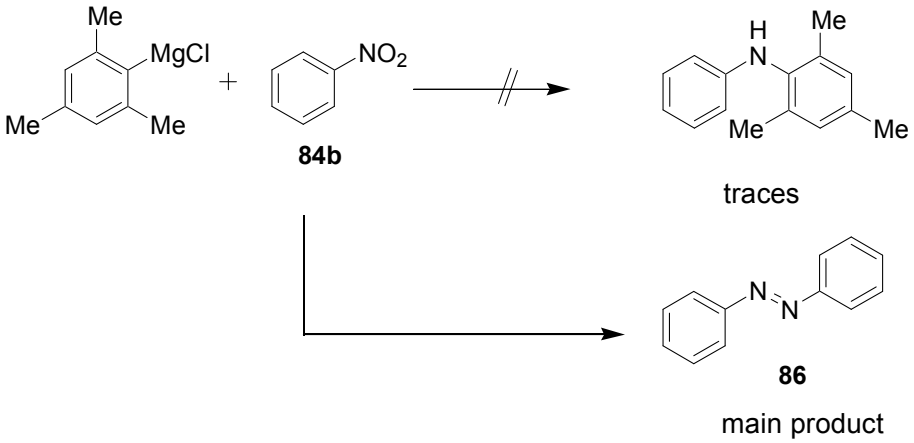
To show again the robustness of this methodology, being nearly unaffected by different electronic or steric effects, 2-, 3- and 4-nitroanisole **84i**, **84m** and **84n** were reacted with phenylmagnesium chloride (Scheme 54). The *meta* substituent acts as an electron withdrawing substituent ($\sigma_m$OMe = 0.10), while the one in *para* position increases the electronic density ($\sigma_p$OMe = −0.28). The *ortho* substituent increases the sterical hindrance and the electron density.




**Scheme 54:** Reaction of phenylmagnesium chloride with *o*-, *m*-, *p*- nitroanisoles **84**.

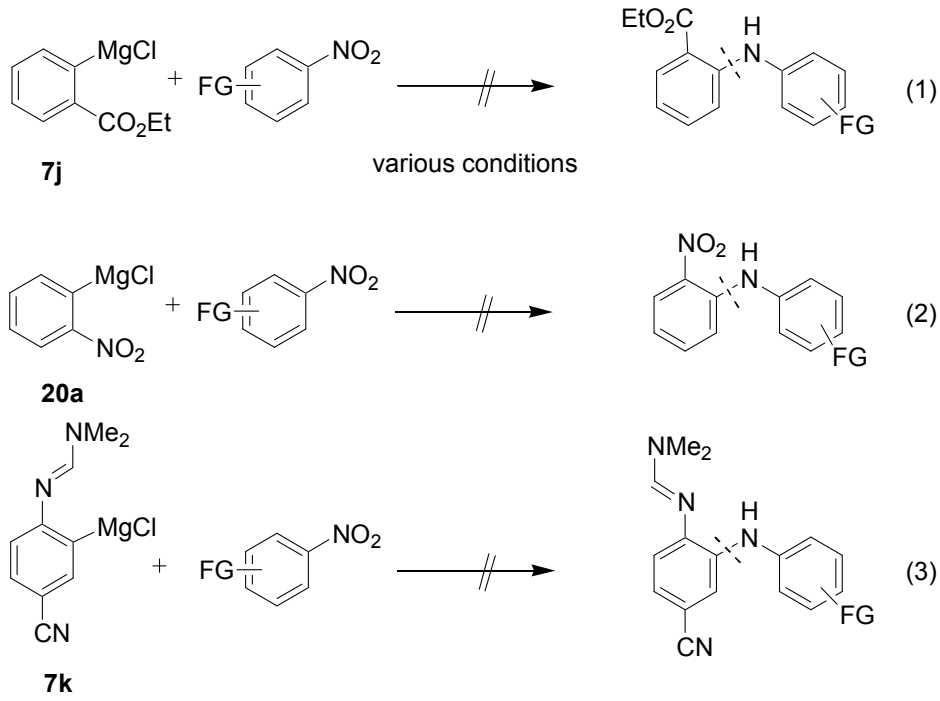
As shown in Scheme 54 all three isomers were isolated in excellent yields, without showing a strong electronic influence on the yield. Steric hindrance on the nitro compound, as mentioned above (Table 7, entries 3, 9, 14, 16, 19, 28, 29) increased the reaction time, but without lowering the yield.

Unfortunately, steric hindrance of the Grignard reagent turned out to prevent the reaction. This is in accordance with the results obtained in chapter 3.3. Azobenzene **86** was observed as the main product of the reaction using mesitylmagnesium bromide and nitrobenzene **84b** (Scheme 55).



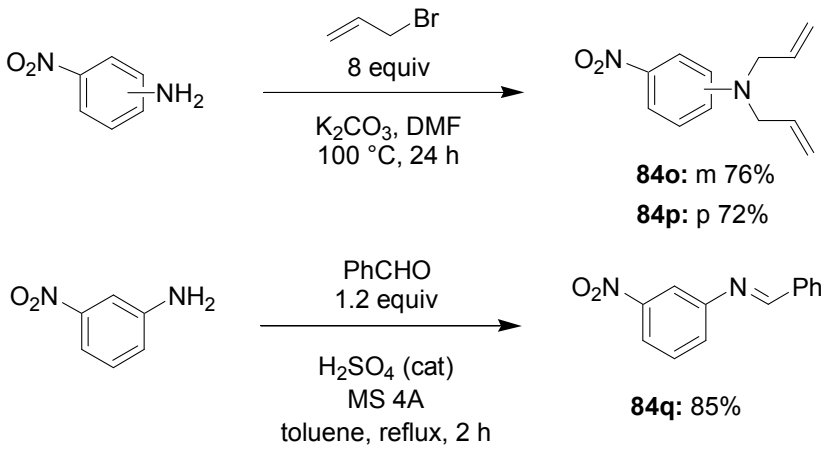

**Scheme 55:** Attempts to prepare a mesitylamine derivative.

The same is true for *ortho*-chelating groups on the Grignard reagents. Alas, all attempts to react 2-carbethoxyphenylmagnesium chloride (**7j**) with nitroarenes were in vain (eq. 1, Scheme 56). Different solvents and reaction temperatures were tested without success. The same is true for Grignard reagents **20a** and **7k** bearing different *ortho*-chelating groups, shown in eqs. 2 and 3 of Scheme 56.



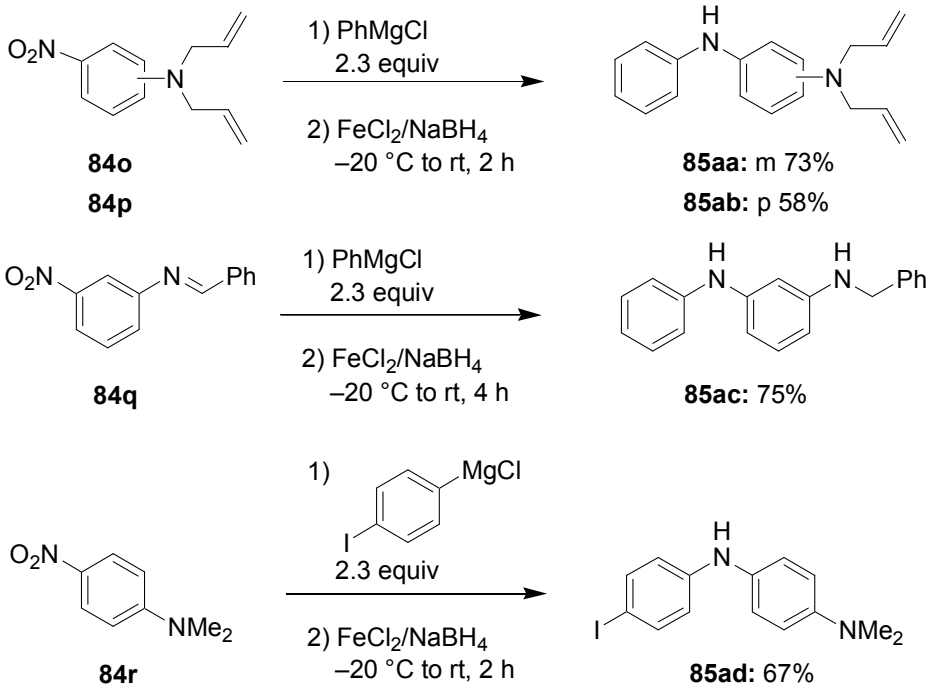

**Scheme 56:** Attempts to react *o*-functionalized Grignard reagents with nitrobenzenes.

Additionally, the possibility of applying this methodology to protected nitroanilines, leading to polyfunctional 1,3- and 1,4-disubstituted anilines was studied. Therefore, 1,3- and 1,4-nitroaniline were converted, to the corresponding protected derivatives using standard protecting group precursors (Scheme 57).[86]




**Scheme 57:** Synthesis of *m*- and *p*-protected nitroanilines **84o-q**.

With these substrates in hand, the addition of phenylmagnesium chloride under the above reaction conditions was carried out. Better results were obtained for protected 3-nitroanilines compared to protected 4-nitroanilines (Scheme 58).

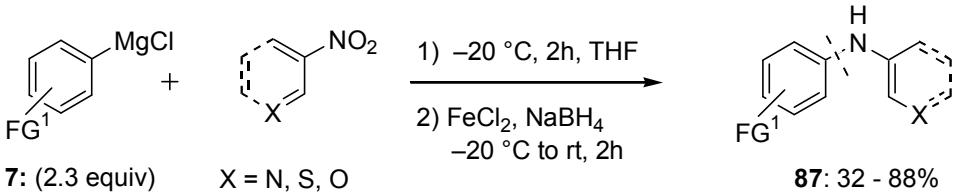



**Scheme 58:** Synthesis of 1,3- and 1,4-disubstituted anilines **85aa-ad**.

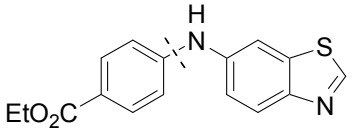
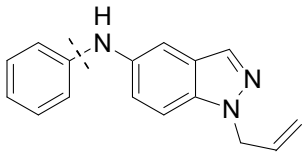
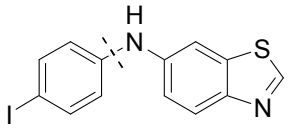
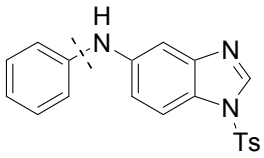
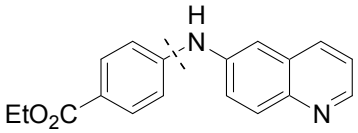
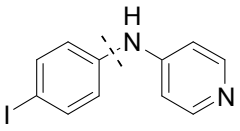
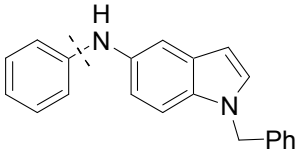
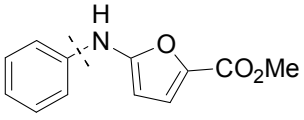
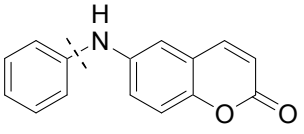
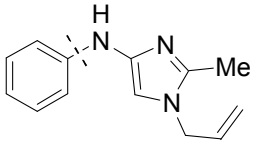
Thus, addition of phenylmagnesium chloride to *N,N*-diallyl-4-nitro-aniline (**84p**) afforded aromatic diamine **85ab** in 58% yield, whereas the addition to *N,N*-diallyl-3-nitro-aniline (**84o**) furnished 1,3-substituted diamine **85aa** in 73% yield. For the benzimine **84q** a reduction to the benzyl group was observed during the reductive work-up, delivering compound **85ac** in 75% yield. Finally, 4-iodophenylmagnesium chloride (**7b**) was reacted with commercially available *N,N*-dimethyl-4-nitroaniline (**84r**) leading to product **85ad** in 67% isolated yield. These examples show that alkyl- and methyl-amines are well tolerated by this methodology.

### 4.2.3 Preparation of Polyfunctionalized Heteroaromatic Diarylamines 87 by the Addition of Functionalized Arylmagnesium Compounds to Nitro functionalized Heterocycles

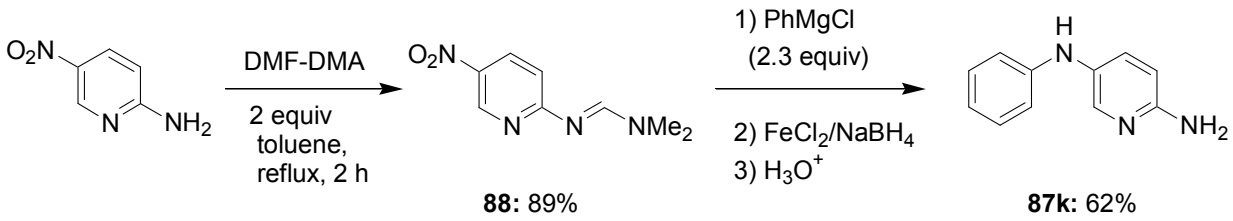
Despite these limitations we were encouraged to examine the feasibility of preparing heterocyclic compounds using this methodology. A variety of nitro-functionalized heterocycles are commercially available and we found that the developed reaction conditions were applicable to this substance class although with varying degrees of success (Scheme 59 and Table 9).




**Scheme 59 and Table 9:** Heterocyclic diarylamines **87** obtained by the reaction of arylmagnesium halides **7** with heterocyclic nitroarenes.

| Entry | Product **87** | Isolated yield (%) | Entry | Product **87** | Isolated yield (%) |
|---|---|---|---|---|---|
| 1 |  **87a** | 77 | 6 |  **87f** | 80 |
| 2 |  **87b** | 64 | 7 |  **87g** | 75 |
| 3 |  **87c** | 59 | 8 |  **87h** | 44 |
| 4 |  **87d** | 88 | 9 |  **87i** | 32 |
| 5 |  **87e** | --- | 10 |  **87j** | --- |

Thus, the reaction of 4-carbethoxyphenylmagnesium chloride (**7c**) or 4-iodophenylmagnesium chloride (**7b**) with 6-nitrobenzothiazole led, under the normal reaction conditions, to the desired arylated amines **87a** and **87b** in 77% and 64% yield, respectively (entries 1 and 2, Table 9). Similarly, reaction of 6-nitroquinoline with 4-carbethoxyphenylmagnesium chloride (**7c**) furnished the aminoquinoline **87c** in 59% yield (entry 3). Several protected heterocycles, such as a *N*-benzylated indole, an *N*-allylated indazole or a *N*-tosyl protected benzimidazole reacted under these conditions with phenylmagnesium chloride, delivering products **87d**, **87f** and **87g** in yields from 75-88% (entries 4, 6 and 7). Remarkably, 4-nitropyridine underwent a reaction with 4-iodophenylmagnesium chloride (7**b**), leading to the desired amine **87h** in 44% yield (entry 8). The addition to methyl 5-nitrofuroate was more complicated, allowing the isolation of product **87i** in only 32% yield (entry 9) only after reaction at lower temperatures (−78 °C). Higher temperatures led to complicated reaction mixtures. Despite several attempts, the addition of phenylmagnesium chloride to 6-nitrocoumarin and 4-nitroimidazoles failed.
Finally, we were able to apply our methodology to the selective synthesis of 5-aminophenyl-2-aminopyridine (**87k**). Starting from 5-nitro-2-aminopyridine, the amino group was first protected as its formamidine, leading to compound **88**. Selective amination of the nitro group and cleavage of the amino protecting group during acidic work-up conditions (HCl) furnished product **87k** in 61% yield (Scheme 60). This substance class of aminopyridines was of special interest for Aventis Pharma, Frankfurt a. M., and several derivatives were prepared at the Aventis laboratories with this methodology, using different protecting groups, as well as different substitution patterns.[87]

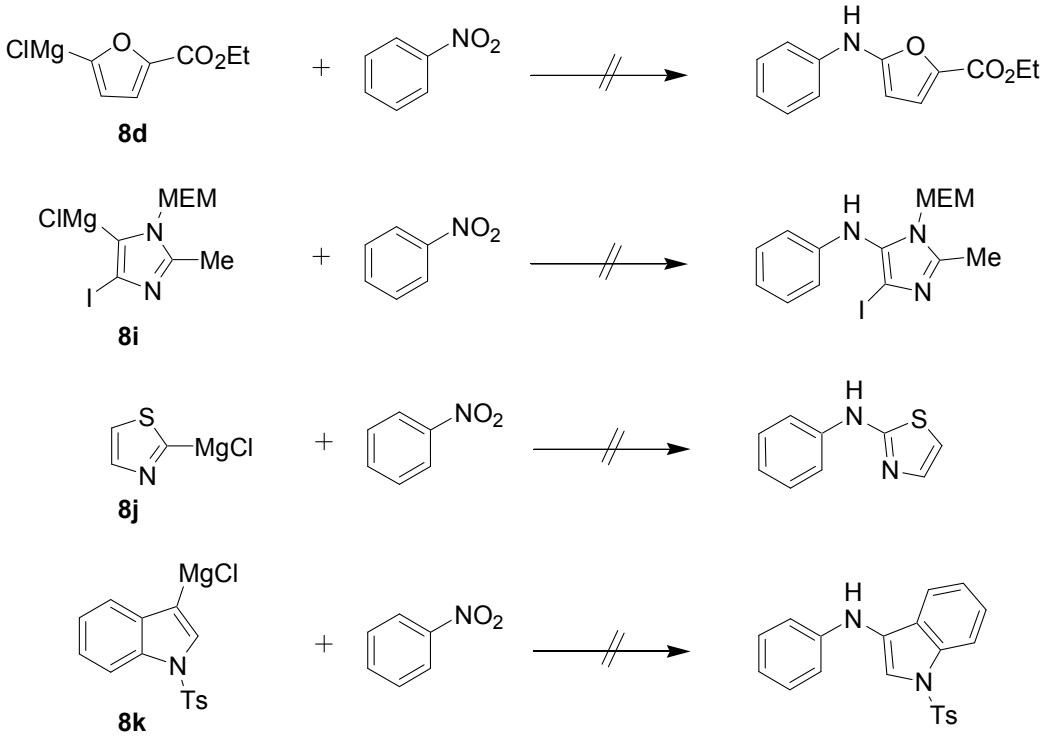



**Scheme 60:** Synthesis of compound **87k**.

Compared to other procedures described for the synthesis of diarylamines, our method led to agreeable yields under standard conditions, although depending on the electronic properties of the heterocycle.

### 4.2.4 Attempts for the Preparation of Polyfunctionalized Heteroaromatic Diarylamines 87 by the Addition of Functionalized Heteroarylmagnesium Compounds to Nitroarenes

Our attempts to apply this methodology to heterocyclic Grignard reagents **8** proved less successful. Thus, the addition of heterocyclic Grignard reagents **8d**, **8i**, **8j** and **8k**, all prepared through an I/Mg exchange starting from the corresponding iodides (see also Scheme 8), led to no amination products, but instead gave complex reaction mixtures (Scheme 61).

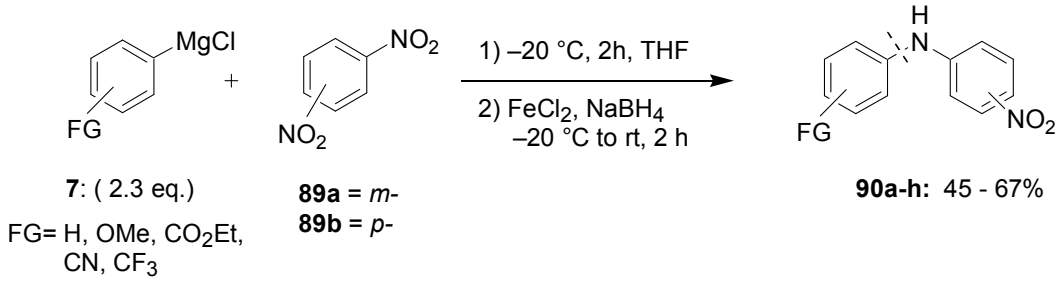



**Scheme 61:** Attempts to generate heterocyclic diarylamines **87**.

### 4.2.5 Selective Mono-Amination of Dinitrobenzenes 89

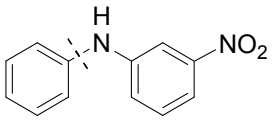
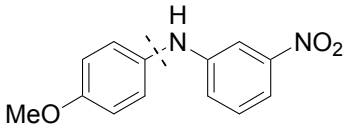
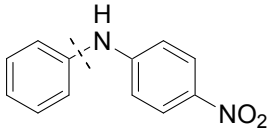
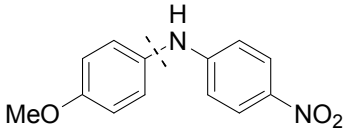
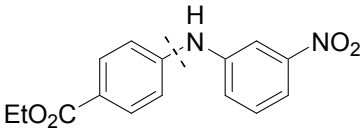
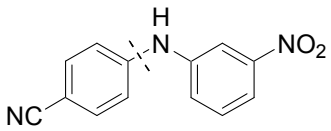
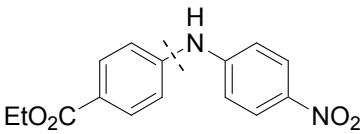
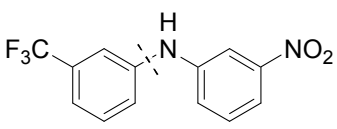
Encouraged by the results, the selective mono-functionalization of dinitrobenzenes **89**, a longstanding problem in organic syntheses[88,89] which had attracted both academic and industrial interest, was studied. The chemoselective differentiation between two nitrogen atoms in phenylenediamines is especially useful since this moiety is present in some biologically active molecules as well as in industrial chemicals like dyes and polymers.[90] Several *N,N′*-substituted *p*-phenylenediamines are used as antidegradant and antiozonant agents for diene rubber and are by far the most effective and widely used radical scavengers in the rubber industry.[91] To our knowledge, palladium catalyzed amination reactions do not allow in a general way the monofunctionalization of aromatic dibromides, diiodides or diamines, although this method is widely used for the preparation of various aryl amines as mentioned before.[79,80]

Application of the methodology described in chapter 4.2.2 to dinitroarenes **89** seemed suitable for a selective monoamination. Good yields were obtained for both 1,3-dinitrobenzene (**89a**) and 1,4-dinitrobenzene (**89b**) (Scheme 62 and Table 10). However, the use of 1,2-dinitrobenzene led to no selective formation of the desired product.




**Scheme 62:** Selective mono-functionalization of dinitrobenzenes **89**.

**Table 10:** Nitrofunctionalized amines **90** obtained through the reaction of arylmagnesium halides with dinitrobenzenes **89**.

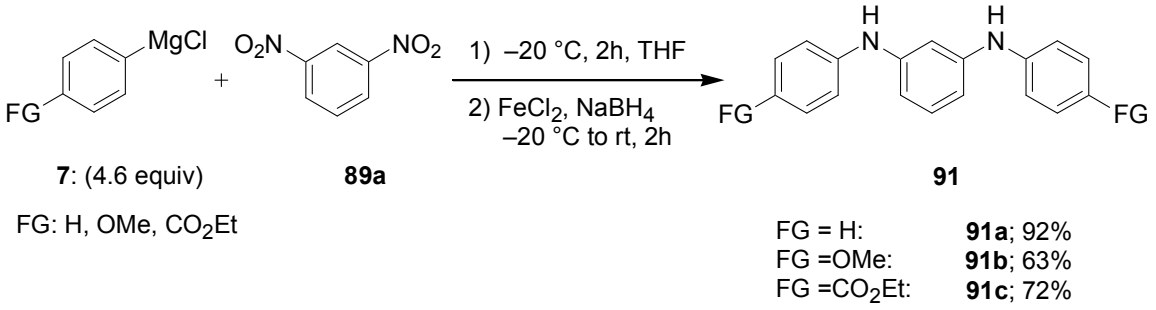
| Entry | Product **90** | Isolated yield (%) | Entry | Product **90** | Isolated yield (%) |
|---|---|---|---|---|---|
| 1 |  **90a** | 67 | 5 |  **90e** | 64 |
| 2 |  **90b** | 63 | 6 |  **90f** | 47 |
| 3 |  **90c** | 55 | 7 |  **90g** | 45 |
| 4 |  **90d** | 55 | 8 |  **90h** | 68 |

The addition of phenylmagnesium chloride to 1,3-dinitrobenzene (**89a**) and, 1,4-dinitrobenzene (**89b**) yielded compound **90a** and **90b** in 67% and 63% yield, respectively (entries 1 and 2, Table 10). The Grignard reagent could bear either electron-withdrawing (entries 3 and 4) or electron-donating groups (entries 5 and 6) and added in good yield to the dinitrobenzenes **89**. Thus, addition of 4-carbethoxymagnesium bromide (**7c**) to 1,3- and 1,4-dinitrobenzene (**89a**) and (**89b**) provided, after reductive workup, functionalized *N*-

phenylated nitroanilines **90c** and **90d** in 55% yield. The more electron-rich *p*-methoxyphenylmagnesium bromide (**7h**) led to diarylamine **90e** in good yield (65%) while the addition to 1,4-dinitrobenzene gave compound **90f** in only 47% yield (entries 5 and 6). Grignard reagents **7d** and **7e**, prepared from the corresponding iodides *via* I/Mg exchange reaction furnished compounds **90g** and **90h** in 45% and 68% yield, respectively.

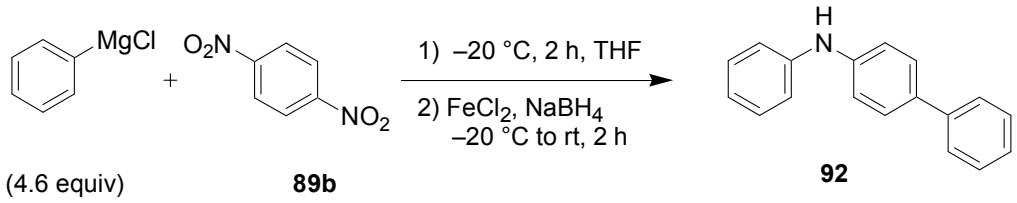
### 4.2.6 Synthesis of 1,3-Diamines 91 Starting from Dinitrobenzenes 89

The use of a larger excess of Grignard reagent (4.6 equiv) allowed for the reduction of both nitro groups in one step, resulting in the isolation of 1,3-diamines **91** in good to excellent yields (Scheme 63). The reduction proceeded under very mild reaction conditions. Methoxy- or ester-functionalized Grignard reagents were also used in this diamination reaction, providing products **91b** and **91c** in 63 and 72% yield, respectively (Scheme 63).




**Scheme 63:** Synthesis of phenylated 1,3-diamines **91**.

The use of a larger excess of Grignard reagent in order to generate phenylated 1,4-diamines resulted in the formation of significant amounts of substitution products, like **92** (Scheme 62).

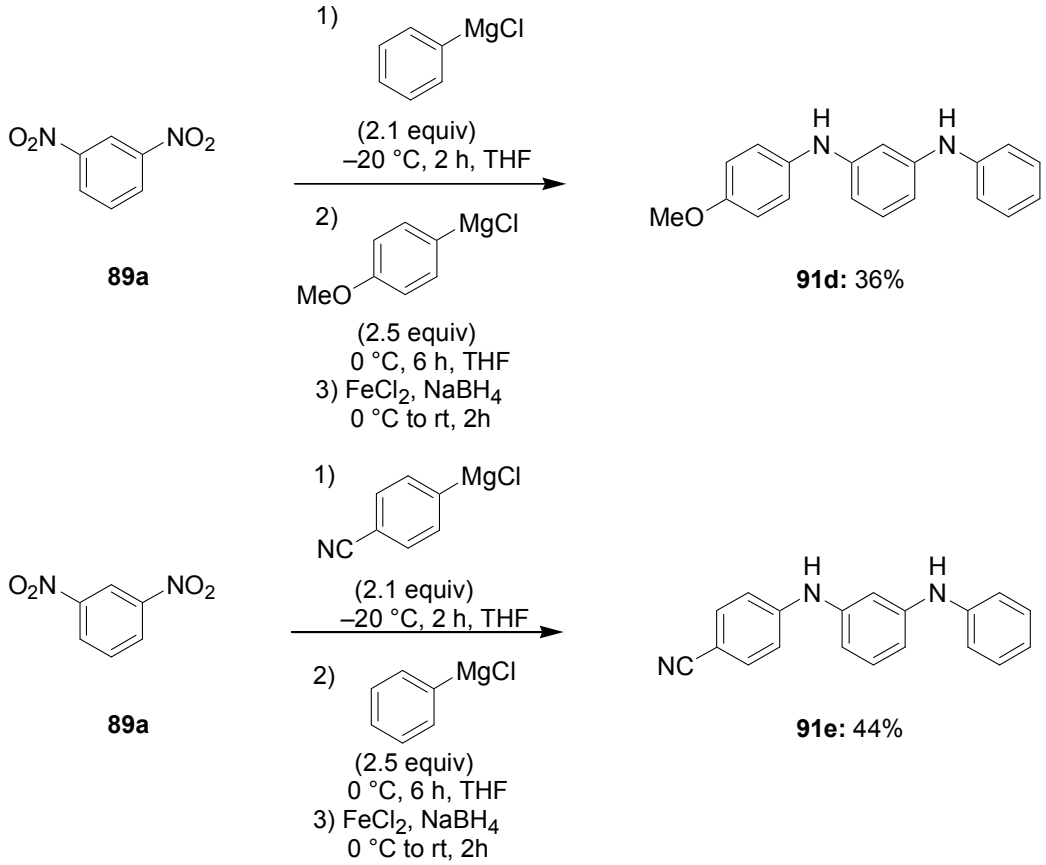



**Scheme 64:** Attempts to generate phenylated 1,4-diamines.

### 4.2.7 Stepwise One-Pot Di-Amination of Dinitrobenzenes 89

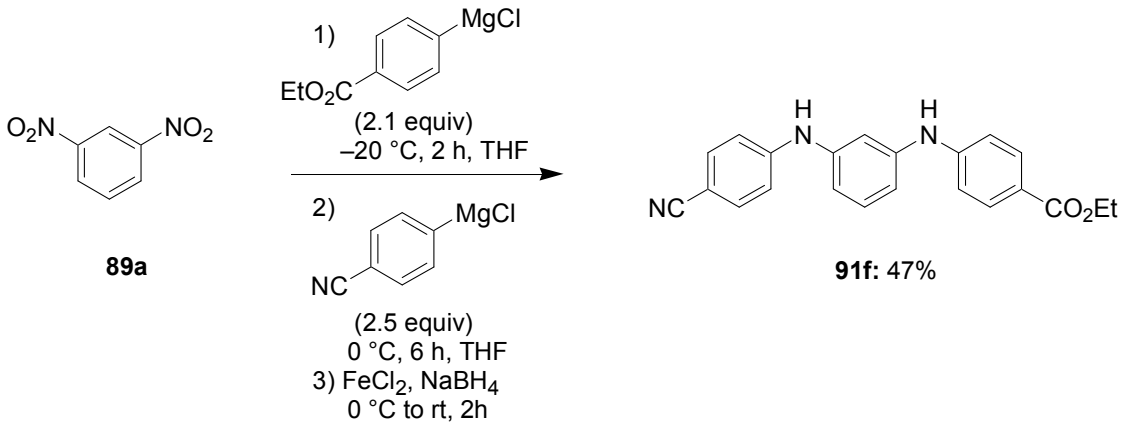
Encouraged by the results obtained in the previous part, we envisioned the possibility of a stepwise addition to both nitro groups with two different Grignard reagents, in a one-pot synthesis. This should be possible in principle, but several difficulties were faced. First, the slight excess of Grignard reagent used for the first reductive amination could add to the second nitro group. Second, lowering the amount of Grignard reagent in the first step, could lead to an addition of the second Grignard reagent to unreacted dinitrobenzene **89**. Third, the stability of unsymmetrical diarylamines proved troublesome, leading in most cases to

red oils or very light sensitive solids, which could decompose during the aqueous work-up. Nevertheless, we succeeded in the preparation of such unsymmetrical 1,3-diarylamines **91**, as shown in Scheme 65**,** with moderate yields of 36% and 46%.




**Scheme 65:** Synthesis of unsymmetrical diarylamines **91**.

As shown in Scheme 65, the addition of an electron-poor or electron-rich Grignard reagent was possible, although the second addition was considerably slower.
Finally, the preparation of diarylamine **91f** was carried out, bearing two different functional groups (Scheme 66).

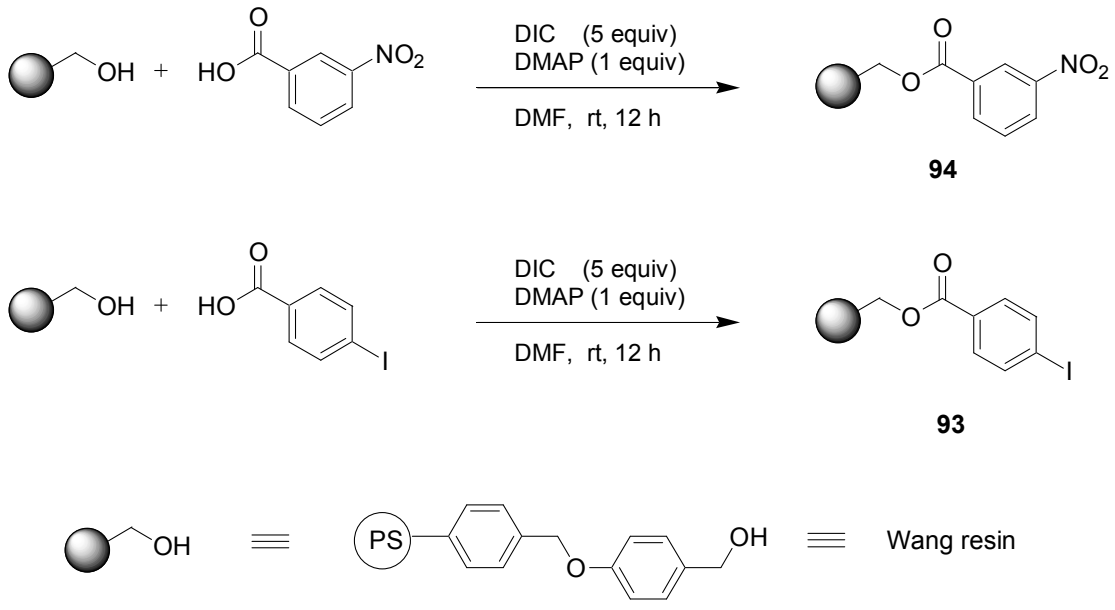



**Scheme 66:** Synthesis of unsymmetrical diphenyldiamines **91f**.

In summary, this venture shows the limitations of this new methodology as well as the wide applicability, although the isolated yields have to be improved. By choosing the amount of Grignard reagent used, a mono- or diamination is possible, emphasizing that this method is complementary to transition metal catalyzed aminations.

### 4.2.8 Amination of Solid Phase Supported Nitrobenzenes using Arylmagnesium Reagents

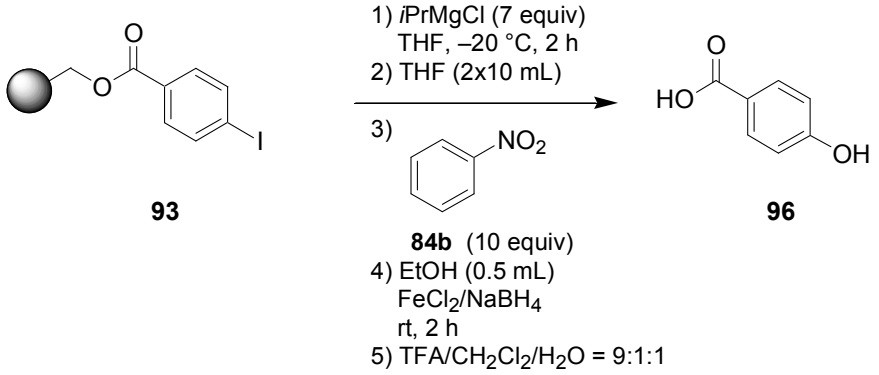
In the first part of this chapter, focus was placed on the amination of nitroarenes in solution. In previous work from our research group, Dr. M. Rottlaender and later Dr. W. Dohle showed, that the I/Mg exchange reaction could be extended to resin-bound aryl iodides using an excess of *i*PrMgCl at low temperatures.[16,92] Considering the wide range of functional groups that were tolerated in solution and the variety of commercially available aromatic nitro compounds, we regarded this method as useful for a library synthesis.
If *N*-arylation occurs in the first step, a resin-attached Grignard reagent should lead to an easy method for generating diversity. On the other hand, if the *O*-arylation was the first step in this reaction sequence, a solid-supported nitro-compound would instead lead to the desired structures. Both, a resin-bond iodoarene **93** and nitroarene **94** were prepared, attached to Wang resin with the corresponding carboxylic acids, according to standard procedures (Scheme 67).[93] Wang resin was treated with the appropriate carboxylic acid (10 equiv) in the presence of DIC and DMAP in DMF. The resins were washed, dried and quantitative loading was determined by cleavage of a small amount of resin with TFA.




**Scheme 67:** Synthesis of Wang-resin supported nitroarene **94** and iodoarene **93**.

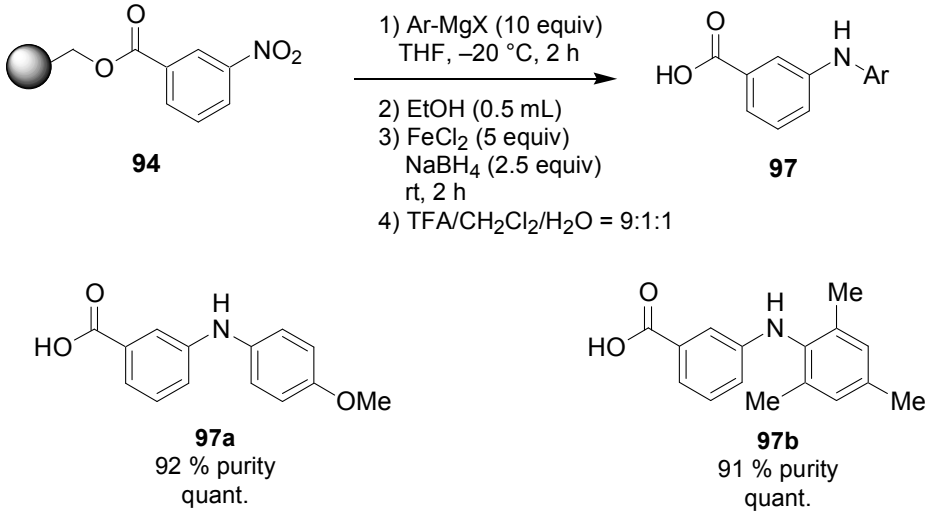
We first studied the reaction of polymer supported Grignard reagent **95** with nitrobenzene **84b**. The exchange was performed according to the procedures developed in our group, using 7 equiv of *i*PrMgCl. After 1 h the solvent was removed *via* syringe and the resin washed twice with dry THF to ensure complete removal of excess *i*PrMgCl. Subsequently, a

solution of nitrobenzene in THF was added and the usual procedure was performed. After work-up and acidic cleavage of the resin, only 4-hydroxybenzoic acid (**96**) was isolated in quantitative yield and good HPLC purity (98%) (Scheme 68).




**Scheme 68:** Failed polymer supported synthesis of diarylamines.

These results will be discussed in more detail in chapter 4.2.9. To our delight, the second approach, starting from solid phase supported nitrobenzene **94** led to the desired product **97** (Scheme 69). Thus, we were able to show the applicability of this methodology to solid phase, although it is no longer as convenient as a polymer-bound Grignard reagent would have been, since the commercial availability of nitroarenes is superior. In the case of immobilized nitroarenes, side-reactions, such as the dimerization of reactive intermediates (nitrosobenzene) was suppressed, allowing the synthesis of amine **97b**, which failed in solution.




**Scheme 69:** Synthesis of derivatives **97** *via* arylation of polymer supported nitrobenzene **94**.

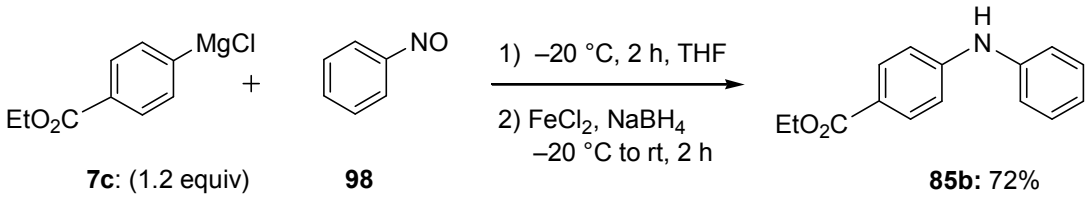
## 4.2.9. Limitations and Mechanistic Studies of the Preparation of Polyfunctionalized Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Nitroarenes

Some of the limitations already discussed in this chapter are summarized again:

1. the necessity of at least two equivalents of Grignard reagent,
2. the limitation to aromatic Grignard reagents,
3. decreased reactivity for sterical hindered and *ortho*-chelating substituents and,
4. the failure of heterocyclic Grignard reagents.

In order to overcome these problems, we studied more carefully the proposed mechanisms from chapter 4.2.1. Although, both mechanisms can be rationalized, we believe that the second mechanism suits best our observations, which will be discussed in detail. The observations made favor the mechanism proposed by Koebrich, who postulated an *O*-arylation in the first step. Good evidence stems from the following experiments:

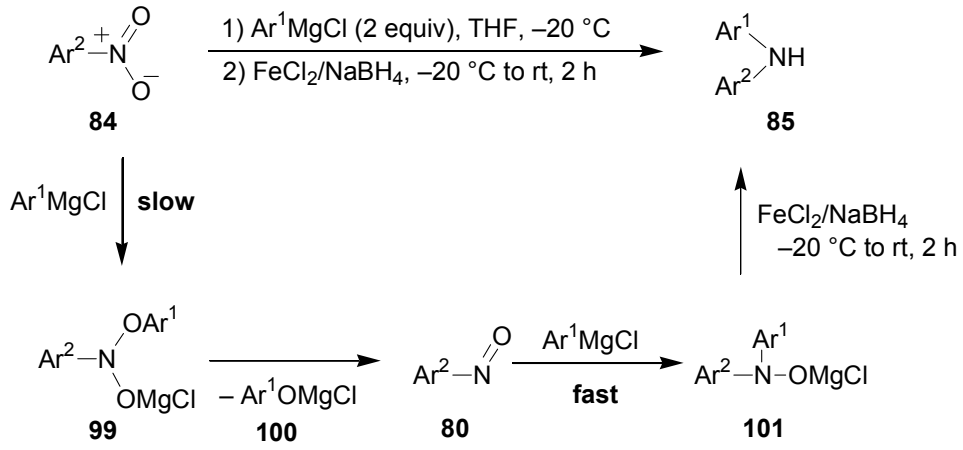
1. The reaction of nitrobenzene **84b** with phenylmagnesium chloride required at least 2.2 equiv of phenylmagnesium chloride to give complete conversion of nitrobenzene to diarylamine **85b** and 1 equiv of phenol was formed during the reaction. Addition of less than two equiv of phenylmagnesium chloride led only to a partial reduction of nitrobenzene **84b**. In contrast, no phenol formation was observed in the reaction of nitrosobenzene **98** with 4-carbethoxyphenylmagnesium chloride **7c** and 1.2 equiv of Grignard were sufficient to convert starting material to diarylamine **85b** completely (Scheme 70).




**Scheme 70:** Synthesis of diarylamine **85b** starting from nitrosobenzene.

2. During the reaction of mesitylmagnesium bromide with nitrobenzene, azobenzene **87** was isolated as the main product. This can be explained by a dimerization of nitrosobenzene, which was formed in the initial step of this reaction (Scheme 55).
3. Solid supported Grignard reagent **95** delivered only the corresponding phenol **96**, indicating again an *O*-arylation as the first step (Scheme 68).

Our postulated mechanism is as follows and good evidence is given for this by the above mentioned experiments:




**Scheme 71:** Proposed mechanism for the reaction of aryl magnesium compounds with nitroarenes **84**, leading to diarylamines **85**.

The first aryl group is transferred to the oxygen of the nitro group furnishing **99** which can produce as an intermediate arylnitroso derivative **80** after elimination of magnesium phenolate **100**. Reaction of this intermediate nitroso species with the second equivalent of Grignard reagent leads to the formation of the C-N bond and produces the air-sensitive diarylhydroxylamide **101** which is then converted to diarylamine **85**, by the addition of $FeCl_2$ and $NaBH_4$.

In summary, several experiments, especially the solid-phase supported reactions (Scheme 68 and 69) clearly indicate that the mechanism proposed by H. Gilman, R. McCracken and Y. Yost, is incorrect.[73,75]

Considering our mechanism, one possibility to reduce the amounts of Grignard reagent would be to start from the corresponding nitrosobenzenes (**80**). Indeed, F. Kopp showed in his diploma thesis that the addition of aromatic Grignard reagents to functionalized nitrosobenzenes was possible with only 1.2-1.4 equiv of Grignard reagent. Nevertheless, the yields were significantly lower than the ones obtained by the addition to nitroarenes, due to the lower stability of nitroso compounds. Even more disconcerting was the fact that the use of nitroso compounds did not solve the problem of the steric hindrance or *ortho*-chelation. These substrates remained unreactive. Furthermore, no general procedure for the preparation of nitroso compounds has been yet developed, narrowing the accessibility of this substance class.

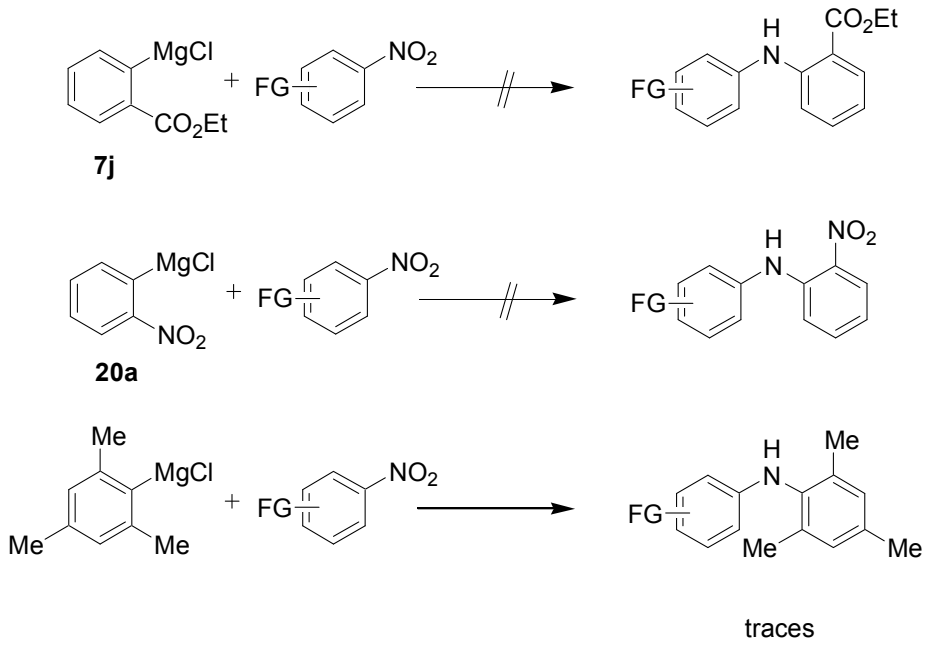
All attempts to reduce the nitro group *in situ* or to activate the group by oxophilic substrates were in vain.

Despite the above-mentioned drawbacks, our method represents an extension to the methods used previously for the synthesis of diarylamines and encouraged us to further examine the electrophlic amination, using other nitrogen electrophiles.

# 5. Synthesis of Polyfunctional Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Arylazosulfones

## 5.1 Introduction

As discussed in the previous chapter, the preparation of polyfunctional diarylamines **85** is an important synthetic goal, since these building blocks are present in many pharmaceuticals and various fine chemicals. Although nitroarenes **84** prove to be excellent electrophilic nitrogen synthons, this method has several limitations. One major drawback is the need for two equivalents of Grignard reagent **7**, one equivalent being lost during the reduction of the nitroarene **84** to an intermediate arylnitroso $Ar^1$-NO **80**, as shown in Scheme 71. Even more limiting is the fact that well-stabilized Grignard reagents, bearing an *ortho*-chelating group, such as 2-ethoxycarbonylphenylmagnesium chloride (**7j**) or 2-nitrophenylmagnesium chloride (**20a**), do not add to either nitro- **84** nor nitroso arenes **80** (Scheme 56 and 72). In addition sterically hindered *ortho*-substituents decrease the reactivity of the Grignard reagent, resulting in a slower addition to the very reactive nitroso compound. Therefore, sterically hindered Grignard reagents, such as mesitylmagnesium bromide**,** give only traces of the desired diarylamine **86**.



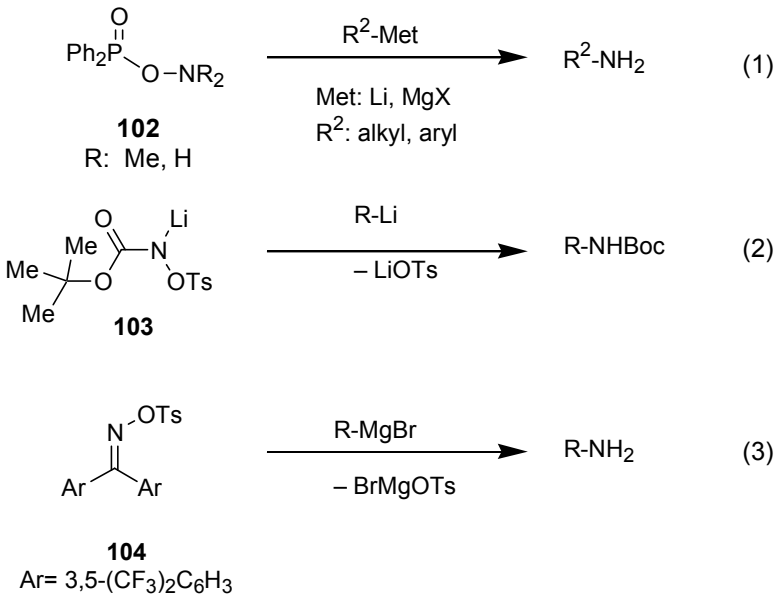

**Scheme 72:** Limitations of the amination with aromatic Grignard reagents using nitroarenes **84**.

Additionally, one can consider the fact that only aromatic Grignard reagents undergo this addition as another limitation of this electrophilic nitrogen source.

Despite all these limitations, the addition of functionalized arylmagnesium compounds to nitroarenes represents one of the easiest and most convenient procedures known for the preparation of such aniline derivatives.

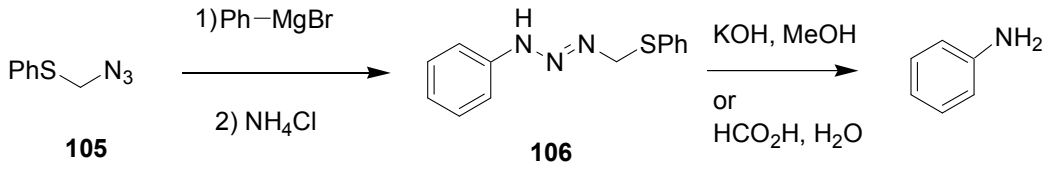
## 5.2 Electrophilic aminations

The need for a more general method for the preparation of alkyl-substituted aniline derivatives and diarylamines made a more careful examination of possible electrophilic nitrogen synthons obligatory. Several methods for the conversion of alkyl- or arylorganometallics to primary amines are known (Scheme 19 and 73), the most important ones being treatment of the corresponding organometallic with a hydroxylamine derivative, a dialkyl azodicarboxylate or with certain azides.[29,46] For the first method, the treatment of a hydroxylamine derivative **102** (eq. 1, Scheme 73) or a lithium alkoxyamide **103** (eq. 2) with an organometallic (R-Met) leads to the formation of $RNH_2$ and can be extended to the formation of secondary and tertiary amines by the use of mono- or di-*N*-substituted hydroxylamines (eq. 1).[94]



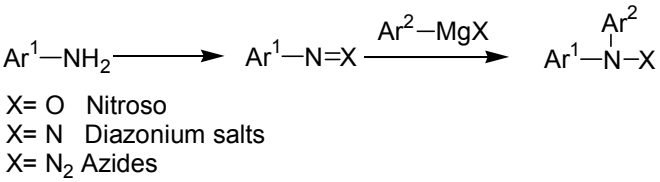

**Scheme 73:** Synthesis of amines using hydroxylamine derivatives **102-104**.

More recently, K. Narasaka developed a procedure that allows the conversion of tosylhydroxylamines **104** to primary amines through the addition of Grignard reagents.[95] In the case of the azides, tosyl azide ($TsN_3$),[96] the azidomethyl phenyl sulfide (**105**) ($PhSCH_2N_3$) developed by B. M. Trost[97] and allyl azide,[98] are most often used.[99] These reagents all have several drawbacks, compared with the hydroxylamines, mainly the difficult preparation and the instability of these very reactive compounds. $PhSCH_2N_3$, with a poor leaving group attached to the $N_3$, provides a possible solution to this problem, and the initially formed triazene can be reduced selectively, after addition of an organometallic species, with strong alkali to give the amine (Scheme 74). Thus, the reaction of phenylmagnesium chloride with azidomethyl phenyl sulfide (**105**) leads to intermediate **106**, which can by easily hydrolized to furnish aniline.



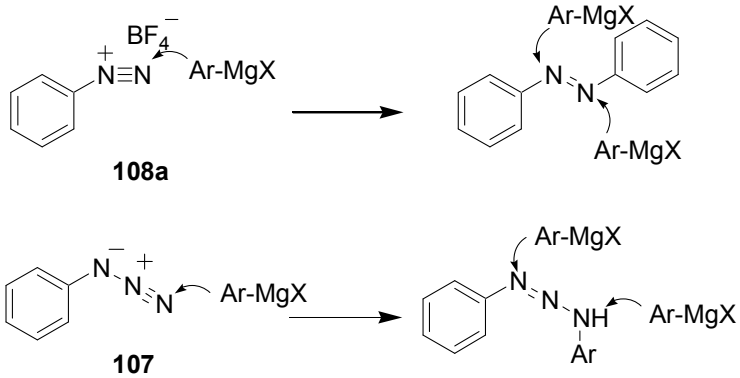

**Scheme 74:** Synthesis of primary amines using $PhSCH_2N_3$ **105**.

However, according to B. M. Trost, this route fails for heteroaromatic organometallic compounds. Genet finally showed that alkyl azodicarboxylates can act as $NH_2^+$ sources, leading to primary amines, after addition of carbon nucleophiles.[100]
All of the reagents mentioned above are very powerful, leading to aromatic and aliphatic amines in good to excellent yields, but no formation of diarylamines was ever reported.
Diarylamine formation is more difficult, because the corresponding hydroxylamines are not as easy to handle and only few examples have been reported,[47] where the direct conversion of an aromatic amine to a diarylamine was successful.
The high electronegativity of nitrogen (EN=3.0) limits the possible counterpart atoms to fluorine, oxygen, which has already been used in the arylation of nitroarenes, and nitrogen itself, as shown above and in Scheme 75.




**Scheme 75:** Possible transformations to an electrophilic nitrogen.

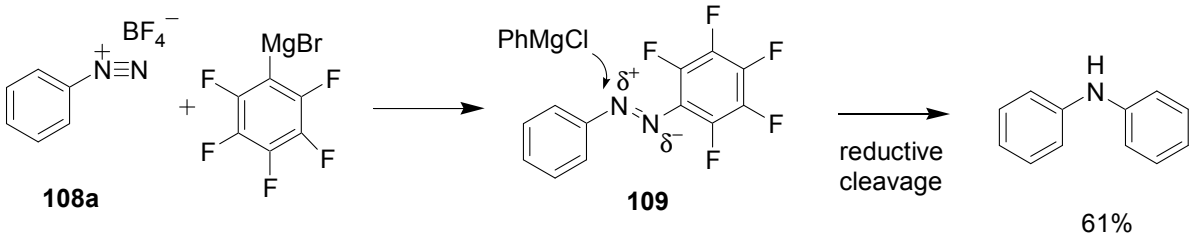
Utilizing aromatic azides **107** or diazonium salts **108** as substrates would not solve this problem due to a lack of selectivity for the second addition of a Grignard reagent (Scheme 76).




**Scheme 76:** Possible reactions of diazonium salts **108** and azides **107**.

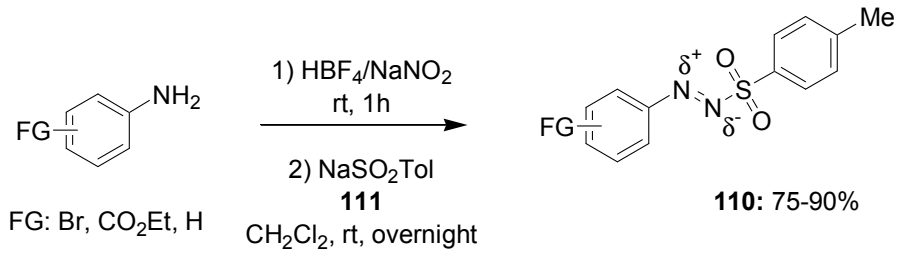
A more selective addition was anticipated by adding a very electron poor substituent to azo compound **109**. This possibility was examined by adding pentafluorophenylmagnesium

bromide to phenyldiazonium tetrafluoroborate (**108a**) and the desired azo-compound **109** was isolated in satisfactory yields (Scheme 77). Addition of phenylmagnesium chloride gave good selectivity for the addition, allowing the attack of the Grignard reagent only at the less electron-poor nitrogen leading after reductive cleavage to diphenylamine in moderate yield.



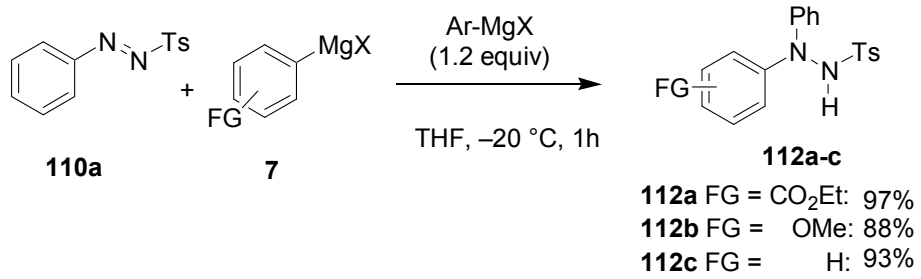

**Scheme 77:** Pentafluorophenyl azobenzene as an electrophilic nitrogen synthon.

However, the synthesis of the starting material turned out to be difficult, when scaling up this reaction. The isolated yields varied between 40 and 60% when running this reaction on 10 mmol scale. In addition, the starting materials are very expensive and not easily synthesized. Therefore, another approach was considered, starting again from phenyldiazonium tetrafluoroborates **108**. This reaction is very easy to carry out on a multi-gram scale and yields are reproducibly good. In a second step, the diazonium salt was transferred to the corresponding areneazosulfone **110** by simply stirring with sodium *p*-toluenesulfinic acid (NaTs) **111**, a commercially available, cheap, bulk chemical (Scheme 78).[101]




**Scheme 78:** Synthesis of areneazosulfones **110**.

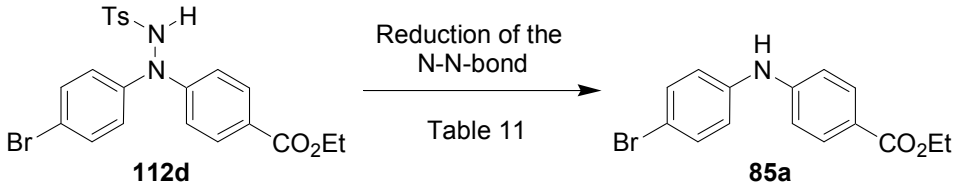
With these arylazosulfones in hand, several addition reactions of aromatic Grignard reagents were examined and the addition products **112** were isolated in good to excellent yields (Scheme 79) by using only 1.2 equiv of the organometallic reagent.




**Scheme 79:** Addition of functionalized Grignard reagents 7 to phenyl-4-tolylazo sulfone (**110a)**.

Under very mild conditions, these arylazosulfones **110** showed an excellent reactivity towards arylmagnesium reagents. Thus, phenylmagnesium chloride added to phenyl azosulfone **110a**, leading to trisubstituted hydrazine **112c** in 93% yield. Functionalized Grignard reagents such as the 4-carbethoxyphenylmagnesium chloride (**7c**) furnished product **112a** in 97% yield and the addition of 4-methoxyphenylmagnesium bromide delivered compound **112b** in 88% yield.

Although several procedures for the reductive cleavage of the N-N bond in hydrazines and azo compounds were reported, the reaction turned out to be troublesome.[102] Hydrazine **112d** was used as a test system for optimization of the reduction conditions. Table 11 shows the various attempts to cleave the N-N bond (Scheme 80).




**Scheme 80 and Table 11:** Attempts to cleave the N-N-bond in **112d** with various reagents.[103]

| Entry | Conditions and Reagents | Isolated yield of **85a** (%) |
|---|---|---|
| 1 | $FeCl_2 \cdot NaBH_4$ [103d,e] EtOH | -- |
| 2 | $NiCl_2 \cdot NaBH_4$ [103d,e] EtOH | 24 |
| 3 | $CoCl_2 \cdot NaBH_4$ [103d,e] EtOH | -- |
| 4 | $SmI_2$ (5 equiv) [103c] THF/MeOH = 5/1 | traces |
| 5 | Zn (10 equiv) THF/HCOOH = 1/5 | -- |
| 6 | Zn (10 equiv) [103a] THF/$HCOONH_4$ | -- |

| Entry | Conditions and Reagents | Isolated yield of **85a** (%) |
|---|---|---|
| 7 | Zn (10 equiv) [103f] HCOOH. | traces |
| 8 | Zn (10 equiv) [103f] AcOH | traces |
| 9 | Zn (10 equiv) HCl (conc.) | traces |
| 10 | Raney-Ni/$H_2$ (1 bar) [103f] EtOH | -- |
| 11 | Raney-Ni/$H_2$ (50 bar) [103f] EtOH | 32 + (50 debrominated product) |
| 12 | Raney-Ni [103f] EtOH reflux | 38 + (50 debrominated product) |
| 13 | Fe/AcOH reflux | -- (reduction of electron rich systems) |
| 14 | $PtO_2$/$H_2$ (1 bar) in MeOH/AcOH [103b] (5:1) | -- |

Most of the attempts failed, resulting either in no selective N-N-bond cleavage or in no cleavage at all. Catalytic hydrogenation with Raney-Ni and $H_2$ showed some promising results, but the loss of the bromine substituent made these conditions unattractive (entries 10, 11 and 12, Table 11). In addition, *in situ* formation of a very active nickel hydride through reduction of $NiCl_2$ with $NaBH_4$, seemed worthy of more detailed study (entry 2). Nevertheless, all changes in conditions did not lead to higher yields of the desired diarylamine **85a** and the 24% reported in Table 10 was not improved upon. Interestingly, the use of iron in glacial acetic acid led to a reduction of more electron-rich hydrazines (entry 13, Table 11). This observation and the failure of all the other methods using acetic media turned our interest to a more careful study of the conditions. Despite our fruitless attempts, strong organic acids like formic acid, glacial acetic acid or ammonium formate (entries 6, 7 and 8) and strong inorganic acids (entry 9) allowed cleavage of azo- and hydrazo compounds to the corresponding amines in good to excellent yields using zinc as the reducing reagent.[103] While in the reported protocols the hydrazo compounds bore only one aromatic substituent, in this case the second aromatic ring changed the properties of these substrates dramatically. In addition, it was known that tetra-substituted hydrazines are more easily cleaved than the corresponding tri-substituted ones. Taking into account the acidity of the "acids" the reasons for our failed attempts became more obvious (Table 12).

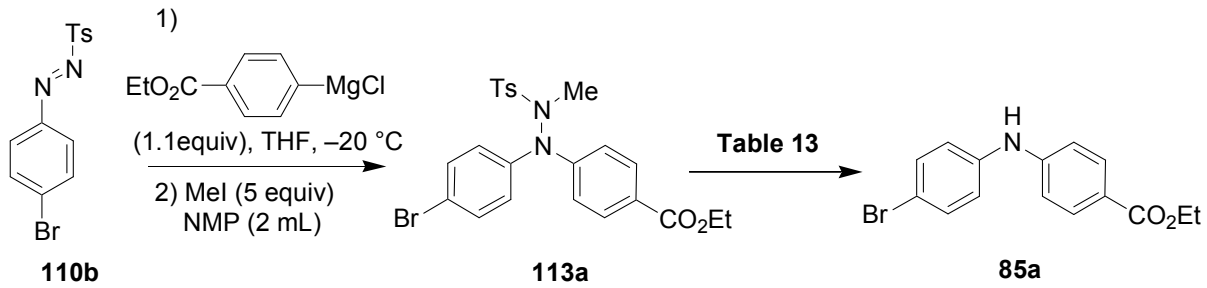
**Table 12:** The p$K_a$ values for selected acids.[104]

| Entry | Acid | Base | Approximate p$K_a$ (relative to water) |
|---|---|---|---|
| 1 | HCl | $Cl^-$ | −7 |
| 2 | $ArSO_3H$ | $ArSO_3^-$ | −6.5 |
| 3 | $Ar_3NH^+$ | $Ar_3N$ | −5 |
| 4 | $HNO_3$ | $NO_3^-$ | −1.4 |
| 5 | $F_3CCOOH$ | $F_3CCOO^-$ | −1.0 |
| 6 | $Cl_3CCOOH$ | $Cl_3CCOO^-$ | −0.65 |
| 7 | $Ar_2NH_2^+$ | $Ar_2NH$ | 1 |
| 8 | $HSO_4^-$ | $SO_4^{2-}$ | 1.99 |
| 9 | $ArNH_3^+$ | $ArNH_2$ | 3-5 |
| 10 | $ArNR_2H^+$ | $ArNR_2$ | 3-5 |
| 11 | HCOOH | $HCOO^-$ | 3.77 |
| 12 | $CH_3COOH$ | $CH_3COO^-$ | 4.76 |
| 13 | $CH_3CH_2COOH$ | $CH_3CH_2COO^-$ | 4.88 |
| 14 | $NH_4^+$ | $NH_3$ | 9.24 |
| 15 | $R_3NH^+$ | $R_3N$ | 10-11 |

Due to the decreased basicity of our substrates, comparable to diarylamine (p$K_b$=13, entry 7, Table 12), the protonation occurred slower or not at all with weaker acids. In order to solve this problem, two transformations were possible, and finally both were used to overcome this problem.

- An additional substituent, which would facilitate an easier N-N-bond cleavage by increasing the p$K_a$ value and,
- the use of stronger acids that would allow an easier reduction, due to accelerated protonation of the hydrazo compound (p$K_a$ < 1, entries 1-6, Table 12).

First, the effects of an additional substituent on the hydrazine were examined, in order to avoid too acidic conditions. Therefore, the tetra-substituted hydrazine **113a**, bearing an additional methyl substituent was synthesized by addition of 5 equiv of methyl iodide and NMP (2 mL) to the intermediately formed magnesium hydrazide. In the absence of NMP no substitution was observed (Scheme 81).



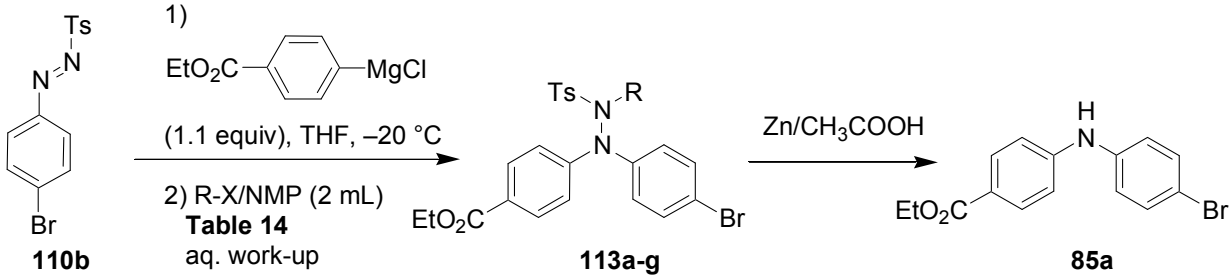

**Scheme 81:** Synthesis of tetra-substituted hydrazine **113a**.

**Table 13:** Attempts to cleave the N-N bond of tetra-substituted hydrazine **113a** with various reagents.

| Entry | Conditions and Reagents | Isolated yield of **85a** (%) |
|---|---|---|
| 1 | Zn (10 equiv)<br>THF/HCOOH =5/1, rt | 52 |
| 2 | $SmI_2$ (5 equiv)<br>THF/MeOH = 5/1, rt | 10 |
| 3 | Zn (10 equiv)<br>AcOH, rt | 57 |
| 4 | Zn (10 equiv)<br>AcOH, 75 °C | 64 |
| 5 | Zn (10 equiv)<br>HCOOH, 75 °C | 50 |

Our initial idea proved correct and, indeed, the cleavage of the N-N bond was facilitated by the introduction of another substituent, as shown in Table 13. The reduction of hydrazine **113a** with glacial acetic acid furnished diarylamine **85a** in 57% yield at ambient temperature and in 64% at 75 °C (entries 3 and 4, Table 13). On the other hand, the use of formic acid led to a faster, but less selective reduction of hydrazine **113a**, providing diarylamine **85a** in only 50% yield (entry 5). In this case, a significant amount of the *N*-methylated hydrazine was isolated, showing that a tuning of both acid strength and electronic properties was essential for a selective N-N bond cleavage.

Therefore, the influence of the fourth substituent was studied more carefully. Several different substituents were introduced and the resulting tetra-substituted hydrazines **113** were reduced (Scheme 82 and Table 14).



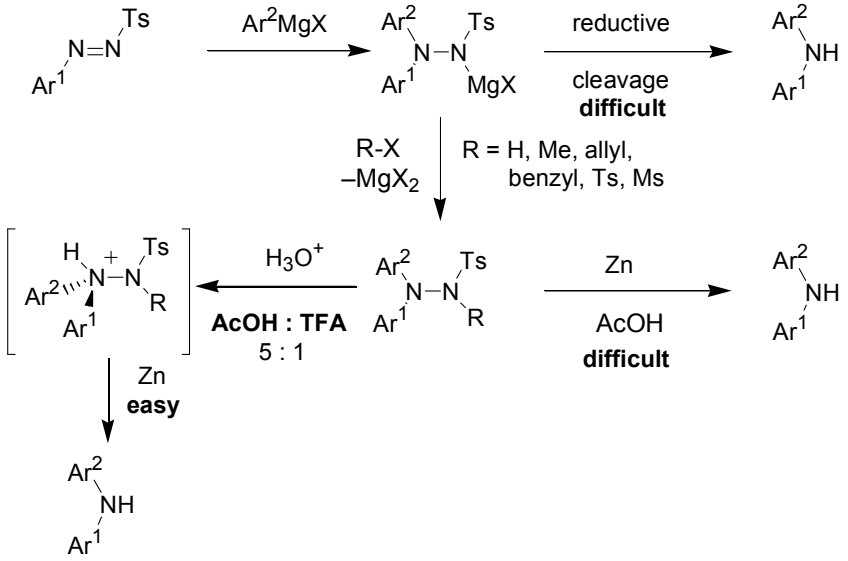

**Scheme 82:** Preparation of various tetra-substituted hydrazines **113a-g** and cleavage to diarylamines.

**Table 14:** Attempts to cleave the N-N bond of various tetra-substituted hydrazines **113** with various reagents.

| Entry | R-X | Isolated yield of **85a** (%) |
|---|---|---|
| 1 | TsCl | -- |
| 2 | MsCl | -- |
| 3 | $Ac_2O$ | -- |
| 4 | $EtO_2CCl$ | -- |
| 5 | $C_3H_5Br$ | 69 |
| 6 | $C_7H_7Br$ | 63 |
| 7 | $CH_3I$ | 50 |
| 8 | $C_3H_5Br$<br>HCOOH | 52 |
| 9 | $C_3H_5Br$<br>AcOH/TFA = 5:1 | 75 |
| 10 | $C_3H_5Br$<br>AcOH 10 mL<br>*p*-$TolSO_3H$ (10 equiv) | 73 |

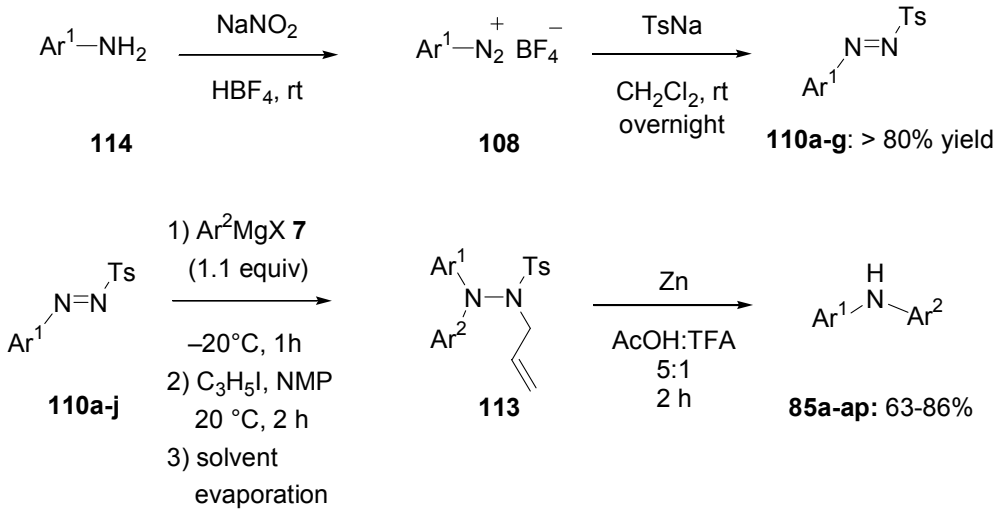
Electron-withdrawing substituents, such as an additional tosylate, a mesylate, an acetate or an ethyl formate, hamper the reaction and led to no reduction product, even at elevated temperatures and elongated reaction times (entries 1, 2, 3 and 4, Table 14), whereas the introduction of more electron-donating substituents, like an allyl or benzyl substituent (entries 5 and 6), increased the yield of diarylamine **84a** significantly. At the same time the amount of side products, in particular the corresponding hydrazine, was decreased. Although a change of solvent to formic acid again facilitated side reactions, leading to lower yields of diarylamine **84a** (entry 8), a 5:1 mixture of AcOH/TFA proved best for this substrate (entry 9) delivering **84a** in impressive 75% overall yield. The reduction was complete within 2 h at 75 °C, allowing a fast reductive cleavage of the N-N bond. A mixture of AcOH and *p*-toluenesulfonic acid gave also high yields of the corresponding diarylamine, but a removal of the *p*-toluenesulfonic acid was more complicated, and thus AcOH/TFA was considered to be the best reagent system.

Scheme 83 summarizes the different stages of optimization.




**Scheme 83:** Optimization of reaction conditions.

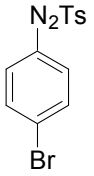
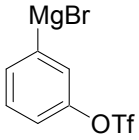
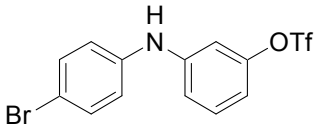
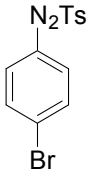
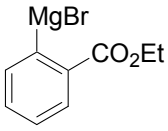
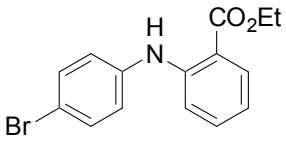
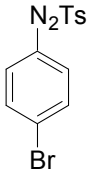
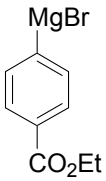
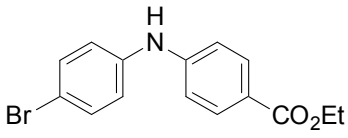
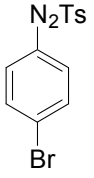
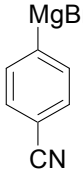
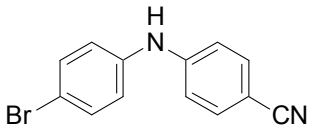
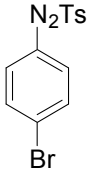
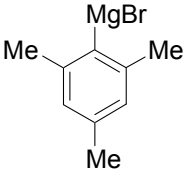
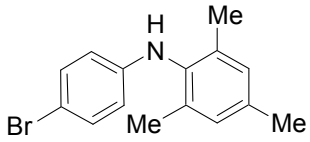
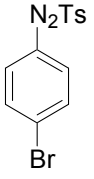
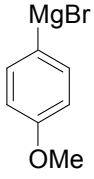
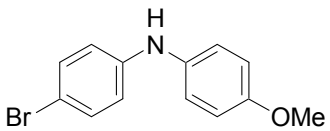
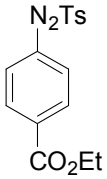
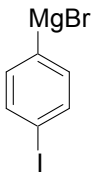
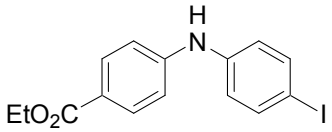
With these optimized conditions in hand, the new methodology was applied to several azosulfones **110** and different functionalized Grignard reagents **7** (Scheme 84). The aryl 4-tolylazo sulfones, were readily prepared from aromatic amines **114** (see also Scheme 78) in a two step-sequence in more than 80% overall yield in most cases (Scheme 84).[101]

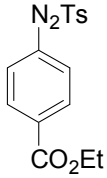
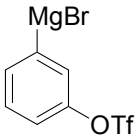
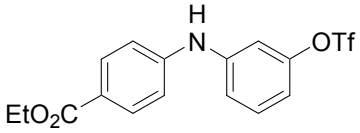
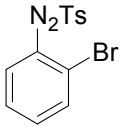
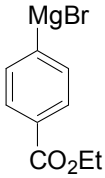
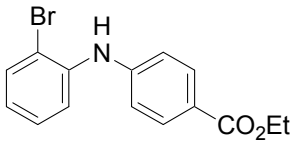
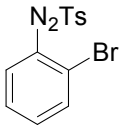
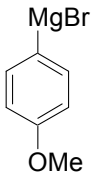
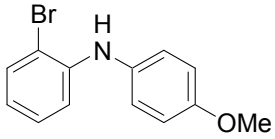
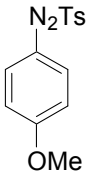
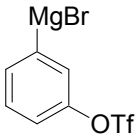
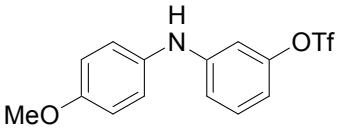
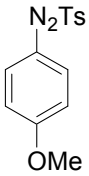
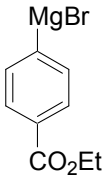
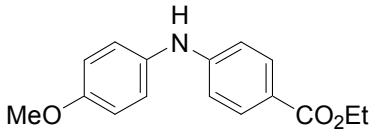
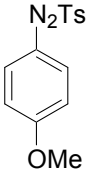
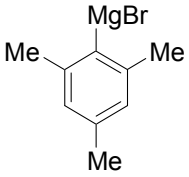
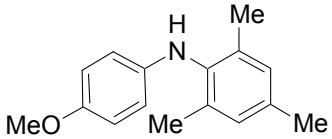
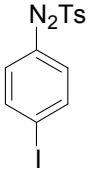
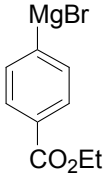
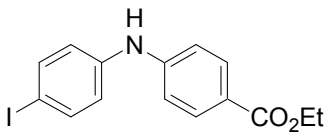


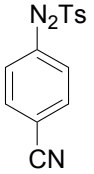
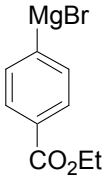
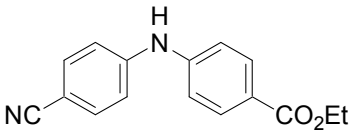
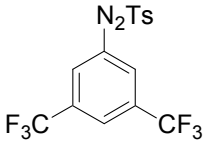
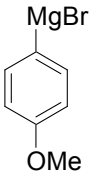
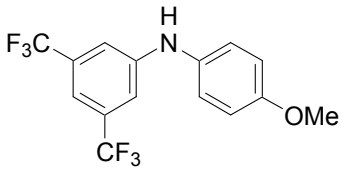
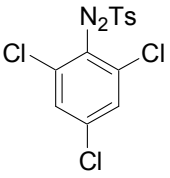
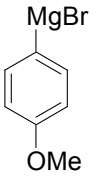
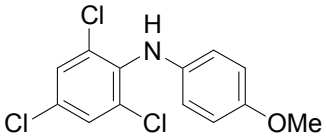
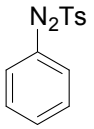
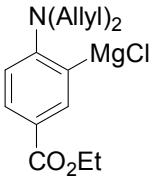
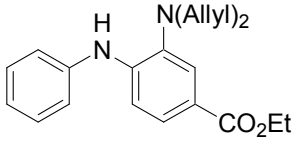

**Scheme 84:** Synthesis of aryl 4-tolylazo sulfones **110** and diarylamines **85**.

Various functionalized aryl 4-tolylazo sulfones **110a-j** underwent the addition of arylmagnesium compounds furnishing in a one-pot procedure, including a change of solvent for the reduction, polyfunctional diarylamines **85** in 63-86% overall yields (Scheme 84 and Table 15).

**Table 15:** Polyfunctional diarylamines **85** obtained by the addition of functionalized Grignard reagents **7** to functionalized aryl 4-tolylazo sulfones **110a-g**.

| Entry | Azo Sulfone **110** | Arylmagnesium Reagent **7** | Product **85** | Yield (%) |
|---|---|---|---|---|
| 1 |  **110b** |  **7l** |  **85ae** | 70[a] |
| 2 |  **110b** |  **7j** |  **85af** | 80 |
| 3 |  **110b** |  **7c** |  **85a** | 83 |
| 4 |  **110b** |  **7d** |  **85ag** | 73[b] |
| 5 |  **110b** |  **7m** |  **85ah** | 69 |
| 6 |  **110b** |  **7h** |  **85u** | 86 |
| 7 |  **110c** |  **7b** |  **85g** | 63 |

| Entry | Azo Sulfone **110** | Arylmagnesium Reagent **7** | Product **85** | Yield (%) |
|---|---|---|---|---|
| 8 |  **110c** |  **7l** |  **85ai** | 80[c] |
| 9 |  **110d** |  **7c** |  **85o** | 65 |
| 10 |  **110d** |  **7h** |  **85aj** | 67 |
| 11 |  **110e** |  **7l** |  **85ak** | 81 |
| 12 |  **110e** |  **7c** |  **85j** | 96 |
| 13 |  **110e** |  **7m** |  **85al** | 83 |
| 14 |  **110e** |  **7c** |  **85g** | 71 |

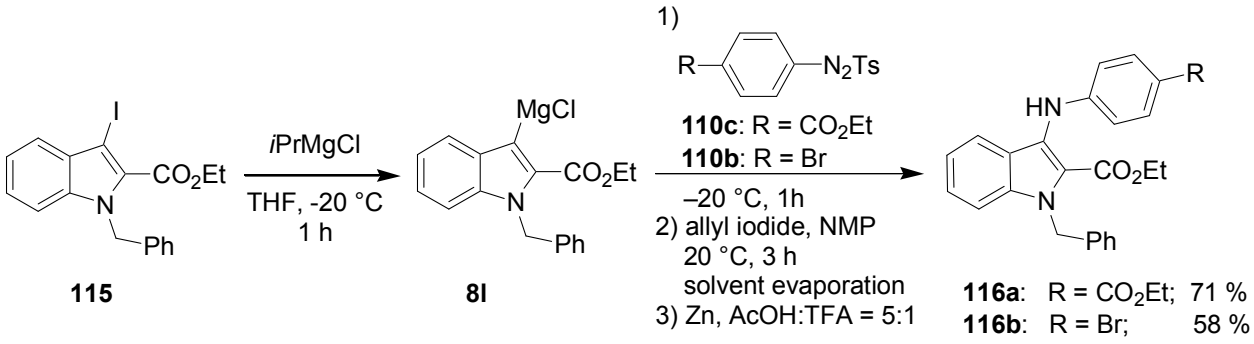
| Entry | Azo Sulfone **110** | Arylmagnesium Reagent **7** | Product **85** | Yield (%) |
|---|---|---|---|---|
| 15 |  **110e** |  **7c** |  **85am** | 64[d] |
| 16 |  **110e** |  **7h** |  **85an** | 60[b] |
| 17 |  **110e** |  **7h** |  **85ao** | 59[e] |
| 18 |  **110e** |  **7n** |  **85ap** | 29 |

[a]reaction time for the reduction: 6 h; [b]reaction time for the reduction: 15 h; [c]reaction time for the reduction 18 h; [d]reaction time for the reduction 12 h; [e]rection time for the reduction 5 h.

As shown in Table 15, the presence of many different electron-withdrawing groups, such as an ester, a halide or a nitrile, as well as electron donating groups, like a methoxy- or dimethylamino substituent, is compatible with a wide range of functionalized Grignard reagents. The addition is usually complete within 1 h at −20 °C and, remarkably, either the Grignard reagent **7** or the aryl 4-tolylazo sulfones **110** can bear a bromide- (entries 1-6, 9-10) or an iodide substituent (entries 7 and 14). A highly electrophilic functionality like a triflate (entries 1, 8 and 11) was also compatible with the reaction conditions. This is in contrast to Pd-, Cu- or Ni-catalyzed amination reactions of aromatic halides and makes this method again complementary to the Buchwald-Hartwig amination procedure. Steric hindrance was no longer problematic, since in both the aryl 4-tolylazo sulfones **110** as well as in the Grignard reagent **7** the presence of one (entries 2, 9 and 10) or two *ortho*-substituents (entries 5, 13 and 17) did not reduce the yields for the amination reactions significantly.

This procedure was successfully applied to heterocyclic systems as well. Thus, the functionalized 3-indolylmagnesium reagent **8l**, prepared from the corresponding heterocyclic iodide **115** *via* an I/Mg exchange, reacted with the aryl 4-tolylazo sulfones

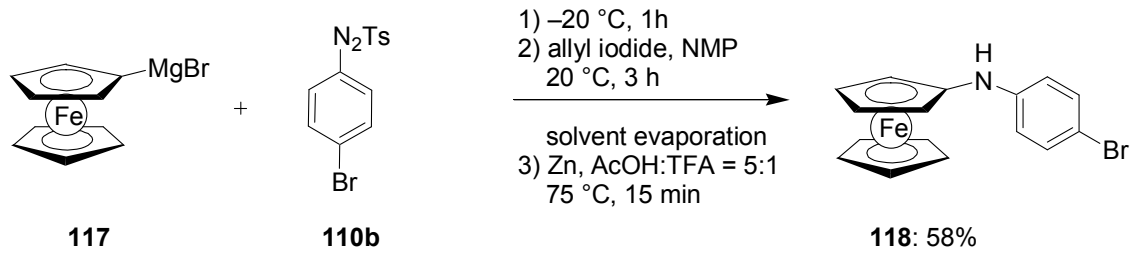
**110b** and **110c** under the usual reaction conditions, providing the new 3-arylaminated indole derivatives **116a** and **116b** in 58-71% yield (Scheme 85).




**Scheme 85:** Synthesis of 3-arylamino-indole derivatives **116**.

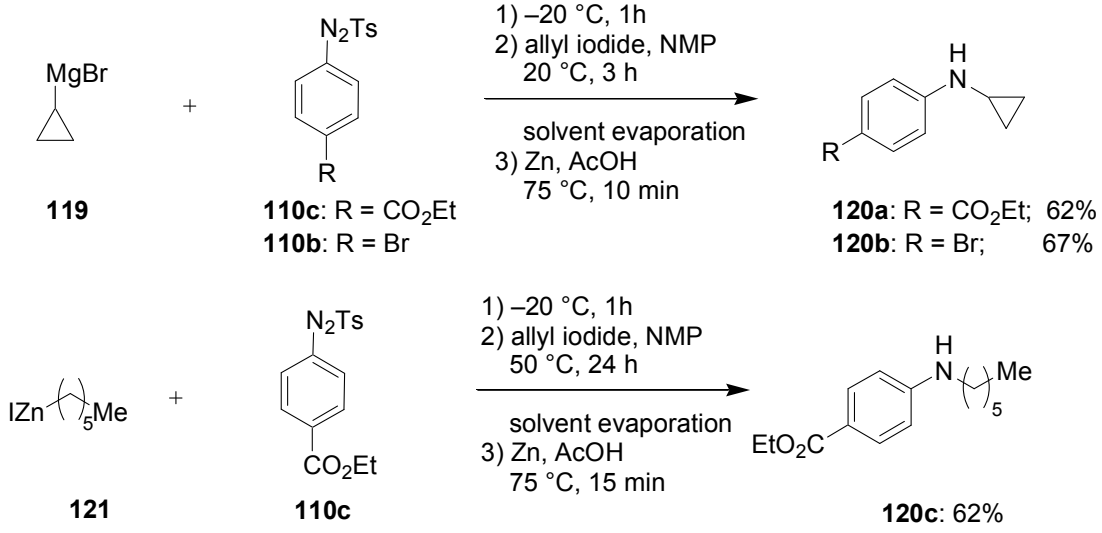
This new class of 3-arylaminated indoles was for the first time accessible, since all other methods, including transition metal catalyzed reactions, failed.

Finally, the scope of this new amination reaction was extended to other classes of organomagnesium reagents. Thus, the preparation of elusive ferrocenyl aryl amines[105] was achieved by treating ferrocenylmagnesium bromide **117**, prepared from tributylstannylferrocene[106] with the arylazo tosylate **110b** (−20 °C, 1 h) followed by usual reductive workup (Zn, AcOH:TFA = 5:1, 75°C, 15 min). Under these conditions, the novel aminated ferrocenyl derivative **118** was obtained in 58% yield (Scheme 86).



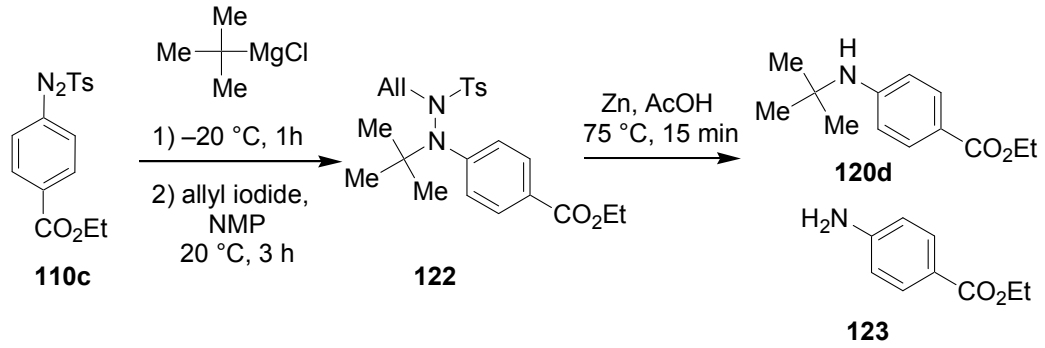

**Scheme 86:** Synthesis of ferrocenylamine **118**.

Aliphatic organomagnesium and organozinc reagents underwent the amination reaction as well (Scheme 87). Thus, cyclopropylmagnesium bromide **119** reacted with the aryl 4-tolylazo sulfones **110b** and **110c,** affording the expected *N*-arylcyclopropylamines **120a-b**[107] in 62% and 67% isolated yield, respectively. The addition of *n*hexylzinc iodide (**121**) to arylazo sulfone **110c** proceeded at −20 °C in 2 h, leading to the zinc hydrazide, which was significantly less reactive than the corresponding magnesium hydrazide, requiring higher temperatures and longer reaction times for the allylation reaction to occur. Nevertheless, after reductive cleavage of the hydrazine, amine **121c** was isolated in 62% yield. In these cases, it turned out that the use of TFA was not essential for the cleavage of the N-N bond and glacial acetic acid alone was sufficient.



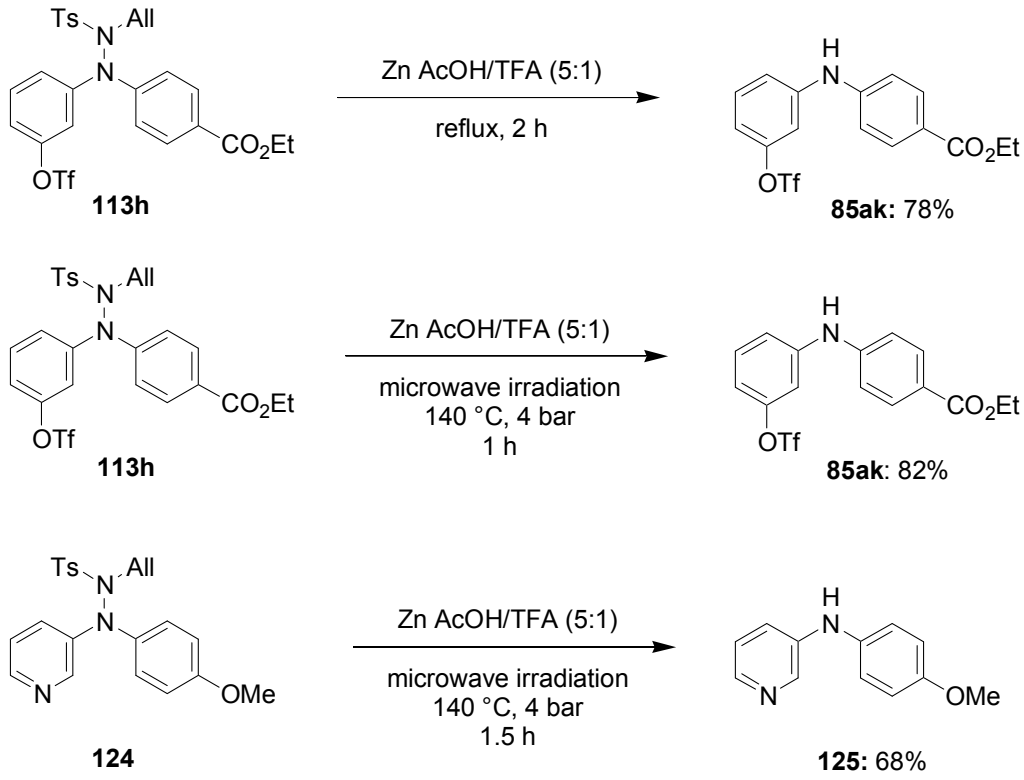

**Scheme 87:** Amination of alkyl-organomagnesium and organozinc reagents.

The preparation of *t*butylaminoaniline derivatives failed, due to cleavage of the *t*butyl group under reaction conditions. While the addition of *t*BuMgCl to arylazo sulfone **110c** and subsequent allylation proceeded very well, leading to compound **122**, the reduction of hydrazine **122** led to a complex mixture of products, with small amounts of the desired amine **120d** and ethyl 4-aminobenzoate (**123**) as the main product, although again less acidic conditions were used (only AcOH) (Scheme 88).




**Scheme 88:** Attempted synthesis of *t*butyl-substituted amines **120d**.

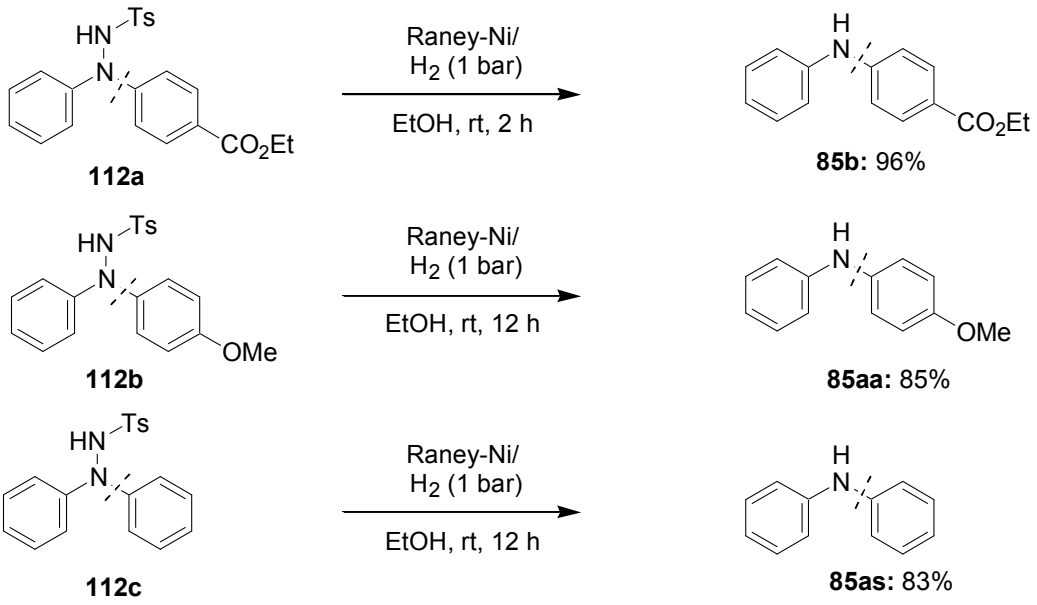
As shown above, this methodology allowed the preparation of a wide range of functionalized diarylamines and aryl-alkylamines. Nevertheless, several substrates that gave stable hydrazine derivatives could not be transformed into the corresponding amines by the reduction method. As mentioned before, varying reaction times were required for the reduction, depending on the electronic properties of the hydrazine. The more electron-poor the substituents were, the longer the reaction took. One possible solution to this problem was heating the reaction to reflux, sometimes resulting not only in shorter reaction times, but in lower selectivity as well. Another possibility was the use of microwave irradiation, in order to increase temperature and pressure at once, resulting also in a faster, but again less selective reduction. Some examples, illustrating these effects are given in Scheme 89.




**Scheme 89:** Microwave assisted reduction of hydrazines **113h** and **124**.

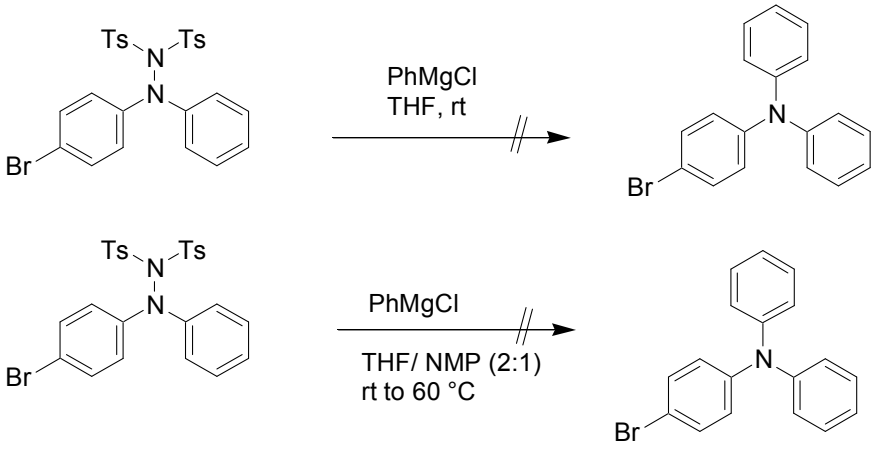
Thus, the reduction of hydrazine **113h**, bearing two electron-withdrawing substituents was accelerated without loss of selectivity (2 h instead of 18 h). Even more impressive is the fact that the reduction of 3-pyridyl substituted hydrazine **124** was accomplished only by using microwave irradiation. Under conventional heating, no reduction to **125** was observed for these derivatives.

Although, one major goal was to tolerate as many functional groups as possible, a more atom economic procedure was desirable in order to make this methodology more attractive for large scale synthesis. As shown in Table 11, Raney-Ni/$H_2$ in ethanol allowed quantitative cleavage of the trisubstituted hydrazines (entries 10-12) and, therefore, this method was chosen for further investigations, although halogen atoms, in particular bromides and iodides, were not tolerated under these reaction conditions. Three different tri-substituted hydrazines **112a-c** were prepared – all without a halogen substituent – and different reaction conditions were applied. The first experiments clearly indicated, that a catalytic amount of Raney-Ni was not sufficient, and the reaction was indifferent to the presence of $H_2$. Therefore, the reaction can be regarded as more of an oxidative cleavage of the N-N bond through insertion of nickel rather than as a catalytic hydrogenation.




**Scheme 90:** N-N bond cleavage with Raney-Ni of tri-substituted hydrazines **112**.

Another problem, already faced in the amination reaction using nitro arenes and Grignard reagents, was the synthesis of triarylamines. A substitution reaction was anticipated for the *bis*tosyl-substituted hydrazines. However, several attempts to run a substitution reaction on these substrates were unsuccessful (Scheme 91).




**Scheme 91:** Failed attempts to convert hydrazines to triarylamines.

In summary, aryl 4-tolylazo sulfones **110**, are easily prepared from arylamines **114** and are excellent synthetic equivalents for electrophilic arylamines. They react with various aromatic and heterocyclic magnesium compounds, providing a range of new polyfunctional amines. The method has a wide scope, allowing the addition of almost any carbon nucleophile, and the application to other types of electrophiles should be further examined. Starting from amines, the method is complementary to the reaction sequence developed in chapter 4 – amination using nitroarenes – and allows the preparation of a number of substrates that were neither accessible by transition metal catalysed amination reactions nor by the amination of nitro arenes.

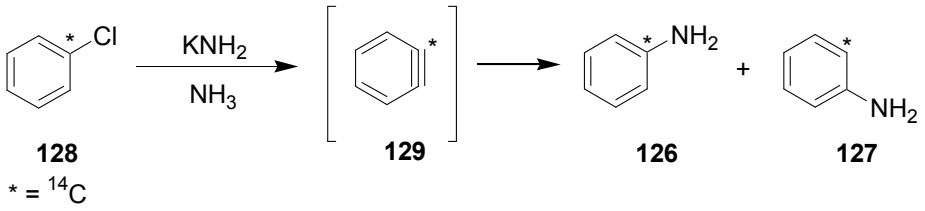
# 6. Generation of Polyfunctionalized Arynes and Their Applications to Amination Chemistry

## 6.1 Introduction

Although several procedures for electrophilic amination have been developed herein, one major goal, the synthesis of triarylamines has not been achieved. Taking into account the great interest in this substance class, a different approach was demanded.

Another possibility of synthesizing such amines, as discussed in the introduction, involves benzynes as very reactive intermediates. These can be trapped with a variety of nucleophiles, including amides and thus a more careful study of this transformation was attempted.

Functional group substitution on aromatic compounds plays a pivotal role in synthetic chemistry, and one important reaction serving this purpose proceeds through arynes. As early as 1942 Wittig proposed a benzyne molecule to explain the remarkable ease of nucleophilic substitution reactions of inactivated haloarenes, when reacted with strong bases. These early studies were undertaken in order to explain the phenomenon of *cine* substitution on aromatic rings. The first decisive evidence came through the observation that equal amounts of both anilines **126** and **127** were formed in the reaction of $^{14}C$-labeled chlorobenzene **128** with $KNH_2$ in liquid ammonia. This observation could be explained by invoking a symmetrical intermediate such as benzyne **129** (Scheme 92).[42]




**Scheme 92:** Reaction of chlorobenzene **128** with $KNH_2$.

Additional support for aryne intermediates has been found in the isolation of Diels-Alder products from reactions proposed to involve benzyne.[108] Since then, the structure of benzyne has been the focus of many experimental and theoretical studies. For instance, its IR spectrum was reported in 1992 recorded by low temperature solid matrix photolysis of the precursor benzocyclobutanedione.[109] Semiemperical and *ab initio* calculations predicted an "arynic bond", which was found to be longer than a regular triple bond with the other C-C bonds being similar in length to those in benzene. The two additional electrons do not destroy the aromaticity and are located in two orbitals that lie in the ring plain overlapping symmetrically. The ground state of benzyne is calculated to be a singlet.

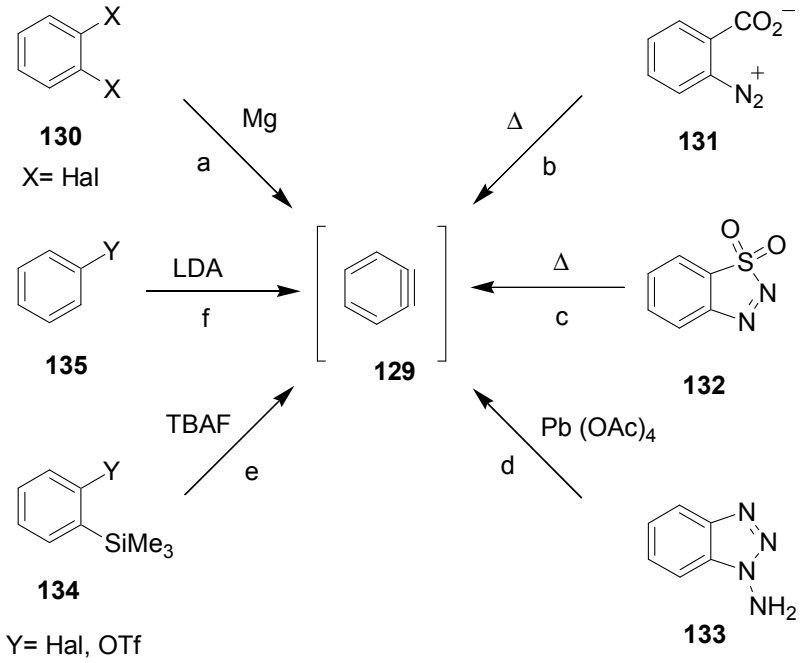
The high reactivity of benzyne was explained in terms of its high enthalpy of formation, which was experimentally determined to be around 500 kJ/mol.[110] Besides its general reactivity, benzyne also exhibits marked electrophilicity. Therefore, the energy of its LUMO is of special importance. The HOMO of benzyne is calculated to be close to that of acetylene (−9.58 eV). However, the LUMO is estimated to be at 1.33 eV, which is significantly lower in energy than the corresponding one in acetylene.[111] This decreases the

energy gap between the benzyne LUMO and the HOMO of the attacking nucleophile and makes a reaction much easier. Hence, many nucleophiles that do not react with acetylene readily add to benzynes.

## 6.2 Methods for the Generation of Benzynes

The high reactivity of benzyne and its derivatives requires an *in situ* generation of the reactive species in the presence of suitable reaction partners, while maintaining its stationary concentration as low as possible, since it rapidly oligomerizes in the absence of other reaction partners.

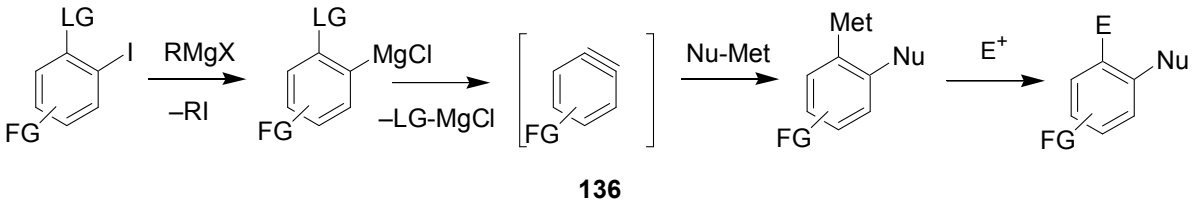
Most of the early work in this area focused on an approach using an aryl halide and a strong base, but a variety of different methods have been reported (Scheme 93).[41,112] Scheme 93 shows some of the most popular ones, like metalation of *o*-dihalobenzenes **130** (a), thermal decomposition of benzenediazonium-2-carboxylate (**131**) (b), 1,2,3-benzothiadiazole-1,1-dioxide (**132**) (c) or the oxidation of 1-aminobenzotriazole (**133**) (d). More recently, *o*-trimethylsilylhalides and sulfonates **134** (e) as well as the direct metalation of arenes, bearing a good leaving group **135**, with LDA (f) were used.




**Scheme 93:** Selected methods for the generation of benzyne **129**.

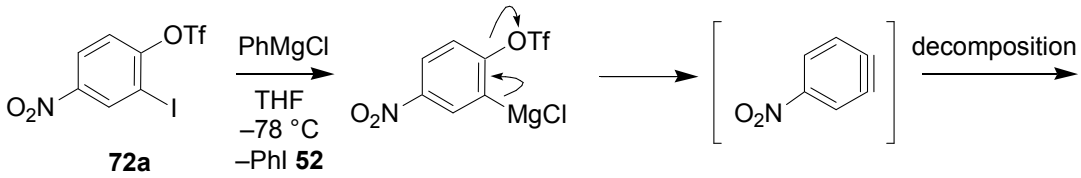
## 6.3 Preparation of Functionalized Benzynes

Whereas a number of methods for the generation of benzyne itself are known, the preparation of functionalized arynes is often incompatible with the harsh reaction conditions necessary for their generation. We envisioned the possibility using the iodine-magnesium exchange reaction for the generation of functionalized benzynes **136** (Scheme 94).



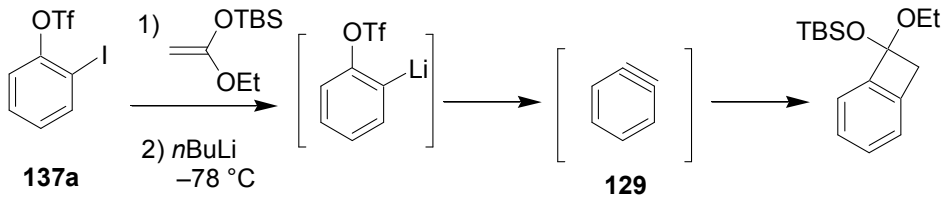

**Scheme 94:** Synthesis of functionalized benzynes **136**.

As already mentioned in part 3.2.2, the I/Mg exchange reaction on compound **72a** led to formation of one equivalent of iodobenzene **52**, indicating that an exchange reaction took place, but the products readily decomposed at low temperatures (−78 °C) (Scheme 95).




**Scheme 95:** Anticipated elimination of the triflate in compound **72a**.

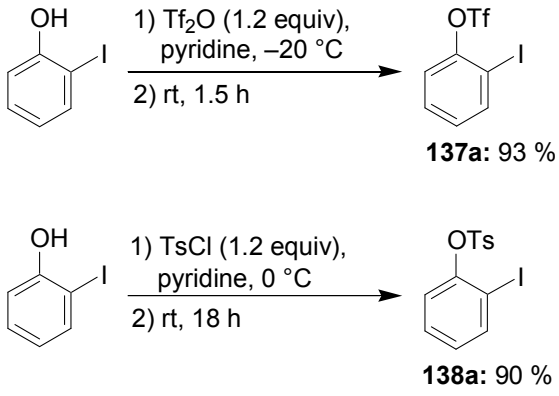
Earlier, K. Suzuki and co-workers reported the formation of benzyne, when treating 2-iodophenyltriflate (**137a**) with *n*BuLi in THF. They were able to trap the benzyne intermediate in a [2+2] cycloaddition with several silyl enol ethers (Scheme 96).[113]




**Scheme 96:** Generation of benzyne **129** through I/Li exchange.

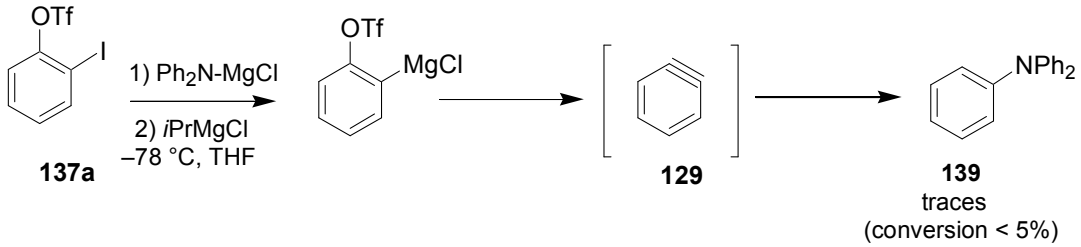
However, no optimization of the reaction conditions was possible, and the functional group tolerance was modest. Moreover, the organometallic species was not detectable, indicating the good leaving group abilities of triflate.

Two different leaving groups were first examined on unfunctionalized derivatives in order to test if this approach was applicable to the corresponding magnesium derivatives. Thus, 2-iodophenyltriflate (**137a**) and 2-iodophenyltosylate (**138a**) were prepared under standard conditions (Scheme 97) starting from the corresponding 2-iodophenol.



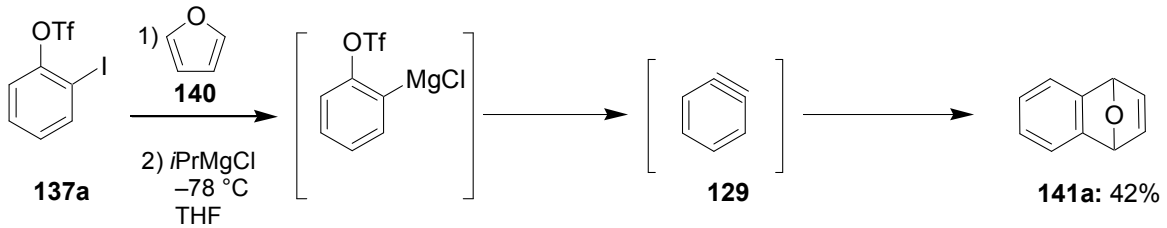

**Scheme 97:** Synthesis of derivatives **137a** and **138a**.

As mentioned in the introduction, arynes have been used for the selective amination using magnesium amides. We applied this procedure to triflate **137a** (Scheme 98).




**Scheme 98:** Attempts for the synthesis of triarylamines **139**.

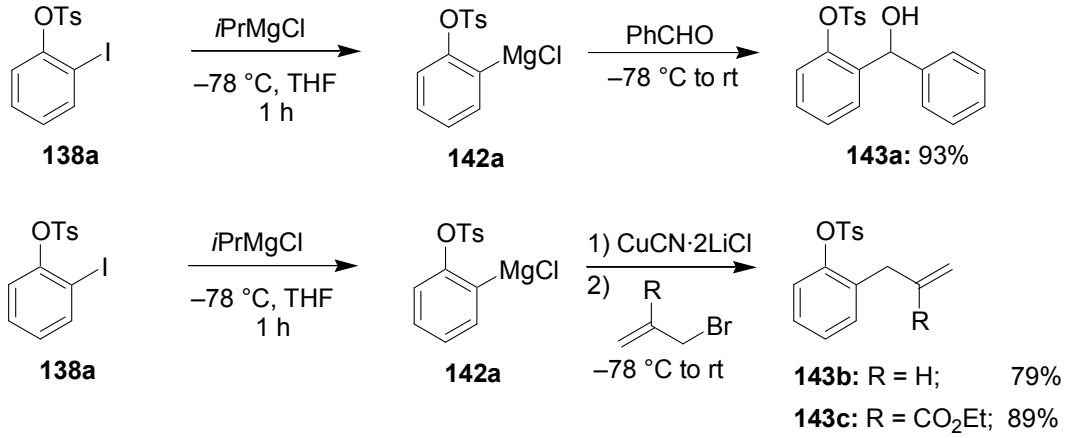
The reaction led only to traces of the desired triarylamine **139**, possibly due to a fast formation of benzyne (**129**) at low temperatures. An inverse addition of the reaction partners and different reaction conditions did not improve the conversion to triarylamines **139**. Since diarylamines are known to be weak nucleophiles, furan (**140**) was used for the addition to benzyne (**129**) to test the formation of the reactive intermediate (Scheme 99).




**Scheme 99:** Synthesis of compound **141a**.

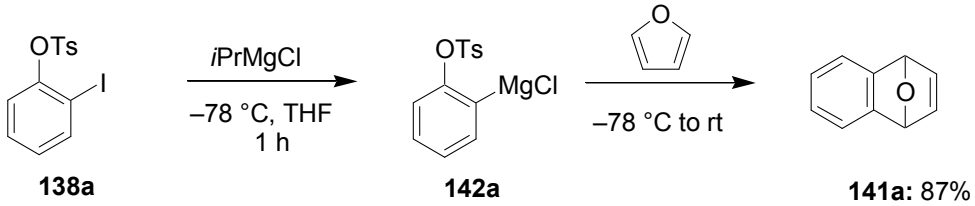
Thus, the addition of *i*PrMgCl to a mixture of 2-iodophenyl triflate **137a** and furan (**140**) in THF at −78 °C furnished 1,4-dihydro-1,4-epoxynaphthalene (**141a**) in 42% yield after 30 min. This experiment proved the formation of benzyne **129** although the yield was only moderate. Several other dienophiles, like cyclohexadiene, cyclopentadiene and anthracene were used for the reaction with the formed benzyne. All of these reactions gave complex reaction mixtures, based on GC analysis. The addition of sodium methyl thiolate, which was shown to react with benzyne as a nucleophile,[41] also failed here. One reason for the failure

could be the low temperature employed for the formation of benzyne, leading to an unselectively generated benzyne in high concentrations.
Therefore, a tosyl group, which should be less prone to an elimination at low temperatures, was used as the leaving group. This gives rise to an elimination at higher temperatures and should generate significantly lower concentrations of benzyne at a given temperature. The exchange reaction was considerably slower and required 1 h at −78 °C for full conversion (Scheme 100).



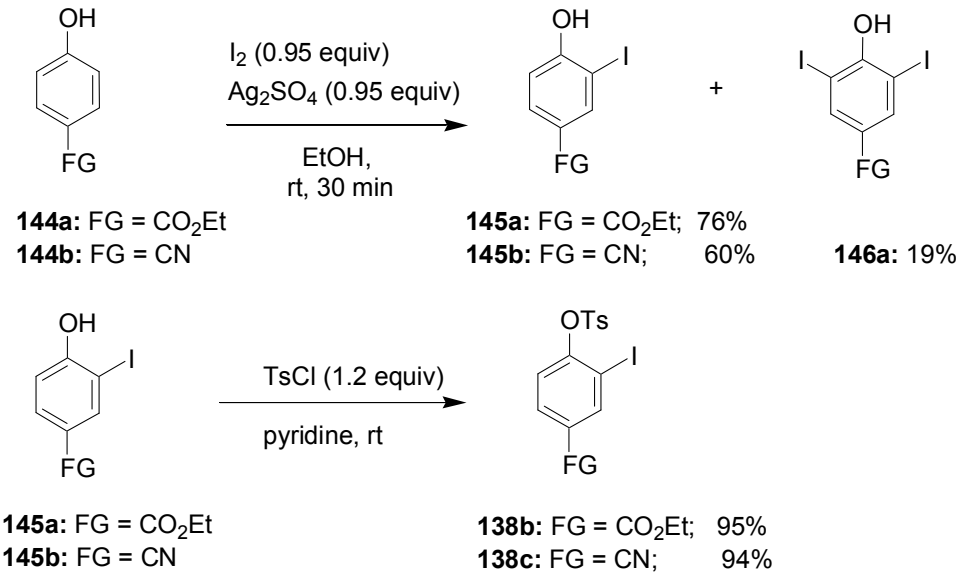

**Scheme 100:** I/Mg exchange on compound **138a** and reactions of Grignard reagent **142a** with electrophiles.

This Grignard reagent **142a** is perfectly stable at a temperature of −78 °C and was reacted directly with benzaldehyde **22**, leading to the corresponding benzylic alcohol **143a** in 93% yield. Additionally, a transmetalation to copper allowed the reaction with allyl bromide **45** and ethyl (2-bromomethyl) acrylate (**46**), furnishing the desired products **143b** and **143c** in 79% and 89% yield, respectively.
At low temperatures (−78 °C) no reaction with furan (**140**) occurred, but warming to ambient temperature led to product **141a** in 87% yield (Scheme 101).




**Scheme 101:** Synthesis of compound **141a**.

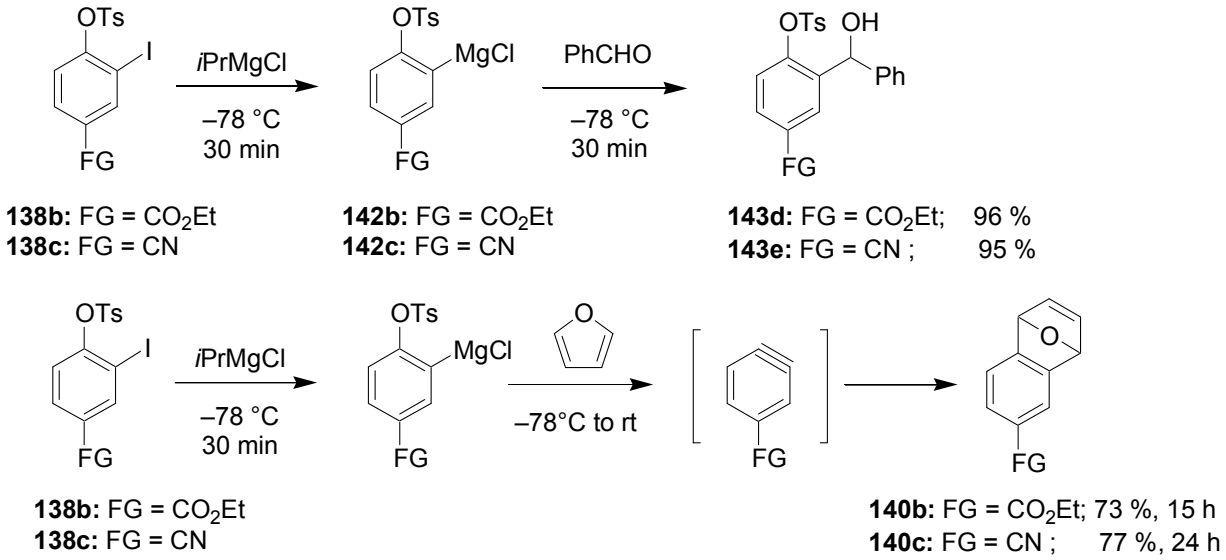
With these very promising results in hand, we investigated the functional group tolerance of this method. Thus, the ester and nitrile functionalized derivatives were prepared in a two-step synthesis starting from the corresponding phenols (Scheme 102).




**Scheme 102:** Synthesis of compounds **138b** and **138c**.

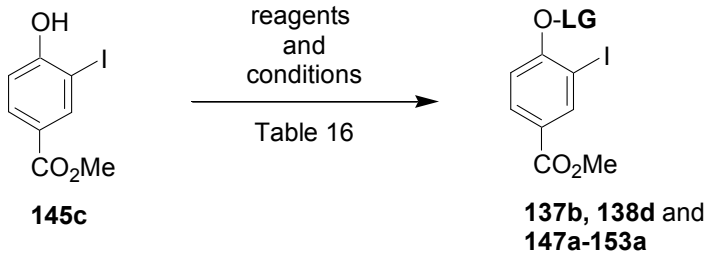
The synthesis started with an iodination of the commercially available phenols **144a** and **144b**, leading to mono- and diiodinated products **145** and **146**, which could be easily separated by column chromatography. Subsequent conversion to the tosylates under standard conditions furnished products **138b** and **138c** in high yields of 95% and 94%, respectively (Scheme 102).

The iodine-magnesium exchange on these substrates was faster, due to the electron withdrawing properties of the substituents, and complete conversion was observed after 30 min at −78 °C (Scheme 103). Furthermore, the resulting Grignard reagents **142b** and **142c** were stable at this temperature for elongated periods of time and thus were reacted with benzaldehyde, leading to the corresponding benzylic alcohols **144d** and **144e** in excellent yields.




**Scheme 103:** Generation of functionalized benzynes.

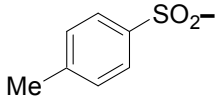
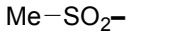
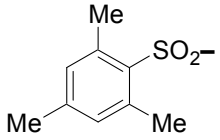
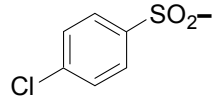
In the presence of furan, increasing the temperature to ambient temperature, led to the Diels-Alder cycloaddition products of type **140** in good yields, indicating the formation of functionalized benzyne. However, the reaction times were very long and for the cyano-substituted substrate, the reaction mixture was hydrolyzed after 24 h, although GC analysis indicated unreacted starting material (Scheme 103). The stability of these Grignard reagents, led to a very slow elimination of the tosylate. Thus, a better leaving group, showing a similar good stability as substrates **142** at low temperature, but with a higher tendency to eliminate at higher temperatures was desired.
Therefore, substrates with several other leaving groups on the phenol were synthesized, as shown in Scheme 104 and Table 16.

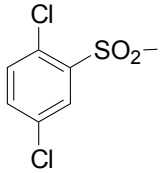
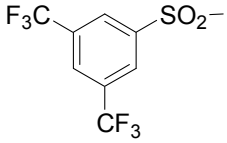
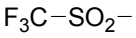
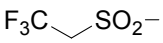
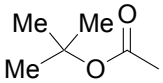



**145c**

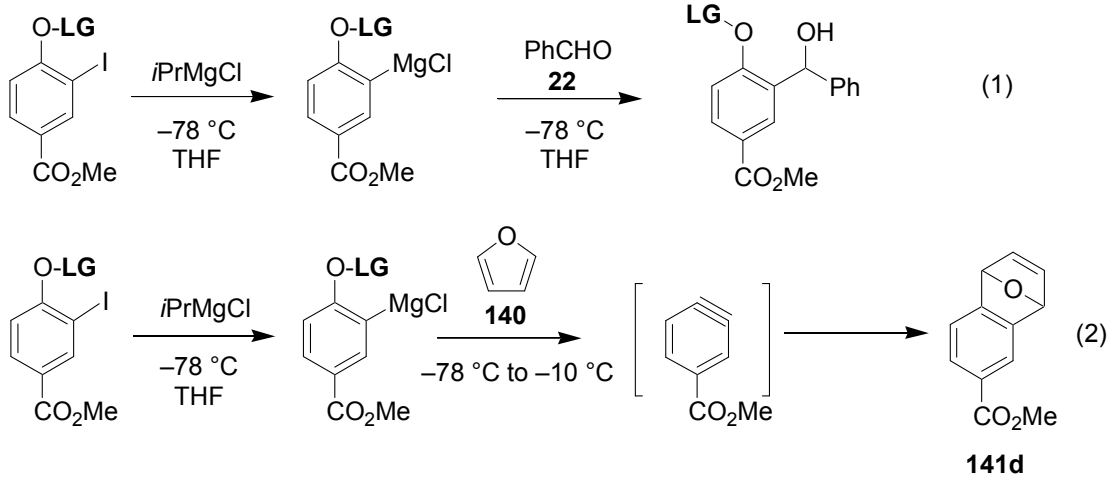
**137b, 138d** and **147a-153a**

**Scheme 104 and Table 16:** Synthesis of protected phenols **137b, 138d** and **147a-153a**.

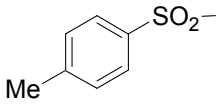
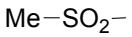
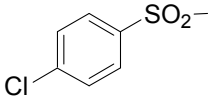
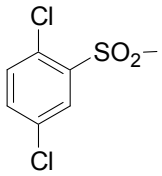
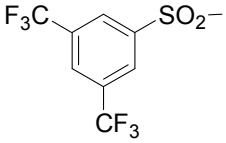
| Entry | Reagents and Conditions | Leaving Group (LG-) | Yield of **148** (%) |
|---|---|---|---|
| 1 | TsCl (1.2 equiv)<br>pyridine<br>0 °C to rt, overnight |  <br>**138d** | 95 |
| 2 | MsCl (1.2 equiv)<br>pyridine<br>0 °C to rt, overnight |  <br>**147a** | 79 |
| 3 | 2,4,6-trimethylphenyl-sulfonyl chloride (1.2 equiv)<br>pyridine<br>0 °C to rt, overnight |  <br>**148a** | 81 |
| 4 | 4-chlorophenyl-sulfonyl chloride (1.2 equiv)<br>pyridine<br>0 °C to rt, overnight |  <br>**149a** | 96 |

| Entry | Reagents and Conditions | Leaving Group (LG-) | Yield of **148** (%) |
|---|---|---|---|
| 5 | 2,5-dichlorophenyl-sulfonyl chloride (1.2 equiv) pyridine 0 °C to rt, overnight |  **150a** | 96 |
| 6 | 3,5-bistrifluoromethylphenyl-sulfonyl chloride (1.2 equiv) pyridine 0 °C to rt, overnight |  **151a** | 95 |
| 7 | $Tf_2O$ (1.2 equiv) pyridine −20 °C to rt, overnight |  **137b** | 85 |
| 8 | 2,2,2 trifluoroethane-sulfonyl chloride (1.2 equiv) pyridine −20 °C to rt, overnight |  **152a** | 83 |
| 9 | $Boc_2O$ (1.2 equiv) DMAP (0.1 equiv) THF, rt, overnight |  **153a** | 94 |

One major objective was to generate a stable Grignard reagent, which could form the benzyne selectively at higher temperatures. Thus, in an initial experiment, substrates **137b**, **138d** and **147a-153a** were reacted with *i*PrMgCl at −78 °C, and the resulting Grignard reagents were treated with benzaldehyde **22** (Scheme 105, eq. (1) and Table 17). In independent, second experiments, substrates which gave rise to stable Grignard reagents were treated subsequently with furan and the reaction mixture was allowed to warm up to −10 °C (Scheme 105, eq. (2) and Table 17).

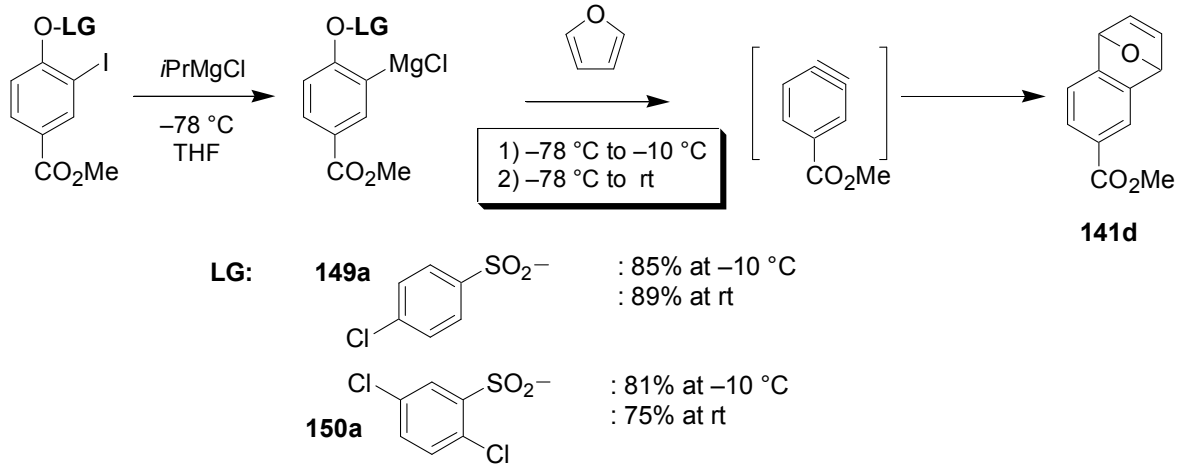


**Scheme 105 and Table 17:** Reactions of compounds **138d** and **147a-151a** with benzaldehyde (**22**) and furan (**140**).

| Entry | Leaving Group (LG-) | Yield for reaction with benzaldehyde **22** (%) | Time for the reaction with furan **140** | GC conversion (%) of **141d** for the reaction with furan **140** |
|---|---|---|---|---|
| 1 |  **138d** | 90 **143f** | 5 h | 17[a] |
| 2 |  **147a** | 72 **154a** | 5 h | 10[a] |
| 3 |  **149a** | 93 **155a** | 4 h | quant. |
| 4 |  **150a** | 87 **156a** | 1 h | quant. |
| 6 |  **151a** | 78 **157a** | 1 h | quant. |

[a] full conversion was obtained after additional stirring for 18 h at ambient temperature

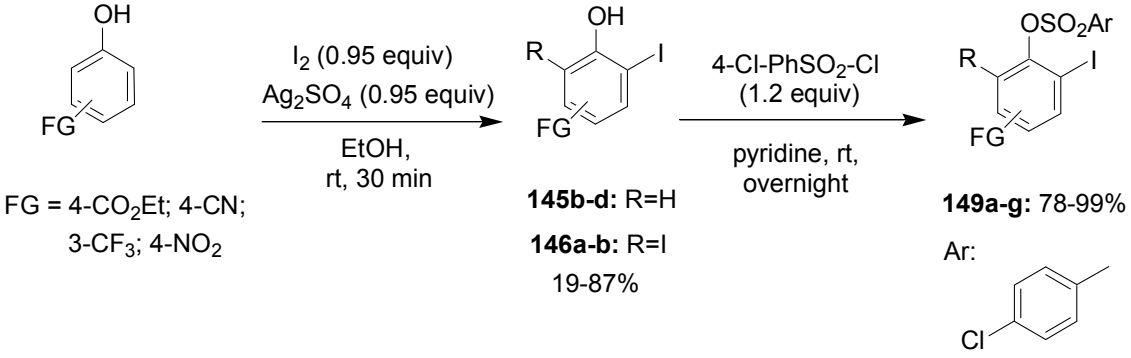
Table 17 shows those results for which the first reaction was successful, leading to the benzylic alcohols **143f, 154a-157a** in good yield. Compounds **137b, 152a** and **153a** (entries 7-9, Table 16) did not give significant amounts of the corresponding Grignard reagent, indicating formation of benzyne even at −78 °C. The best yield for the nucleophilic addition to benzaldehyde (**22**), combined with an acceptable time for benzyne formation at −10 °C was found for the 4-chlorophenylsulfonate **149a** (entry 4, Table 17). Thus, the reaction with benzyne was carried out for this example and the second best group, 2,5-dichlorophenyl substituted compound **150a** (entry 5), again on an appropriate scale at two different temperatures and the reaction products were isolated (Scheme 106).



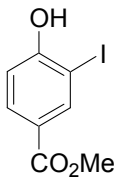
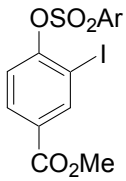

**Scheme 106:** Testing of the leaving group properties in **149a** and **150a**.

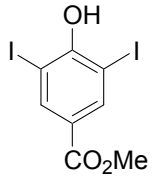
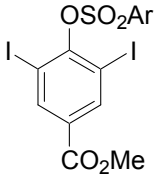
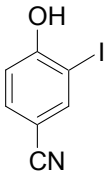
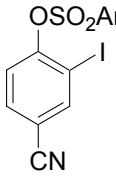
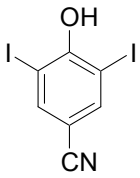
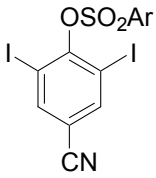
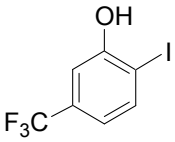
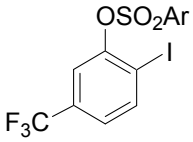
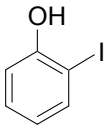
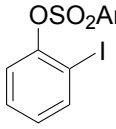
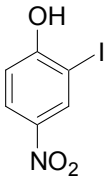
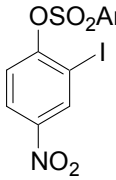
Both reactions gave comparable isolated yields at −10 °C furnishing product **140d** in 85% and 81% yield, respectively. However, the 4-chlorophenylsulfonate **149a** led to the desired product in 89% yield at room temperature, while compound **150a** decomposed faster, leading to product **141d** in only 75% yield. This result can be explained by a faster benzyne formation at ambient temperature for **150a**, which led in this case to unselective side reactions. In strong contrast, compound **149a** formed benzyne rapidly enough to react with furan (**140**) in a [4+2] cycloaddition without giving rise to side reactions.

With these results in hand, establishing the best leaving group for our purpose, the functional group tolerance of the transformation was studied. Several functionalized 2-iodophenols were synthesized according to the procedure mentioned above and converted to the 4-chlorophenyl sulfonates **149** (Scheme 107).




**Scheme 107 and Table 18:** Synthesis of functionalized 4-chlorophenylsulfonates **149**.

| Entry | Iodination Products | Yield (%) | Product **149** | Yield (%) |
|---|---|---|---|---|
| 1 |  **145c** | 56 |  **149a** | 99 |

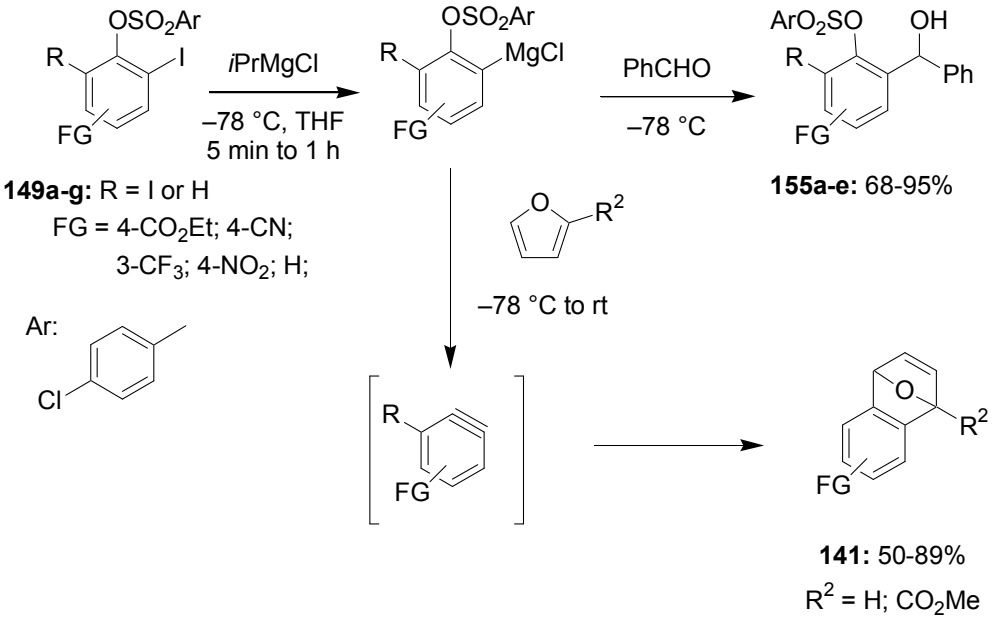
| Entry | Iodination Products | Yield (%) | Product **149** | Yield (%) |
|---|---|---|---|---|
| 2 |  **146b** | 20 |  **149b** | 95 |
| 3 |  **145b** | 62 |  **149c** | 78 |
| 4 |  **146a** | 19[a] |  **149d** | 81 |
| 5 |  **145d** | 86 |  **149e** | 91 |
| 6 |  | --[a] |  **149f** | 93 |
| 7 |  **69** | 60 |  **149g** | 92 |

[a] commercially available; Ar: 4-Cl-$C_6H_4$-

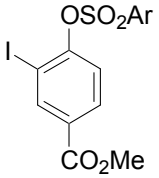
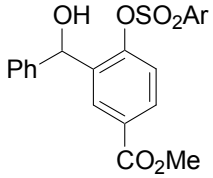
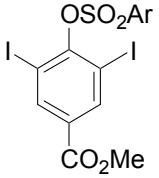
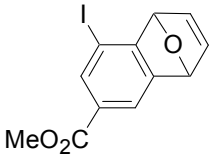
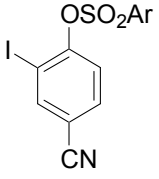
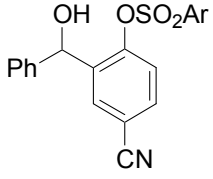
A selective monoiodination was only possible for the *meta*-$CF_3$ substituted substrate leading to **145d** in good yield. For all other compounds, mono- **145** and diiodinated **146** products were obtained, which were separated by column chromatography. Protection of the iodophenols generally worked very well, and furnished the desired 4-chlorophenylsulfonates **149** in good to excellent yields (Table 18).

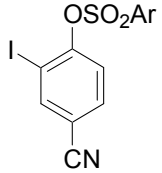
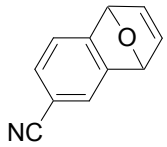
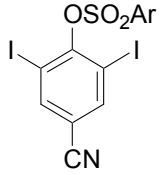
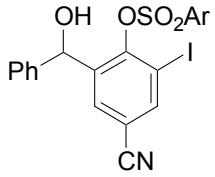
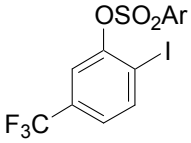
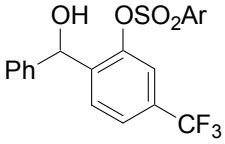
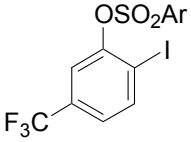
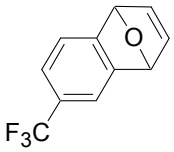
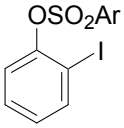
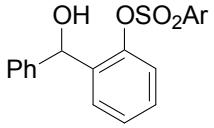
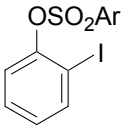
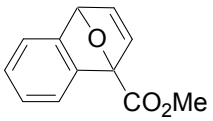
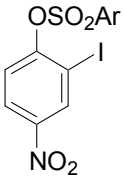
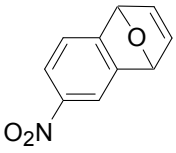
In all cases a selective I/Mg exchange reaction was possible, allowing subsequent reaction with benzaldehyde **22** at −78 °C. The benzylic alcohols **155** were isolated in good to excellent yields. Additionally, increasing the temperature and addition of furan derivatives

led to the cycloaddition products, which were isolated in good yields (Scheme 108 and Table 19).




**Scheme 108 and Table 19:** I/Mg exchange reaction on compounds **149** and reaction with benzaldehyde (**22**) and [4+2] cycloaddition with furan derivatives furnishing compounds of type **155** and **141**.

| Entry | Compound **149** | Reagents and Conditions | Product **155** or **141** | Yield (%) |
|---|---|---|---|---|
| 1 |  **149a** | 1) *i*PrMgCl<br>30 min, −78 °C<br>2) PhCHO, −78 °C<br>1 h |  **155a** | 93 |
| 2 |  **149b** | 1) *i*PrMgCl<br>30 min, −78 °C<br>2) furan, −78 °C to rt<br>4 h |  **141e** | 71 |
| 3 |  **149c** | 1) *i*PrMgCl<br>15 min, −78 °C<br>2) PhCHO, −78 °C<br>1 h |  **155b** | 95 |

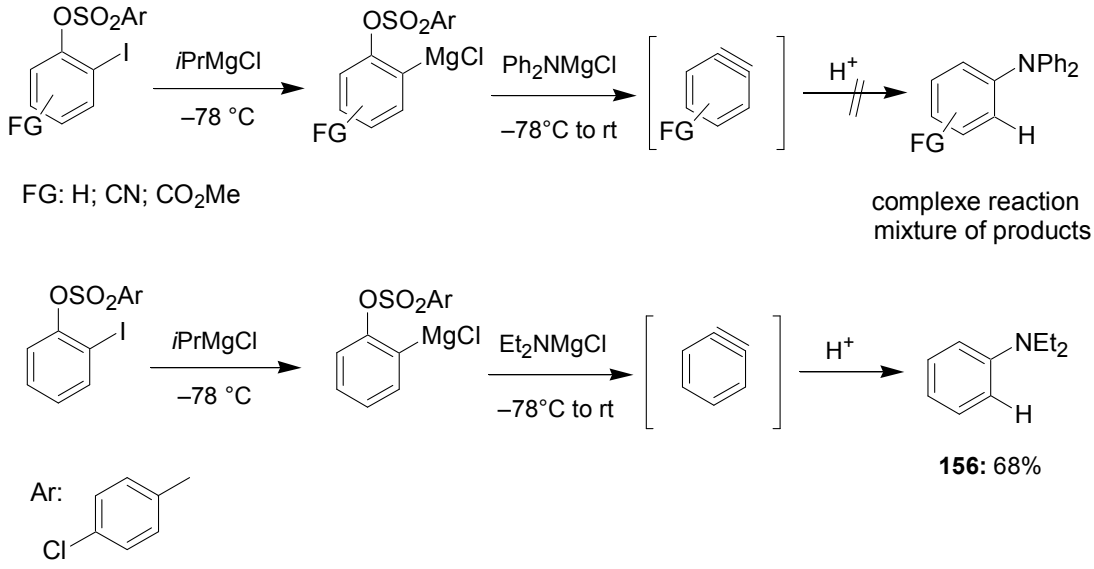
| Entry | Compound **149** | Reagents and Conditions | Product **155** or **141** | Yield (%) |
|---|---|---|---|---|
| 4 |  **149c** | 1) *i*PrMgCl 15 min, −78 °C 2) furan, −78 °C to rt 6 h |  **141c** | 78 |
| 5 |  **149d** | 1) *i*PrMgCl 15 min, −78 °C 2) PhCHO, −78 °C 1 h |  **155c** | 68 |
| 6 |  **149e** | 1) *i*PrMgCl 30 min, −78 °C 2) PhCHO, −78 °C 1 h |  **155d** | 91 |
| 7 |  **149e** | 1) *i*PrMgCl 30 min, −78 °C 2) furan, −78 °C to rt 5 h |  **141f** | 75 |
| 8 |  **149f** | 1) *i*PrMgCl 1 h, −78 °C 2) PhCHO, −78 °C 1 h |  **155e** | 95 |
| 9 |  **149f** | 1) *i*PrMgCl 30 min, −78 °C 2) methyl-2furoate, −78 °C to rt 12 h |  **141g** | 50 |
| 10 |  **149g** | 1) PhMgCl 10 min, −78 °C 2) furan, −78 °C to rt 12 h |  **141h** | 78 |

Thus, the iodine-magnesium exchange reaction was remarkably fast at −78 °C, leading to the functionalized Grignard reagents within 10 to 30 min. These Grignard reagents reacted very well with benzaldehyde (**22**), furnishing the desired products in 68-95% yield (entries 1, 3, 5, 6 and 8, Table 19). The addition of furan and subsequent warming to ambient

temperature led to a fast and selective formation of benzyne, which gave rise to the cycloaddition products in good yields (entries 2, 4 and 7). Remarkably, by using phenylmagnesium chloride, a nitro group was also tolerated, leading to nitro-functionalized benzyne at higher temperatures without any significant addition to the nitro group. Thus, compound **141h** was isolated in 78% yield (entry 10). Other furan derivatives, such as methyl 2-furoate underwent a cycloaddition reaction as well, delivering compound **141g** in moderate yield (entry 9). The reactivity of methyl 2-furoate is significantly lower compared with furan, thus, giving rise to side reactions of benzyne again.

With these optimized reaction conditions, the initial idea of a very reactive electrophile, which should facilitate the addition of less reactive nucleophiles, such as a diarylamides, was investigated again.

Magnesium diphenylamide did not react under these reaction conditions, leading to complicated mixtures of oligomerization products of benzyne (Scheme 109). However, to prove that the initial idea was correct, other more reactive nitrogen nucleophiles were used, and the addition of magnesium diethylamide furnished *N,N*-diethylaniline (**156**) in 68% yield. GC and GC-MS analysis of the reaction mixture indicated side products, 2-phenyl-diethylanline and 2-biphenyl-diethylaniline, which arose from another addition of the formed Grignard reagent to a molecule of benzyne.




**Scheme 109:** Attempts for the synthesis of triarylamines.

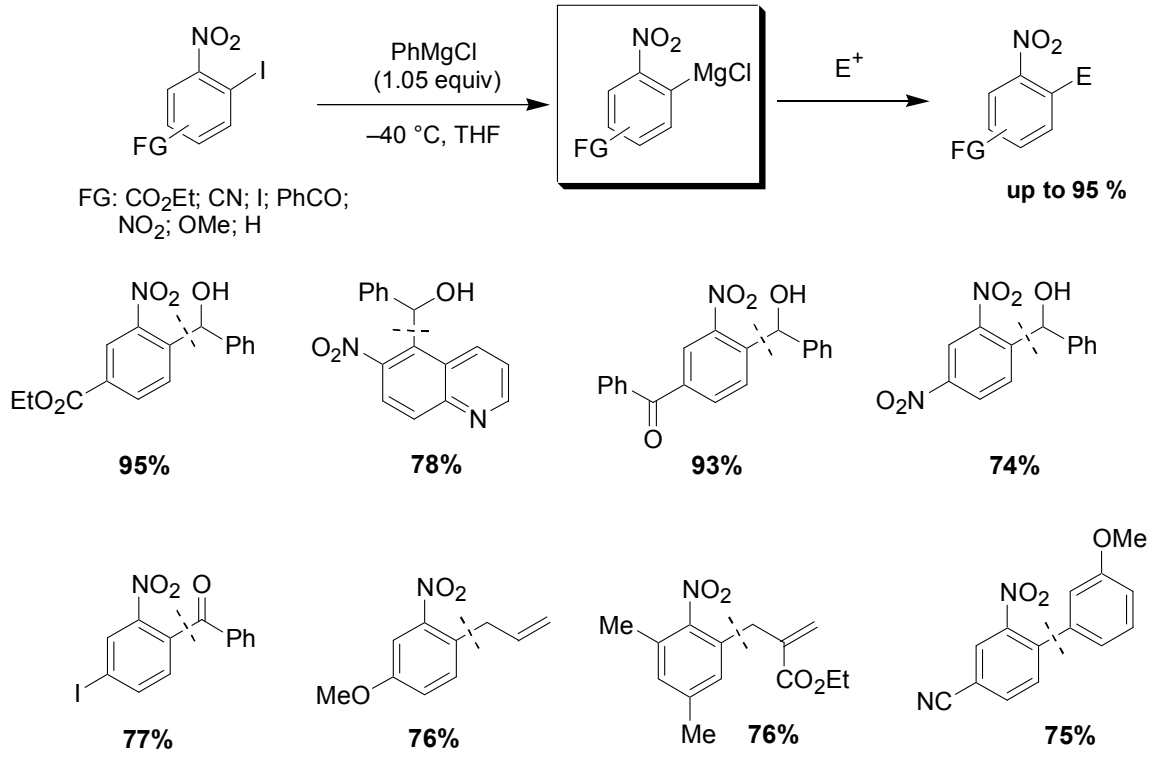
Despite the failed attempts, for the synthesis of triarylamines, this new method for the formation of functionalized benzynes through an I/Mg exchange reaction is very mild and shows a remarkable functional group tolerance.

# 7. Summary and Outlook

This work focused on the formation of new functionalized Grignard reagents using a low-temperature iodine-magnesium exchange reaction. Furthermore, novel amination reactions were developed.

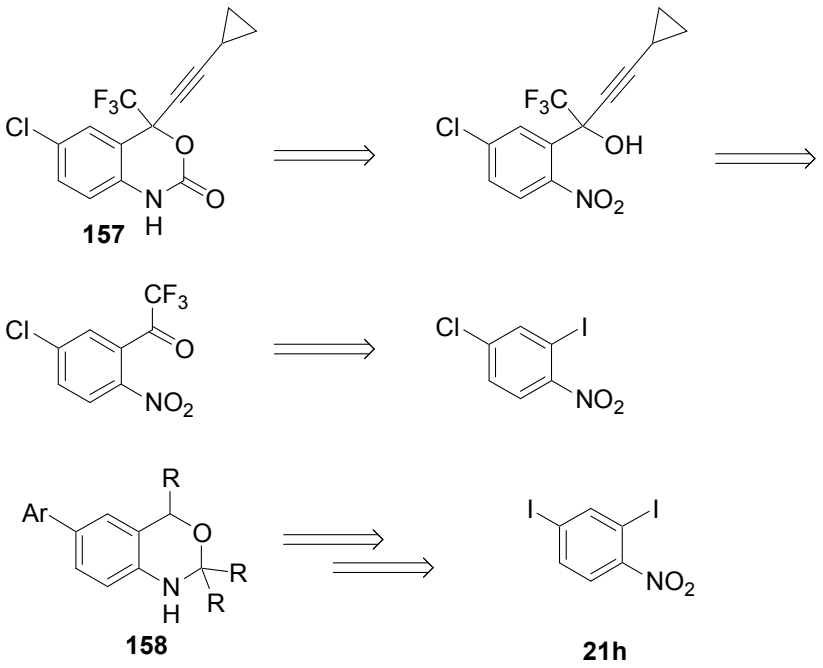
## 7.1 Synthesis of *ortho*-Nitro-Functionalized Aryl and Heteroaryl Grignard Reagents

In the first project, the preparation of new nitro-functionalized aromatic and heteroaromatic Grignard reagents, bearing a variety of different functional groups was described. These reagents were reacted with several aldehydes in good yields. Transmetalation to copper or zinc enabled transition-metal catalyzed or -mediated transformations (Scheme 110).




**Scheme 110:** Synthesis and reaction of functionalized *ortho*-nitroarylmagnesium halides.

As an extension, the application to several interesting target molecules could be investigated. For example, several analogues of Efavirenz **157**,[114] a HIV-1 reverse transcriptase inhibitor, should be accessible with this method without the use of protecting groups (Scheme 110).

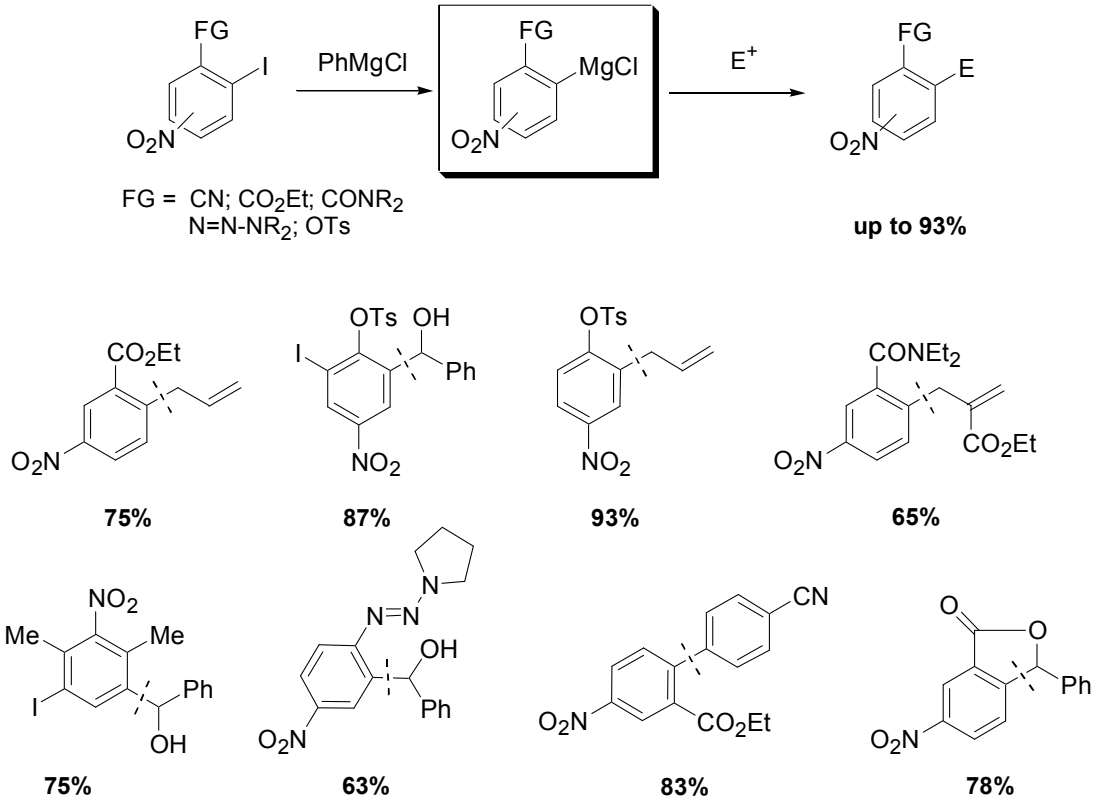



**Scheme 111:** Retrosynthetic analysis of Evafirenz **157** and compound **158**.

The same holds true for the synthesis of 6-aryl benzoxazines **158**,[115] which proved to be a very potent progesterone receptor agonists. Here, compound **21h** could be used as building block for library synthesis.

## 7.2 Synthesis of *meta* and *para*-Nitro-Functionalized Aryl Grignard Reagents

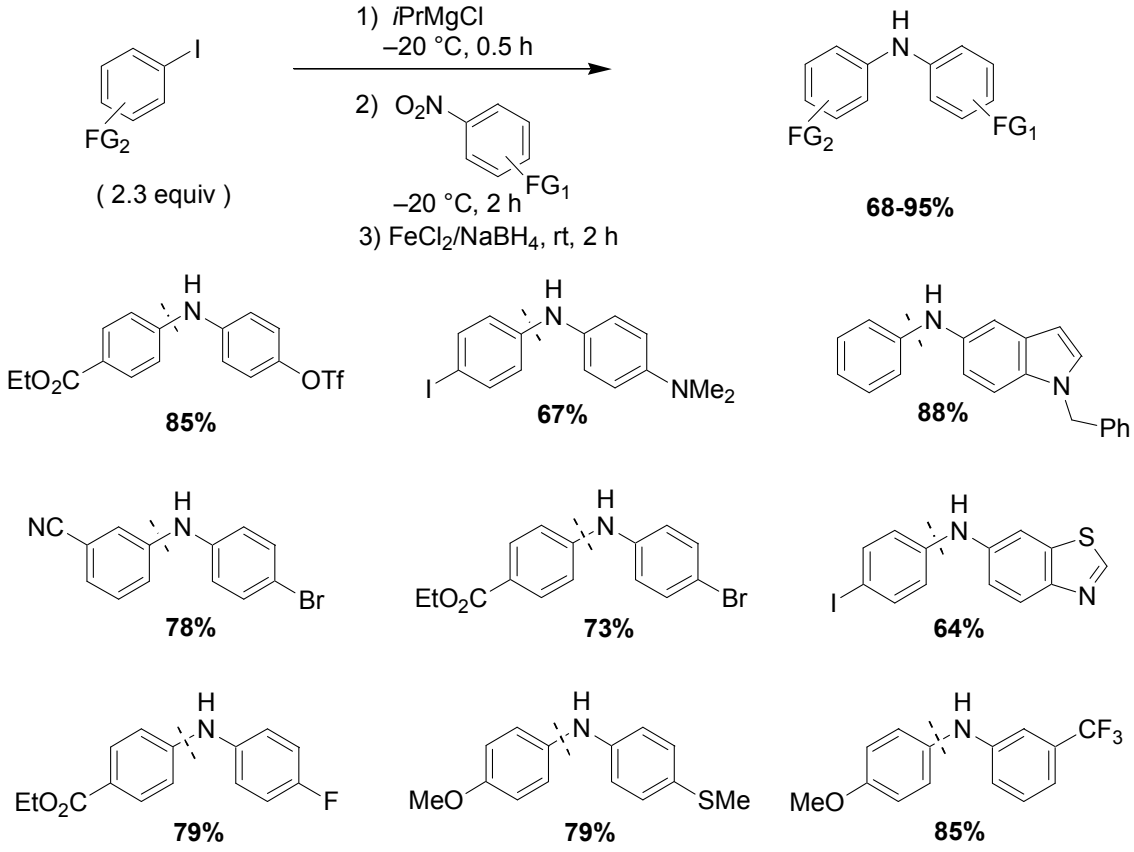
The incorporation of chelating functional groups and sterically encumbered substituents allowed for the first time the formation of *meta*- and *para*-nitro-substituted arylmagnesium halides. The use of these compounds in transition-metal catalyzed reactions, after transmetalation, was also presented (Scheme 112).




**Scheme 112**: Synthesis and reaction of functionalized *meta*- and *para*-nitroarylmagnesium halides.

## 7.3 Synthesis of Diarylamines using Nitroarenes and Aromatic Grignard Reagents

As a result of careful side reaction observation and optimization, a new potent one-pot synthesis of highly functionalized diarylamines using functionalized Grignard reagents and nitroarenes was developed (Scheme 113).

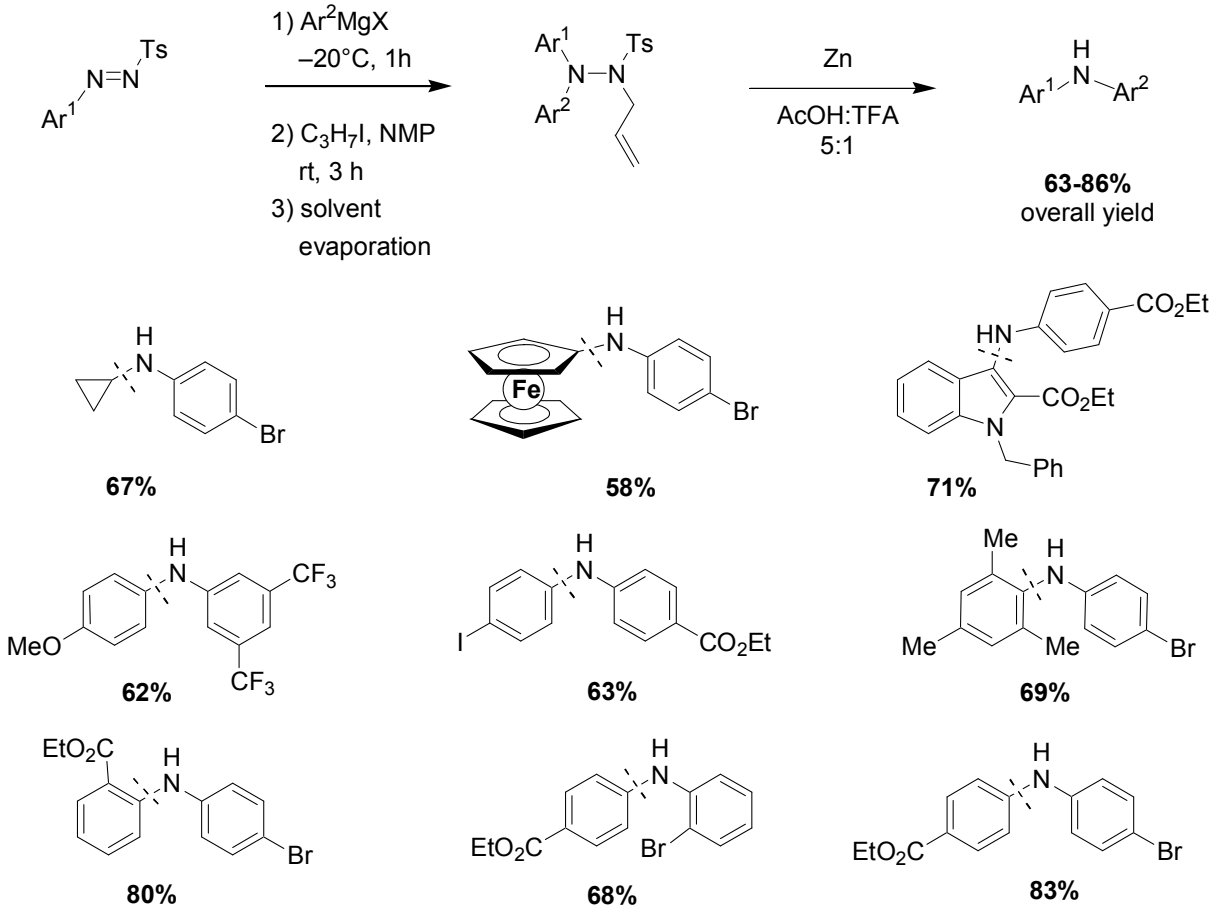



**Scheme 113:** Synthesis of diarylamines using nitroarenes and heteroarenes and aromatic Grignard reagents.

This method is complementary to known amination procedures, starting from a new substrate class and, therefore, allows an access to a new class of substances not yet synthesized by common amination procedures. Additionally, an excellent compatibility with halogens and sulfoxide-substituents, is observed. Further applications of this method as a powerful lever in combinatorial synthesis of this interesting substance class can be envisioned, and Aventis Pharma have already explored this potential.

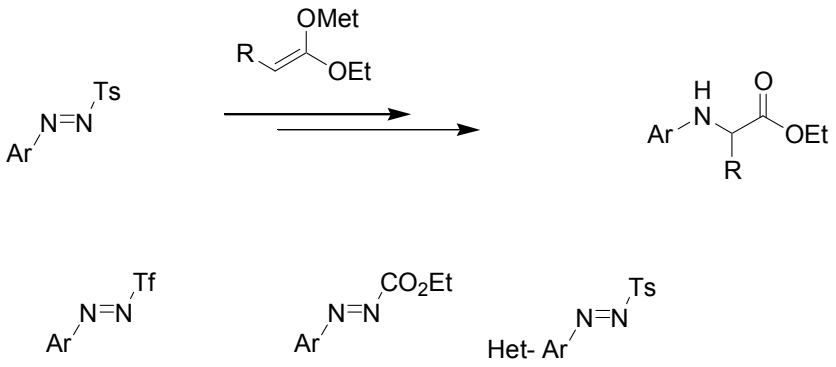
## 7.4 Synthesis of Diarylamines and Alkylarylamines using Aryltolylazo Sulfones and Aromatic Grignard Reagents

Moreover, another new amination procedure, starting from anilines, was developed. This method allows the use of a variety of carbon nucleophiles, which readily add to aryl tolylazo sulfones in good yields. Selective N-N bond cleavage of the intermediately formed hydrazines furnishes the aniline derivatives in good yields (Scheme 114).




**Scheme 114:** Synthesis of diarylamines and alkyl-arylamines using aryltolylazo sulfones and aromatic Grignard reagents.

This method should allow the addition of any carbon nucleophile and therefore a variety of different organometallic species should be applicable. For example, the addition of esterenolates should furnish *N*-aryl amino acids, which show interesting biological activities (Scheme 115).

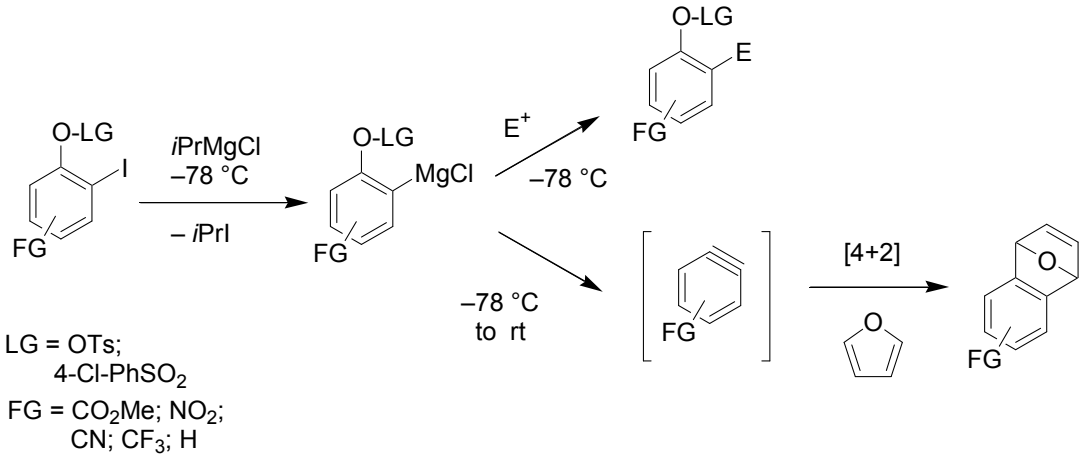



**Scheme 115:** Further applications of arylazo sulfones as arylamine synthons.

Furthermore, this method should be extended to heterocyclic azo sulfones and the introduction of other sulfonates in order to find milder cleavage conditions, should be investigated.

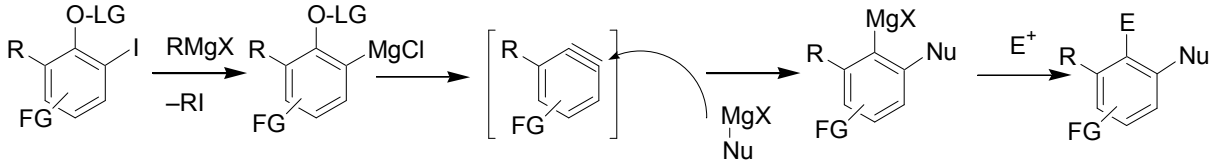
## 7.5 Generation of Highly Functionalized Benzynes

Finally, the iodine-magnesium exchange was applied to the synthesis of highly functionalized benzynes. The leaving group abilities of several sulfonates were studied and allowed either a reaction of the Grignard reagent at low temperature or, at higher temperatures, a generation of the benzyne (Scheme 116).




**Scheme 116:** Selective generation of functionalized benzynes.

This method opens a range of possible new applications in carbon-carbon and carbon-heteroatom bond formation reactions. These applications should be investigated in more detail. The unique possibility to further functionalize the precursors gives this method an advantage over other benzyne formation reactions and increases the diversification potential (Scheme 117).




**Scheme 117:** Applications of benzynes in new carbon-carbon and carbon-heteroatom bond formations.

Several promising results were already obtained by W. Lin, who showed that the addition of magnesium thiolates leads to the formation of new carbon-sulfur and carbon-magnesium bonds, which could be further functionalized.
A careful mechanistic study of the formation of benzyne should allow an optimisation of the reaction conditions and is therefore desirable. A cooperation with A. Streiter and Prof. Mayr was initiated to address this issue.

# EXPERIMENTAL PART

# 8. General Conditions

All reactions were carried out with magnetic stirring and, if air or moisture sensitive, in flame-dried glassware under argon. Syringes which were used to transfer reagents and solvents were purged with argon prior to use.

## Solvents

Solvents were dried according to standard methods by distillation over drying agents as stated below and were stored under argon.

**$CH_2Cl_2$** was predried over calcium chloride and was distilled from calcium hydride.

**Dimethylformamide** (**DMF**) was heated to refluxed for 14 h over calcium hydride and distilled of.

**Ethanol** was treated with Phthalic anhydride (25 g/L) and sodium, heated to reflux for 6 h and distilled.

**Methanol** was treated with magnesium turnings (20 g/L), refluxed for 6 h and distilled of.

***N*-Methylpyrrolidinone** (**NMP**) was refluxed for 6 h over calcium hydride and distilled.

**Pyridine** was dried over potassium hydroxide and distilled.

**Toluene** was predried over calcium chloride and was distilled from calcium hydride.

**Tetrahydrofuran** (**THF**) was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen.

## Reagents

Reagents of >98 % purity were used as obtained.

***i*PrMgCl**: A dried, three-necked flask equipped with an argon inlet, a dropping funnel and a thermometer was charged with magnesium turnings (Fluka) (3.7 g, 150 mmol). A small amount of THF was added to cover the magnesium, and isopropyl chloride (7.95 g, 100 mmol) in THF (100 mL) was added dropwise, keeping the temperature of the mixture below 30 °C (water bath). After the addition was complete the reaction mixture was stirred at rt for 10 h. The excess magnesium was removed by filtration. Yields between 90 and 95% were obtained.

**4-Methoxyphenylmagnesium bromide** and **mesitylmagnesium bromide** were prepared according to this procedure from the corresponding bromides.

**CuCN·2LiCl** solution (1 M) was prepared by drying CuCN (869 mg, 10 mmol) and LiCl (848 mg, 20 mmol) in a Schlenk flask under vacuum for 5 h at 120 °C. After cooling to rt, dry THF (10 mL) was added and stirring was continued until the salts were dissolved.

**Diisopropylamine** was stirred for 12 h over calcium hydride and distilled.

**$ZnBr_2$** solution (1 M) was prepared by drying $ZnBr_2$ (33.78 g, 150 mmol) under vacuum for 5 h at 150 °C. After cooling to rt, dry THF (150 mL) was added and stirring was continued until the salts were dissolved.

***n*-Butyllithium** was used as 1.5 M solution in hexane purchased by Chemetall.

**Phenylmagnesium chloride** was used as 2 M solution in THF purchased by Chemetall.

**Methylmagnesium chloride** was used as 3 M solution in THF purchased by Chemetall.

The following reagents were prepared according to literature procedures:

ethyl 2-(bromomethyl) acrylate,[65] palladium(II)bis(dibenzylidenacetone),[116] *tris*-o-furylphosphine,[117] 3-iodo-2-methyl-2-cyclopentenone,[118] *n*hexylzinc,[119]tri-*n*-butyltinferrocen,[106] 4-nitropyridine,[120] allyl-5-nitro-1H-indazole.[121]

## Content determination of organometallic reagent

Organolithium and organomagnesium solutions were titrated using the method of Paquette prior to use.[122]
The concentrations of organozinc solutions were determined by back titration of iodine with an aqueous $Na_2S_2O_3$ solution.

## Chromatography

Thin layer chromatography (TLC) was performed using aluminium plates covered with $SiO_2$ (Merck 60, F-254). Spots were visualized under UV light and /or by staining of the TLC plate with one of the solutions below followed by heating with a heat gun:

- $KMnO_4$ (0.3 g), $K_2CO_3$(20 g), KOH (0.3 g) in water (300 mL).
- Phosphormolybdic acid (5.0 g), $Ce(SO_4)_2$ (2.0 g), conc. $H_2SO_4$ (12 mL) in water (230 mL).

Flash column chromatography was performed using $SiO_2$ 60 (0.040-0.063 mm, 230-400 mesh ASTM) from Merck. The diameters of the columns and the amount of silicagel were calculated according to the recommendations of W. C. Still.[123]

## Analytical data

**NMR** spectra were recorded on Brucker ARX 200, AC 300, WH 400 or AMX 600 instruments. Chemical shifts are reported as δ-values in ppm relative to the deuterated solvent peak: $CDCl_3$ ($\delta_H$: 7.25, $\delta_C$: 77.0), $C_6D_6$ ($\delta_H$: 7.15, $\delta_C$: 128.0), DMSO-$d_6$ ($\delta_H$: 2.50, $\delta_C$: 39.4), acetone-$d_6$ ($\delta_H$: 2.04, $\delta_C$: 29.3). For the characterization of the observed signal multiplicities the following abbreviations were applied: s (singlet), d (doublet), dd (double doublet), dt (double triplet), t (triplet), q (quartet), quint (quintet), m (multiplet), as well as br (broad).

**Melting points** are uncorrected and were measured on a Büchi B-540 apparatus.

**Infrared** spectra were recorded from 4000–400 $cm^{-1}$ on a Nicolet 510 FT-IR or a Perkin-Elmer 281 IR spectrometer. Samples were measured either as a film between potassium bromide (KBr) plates or (for solids) as potassium bromide (KBr) tablets. The absorption bands are reported in wave numbers ($cm^{-1}$). For the band characterization the following abbreviations were applied: br (broad), s (strong), m (medium), vs (very strong), w (weak).

**Gas chromatography** (GC) was performed using a Hewlett-Packard 6890 or 5890 Series II.

- Column A: 5 % phenylmethylpolysiloxane (HP Ultra 2) 12 m x 0.2 mm
- Column B: 5 % phenylmethylpolysiloxane (HP %) 5 m x 0.25 mm

The compounds were detected with a flame ionisation detector.

**Mass spectroscopy**: Mass spectra were recorded on a Finnigan MAT 95Q or Finnigan Mat 90 instrument for electron impact ionisation (EI). High resolution mass spectra (HRMS) were recorded on the same instruments instrument. Fast atom bombardment (FAB) samples were recorded in either a 2-nitrobenzyl alcohol- or glycerine-matrix. Additionally, for the combination of gas chromatography with mass spectroscopic detection, a GC/MS from Hewlett-Packard HP 6890/MSD 5973 was used.

- Column C: 5% phenylmethylpolysiloxane (HP 5) 30m x 250 µm x 0.25 µm

**Elemental analysis** was carried out on a Heraeus CHN-Rapid-Elementanalyzer in the microanalytical laboratories of the Department Chemie und Pharmazie, Ludwig-Maximilians Universität, Munich.

**High Performance Liquid Chromatography (HPLC)** was performed using a Gynkotec-HPLC with a diode-array detector (DAD) 215-280 nm. Reverse phase column RP-18 (125 mm x 3 mm) from Fa. Macherey & Nagel. Eluent: acetonitrile/water (0.1% TFA). Gradient: 5-100% acetonitrile in 20 min with a flow of 0.8 mL/min.

# 9. Typical procedures (TP)

## 9.1 Typical procedure for the nitration of arenes (TP 1)

A cold mixture of 1.9 mL nitric acid ($HNO_3$, 100%) and 2.7 mL sulfuric acid ($H_2SO_4$, 100%) was added slowly to a solution of the corresponding arene (10 mmol) dissolved in 5 mL sulphuric acid ($H_2SO_4$, 100%) within 30 min with vigorous stirring. Upon completion of the addition the solution was allowed to warm to ambient temperature and stirring was continued for 5 h and poured crushed ice (100 g). The solid was filtrated taken up in ethyl acetate (100 mL) and washed with saturated $NaHCO_{3(aq.)}$ (100 mL), dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. Recrystallization from ethanol yielded the pure product.

## 9.2 Typical procedure for the iodination of arenes using silver sulfate (TP 2)[61]

A 250 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with iodine (5.08 g, 20.0 mmol) and silver sulfate (6.23 g, 20.0 mmol) in ethanol (100 mL). The aromatic compound (20 mmol) was then added and the mixture was stirred vigorously at rt until tlc analysis indicated complete conversion (typically 30min-2 h). The reaction mixture was filtered through a glass sinter, the solids on the sinter were washed with ethyl acetate (2 x 100 mL) and the filtrate was concentrated *in vacuo*. The residue was taken up in $CH_2Cl_2$ (100 mL), washed with 2 M NaOH (100 mL), water (100 mL), dried over $Na_2SO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel furnished the product.

## 9.3 Typical procedure for the performance of an iodine-magnesium exchange reaction on functionalised *o*-iodonitroarenes (TP 3)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with the *o*-iodo-nitrobenzene (2 mmol). Dry THF (5 mL) was added, the mixture cooled to −40 °C and PhMgCl (2.2 mmol, solution in THF) was then added dropwise. The I/Mg exchange was usually complete after 5 min (checked by GC analysis of reaction aliquots) and if necessary CuCN·2LiCl (2 mL, 1.0 M in THF) was added prior to the addition of the electrophile. The reaction mixture was stirred for 30 min at −40 °C, the cooling bath was removed and the mixture stirred for additional 30 min at room temperature. The reaction mixture was quenched with saturated $NH_4Cl_{(aq)}$ (2 mL) and poured into water (25 mL). The aqueous phase was extracted with ethyl acetate (2 x 40 mL), the collected organic phases were washed with brine (30 mL), dried over $Na_2SO_4$ and concentrated *in vacuo*. Purification by flash chromatography furnished the product.

## 9.4 Typical procedure for the preparation of nitro-substituted polyfunctional biphenyls by Negishi cross-coupling of *o*-nitroarylzinc reagents (TP 4)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with the 2-iodonitroarene (1.00 mmol). Dry THF (5 mL) was added, the mixture cooled to −40 °C and mesitylmagnesium bromide (1.6 mL, 1.1 mmol, 0.70 M in THF) was added dropwise. The I/Mg exchange was complete after 15 min (checked by GC analysis of reaction aliquots) and zinc bromide (1.1 mL, 1.1 mmol, 1.0 M in THF) was added to the magnesiated nitroarene. Another dry two-necked flask equipped with a magnetic stirrer and

a septum was charged with *bis*-(dibenzylideneacetone)palladium(0) ($Pd(dba)_2$) (29 mg, 5 mol %) and *tris*-*o*-furylphosphine (tfp) (25 mg, 10 mol %) followed by THF (2 mL). The initial red colour disappeared after 2 min leading to a yellow solution and haloarene (1.5 mmol) was added. This solution was added *via cannula* after 10 min of stirring to the reaction mixture at −40 °C and the cooling bath was removed. The reaction was stirred for 5 h at room temperature, treated with ethanol (2 mL) and poured into water (25 mL). The aqueous phase was extracted with ethyl acetate (3 x 40 mL), the collected organic phases were washed with brine (30 mL), dried over $Na_2SO_4$ and concentrated *in vacuo*. Purification by flash chromatography furnished the product.

## 9.5 Typical procedure for the performance of an iodine-magnesium exchange reaction on functionalised *m*- and *p*-iodonitroarenes (TP 5)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with the *m*- or *p*-iodo-nitrobenzene (1 mmol). Dry THF (5 mL) was added, the mixture cooled to −78 °C and PhMgCl (1.1 mmol, solution in THF) was then added dropwise. The I/Mg exchange was usually complete after 30 min (checked by GC analysis of reaction aliquots) and if necessary CuCN·2LiCl (2 mL, 1.0 M in THF)was added prior to the addition of the electrophile. The reaction mixture was stirred for 30 min at −78 °C, the cooling bath was removed and the mixture stirred for additional 30 min at ambient temperature. The reaction mixture was quenched with saturated $NH_4Cl_{(aq)}$ (2 mL) and poured into water (25 mL). The aqueous phase was extracted with ethyl acetate (2 x 40 mL), the collected organic phases were washed with brine (30 mL), dried over $Na_2SO_4$ and concentrated *in vacuo*. Purification by flash chromatography furnished the product.

## 9.6 Typical procedure for the preparation of nitro-substituted polyfunctional biphenyls by Negishi cross-coupling of *m*- and *p*-nitroarylzinc reagents (TP 6)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with *m*- or *p*-iodonitrobenzene (1.0 mmol). Dry THF (5 mL) was added, the mixture cooled to −78 °C and PhMgCl (0.65 mL, 1.05 mmol, solution in THF) was added dropwise. The I/Mg exchange was complete after 10 min (checked by GC analysis of reaction aliquots) and zinc bromide (1.1 mL, 1.1 mmol, 1.0 M in THF) was added to the magnesiated benzoate at −78 °C. Another dry two-necked flask equipped with a magnetic stirrer and a septum was charged with *bis*-(dibenzylideneacetone)palladium(0) ($Pd(dba)_2$) (29 mg, 5 mol %) and *tris*-*o*-furylphosphine (tfp) (25 mg, 10 mol %) followed by THF (2 mL). The initial red colour disappeared after 2 min leading to a yellow solution and the iodobenzene (2 mmol) was added. This solution was added *via cannula* after 10 min of stirring to the reaction mixture at −78 °C and the cooling bath was removed. The reaction mixture was stirred for 2 h at room temperature, treated with ethanol (2 mL) and poured into water (25 mL). The aqueous phase was extracted with ethyl acetate (3 x 40 mL), the collected organic phases were washed with brine (30 mL), dried over $Na_2SO_4$ and concentrated *in vacuo*. Purification by flash chromatography furnished the product.

## 9.7 Typical procedure for the reductive amination of nitroarenes with functionalized arylmagnesium halides (TP 7)

In a dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, the aryl halide (3.5 mmol) was dissolved in dry THF (8 mL), cooled to −20 °C and *i*PrMgCl (3.6 mmol, solution in THF) was added dropwise. The I/Mg exchange was complete after 30 min (indicated by GC analyses of reaction aliquots) and the functionalized nitrobenzene (1.5 mmol) was added. After 2 h of stirring at –20 °C, the reaction mixture was quenched with ethanol (1 mL), $FeCl_2$ (3 mmol) and $NaBH_4$ (1.5 mmol) were added and stirring was continued for 2 h at room temperature. The reaction mixture was poured into water (25 mL), the aqueous phase was extracted with diethyl ether (3 x 40 mL) and the organic fractions were washed with successively with 2 M NaOH solution (30 mL), brine (30 mL), dried over $Na_2SO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel furnished the product.

## 9.8 Typical procedure for the preparation of arylazo sulfonates (TP 8)

A 50 mL round bottom flask, equipped with a magnetic stirring bar and a dropping funnel, was charged with the aniline (10.0 mmol), dissolved in 15 mL of aq. $HBF_4$-solution (50 %), cooled to 0 °C and a solution of $NaNO_2$ (760 mg, 11 mmol) in water (5 mL) was added dropwise. After 30 min of stirring, the reaction mixture was allowed to warm to room temperature and was stirred for an additional hour. The white precipitate was filtered off and washed subsequently with aq. $HBF_4$-solution (10 mL), ethanol (10 mL) and diethyl ether (20 mL). The white crystalline powder was suspended in $CH_2Cl_2$ without further purification or drying, sodium 4-toluenesulfinic acid (NaTs) (2.14 g, 12.0 mmol) was added and the reaction mixture was stirred overnight. The salts were removed by filtration and the crude reaction mixture was concentrated *in vacuo*. Recrystallization from ethanol yielded the desired arylazo sulfon.

## 9.9 Typical procedure for the preparation of arylamines using arylazosulfones (TP 9)

A dry and argon flushed 25 mL round bottom flask equipped with a magnetic stirrer and a septum was charged with iodoarene (1.10 mmol) dissolved in dry THF (5 mL) and cooled to −20 °C. *i*PrMgCl (1.10 mmol, solution in THF) was added dropwise and the I/Mg-exchange was checked by GC analysis of reaction aliquots until completion (30 min). Afterwards the arylazo sulfone (1.00 mmol) was dissolved in THF (3 mL) and added dropwise to the Grignard reagent. After 1 h of stirring at −20 °C, the reaction mixture was treated with allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) and stirred for additional 2 h at room temperature. The solvents were removed in vacuo and the residue taken up in of glacial acetic acid (10 mL). Zinc powder (10 mmol) and TFA (2 mL) were added and the reaction mixture was heated to 75 °C until no starting material was observed by TLC-analysis (2-16 h). The reaction mixture was allowed to cool to room temperature and was poured on crushed ice (ca. 30 g) and 20 mL of 2 M NaOH. The aqueous phase was extracted with diethyl ether (3 x 30 mL) and the combined organic phases were washed with saturated $NaHCO_{3(aq)}$ and brine successively. The organic phases were dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. Flash chromatography on silica gel furnished the product.

## 9.10 Typical procedure for the reductive amination of nitroarenes with functionalized arylmagnesium halides (TP 10)

In a dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, the aryl halide (3.5 mmol) was dissolved in dry THF (8 mL), cooled to −20 °C and *i*PrMgCl (3.6 mmol, solution in THF) was added dropwise. The I/Mg exchange was complete after 30 min (indicated by GC analyses of reaction aliquots) and the functionalized nitrobenzene (1.5 mmol) was added. After 2 h of stirring at –20 °C, the reaction mixture was quenched with ethanol (1 mL), $FeCl_2$ (3 mmol) and $NaBH_4$ (1.5 mmol) were added and stirring was continued for 2 h at room temperature. The reaction mixture was poured into water (25 mL), the aqueous phase was extracted with diethyl ether (3 x 40 mL) and the organic fractions were washed with successively with 2 M NaOH solution (30 mL), brine (30 mL), dried over $Na_2SO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel furnished the product.

## 9.11 Typical procedure for loading on resin (TP 11)

In a cap-glass, Wang resin (2.0 g, 1.5 mmol) was suspended in DMF (20 mL) and the corresponding carboxylic acid (15 mmol), DIC (947 mg, 7.5 mmol), and DMAP (183 mg, 1.5 mmol) were added subsequently. The mixture was shook overnight, the resin filtered and washed 3 times with THF, DMF and MeOH (20 mL of each solvent). After this careful washing the resin was washed again with $CH_2Cl_2$ (3x20 mL) and dried in an oven at 55 C overnight. Loading and HPLC purity of the resin were determined by cleaving of 50 mg of resin according to TP 2.10 with TFA/$CH_2Cl_2$/$H_2O$=9:1:1 mixture (20 min).

## 9.12 Typical procedure for the cleavage of resin bond derivatives from Wang-Resin (TP 12)

A 2 ml syringe with filter inlet was charged with resin and a mixture of TFA/ $CH_2Cl_2$/$H_2O$=9:1:1 was added (1-1.5 mL) and the mixture was shaken for 30 min at rt. The solution was filtered in a 10 mL round-bottom flask and the resin was washed with $CH_2Cl_2$ (3x1 mL). The solvent was evaporated *in vacuo* and afterwards at 50 C for several hours on the high-vacuum and yield was determined.

## 9.13 Typical procedure for the reductive amination of polymer attached nitroarenes with functionalized arylmagnesium halides (TP 13)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with resin (0.15 mmol), dry THF (8 mL) was added and the suspension cooled to −20 °C. The arylmagnesium reagent (1.5 mmol) was added dropwise and the reaction mixture was stirred for 2 h at –20 °C. The reaction mixture was quenched with ethanol (2 mL), $FeCl_2$ (1 mmol) and $NaBH_4$ (0.5 mmol) were added and stirring was continued for 4 h at room temperature. The resin was then filtered and washed 3 times with THF, DMF and MeOH (5 mL of each solvent). After this washing the resin was washed again with $CH_2Cl_2$ (3x5 mL) and dried in an oven at 55 C overnight. Cleavage from the resin was performed by treatment with a solution of TFA/$CH_2Cl_2$/$H_2O$=9:1:1 (2 mL) mixture (20 min). Excess TFA was removed under vacuum affording the desired product.

## 9.14 Typical procedure for the formation of alkyl- and aryl-sulfonates from the corresponding phenols (TP 14)

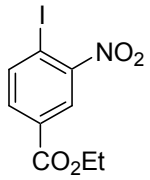
A 100 mL round–bottom flask, equipped with a magnetic stirring bar, was charged with the corresponding phenol (10.0 mmol) and dry pyridine (20 mL) was added. The solution was cooled to 0 °C and the aryl or alkyl sulfonyl chloride (12.0 mmol) was added portionwise. On completion of the addition, the reaction mixture was stirred for additional 15 min at 0 °C and was then allowed to warm to room temperature and was stirred overnight. The reaction mixture was poured onto ice (50 g) and ethyl acetate (100 mL), 2M HCl (30 mL) was added and the phases were separated. The organic phase was washed with 2M HCl (30 mL), saturated $NaHCO_{3(aq)}$ (50 mL), brine (50 mL), dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. Flash chromatography on silica gel furnished the product.

## 9.15 Typical procedure for the generation and trapping of functionalized arynes (TP 15)

A dry and argon-flushed 10 mL Schlenk tube, equipped with a magnetic stirrer and a septum, was charged with a solution of the corresponding precursors (1 mmol) in dry THF (5 mL). *i*PrMgCl (1.05 mmol, solution in THF) was then added dropwise at –78 °C. After 30 min, either furan (0.3 mL, 5 equiv) or an appropriate electrophile (2 equiv) was added slowly at –78 °C, and the resulting mixture was warmed to the desired temperature and stirred for 2 h. Saturated $NH_4Cl_{(aq.)}$-solution was then added, and the resulting mixture was extracted with $CH_2Cl_2$. The organic extracts were dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. Purification by flash chromatography furnished the desired products.

# 10. Preparation of Functionalized Nitroarylmagnesium Halides *via* an Iodine-Magnesium Exchange

## Synthesis of ethyl 4-iodo-3-nitrobenzoate (21d)[124]




Prepared according to **TP 1** from $HNO_3$ (100%, 1.9 mL), $H_2SO_4$ (100%, 2.7 mL) and ethyl 4-iodobenzoate (5.52 g, 20.0 mmol). Recrystallization from ethanol furnished the title compound **21d** as a yellow solid (5.48 g, 86%).

**mp.:** 89 °C (Lit.: 89.5 °C).

**$^1$H-NMR** ($CDCl_3$, 300 MHz, 25 °C): $\delta$ = 8.36 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.06 (d, $^3J$(H,H) = 8.9 Hz 1 H), 7.80 (dd, $^3J$(H,H) = 8.9 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 4.35 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.34 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

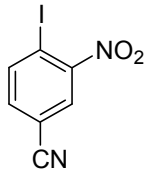
**$^{13}$C-NMR** ($CDCl_3$, 75 MHz, 25 °C): $\delta$ = 164.4, 153.6, 142.7, 133.8, 132.3, 126.3, 92.3, 62.5, 14.6.

**MS** (70 eV, EI), *m/z* (%): 321 (88) [$M^+$], 293 (100), 276 (99), 260 (12), 247 (26), 230 (37), 219 (4), 201 (12), 191 (11), 176 (2), 149 (1), 136 (8), 119 (5), 103 (34), 92 (13), 75 (40), 63 (5), 53 (2).

**IR** (KBr): $\tilde{\nu}$ = 2982 (m), 1708 (vs), 1600 (s), 1561 (m), 1532 (vs), 1469 (s), 1385 (m), 1366 (m), 1341 (vs), 1285 (vs), 1238 (vs), 1158 (s), 1136 (m), 1116 (m), 1018 (s), 916 (w), 864 (w), 854 (m), 834 (m), 768 (m), 743 (s), 727 (m), 658 (w).

**$C_9H_8INO_4$:** required: C: 33.67; H: 2.51; N: 4.36;
found: C: 33.76; H: 2.35; N: 4.33.

## Synthesis of 4-iodo-3-nitrobenzonitrile (21e)




Prepared according to **TP 1** from $HNO_3$ (100%, 0.96 mL), $H_2SO_4$ (100%, 1.4 mL) and 4-iodobenzonitrile (2.30 g, 10.0 mmol). Recrystallization from ethanol furnished the title compound **21e** as a yellow solid (1.84 g, 67%).

**mp.:** 132-133 °C.

**$^1$H-NMR** ($CDCl_3$, 300 MHz, 25 °C): δ = 8.16 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 8.05 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.45 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H).

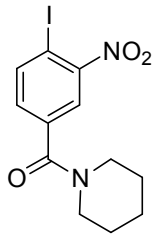
**$^{13}$C-NMR** ($CDCl_3$, 75 MHz, 25 °C): δ = 151.0, 143.7, 135.8, 128.8, 116.4, 114.0, 93.1.

**MS** (70 eV, EI), *m/z* (%): 274 (100) [$M^+$], 258 (2), 228 (50), 216 (6), 127 (5), 117 (12), 101 (31), 75 (7), 50 (10).

**IR** (KBr): $\tilde{\nu}$ = 3091 (w), 3066 (w), 2236 (s), 1597 (m), 1548 (s), 1530 (vs), 1464 (m), 1352 (s), 1264 (w), 1024 (w), 843 (w), 788 (w), 671 (w), 55 (w).

**HRMS** for **$C_7H_3IN_2O_2$** (273.9239): found: 273.9245.

## Synthesis of pyperidino-4-iodo-3-nitro-benzamide (21f)




Prepared according to **TP 1** from $HNO_3$ (100%, 1.9 mL), $H_2SO_4$ (100%, 2.7 mL) pyperidino-4-iodo-benzamide (4.73 g, 15.0 mmol). Recrystallization from ethanol furnished title compound **21f** as colourless solid (4.50 g, 83%).

**mp**.: 155.5-156.5 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 8.06 (d, $^3J$(H,H) = 8.0 Hz, 1 H), 7.86 (d, $^4J$(H,H) = 1.9 Hz, 1 H), 7.27 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.9 Hz, 1 H), 3.67 (s_br, 2 H), 3.31 (s_br, 2 H), 1.72-1.42 (m, 6 H).

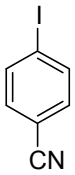
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 166.7, 152.8, 142.1, 137.7, 131.5, 123.9, 87.2, 48.8, 43.4, 26.5, 25.4, 24.3.

**MS** (70 eV, EI), *m/z* (%): 359 (100) [$M^+$], 34 (31), 325 (15), 313 (10), 275 (95), 229 (36), 186 (30), 158 (4), 127 (23), 103 (63), 84 (16), 75 (44).

**IR** (KBr): $\tilde{\nu}$ = 2952 (m), 1608 (vs), 1598 (vs), 1527 (vs), 1443 (m), 1341 (s), 1248 (m), 1021 (m), 1010 (m), 844 (m), 742 (m).

**HRMS** for **$C_{12}H_{13}IN_2O_3$** (359.9971): found: 359.9954.

**Synthesis of 4-iodbenzonitrile (25)**




A 250 mL round-bottom flask, equipped with a magnetic stirring bar and a dropping funnel, was charged with 4-iodobenzoyl chloride (5.32 g, 20.0 mmol) and $CH_2Cl_2$ (100 mL). The reaction mixture was cooled to 0 °C and ammonia (10 mL, 25%$_{(aq)}$) was added dropwise over a period of 30 min. On completion of the addition, the ice bath was removed and the reaction mixture was heated to 50 °C for an additional hour. The crude product was filtrated, washed with ethanol, diethyl ether and pentane furnishing 4-iodobenzamide. This white powder was then transferred into a 100 mL round bottom-flask equipped with a magnetic stirring bar and a reflux condenser, and a large excess of thionyl chloride (30 mL) was added. The reaction mixture was heated to reflux for 6 h and afterwards the excess of thionyl chloride was evaporated under vacuum. The residue was washed with $CHCl_3$ (2 x 50 mL) and the solvent was again removed *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded **25** as white fluffy powder (3.83 g, 84%).

**mp**.: 125-126 °C (Lit.: 124-125.5).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.78 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.30 (d, $^3J$(H,H) = 8.9 Hz, 2 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 138.9, 133.5, 118.6, 112.2, 100.7.

**MS** (70 eV, EI), *m/z* (%): 228 (100) [$M^+$], 102 (90), 91 (22), 77 (19), 57 (18), 44( 53).

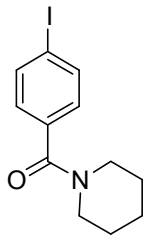
**IR** (KBr): $\tilde{\nu}$ = 3077 (w), 2228 (vs), 1909 (w), 1788 (w), 1645 (w), 1588 (m), 1579 (m), 1475 (m), 1392 (m), 1274 (w), 1244 (w), 1111 (w), 1056 (m), 1012 (m), 962 (w), 819 (vs), 766 (w), 700 (w), 541 (vs), 525 (w), 424 (w)

**HRMS** for **$C_7H_4IN$** (228.9388): found: 228.9407.

| | | |
|---|---|---|
| **$C_7H_4IN$**: | required: | C: 36.71; H: 1.76; N: 6.12; I: 55.41; |
| | found: | C: 36.60; H: 1.78; N: 6.03; I: 55.39. |

Spectral data match those of the literature.[125]

## Synthesis of pyperidino-4-iodo-benzamide (26)



A 250 mL round-bottom flask, equipped with a magnetic stirring bar and a dropping funnel, was charged with 4-iodobenzoyl chloride (5.32 g, 20.0 mmol) and $CH_2Cl_2$ (100 mL). The reaction mixture was cooled to 0 °C and pyperidine (2.55 g, 30.0 mmol) was added dropwise over a period of 20 min. On completion of the addition, the ice bath was removed and the reaction mixture was stirred at rt for 2 h. The reaction mixture was then poured into water, extracted with $CH_2Cl_2$ (3 x 100 mL), and the combined organic fractions were washed with water, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Recrystallization from ethanol, furnished the title compound **26** as white solid (5.92 g, 94%).

**mp**.: 135-135.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.70 (d, $^3J$(H,H) = 8.6 Hz, 2 H), 7.09 (d, $^3J$(H,H) = 8.6 Hz, 2 H), 3.63 (s_br, 2 H), 3.28 (s_br, 2 H), 1.74-1.42 (m, 6 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 169.3, 137.6, 135.9, 128.6, 95.4, 49.0, 43.3, 26.6, 25.3, 24.5.

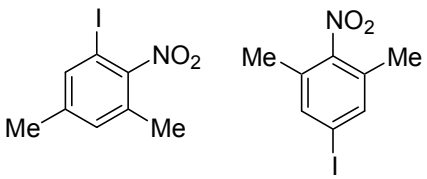
**MS** (70 eV, EI), *m/z* (%): 315 (31) [$M^+$], 314 (100), 230 (67), 202 (17), 188 (4), 160 (2), 127 (9), 104 (10), 76 (23).

**IR** (KBr): $\tilde{\nu}$ = 2937 (m), 1621 (vs), 1587 (s), 1453 (s), 1442 (s), 1288 (m), 1275 (m), 1107 (w), 1001 (m), 885 (w), 849 (w), 826 (m), 751 (m).

**HRMS** for **$C_{12}H_{14}INO$** (315.0120): found: 315.0102.

Spectral data match those of the literature.[126]

## Synthesis of 2-iodo-4,6-dimethyl-nitrobenzene (21g) and 5-iodo-1,3-dimethyl-2-nitrobenzene (29)



**21g** **29**

A 25 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with $HNO_3$ (65%, 15 mL), cooled to 0 °C and 3,5-dimethyl-iodobenzene (4.64 g, 20.0 mmol) was added dropwise. On completion of the addition, the cooling bath was removed and the mixture was heated to 50 °C for 4 h. The reaction mixture was poured onto ice (20 g), neutralized with saturated $NaHCO_{3(aq)}$-solution and extracted with diethyl ether (3 x 50 mL). The combined organic phases were washed with brine, dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 99:1) yielded **21g** and **29** as a pale yellow solids (**21g**, 2.4 g, 44%) and (**29**, 2.3 g, 41%).

**Compound 21g**

**mp**.: 46.2-47.2 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.46 (s, 1 H), 6.97 (s, 1 H), 2.23 (s, 3 H), 2.21 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 153.9, 142.2, 138.4, 132.2, 131.2, 85.2, 21.1, 18.3.

**MS** (70 eV, EI), *m/z* (%): 277 (93) [$M^+$], 260 (100), 184 (7), 133 (63), 104 (55), 91 (17), 78 (25), 63 (10), 51 (8), 43 (10).

**IR** (KBr): $\tilde{\nu}$ = 2924 (m), 1599 (s), 1580 (m), 1565 (s), 1529 (vs), 1448 (s), 1368 (vs), 1282 (m), 1225 (m), 1084 (m), 1039 m), 844 (vs), 792 (s), 735 (m), 728 (m), 604 (m), 588 (m).

**HRMS** for **$C_8H_8INO_2$** (276.9600): found: 276.9588.

**$C_8H_8INO_2$**: required: C: 34.68; H: 2.91; N: 5.06;
found: C: 34.74; H: 3.04; N: 5.05.

**Compound 29**

**mp**.: 73-73.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.43 (s, 2 H), 2.19 (s, 6 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 151.9, 138.0, 131.9, 96.4, 17.5.

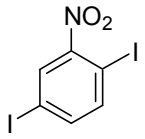
**MS** (70 eV, EI), *m/z* (%): 277 (82) [$M^+$], 260 (100), 197 (13), 184 (16), 133 (65), 104 (64), 91 (20), 78 (34), 63 (15), 50 (16), 43 (17).

**IR** (KBr): $\tilde{\nu}$ = 1594 (s), 1563 (s), 1520 (vs), 1470 (s), 1459 (s), 1438 (s), 1409 (m), 1399 (m), 1382 (s), 1365 (vs), 1280 (s), 1260 (s), 1245 (m), 1133 (s), 1084 (m), 1035 (m), 855 (vs), 712 (m), 589 (m), 582 (m).

**HRMS** for **$C_8H_8INO_2$** (276.9600): found: 276.9622.

**$C_8H_8INO_2$**: required: C: 34.68; H: 2.91; N: 5.06;
found: C: 34.44; H: 2.56; N: 4.91.

## Synthesis of 2,5-diiodo-nitrobenzene (21h)




A 50 mL round-bottom flask, equipped with a magnetic stirring bar and a dropping funnel was charged with water (3.8 mL) and $H_2SO_4$ (100%, 3.5 mL). Glacial acetic acid (3.5 mL) and 4-iodo-2 nitroaniline[61] (1.32 g, 5.00 mmol) were then added at 0 °C. Afterwards, a solution of $NaNO_2$ (380 mg, 5.5 mmol, in 1.5 mL $H_2O$) was added dropwise over a period of 1 h. On completion of the addition the mixture was stirred for 30 min and a solution of KI (1.0 g, 6 mmol, in 1.5 mL $H_2O$) was added dropwise with a strong evolution of gas ($N_2$). On completion of addition the sticky mixture was heated to 60 °C for 1 h, cooled again to 0 °C and diethyl ether was added until all precipitate was dissolved and the reaction mixture was poured into saturated $NaHCO_{3(aq)}$ solution (30 mL) in a separatory funnel. After extraction with diethyl ether (2 x 30 ml) the organic phases were washed with brine, dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. The residue was recrystallized from ethanol to give compound **21h** as a yellow-orange powder (1.27 g, 95%).

**mp.:** 106.5-107.2 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.07 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.67 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.47 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H).

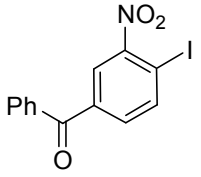
**$^{13}$C-NMR** (750 MHz, $CDCl_3$, 25 °C): δ = 143.4, 142.7, 134.4, 100.0, 93.2, 85.9.

**MS** (70 eV, EI), *m/z* (%): 375 (100) [$M^+$], 329 (31), 317 (4), 218 (7), 202 (21), 127 (3), 75 (39).

**IR** (KBr): $\tilde{\nu}$ = 1567 (w), 1544 (w), 1525 (vs), 1451 (w), 1350 (s), 1252 (w), 1081 (w), 1016 (s), 888 (w), 865 (w), 817 (m), 750 (w), 724 (w).

**$C_6H_3I_2NO_2$**: required: C: 19.22; H: 0.81; I: 67.70; N: 3.74;
found: C: 19.27; H: 0.79; I: 67.66; N: 3.72.

## Synthesis of 4-iodo-3-nitrobenzophenone (21i)




Prepared according to the procedure of Baik and Wong[63] from 4-amino-3-nitrobenzophenone (726 mg, 3.00 mmol), $KNO_2$ (510 mg, 6.00 mmol), HI (2.8 mL,

15 mmol, 50%$_{(aq)}$), CuI (570 mg, 3.00 mmol) and DMSO (20 mL) at 60 °C. Recrystallization from ethanol yielded compound **21i** as yellow solid (750 mg, 73%).

**mp.:** 116.7-117.3 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.21-8.17 (m, 2 H), 7.79-7.75 (m, 2 H), 7.68-7.62 (m, 2 H), 7.55-7.49 (m, 2 H).

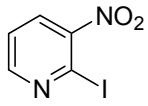
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 193.3, 153.0, 142.2, 138.6, 135.9, 133.6, 133.5, 129.9, 128.8, 126.2, 91.3.

**MS** (70 eV, EI), *m/z* (%): 353 (55) [$M^+$], 275 (12), 229 (5), 180 (3), 152 (4), 127 (2), 105 (100), 77 (42), 51 (8).

**IR** (KBr): $\tilde{\nu}$ = 1651 (vs), 1590 (vs), 1534 (vs), 1340 (m), 1280 (vs), 1245 (s), 1021 (m), 975 (m), 795 (w), 719 (vs), 697 (m), 672 (m).

**HRMS** for **$C_{13}H_8INO_3$** (352.9549): found: 352.9521.

## Synthesis of 2-iodo-3-nitropyridine (33)




Prepared according to the procedure of Baik and Wong from 2-amino-3-nitropyridine (696 mg, 5.00 mmol), $KNO_2$ (850 mg, 10.0 mmol), HI (3.8 mL, 25 mmol, 50%$_{(aq)}$), CuI (475 mg, 2.50 mmol) and DMSO (45 mL) at 60 °C. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded compound **33** as yellow solid (784 mg, 63%).

**mp.:** 130.2-131.8 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.55 (dd, $^{3}J$(H,H) = 4.9 Hz, $^{4}J$(H,H) = 1.8 Hz, 1 H), 8.05 (dd, $^{3}J$(H,H) = 8.0 Hz, $^{4}J$(H,H) = 1.8 Hz, 1 H), 7.50 (dd, $^{3}J$(H,H) = 8.0 Hz, $^{3}J$(H,H) = 4.9 Hz, 1 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 153.4, 151.0, 132.8, 123.4, 110.4.

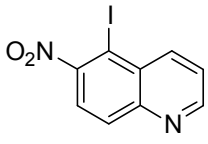
**MS** (70 eV, EI), *m/z* (%): 249 (100) [$M^+$], 203 (34), 126 (8), 77 (22), 53 (22).

**IR** (KBr): $\tilde{\nu}$ = 3037 (m), 1574 (vs), 1555 (vs), 1526 (vs), 1447 (w), 1401 (vs), 1347 (vs), 1245 (m), 1221 (m), 1053 (m), 1039 (s), 854 (s), 827 (s), 740 (s), 720 (s), 633 (m), 565 (w).

**HRMS for $C_{12}H_{10}N_2O_2$** (249.9239)**:** found: 249.9208.

**$C_5H_3IN_2O_2$**: required: C: 24.02; H: 1.21; N: 11.21;
found: C: 24.13; H: 1.08; N: 11.18.

## Synthesis of 5-iodo-6-nitroquinoline (34)




Prepared according to the procedure of Baik and Wong from 5-amino-6-nitroquinoline (946 mg, 5.00 mmol), $KNO_2$ (935 mg, 11.0 mmol), HI (3.9 mL, 27 mmol, $50\%_{(aq)}$) CuI (950 mg, 5.00 mmol) and DMSO (45 mL) at 60 °C. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded compound **34** as green-yellow solid (1.26 g, 84%).

**mp.:** 159.7-161.9 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 9.01 (s_br, 1 H), 8.66 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 8.21 (d, $^3J$(H,H) = 9.3 Hz, 1 H), 8.91 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 7.50 (dd, $^3J$(H,H) = 8.9 Hz, $^3J$(H,H) = 4.5 Hz, 1 H).

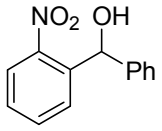
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C): δ = 153.3, 153.2, 148.5, 142.9, 131.9, 129.8, 124.5, 124.2, 92.8.

**MS** (70 eV, EI), *m/z* (%): 300 (100) $[M]^+$, 254 (31), 242 (15), 145 (18), 127 (44), 115 (14), 101 (11), 74 (7),

**IR** (KBr): $\tilde{\nu}$ = 1597 (w), 1561 (vs), 1524 (vs), 1488 (s), 1335 (s), 1325 (s), 1307 (m), 1299 (m), 963 (m), 838 (m), 806 (s), 772 (m), 731 (w).

**HRMS for $C_9H_5IN_2O_2$** (299.9396)**:** found: 299.9409.

## Synthesis of (2-nitrophenyl)-(phenyl)-methanol (23a)




Prepared according to **TP 3** from 2-iodonitrobenzene (**21a**) (498 mg, 2.00 mmol) PhMgCl (1.1 mL, 2.2 mmol, 2.0 M in THF) and benzaldehyde (255 mg, 2.40 mmol). Reaction time: 0.5 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the benzylic alcohol **23a** as a red oil (400 mg, 87%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.84 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 7.65 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 7.54 (dt, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.3 Hz, 1 H), 7.36 (dt, $^3J$(H,H) = 8.6 Hz, $^4J$(H,H) = 1.3 Hz, 1 H), 7.25-7.17 (m, 5 H), 6.34 (s_br, 1 H), 2.83 (s_br, 1 OH).

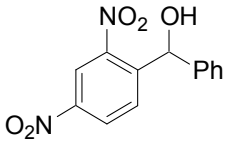
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 148.8, 141.9, 138.9, 133.8, 129.8, 129.0, 128.4, 127.3, 126.9, 125.1, 71.9.

**MS** (70 eV, EI), *m/z* (%): 229 (0.1) [$M^+$], 211 (5), 194 (46), 181 (21), 167 (100), 152 (57), 39 (10), 127 (5), 115 (5), 105 (17), 92 (2), 77 (46), 65 (4), 51 (12).

**IR** (KBr): $\tilde{\nu}$ = 3412 (m, br), 3064 (m), 1955 (w), 1740 (w), 1667 (w), 1598 (m), 1578 (m), 1525 (vs), 1452 (s), 1349 (vs), 1260 (s), 1178 (s), 1022 (s), 861 (m), 787 (m), 760 (s), 736 (s), 701 (vs), 647 (w), 601 (w).

**HRMS** for **$C_{13}H_{11}NO_3$** (229.0739): found: 229.0518.

## Synthesis of (2,4-dinitrophenyl)(phenyl)methanol (23b)




Prepared according to **TP 3** from 2,4-dinitro-iodobenzene (**21b**) (588 mg, 2.00 mmol), PhMgCl (1.1 mL, 2.1 mmol, 2.0 M in THF) and benzaldehyde (424 mg, 4.00 mmol). Reaction time: 0.5 h. Purification by flash chromatography ($CH_2Cl_2$) yielded (2,4-dinitrophenyl)(phenyl)methanol (**23b**) (442 mg, 81%) as an orange oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.66 (d, $^4J$(H,H) = 2.1 Hz, 1 H), 8.39 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.1 Hz, 1 H), 8.07 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.30-7.18 (m, 5 H), 6.47 (s, 1 H), 2,46 (s_br, 1 OH).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 146.9, 146.1, 143.9, 139.3, 129.4, 128.0, 127.8, 126.2, 126.1, 119.2, 70.3.

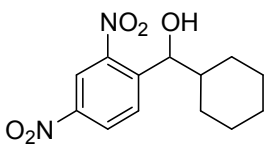
**MS** (70 eV, EI), *m/z* (%): 256 (11) [$M-H_2O]^+$, 239 (100), 210 (17), 193 (15), 180 (25), 166 (85), 152 (68), 139 (32), 127 (11), 105 (31), 77 (76), 63 (8), 51 (14).

**IR** (KBr): $\tilde{\nu}$ = 3542 (s), 3111 (s), 1605 (s), 1538 (vs), 1454 (s), 1348 (vs), 1176 (m), 1036 (s), 919 (m), 836 (s), 758 (s), 740 (s), 701 (s).

**HRMS** for **$C_{13}H_{10}N_2O_5$** (274.0590): found: 272.0432 [$M-2H]^+$.

**$C_{13}H_{10}N_2O_5$**: required: C: 56.94, H: 3.68, N: 10.22;
found: C: 57.13, H: 3.71, N: 10.01.

## Synthesis of cyclohexyl(2,4-dinitrophenyl)methanol (23c)



Prepared according to **TP 3** from 2,4-dinitro-iodobenzene (**21b**) (588 mg, 2.00 mmol), PhMgCl (1.1 mL, 2.1 mmol, 2 M in THF) and cyclohexanecarbaldehyde (560 mg, 5.00 mmol). Reaction time: 0.5 h. Purification by flash chromatography ($CH_2Cl_2$/pentane = 4:1) yielded cyclohexyl(2,4-dinitrophenyl)methanol (**23c**) (416 mg, 74%) as an orange oil

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.67 (d, $^4J$(H,H) = 2.1 Hz, 1 H), 8.37 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.1 Hz, 1 H), 7.61 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 5.19 (d, $^3J$(H,H) = 5 Hz, 1 H), 2.18 (s_br, 1 OH), 1.69-157 (m, 5 H), 1.44-1.41 (m, 1 H), 1.18-1.03 (m, 5 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 148.3, 147.1, 146.1, 131.1, 127.1, 120.2, 73.3, 44.8, 30.2, 27.2, 26.5, 26.4, 26.2.

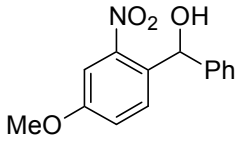
**MS** (70 eV, EI), *m/z* (%): 261 (2) $[M-H_2O]^+$, 245 (5), 217 (4), 198 (90), 180 (100), 164 (8), 151 (14), 134 (31), 124 (5), 103 (9), 83 (50), 77 (13), 67 (7), 55 (75).

**IR** (KBr): $\tilde{\nu}$ = 3562 (br, s), 3111 (m), 2926 (vs), 1605 (m), 1538 (vs), 1450 (s), 1353 (vs), 1262 (m), 1188 (m), 1083 (s), 1024 (m), 916 (m), 836 (s), 745 (s), 720 (s).

**HRMS** for **$C_{13}H_{16}N_2O_5$** (280.1059): found: 263.0999$[M-OH]^+$.

**$C_{13}H_{16}N_2O_5$**: required: C: 55.71, H: 5.75, N: 9.99;
found: C: 55.60, H: 5.78, N: 9.62.

## Synthesis of (4-methoxy-2-nitrophenyl)(phenyl)methanol (23d)




Prepared according to **TP 3** from 1-iodo-4-methoxy-2-nitrobenzene (**21c**) (418 mg, 1.50 mmol), PhMgCl (1.0 mL, 1.7 mmol, 1.7 M in THF) and benzaldehyde (190 mg, 1.80 mmol). Reaction time: 0.5 h. Purification by flash chromatography ($CH_2Cl_2$) yielded (4-methoxy-2-nitrophenyl)(phenyl)methanol (**23d**) (279 mg, 72%) as a yellow oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.48 (d, $^3J$(H,H) = 8.5 Hz, 1 H), 7.35(d, $^4J$(H,H) = 1.9 Hz, 1 H), 7.26-7.18 (m, 5 H), 7.05 (dd, $^3J$(H,H) = 8.5 Hz, $^4J$(H,H) = 1.9 Hz, 1 H), 6.25 (s, 1 H), 3.78 (s, 3 H), 2.61 (s_br, 1 OH).

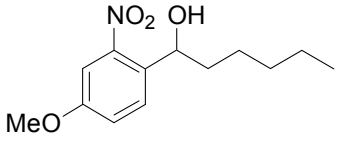
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 159.6, 149.4, 142.2, 131.1, 131.0, 128.9, 128.2, 127.2, 120.1, 109.8, 71.6, 56.3.

**MS** (70 eV, EI), *m/z* (%): 241 (26) $[M-H_2O]^+$, 224 (48), 211 (27), 196 (32), 182 (100), 168 (50), 154 (87), 140 (22), 135 (26), 127 (11), 115 (18), 105 (22), 92 (12), 77 (80), 63 (18), 51 (17).

**IR** (KBr): $\tilde{\nu}$ = 3400 (m), 2840 (w), 1621 (m), 1530 (vs), 1352 (s), 1244 (s), 1181 (m), 1066 (m), 1033 (s), 759 (m), 700 (s), 549 (w).

**$C_{14}H_{13}NO_4$:** required: C: 64.86, H: 5.40, N: 5.40;
found: C: 65.22, H: 5.13, N: 5.23.

## Synthesis of 1-(4-methoxy-2-nitrophenyl)-1-hexanol (23e)




Prepared according to **TP 3** from 3-iodo-4-nitroanisole (**21c**) (418 mg, 1.50 mmol), PhMgCl (0.85 mL, 1.6 mmol, 1.9 M in THF) and hexanal (201 mg, 2.00 mmol). Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 7:1) yielded 1-(4-methoxy-2-nitrophenyl)-1-hexanol (**23e**) (270 mg, 71%) as a colourless oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.60 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.29 (d, $^4J$(H,H) = 1.9 Hz, 1 H), 7.06 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.9 Hz, 1 H), 5.07-5.03 (m, 1 H), 3.78 (s, 3 H), 2.37 (s_br, 1 OH), 1.68-1.21 (m, 8 H), 0.83-0.78 (m, 3 H).

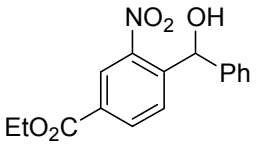
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 159.2, 148.9, 132.6, 129.5, 120.4, 109.1, 69.4, 56.2, 38.4, 31.9, 26.2, 22.9, 14.4.

**MS** (70 eV, EI), *m/z* (%): 253 (0.1) [$M^+$], 235 (32), 213 (14), 197 (39), 183 (100), 170 (28), 153 (81), 140 (14), 135 (13), 126 (22), 115 (25), 77 (5), 63 (3) (43 (26).

**IR** (KBr): $\tilde{\nu}$ = 3401 (m), 2956 (s), 1621 (m), 1530 (vs), 1498 (m), 1463 (m), 1351 (s), 1297 (m), 1242 (s), 1184 (m), 1119 (w), 1066 (m), 1037 (s), 929 (w), 854 (w), 832 (w), 761 (w).

**HRMS** for **$C_{13}H_{19}NO_4$** (253.1314): found: 254.1136 $[M+H]^+$.

## Synthesis of ethyl 4-[hydroxy(phenyl)methyl]-3-nitrobenzoate (23f)




Prepared according to **TP 3** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (642 mg, 2.00 mmol), PhMgCl (1.1 mL, 2.2 mmol, 2.0 M in THF) and benzaldehyde (254 mg, 2.40 mmol). Reaction time: 0.5 h. Purification by flash chromatography (pentane/ $CH_2Cl_2$ = 4:1) yielded ethyl 4-[hydroxy(phenyl)methyl]-3-nitrobenzoate (**23f**) (564 mg, 94%) as a pale yellow oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.45 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.19 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.84 (d, $^3J$(H,H) = 8.4 Hz 1 H), 7.25-7.18 (m, 5 H), 6.40 (d, $^3J$(H,H) = 3.5 Hz, 1 H), 4.34 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 2.85 (d, $^3J$(H,H) = 3.5 Hz, 1 OH), 1.33 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

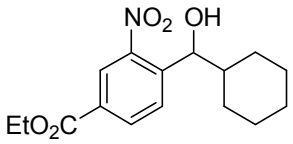
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.7, 148.5, 143.1, 141.4, 134.2, 131.4, 129.8, 129.1, 128.8, 127.4, 126.1, 71.8, 62.3, 14.6.

**MS** (70 eV, EI), *m/z* (%): 283 (14) $[M-H_2O]^+$, 266 (26), 256 (16), 238 (41), 222 (20), 211 (14), 194 (100), 180 (23), 167 (72), 152 (69), 139 (8), 127 (5), 115 (6), 105 (41), 77 (54), 65 (4), 51 (9).

**IR** (KBr): $\tilde{\nu}$ = 3478 (s), 2984 (m), 1728 (vs), 1620 (s), 1538 (vs), 1493 (s), 1454 (s), 1355 (s), 1288 (s), 1152 (s), 1021 (s), 919 (m), 838 (m), 764 (vs), 749 (vs), 701 (vs), 665 (w), 557 (w).

**HRMS** for **$C_{16}H_{15}NO_5$** (301.0950): found: 302.1031 $[M+H]^+$.

## Synthesis of ethyl 4-[cyclohexyl(hydroxy)methyl]-3-nitrobenzoate (23g)




Prepared according to **TP 3** from ethyl 4-iodo-3-nitro-benzoate (**21d**) (583 mg, 1.80 mmol), PhMgCl (1.0 mL, 2.0 mmol, 2.0 M in THF) and cyclohexanecarbaldehyde (249 mg, 2.20 mmol). Reaction time: 1 h. Purification by flash chromatography (pentane/ $CH_2Cl_2$ = 7:3) yielded ethyl 4-[cyclohexyl(hydroxy)methyl]-3-nitrobenzoate (**23g**) (355 mg, 64%) as an orange-yellow oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): 8.41 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.16 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.76 (d, $^3J$(H,H) = 8.4 Hz 1 H), 5.06 (d, $^3J$(H,H) = 5.5 Hz, 1 H), 4.35 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 2.15 (s_br, 1 OH), 1.68-1.58 (m, 6 H), 1.34 (t, $^3J$(H,H) = 7 Hz, 3 H), 1.11-1.05 (m, 5 H).

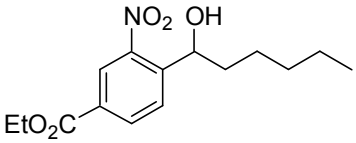
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): 183.8, 164.9, 148.7, 143.6, 133.6, 130.9, 129.8, 125.7, 73.6, 62.2, 44.6, 30.2, 27.7, 26.6, 26.3, 14.6.

**MS** (70 eV, EI), *m/z* (%): 288 (5), 272 (18), 262 (18), 244 (13), 224 (11), 207 (100), 191 (27), 179 (56), 162 (30), 151 (30), 135 (8), 123 (36), 118 (6), 105 (12), 83 (20), 77 (15), 65 (10), 55 (46).

**IR** (KBr): $\tilde{\nu}$ = 3497 (br, m), 2929 (vs), 2854 (vs), 1726 (vs), 1619 (m), 1535 (vs), 1450 (m), 1355 (s), 1285 (br, vs), 1189 (m), 1096 (m), 1020 (s), 919 (w), 863 (m), 838 (m), 759 (vs), 718 (w), 705 (w).

**HRMS** for **$C_{16}H_{21}NO_5$** (307.1420): found: 308.1485 $[M+H]^+$.

## Synthesis of ethyl 4-(1-hydroxyhexyl)-3-nitrobenzoate (23h)




Prepared according to **TP 3** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (483 mg, 1.50 mmol), PhMgCl (0.85 mL, 1.6 mmol, 1.9 M in THF) and hexanal (201 mg, 2.00 mmol). Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 5:1) yielded ethyl 4-(1-hydroxyhexyl)-3-nitrobenzoate (**23h**) (383 mg, 87%) as a colourless oil.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.43 (d, $^{4}J$(H,H) = 1.8 Hz, 1 H), 8.18 (dd, $^{3}J$(H,H) = 8.4 Hz, $^{4}J$(H,H) = 1.8 Hz, 1 H), 7.82 (d, $^{3}J$(H,H) = 8.4 Hz, 1 H), 5.21-5.17 (m, 1 H), 4.36 (q, $^{3}J$(H,H) = 7.1 Hz, 2 H), 2.41 (s_br, 1 OH), 1.85-1.29 (m, 8 H), 0.92-0.85 (m, 3 H).

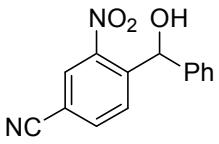
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.5, 147.6, 144.9, 133.8, 130.5, 128.4, 125.4, 69.3, 61.8, 38.3, 32.7, 25.6, 22.9, 14.2, 14.0.

**MS** (70 eV, EI), *m/z* (%): 295 (4) [$M^+$], 278 (9), 250 (12), 224 (100), 207 (26), 176 (58), 162 (14), 149 (17), 121 (11), 105 (14), 77 (7), 65 (13), 43 (31).

**IR** (KBr): $\tilde{\nu}$ = 3440 (m), 2957 (s), 1727 (vs), 1620 (m), 1534 (vs), 1466 (m), 1354 (s), 1286 (vs), 1113 (s), 1020 (m), 920 (w), 862 (w), 772 (m), 759 (m), 717 (w).

**HRMS** for **$C_{15}H_{21}NO_5$** (295.1420): found: 296.1490 $[M+H]^+$.

## Synthesis of [hydroxy(phenyl)methyl]-4-nitrobenzonitrile (23i)




Prepared according to **TP 3** from 4-iodo-3-nitrobenzonitrile (**21e**) (274 mg, 1.00 mmol), PhMgCl (0.55 mL, 1.1 mmol, 2.0 M in THF) and benzaldehyde (128 mg, 1.20 mmol). Reaction time: 0.5 h. Purification by flash chromatography ($CH_2Cl_2$) yielded [hydroxy(phenyl)methyl]-4-nitrobenzonitrile (**23i**) (240 mg, 94%) as a yellow oil.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.10 (d, $^{4}J$(H,H) = 1.8 Hz, 1 H), 7.87 (d, $^{3}J$(H,H) = 8.4 Hz, 1 H), 7.66 (dd, $^{3}J$(H,H) = 8.4 Hz, $^{4}J$(H,H) = 1.8 Hz, 1 H), 7.31-7.18 (m, 5 H), 6.36 (d, $^{3}J$(H,H) = 3.6 Hz, 1 H), 2.7 (d, $^{3}J$(H,H) = 3.6 Hz, 1 OH).

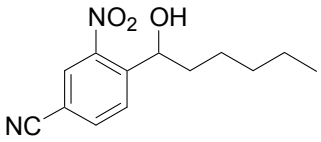
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.1, 139.4, 138.8, 132.1, 131.0, 128.6, 128.0, 127.5, 126.1, 124.2, 116.0, 69.9.

**MS** (70 eV, EI), *m/z* (%): 236 (11) $[M-H_2O]^+$, 219 (73), 206 (25), 192 (100), 177 (23), 165 (15), 151 (27), 129 (7), 105 (20), 77 (59), 63 (5), 51 (11).

**IR** (KBr): $\tilde{\nu}$ = 3468 (br, s), 3085 (s), 2238 (s), 1673 (w), 1601 (m), 1584 (vs), 1454 (s), 1350 (vs), 1299 (s), 1146 (m), 1077 (m), 1023 (s), 917 (w), 846 (vs), 759 (s), 701 (vs), 592 (w), 554 (w).

**HRMS** for $\mathbf{C_{14}H_{10}N_2O_3}$ (254.0691): found: 252.0546 $[M-2H]^+$.

## Synthesis of 1-(4-cyano-2-nitrophenyl)-1-hexanol (23j)




Prepared according to **TP 3** from 3-iodo-4-nitrobenzonitrile (**21e**) (411 mg, 1.50 mmol), PhMgCl (0.85 mL, 1.6 mmol, 1.9 M in THF) and hexanal (225 mg, 2.30 mmol). Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded 1-(4-cyano-2-nitrophenyl)-1-hexanol (**23j**) (234 mg, 63%) as a pale yellow oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.17 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.00 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.87 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 5.33-5.29 (m, 1 H), 2.47 (s_br, 1H), 1.81-1.25 (m, 8 H), 1.33-1.26 (m, 3 H).

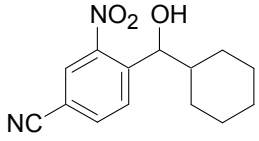
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.3, 147.7, 137.9, 131.4, 129.8, 118.3, 113.9, 70.9, 40.3, 33.1, 27.4, 24.3, 15.7.

**MS** (70 eV, EI), *m/z* (%) 249 (1) $[M+H]^+$, 177 (100), 160 (51), 145 (9), 129 (27), 117 (11), 104 (11), 77 (3).

**IR** (KBr): $\tilde{\nu}$ = 3438 (m), 2956 (m), 2930 (m), 2238 (s), 1617 (w), 1537 (vs), 1466 (m), 1356 (s), 1055 (m), 849 (m), 818 (w).

**HRMS** for $\mathbf{C_{13}H_{16}N_2O_3}$ (248.1161): found: 249.1262 $[M+H]^+$.

## Synthesis of 4-[cyclohexyl(hydroxy)methyl]-3-nitrobenzonitrile (23k)




Prepared according to **TP 3** from 4-iodo-3-nitrobenzonitrile (**21e**) (274 mg, 1.00 mmol), PhMgCl (0.55 mL, 1.1 mmol, 2.0 M in THF) and cyclohexanecarbaldehyde (224 mg,

2.00 mmol). Reaction time: 1 h. Purification by flash chromatography (pentane/ethyl acetate = 8:1) yielded **23k** as a yellow oil (120 mg, 46%).

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 8.16 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.94 (d, $^3J$(H,H) = 8.1 Hz, 1 H), 7.84 (dd, $^3J$(H,H) = 8.1 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 5.19 (d, $^3J$(H,H) = 5.2 Hz, 1 H), 2.18 (s_br, 1 OH), 1.79-1.58 (m, 5 H), 1.26-1.09 (m, 6 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 148.1, 144.1, 135.5, 130.5, 127.9, 116.5, 112.2, 72.9, 44.4, 29.9, 26.9, 26.1, 26.1, 25.8.

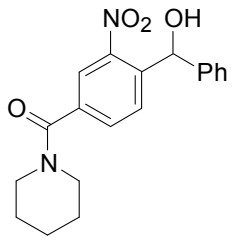
**MS** (70 eV, EI), *m/z* (%): 261 (0.1) $[M+H]^+$, 225 (2), 197 (2), 178 (26), 160 (100), 116 (5), 104 (22), 83 (36), 55 (41).

**IR** (KBr): $\tilde{\nu}$ = 3509 (m), 2929 (m), 2240 (s), 1617 (m), 1536 (vs), 1452 (m), 1405 (m), 1350 (vs), 1308 (s), 1297 (m), 1260 (w), 1180 (w), 1093 (s), 1067 (m), 996 (s), 903 (m), 852 (s), 815 (m), 775 (m), 744 (m), 664 (m), 581 (w), 510 (m).

**HRMS** for **$C_{14}H_{16}N_2O_3$** (260.1161): found: 261.1287 $[M+H]^+$.

**$C_{14}H_{16}N_2O_3$ :** required: C: 64.60; H: 6.20; N: 10.76;
found: C: 64.98; H: 6.00; N: 10.50.

## Synthesis of [2-nitro-4-(1-piperidinylcarbonyl)phenyl](phenyl)methanol (23l)




Prepared according to **TP 3** from 1-(4-iodo-3-nitrobenzoyl)piperidine (**21f**) (360 mg, 1.00 mmol), PhMgCl (0.63 mL, 1.1 mmol, 1.8 M in THF) and benzaldehyde (212 mg, 2.00 mmol). Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded (**23l**) as a colourless oil (285 mg, 84%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.89 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.81 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.58 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.26-7.18 (m, 5 H), 6.41 (d, $^2J$(H,H) = 3.8 Hz, 1 H), 3.68 (s_br, 2 H), 3.50 (d, $^2J$(H,H) = 3.8 Hz, 1 OH), 3.31 (s_br, 2 H), 1.70-1.45 (m, 6 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 167.5, 147.9, 141.4, 140.0, 136.5, 131.5, 129.6, 128.6, 128.1, 127.0, 123.2, 70.9, 48.9, 43.4, 26.5, 25.5, 24.4.

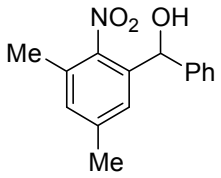
**MS** (70 eV, EI), *m/z* (%): 337 (100) $[M-2H]^+$, 321 (23), 311 (9), 290 (24), 254 (54), 224 (10), 207 (9), 197 (13), 180 (43), 152 (40), 105 (23), 77 (17).

**IR** (KBr): $\tilde{\nu}$ = 3392 (m), 2939 (w), 1616 (vs), 1532 (vs), 1495 (m), 1445 (m), 1353 (m), 1287 (m), 1180 (w), 1117 (s), 1041 (w), 1026 (m), 1010 (w), 906 (w), 854 (w), 752 (m), 700 (m).

**HRMS** for $\mathbf{C_{19}H_{20}N_2O_4}$ (340.1423): found: 338.1263 $[M-2H]^+$.

$\mathbf{C_{19}H_{20}N_2O_4}$: required: C: 67.05; H: 5.92; N: 8.23;
found: C: 66.73; H: 5.89; N: 8.18.

## Synthesis of (3,5-dimethyl-2-nitrophenyl)(phenyl)methanol (23m)




Prepared according to **TP 3** from 2-iodo-4,6-dimethyl-nitrobenzene (**21g**) (277 mg, 1.00 mmol), PhMgCl (0.63 mL, 1.1 mmol, 1.75 M in THF) and benzaldehyde (212 mg, 2.00 mmol). Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 29:1) yielded benzylic alcohol **23m** as a colourless oil (189 mg, 74%).

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 7.34-7.28 (m, 5 H), 7.14 (s_br, 1 H), 7.02 (s_br, 1 H), 5.92 (s, 1 H), 2.31 (s, 3 H), 2.28 (s, 3 H).

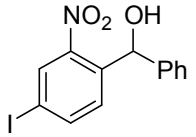
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 147.8, 141.5, 141.0, 135.5, 131.4, 129.9, 128.5, 127.9, 126.7, 126.5, 71.4, 21.3, 17.6.

**MS** (70 eV, EI), *m/z* (%): 257 (not detectable), 239 (12) $[M-H_2O]^+$, 222 (23), 194 (100), 180 (79), 165 (36), 105 (20), 77 (37).

**IR** (KBr): $\tilde{\nu}$ = 3411 (w), 1599 (w), 1524 (vs), 1495 (m), 1451 (w), 1365 (s), 1175 (w), 1051 (m), 842 (m), 759 (w), 701 (s).

$\mathbf{C_{15}H_{15}NO_3}$: required: C: 70.02; H: 5.88; N: 5.44;
found: C: 70.33; H: 5.76; N: 5.24.

## Synthesis of (4-iodo-2-nitrophenyl)(phenyl)methanol (23n)




Prepared according to **TP 3** from 2,5-diiodo-nitrobenzene (**20h**) (563 mg, 1.50 mmol), PhMgCl (0.80 mL, 1.6 mmol, 2.0 M in THF) and benzaldehyde (190 mg, 1.80 mmol).

Reaction time: 0.5 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded (4-iodo-2-nitrophenyl)(phenyl)methanol (**23n**) (458 mg, 86%) as a yellow oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.15 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.86 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.42 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.28-7.18 (m, 5 H), 6.30 (s, 1 H), 2,45 (s_br, 1 H).

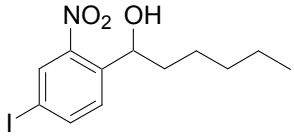
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 141.5, 141.2, 140.0, 137.1, 132.1, 129.8, 127.7, 127.2, 125.9, 91.2, 70.2.

**MS** (70 eV, EI), *m/z* (%): 353 (3) [$M^+$], 337 (18), 320 (82), 308 (6), 293 (38), 260 (8), 231 (13), 182(22), 166 (100), 152 (73), 139 (25), 109 (22), 77 (58), 63 (10), 51 (14).

**IR** (KBr): $\tilde{\nu}$ = 3369 (br), 1530 (vs), 1469 (s), 1347 (vs), 1275 (m), 1179 (m), 1034 (s), 871 (m), 808 (m), 763 (s), 700 (s).

**HRMS** for **$C_{13}H_{10}INO_3$** (354.9705): found: 352.9544 [M−2H]$^+$.

## Synthesis of 1-(4-iodo-2-nitrophenyl)-1-hexanol (23o)




Prepared according to **TP 3** from 2,5-diiodonitrobenzene (**21h**) (562 mg, 1.50 mmol), PhMgCl (0.80 mL, 1.6 mmol, 2.0 M in THF) and hexanal (201 mg, 2.00 mmol). Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded 1-(4-iodo-2-nitrophenyl)-1-hexanol (**23o**) (480 mg, 86%) as a pale yellow oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.12 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.86 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.45 (d, $^3J$(H,H) = 8.4 Hz 1 H), 5.13-5.09 (m, 1 H), 2.37 (s_br, 1 OH), 1.83-1.27 (m, 8 H), 0.92-0.88 (m, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 152.4, 148.1, 142.3, 140.0, 132.7, 129.8, 128.4, 91.5, 69.1, 38.2, 31.4, 25.7, 22.5, 14.0.

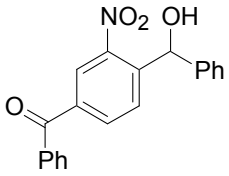
**MS** (70 eV, EI), *m/z* (%): 349 (not detectable), 332 (2) [M−OH]$^+$, 278 (100), 261 (16), 229 (24), 203 (4), 76 (3).

**IR** (KBr): $\tilde{\nu}$ = 3418 (w), 2928 (m), 1529 (vs), 1466 (m), 1347 (vs), 1054 (m), 869 (w), 832 (w), 761 (w).

**HRMS** for **$C_{12}H_{16}INO_3$** (332.0148 [M−OH]$^+$): found: 332.0169 [M−OH]$^+$.

**$C_{12}H_{16}INO_3$**: required: C: 41.28; H: 4.62; I: 36.35; N: 4.01;
found: C: 41.69, H: 4.32; I: 36.76; N: 4.00.

## Synthesis of {3-[hydroxy(phenyl)methyl]-4-nitrophenyl}(phenyl)methanone (23p)




Prepared according to **TP 3** from 4-iodo-3-nitrobenzophenone (**21i**) (353 mg, 1.00 mmol), PhMgCl (0.63 mL, 1.1 mmol, 1.75 M in THF) and benzaldehyde (212 mg, 2.00 mmol). Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded ketone **23p** as a yellow oil (309 mg, 93%).

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 8.29 (d, $^4J$(H,H) = 1.7 Hz, 1 H), 8.04 (dd, $^3J$(H,H) = 8.2 Hz, $^4J$(H,H) = 1.7 Hz, 1 H), 7.96 (d, $^3J$(H,H) = 8.2 Hz, 1 H), 7.79-7.76 (m, 2 H), 7.63 (dt, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 7.54-7.48 (m, 2 H), 7.35-7.31 (m, 5 H), 6.51 (s, 1 H).

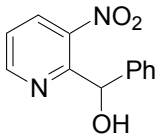
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 193.8, 148.0, 142.2, 141.0, 137.8, 136.3, 133.9, 133.3, 129.9, 129.4, 128.8, 128.7, 128.4, 127.1, 125.9, 70.4.

**MS** (70 eV, EI), *m/z* (%): 331(0.5) $[M-2H]^+$, 315 (15), 300 (38), 270 (6), 238 (24), 224 (9), 194 (56), 166 (11), 152 (11), 105 (100), 77 (45).

**IR** (KBr): $\tilde{\nu}$ = 3437 (m), 3063 (w), 1661 (vs), 1615 (s), 1598 (s), 1577 (m), 1532 (vs), 1493 (m), 1448 (s), 1350 (vs), 1319 (vs), 1281 (vs), 1180 (s), 1074 (m), 1037 (m), 1024 (m), 978 (m), 878 )w), 758 (m), 718 (s), 699 (s), 676 (s).

**HRMS** for **$C_{20}H_{15}NO_4$** (333.1001): found: 331.0826 $[M-2H]^+$.

## Synthesis of (3-nitro-2-pyridinyl)(phenyl)methanol (39)




Prepared according to **TP 3** from 2-iodo-3-nitropyridine (**33**) (125 mg, 0.50 mmol), PhMgCl (0.35 mL, 0.55 mmol, 1.5 M in THF) and benzaldehyde (106 mg, 1.00 mmol) at −78 °C. Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 1:1) yielded benzylic alcohol **39** as a pale yellow oil (64 mg, 55%).

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 8.90 (dd, $^3J$(H,H) = 4.9 Hz, $^4J$(H,H) = 1.7 Hz, 1 H), 8.36 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.7 Hz, 1 H), 7.50 (dd, $^3J$(H,H) = 8.1 Hz, $^3J$(H,H) = 4.9 Hz, 1 H), 7.31-7.21 (m, 5 H), 6.50 (d, $^3J$(H,H) = 6.6 Hz, 1 H), 5.38 (d, $^3J$(H,H) = 6.6 Hz, 1 H).

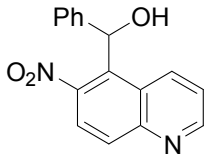
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 156.3, 152.3, 144.2, 141.7, 134.0, 129.0, 128.5, 128.0, 123.8, 72.5.

**MS** (70 eV, EI), *m/z* (%): 230 (5) [$M^+$], 213 (15), 196 (43), 182 (60) 168 (91), 155 (87), 137 (44), 127 (29), 105 (66), 94 (9), 77 (100), 63 (7).

**IR** (KBr): $\tilde{\nu}$ = 3396 (w), 1597 (m), 1567 (m), 1529 (vs), 1453 (m), 1349 (vs), 1188 (m), 1041 (m), 835 (m), 767 (m), 745 (s), 700 (s), 606 (s).

**HRMS** for **$C_{12}H_{10}N_2O_3$** (230.0691): found: 230.0693.

## Synthesis of (6-nitro-5-quinolinyl)(phenyl)methanol (41)




Prepared according to **TP 3** from 5-iodo-6-nitroquinoline (**34**) (300 mg, 1.00 mmol), PhMgCl (0.63 mL, 1.1 mmol, 1.75 M in THF) and benzaldehyde (212 mg, 2.00 mmol). Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 1:1) yielded quinoline derivative **41** as a pale yellow solid (218 mg, 78%).

**mp.:** 138.2-139.5 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C): δ = 8.79 (dd, $^3J$(H,H) = 4.9 Hz, $^4J$(H,H) = 1.7 Hz, 1 H), 8.64 (d, $^3J$(H,H) = 8.1 Hz, 1 H), 8.04 (d, $^3J$(H,H) = 9.0 Hz, 1 H), 7.84 (d, $^3J$(H,H) = 9.0 Hz, 1 H), 7.29 (d, $^3J$(H,H) = 7.3 Hz, 2 H), 7.17-7.14 (m, 2 H), 7.08 (t, $^3J$(H,H) = 7.3 Hz, 1 H), 6.42 (s, 1 H), 6.11 (s_br, 1 OH), 5.38 (d, $^3J$(H,H) = 6.6 Hz, 1 H).

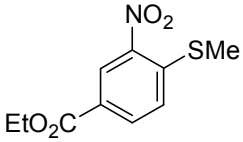
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C): δ = 151.7, 149.0, 147.6, 142.5, 137.3, 135.1, 130.8, 127.9, 126.7, 126.3, 125.5, 122.5, 121.3, 68.8.

**MS** (70 eV, EI), *m/z* (%): 278 (0.2) [M−2H]$^+$, 246 (23), 232 (12), 218 (100), 206 (17), 176 (8), 151 (4), 128 (4), 105 (15), 77 (23).

**IR** (KBr): $\tilde{\nu}$ = 3272 (m), 1597 (w), 1530 (vs), 1499 (s), 1450 (m), 1359 (s), 1260 (w), 1045 (m), 1026 (w), 908 (w), 836 (s), 808 (s), 778 (m), 759 (m), 736 (m), 709 (s), 581(w).

**HRMS for $C_{16}H_{12}N_2O_3$** (280.0848): found: 278.0686 [M−2H]$^+$.

## Synthesis of ethyl 3-nitro-4-thiomethylbenzoate (42)



Prepared according to **TP 3** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (642 mg, 2.00 mmol), PhMgCl (1.1 mL, 2.1 mmol, 2.0 M in THF) and methyl methanethiosulfonate (327 mg, 2.60 mmol). Reaction time: 12 h at 0 °C. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded compound **42** as a yellow solid (170 mg, 38%).

**mp.:** 100-101 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.79 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.13 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.32 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 4.36 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 2.48 (s, 3 H), 1.35 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

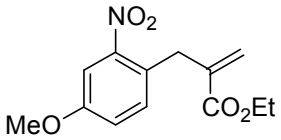
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.7, 147.2, 147.0, 135.8, 129.4, 128.9, 127.7, 63.9, 18.2, 16.4.

**MS** (70 eV, EI), *m/z* (%): 241 (83) [$M^+$], 211 (20), 196 (47), 193 (11), 178 (9), 150 (100), 135 (18), 122 (75), 107 (9), 94 (9), 78 (17), 63 (17).

**IR** (KBr): $\tilde{\nu}$ = 2998 (w), 1715 (vs), 1608 (s), 1516 (s), 1339 (s), 1287 (vs), 1236 (s), 1139 (m), 1025 (m), 832 (w), 770 (w), 750 (m).

**HRMS for $C_{10}H_{11}NO_4S$ (**241.0409): found: 241.0415.

## Synthesis of ethyl 2-(4-methoxy-2-nitrobenzyl)acrylate (44b)




Prepared according to **TP 3** from 1-iodo-4-methoxy-2-nitrobenzene (**21c**) (558 mg, 2.00 mmol), PhMgCl (1.3 mL, 2.2 mmol, 1.7 M in THF), CuCN·2LiCl (2.2 mL, 2.2 mmol, 1.0 M in THF) and ethyl (2-bromomethyl) acrylate (463 mg, 2.40 mmol). Reaction time: 45 min. Purification by flash chromatography (pentane/diethyl ether = 9:1) furnished ethyl 2-(4-methoxy-2-nitrobenzyl)acrylate (**44b**) (381 mg, 72%) as an orange liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.38 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.17 (d, $^3J$(H,H) = 8.5 Hz, 1 H), 7.01 (dd, $^3J$(H,H) = 8.5 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 6.17-6.14 (m, 1 H), 5.29-5.27 (m, 1 H), 4.12 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.82 (s, 2 H), 3.77 (s, 3 H), 1.18 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

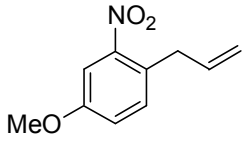
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.4, 157.6, 148.8, 137.7, 132.3, 124.4, 118.6, 108.4, 59.9, 54.8, 33.2, 13.1.

**MS** (70 eV, EI), *m/z* (%): 265 (2) [$M^+$], 248 (23), 236 (100), 220 (52),202 (20), 190 (60), 174 (63), 164 (37), 146 (56), 132 (28), 103 (32), 91 (24), 77 (42), 63 (15), 51 (18).

**IR** (KBr): $\tilde{\nu}$ = 2982 (m), 1715 (s), 1625 (m), 1531 (vs), 1410 (m), 1352 (s), 1252 (s), 1150 (s), 1034 (s), 945 (w), 814 (m), 757 (w).

**HRMS** for **$C_{13}H_{15}NO_5$** (265.0950): found: 264.0888 $[M-H]^+$.

## Synthesis of 1-allyl-4-methoxy-2-nitrobenzene (44c)




Prepared according to **TP 3** from 1-iodo-4-methoxy-2-nitrobenzene (**21c**) (558 mg, 2.00 mmol), PhMgCl (1.3 mL, 2.2 mmol, 1.7 M in THF), CuCN·2LiCl (2.2 mL, 2.2 mmol, 1.0 M in THF) and allyl bromide (290 mg, 2.4 mmol). Reaction time: 45 min. Purification by flash chromatography (pentane/diethyl ether = 19:1) furnished 1-allyl-4-methoxy-2-nitrobenzene (**44c**) (212 mg, 55%) as an orange liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.41 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.23 (d, $^3J$(H,H) = 8.5 Hz, 1 H), 7.01 (dd, $^3J$(H,H) = 8.5 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 5.98-5.88 (m, 1 H), 5.08-5.00 (m, 2 H), 3.83 (s, 3 H), 3.58 (dt, $^3J$(H,H) = 6.4 Hz, $^4J$(H,H) = 1.4 Hz, 2 H).

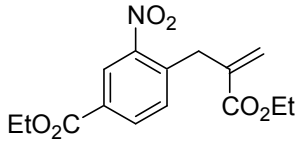
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 158.4, 149.5, 135.5, 132.8, 126.8, 119.7, 116.6, 109.3, 55.8, 36.3.

**MS** (70 eV, EI), *m/z* (%): 193 (27) [$M^+$], 176 (94), 159 (100), 146 (40), 133 (58), 129 (13), 121 (10), 115 (36), 103 (99), 91 (28), 77 (60), 63 (22), 55 (10).

**IR** (KBr): $\tilde{\nu}$ = 2942 (m), 1622 (m), 1531 (vs), 1500 (s), 1463 (m), 1440 (m), 1351 (vs), 1251 (vs), 1036 (s), 920 (m), 812 (m).

**HRMS** for **$C_{10}H_{11}NO_3$** (193.0739): found: 193.0735.

## Synthesis of ethyl 4-[2-(ethoxycarbonyl)-2-propenyl]-3-nitrobenzoate (44d)




Prepared according to **TP 3** from ethyl 4-iodo-3-nitrobenzoate (2**1d**) (642 mg, 2.00 mmol), PhMgCl (1.1 mL, 2.2 mmol, 2.0 M in THF), CuCN·2LiCl (2.2 mL, 2.2 mmol, 1.0 M in THF) and ethyl (2-bromomethyl) acrylate (463 mg, 2.4 mmol). Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 85:15) yielded ethyl 4-[2-(ethoxycarbonyl)-2-propenyl]-3-nitrobenzoate (**44d**) (461 mg, 75%) as a yellow oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.47 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.10 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.39 (d, $^3J$(H,H) = 8.4 Hz 1 H), 6.24 (d, $^2J$(H,H) = 0.9 Hz, 1 H), 5.40 (d, $^2J$(H,H) = 0.9 Hz, 1 H), 4.34 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 4.09 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.95 (s, 2 H), 1.34 (t, $^3J$(H,H) = 7.1 Hz, 3 H), 1.17 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

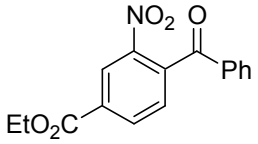
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.4, 164.8, 149.8, 138.7, 138.0, 133.7, 132.8, 130.8, 127.8, 126.2, 62.1, 61.5, 35.2, 14.6, 14.4.

**MS** (70 eV, EI), *m/z* (%): 306 (2) $[M-H]^+$, 278 (16), 261 (100), 244 (7), 233 (67), 217 (24), 206 (21), 188 (29), 172 (15), 160 (29), 144 (24), 134 (13), 115 (33), 103 (13), 89 (14), 77 (14), 63 (7), 55 (5).

**IR** (KBr): $\tilde{\nu}$ = 3429 (br, w), 2984 (m), 1724 (vs), 1620 (m), 1536 (vs), 1494 (w), 1446 (w), 1408 (w), 1367 (s), 1281 (vs), 1263 (vs), 1152 (s), 1113 (s), 1023 (m), 935 (w), 863 (w), 822 (w), 772 (w), 757 (w), 725 (w).

**HRMS** for **$C_{15}H_{17}NO_6$** (307.1056): found: 306.0957 $[M-H]^+$.

## Synthesis of ethyl 4-benzoyl-3-nitrobenzoate (44e)




Prepared according to **TP 3** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (642 mg, 2.00 mmol), PhMgCl (1.2 mL, 2.2 mmol, 1.9 M in THF), CuCN·2LiCl (2.2 mL, 2.2 mmol, 1.0 M in THF) and benzoyl bromide (481 mg, 2.6 mmol). Reaction time: 0.5 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded ethyl 4-benzoyl-3-nitrobenzoate (**44e**) (454 mg, 76%) as a yellow solid.

**mp**.: 93-94 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.79 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.35 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.68-7.64 (m, 2 H), 7.56-7.48 (m, 2 H), 7.41-7.36 (m, 2 H), 4.42 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.38 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

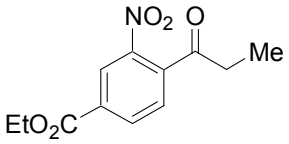
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 193.0, 164.2, 147.1, 140.1, 135.9, 135.1, 134.5, 133.5, 129.6, 129.5, 129.3, 126.0, 62.7, 14.7.

**MS** (70 eV, EI), *m/z* (%): 299 (6) $[M^+]$, 270 (2), 254 (21), 222 (18), 206 (100), 194 (4), 176 (23), 152 (21), 126 (3), 105 (98), 77 (37), 51 (6).

**IR** (KBr): $\tilde{\nu}$ = 3422 (br, w), 2986 (m), 1721 (vs), 1674 (vs), 1597 (w), 1534 (vs), 1492 (m), 1449 (m), 1352 (vs), 1287 (s), 1236 (s), 1163 (s), 1020 (m), 941 (m), 920 (s), 858 (m), 837 (m), 766 (s), 742 (m), 715 (s), 701 (m), 685 (m).

**HRMS** for **$C_{16}H_{13}NO_5$** (299.0794): found: 299.0802.

## Synthesis of ethyl 3-nitro-4-propionylbenzoate (44f)




Prepared according to **TP 3** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (482 mg, 1.50 mmol), PhMgCl (0.97 mL, 1.6 mmol, 1.7 M in THF), CuCN·2LiCl (1.6 mL, 1.6 mmol, 1.0 M in THF) and propionyl chloride (223 mg, 2.25 mmol). Reaction time: 4 h. Purification by flash chromatography (pentane/ethyl acetate = 9:1) furnished the title compound **44f** (231 mg, 61%) as a yellow oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.68 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.29 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.38 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 4.38 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 2.74 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.37 (t, $^3J$(H,H) = 7.1, 3 H), 1.20 (t, $^3J$(H,H) = 7.1, 3 H).

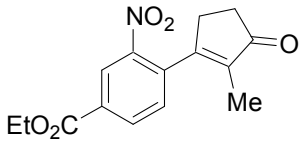
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 201.5, 162.8, 144.7, 140.6, 134.0, 131.9, 126.6, 124.5, 61.2, 35.4, 13.2, 7.0.

**MS** (70 eV, EI), *m/z* (%): 251 (1) [$M^+$], 222 (100), 206 (9), 193 (5), 176 (2), 165 (8), 148 (1), 136 (1), 120 (2), 103 (5).

**IR** (KBr): $\tilde{\nu}$ = 3094 (w), 2984 (s), 2942 (m), 2907 (w), 2880 (w), 1726 (vs), 1622 (m), 1566 (m), 1538 (vs), 1491 (s), 1461 (m), 1403 (m), 1351 (vs), 1311 (vs), 1287 (vs), 1256 (vs), 1211 (vs), 1175 (m), 1155 (s), 1125 (s), 1092 (s), 1069 (w), 1018 (s), 955 (s), 920 (m), 861 (m), 839 (m), 803 (w), 768 (s), 750 (s), 696 (w), 564 (w).

**HRMS** for **$C_{12}H_{13}NO_5$** (251.0794): found: 251.0768.

## Synthesis of ethyl 4-(2-methyl-3-oxo-1-cyclopentenyl)-3-nitrobenzoate (44g)




Prepared according to **TP 3** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (482 mg, 1.50 mmol), PhMgCl (0.97 mL, 1.6 mmol, 1.7 M in THF), CuCN·2LiCl (1.6 mL, 1.6 mmol, 1.0 M in THF) and 3-iodo-2-methyl-2-pentenone (500 mg, 2.25 mmol). Reaction time: 3 h. Purification by flash chromatography (pentane/diethyl ether = 1:2) yielded compound **44g** (266 mg, 61%) as a yellow solid.

**mp.:** 80-81 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.69 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.29 (dd, $^3J$(H,H) = 8.2 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.32 (d, $^3J$(H,H) = 8.2 Hz, 1 H), 4.40 (q,

$^{3}J$(H,H) = 7.1 Hz, 2 H), 2.79-2.75 (m, 2 H), 2.55-2.52 (m, 2 H), 1.52 (s, 3 H), 1.37 (t, $^{3}J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 208.4, 165.1, 164.4, 147.6, 139.3, 137.5, 134.6, 132.5, 130.0, 126.4, 62.5, 34.7, 31.1, 14.6, 9.0.

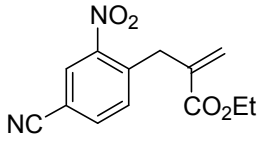
**MS** (70 eV, EI), *m/z* (%): 290 (32) $[M+H]^+$, 244 (74), 234 (57), 218 (100), 204 (73), 192 (83), 176 (50), 144 (24), 141 (36), 128 (37), 115 (60).

**IR** (KBr): $\tilde{\nu}$ = 3432 (m), 1708 (vs) 1721 (vs), 1652 (w), 1619 (m), 1533 (s), 1440 (w), 1398 (w), 1388 (w), 1345 (m), 1289 (s), 1252 (s), 1219 (w), 1160 (w), 1112 (m), 1058 (w), 1021 (m), 865 (w), 837 (w), 774 (w), 729 (m), 664 (w).

**HRMS** for **$C_{15}H_{15}NO_5$** (289.0950): found: 290.1026 $[M+H]^+$.

**$C_{15}H_{15}NO_5$:** required: C: 62.28; H: 5.23; N: 4.84;
found: C: 61.99; H: 5.37; N: 4.74.

## Synthesis of ethyl 2-(4-cyano-2-nitrobenzyl)acrylate (44h)




Prepared according to **TP 3** from 4-iodo-3-nitrobenzonitrile (**21e**) (548 mg, 2.00 mmol), PhMgCl (1.1 mL, 2.1 mmol, 2.0 M in THF), CuCN·2LiCl (2.0 mL, 2.0 mmol, 1.0 M in THF) and ethyl (2-bromomethyl) acrylate (463 mg, 2.40 mmol). Reaction time: 30 min. Purification by flash chromatography (pentane/CH2CL2 = 4:6) furnished title compound **44h** (300 mg, 58%) as a yellow solid.

**mp.:** 62-63 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.23 (d, $^{4}J$(H,H) = 1.8 Hz, 1 H), 7.81 (dd, $^{3}J$(H,H) = 8.4 Hz, $^{4}J$(H,H) = 1.8 Hz, 1 H), 7.56 (d, $^{3}J$(H,H) = 8.4 Hz, 1 H), 6.31 (s, 1 H), 5.38 (m, 1 H), 4.13 (q, $^{3}J$(H,H) = 7.1 Hz, 2 H), 3.95 (s, 2 H), 1.17 (t, $^{3}J$(H,H) = 7.1 Hz, 3 H).

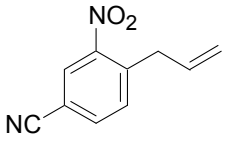
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.8, 149.5, 139.1, 137.0, 135.6, 133.4, 128.4, 128.2, 116.5, 112.1, 61.3, 34.9, 14.0.

**MS** (70 eV, EI), *m/z* (%): 261 (0.1) $[M^+]$, 215 (100), 186 (77), 169 (40), 159 (47),142 (39), 129 (27), 115 (28), 104 (23), 90 (18), 77 (14), 63 (17).

**IR** (KBr): $\tilde{\nu}$ = 3065 (m), 1703 (s), 1703 (vs), 1536 (vs), 1361 (s), 1331 (s), 1310 (s), 1211 (m), 1197 (s), 1159 (m), 1027 (m, 965 (m), 928 (m), 849 (m), 826 (m).

**HRMS** for **$C_{13}H_{12}N_2O_4$** (260.0797): found: 261.0887 $[M+H]^+$.

## Synthesis of 4-allyl-3-nitrobenzonitrile (44i)




Prepared according to **TP 3** from 4-iodo-3-nitrobenzonitrile (**21e**) (411 mg, 1.50 mmol), PhMgCl (0.80 mL, 1.6 mmol, 2.0 M in THF), CuCN·2LiCl (1.6 mL, 1.6 mmol, 1.0 M in THF) and allyl bromide (363 mg, 3.00 mmol). Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded compound **44i** as a yellow oil (128 mg, 53%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.21 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.83 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.53 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 5.97-5.83 (m, 1 H), 5.22-5.08 (m, 2 H), 3.74 (m, 2 H).

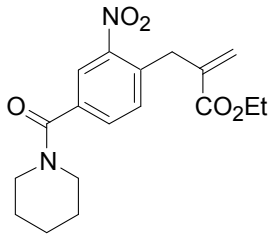
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.7, 139.3, 133.6, 131.2, 129.4, 125.3, 118.7, 118.3, 117.5, 34.4.

**MS** (70 eV, EI), *m/z* (%): 187 (23) $[M-H]^+$, 171 (97), 159 (89), 140 (100), 129 (42), 116 (76), 102 (33), 89 (37), 77 (29), 63 (31), 55 (18).

**IR** (KBr): $\tilde{\nu}$ = 3084 (m), 2237 (s), 1617 (m), 1537 (vs), 1492 (m), 1440 (m), 1356 (vs), 1196 (w), 1074 (w), 996 (m), 925 (s), 847 (m), 813 (s), 761 (w), 591 (w).

**HRMS** for **$C_{10}H_8N_2O_2$** (188.0586): found: 187.0516 $[M-H]^+$.

## Synthesis of ethyl 2-[2-nitro-4-(1-piperidinylcarbonyl)benzyl]acrylate (44j)




Prepared according to **TP 3** from 1-(4-iodo-3-nitrobenzoyl)piperidine (**21e**) (360 mg, 1.00 mmol), PhMgCl (0.63 mL, 1.1 mmol, 1.8 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and ethyl (2-bromomethyl) acrylate (386 mg, 2.00 mmol). Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 1:2) yielded compound **44j** as a pale yellow oil (270 mg, 78%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.94 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.55 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.40 (d, $^3J$(H,H) = 8.0 Hz, 1 H), 6.27 (m, 1 H), 5.44 (m, 1 H), 6.05-5.94 (m, 1 H), 4.16 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.97 (s, 2 H), 3.7 (s_br, 2 H), 3.50 (s_br, 2 H), 1.70-1.45 (m, 6 H), 1.23 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

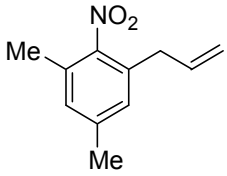
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 167.5, 166.2, 149.2, 137.9, 136.2, 134.9, 132.6, 131.2, 127.2, 123.5, 112.5, 61.1, 48.9, 43.4, 34.6, 25.5, 24.4, 14.1.

**MS** (70 eV, EI), *m/z* (%): 345 (100) [$M^+$], 329 (18), 311 (19), 301 (19), 283 (6), 262 (12), 254 (7), 239 (10), 226 (14), 216 (9), 200 (3), 189 (8), 172 (10), 160 (16), 143 (15), 130 (8), 115 (23), 103 (7), 89 (10), 84 (11), 77 (7), 69 (6), 56 (5).

**IR** (KBr): $\tilde{\nu}$ = 2939 (s), 1715 (vs), 1633 (vs), 1532 (vs), 1498 (s), 1441 (vs), 1351 (vs), 1276 (vs), 1191 (s), 1135 (s), 1124 (m), 1026 (s), 1010 (s), 955 (m), 906 (w), 854 (m), 822 (m), 756 (w), 732 (w), 668 (w).

**HRMS** for **$C_{18}H_{22}N_2O_5$** (346.1529): found: 345.1453 [M−H]$^+$.

## Synthesis of 2-allyl-4,6-dimethyl-1-nitrobenzene (44k)




Prepared according to **TP 3** from 2-iodo-4,6-dimethyl-nitrobenzene (**21g**) (277 mg, 1.00 mmol), PhMgCl (0.73 mL, 1.1 mmol, 1.5 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and allyl bromide (242 mg, 2.00 mmol). Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 49:1) yielded compound **44k** as a yellow oil (149 mg, 78%).

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 6.95-6.92 (m, 2 H), 5.92-5.82 (m, 1 H), 5.11-5.05 (m, 2 H), 3.32 (d, $^3J$(H,H) = 6.7 Hz, 2 H), 2.32 (s, 3 H), 2.27 (s, 3 H).

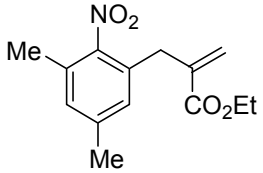
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 140.5, 135.0, 131.5, 130.0, 129.7, 128.7, 117.1, 113.0, 35.6, 21.1, 17.5.

**MS** (70 eV, EI), *m/z* (%): 191 (1) [$M^+$], 174 (100), 159 (7), 144 (17), 131 (29), 115 (23), 105 (9), 91 (21), 77 (14), 65 (5), 55 (28).

**IR** (KBr): $\tilde{\nu}$ = 2925 (m), 1603 (w), 1524 (vs), 1441 (w), 1366 (vs), 1296 (w), 1180 (w), 994 (m), 918 (m), 856 (m), 834 (s), 604 (w).

**HRMS** for **$C_{11}H_{13}NO_2$** (191.0946): found: 191.0949.

## Synthesis of ethyl 2-(3,5-dimethyl-2-nitrobenzyl)acrylate (44l)



Prepared according to **TP 3** from 2-iodo-4,6-dimethyl-nitrobenzene (**21g**) (277 mg, 1.00 mmol), PhMgCl (0.73 mL, 1.1 mmol, 1.5 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and ethyl (2-bromomethyl) acrylate (288 mg, 1.50 mmol). Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded title compound **44l** as a yellow oil (200 mg, 76%).

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 6.96 (s, 1 H), 6.92 (s, 1 H), 6.27 (d, $^2J$(H,H) = 1.0 Hz, 1 H), 5.43 (d, $^2J$(H,H) = 1.0 Hz, 1 H), 4.16 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.60 (s, 2 H), 2.31 (s, 3 H), 2.27 (s, 3 H), 1.24 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

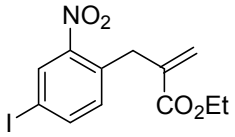
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 166.3, 140.4, 138.1, 130.4, 130.3, 129.9, 129.1, 127.1, 60.9, 36.0, 33.5, 21.1, 17.6, 14.1.

**MS** (70 eV, EI), *m/z* (%): 262 (0.2) $[M-H]^+$, 217 (100), 200 (26), 189 (58), 172 (53), 160 (15), 144 (23), 128 (18), 115 (15), 91 (13), 77 (8).

**IR** (KBr): $\tilde{\nu}$ = 2982 (w), 1717 (vs), 1603 (m), 1525 (vs), 1443 (m), 1366 (s), 1301 (m), 1255 (m), 1194 (m), 1143 (s), 1026 (m), 953 (w), 860 (m), 835 (m), 817 (w).

**HRMS** for **$C_{14}H_{17}NO_4$** (263.1158): found: 262.1094 $[M-H]^+$.

## Synthesis of ethyl 2-(4-iodo-2-nitrobenzyl)acrylate (44m)




Prepared according to **TP 3** from 2,5-diiodo-nitrobenzene (**21h**) (563 mg, 1.50 mmol), PhMgCl (0.85 mL, 1.7 mmol, 2.0 M in THF), CuCN·2LiCl (1.7 mL, 1.7 mmol, 1.0 M in THF) and ethyl (2-bromomethyl) acrylate (345 mg, 1.80 mmol). Reaction time: 45 min. Purification by flash chromatography (pentane/$CH_2Cl_2$ = 2:1) yielded compound **44m** (401 mg, 74%) as a yellow oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.16 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.77 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.04 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 6.21 (d, $^2J$(H,H) = 0.9 Hz, 1 H), 5.38 (d, $^2J$(H,H) = 0.9 Hz, 1 H), 4.10 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.84 (s, 2 H), 1.18 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.1, 148.8, 140.7, 136.7, 132.8, 132.3, 132.3, 126.2, 89.8, 60.1, 33.4, 13.1.

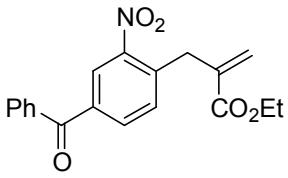
**MS** (70 eV, EI), *m/z* (%): 360 (7) $[M^+]$, 344 (10), 332 (100), 316 (100), 304 (12), 298 (28), 287 (78), 270 (78), 261 (58), 230 (19), 205 (32), 177 (11), 161 (72), 145 (21), 133 (66), 117 (22), 102 (29), 89 (58), 77 (34), 63 (41).

**IR** (KBr): $\tilde{\nu}$ = 2981 (w), 1714 (vs), 1529 (vs), 1475 (m), 1349 (vs), 1299 (m), 1137 (s), 1025 (m), 953 (m), 810 (m), 727 (w), 701 (w).

**HRMS** for $C_{12}H_{12}INO_4$ (360.9811): found: 359.9765 $[M-H]^+$.

$C_{12}H_{12}INO_4$: required: C: 39.91; H: 3.35; N: 3,88;
found: C: 39.90; H: 3.10; N: 3.86.

## Synthesis of ethyl 2-(4-benzoyl-2-nitrobenzyl)acrylate (44n)




Prepared according to **TP 3** from 4-iodo-3-nitrobenzophenone (**21i**) (353 mg, 1.00 mmol), PhMgCl (0.73 mL, 1.1 mmol, 1.5 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and ethyl (2-bromomethyl) acrylate (288 mg, 1.50 mmol). Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded title compound **44n** as a yellow oil (329 mg, 97%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.34 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.99 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.84-7.78 (m, 2 H), 7.69-7.63 (m, 1 H), 7.57-7.51 (m, 3 H), 6.85 (d, $^2J$(H,H) = 0.9 Hz, 1 H), 5.54 (d, $^2J$(H,H) = 0.9 Hz, 1 H), 4.21 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 4.07 (s, 2 H), 1.28 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 194.2, 166.4, 149.7, 138.2, 138.0, 137.5, 136.8, 134.0, 133.6, 132.9, 130.3, 129.1, 127.9, 126.6, 61.5, 35.2, 14.6.

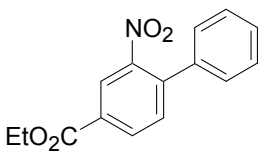
**MS** (70 eV, EI), *m/z* (%): 338 (1) $[M-H]^+$, 310 (8), 293 (27), 265 (14), 248 (8), 189 (5), 160 (4), 144 (5), 115 (8), 105 (100), 77 (55).

**IR** (KBr): $\tilde{\nu}$ = 1715 (vs), 1665 (vs), 1616 (s), 1534 (vs), 147 (s), 1353 (s), 1318 (s), 1301 (s), 1278 (vs), 1191 (s), 1180 (s), 1151 (s), 721 (m), 700 (m).

**HRMS** for $C_{19}H_{17}NO_5$ (339.1107): found: 338.1025 $[M-H]^+$.

**$C_{19}H_{17}NO_5$:** required: C: 67.25; H: 5.05; N: 4.13;
found: C: 67.25; H: 5.30; N: 4.00.

## Synthesis of ethyl 2-nitro[1,1'-biphenyl]-4-carboxylate (51a)



Prepared according to **TP 4** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (482 mg, 1.50 mmol), PhMgCl (0.89 mL, 1.7 mmol, 1.9 M in THF), $ZnBr_2$ (1.7 mL, 1.7 mmol, 1.0 M in THF), $Pd(dba)_2$ (44.0 mg, 0.075 mmol) and tfp (35 mg, 0.15 mmol). Reaction time: 3 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded biphenyl **51a** as a yellow oil (317 mg, 78%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.47 (d, $^4J$(H,H) = 1.8 Hz, 1H), 8.25 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1H), 7.53 (d, $^3J$(H,H) = 8.0 Hz, 1 H), 7.46-7.40 (m, 3 H), 7.34-7.31 (m, 2 H), 4.44 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.43 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

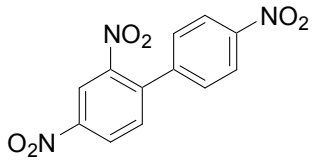
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.3, 149.2, 140.2, 136.8, 132.8, 132.1, 130.7, 128.8, 127.7, 125.1, 113.2, 61.8, 14.3.

**MS** (70 eV, EI), *m/z* (%): 271 (23) [$M^+$], 254 (49), 243 (100), 226 (61), 214 (22), 198 (38), 187 (45), 182 (12), 170 (51), 151 (91), 142 (30), 126 (9), 115 (26), 75 (5).

**IR** (KBr): $\tilde{\nu}$ = 2984 (m), 1723 (vs), 1618 (m), 1535 (vs), 1447 (m), 1360 (s), 1303 (s), 1285 (vs), 1236 (s), 1153 (m), 1113 (s), 1008 (m), 918 (w), 860 (m), 836 (w), 770 (m), 752 (s), 699 (s), 677 (w).

**HRMS** for **$C_{15}H_{13}NO_4$** (271.0845): found: 271.0846.

## Synthesis of 4'-nitro-2,4-dinitro-biphenyl (51b)




Prepared according to **TP 4** from 1-iodo-2,4-dinitrobenzene (**21b**) (441 mg, 1.50 mmol), mesitylmagnesium bromide (2.5 mL, 1.7 mmol, 0.72 M in THF), $ZnBr_2$ (1.7 mL, 1.7 mmol, 1.0 M in THF), $Pd(dba)_2$ (39.5 mg, 0.075 mmol), tfp (35 mg, 0.15 mmol) and ethyl 4-iodo-nitrobenzene (560 mg, 2.25 mmol). Reaction time: 4 h. Purification by flash chromatography (pentane/ethyl acetate = 5:1) yielded biphenyl **51b** as a yellow solid (240 mg, 55%).

**mp**.: 177-178°C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.79 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.49 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.4 Hz, 1 H), 8.28 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 7.63 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.46 (d, $^3J$(H,H) = 8.8 Hz, 2 H).

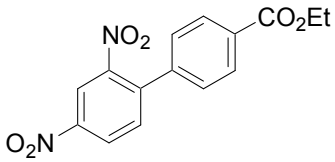
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 147.6, 147.4, 146.8, 140.9, 139.2, 132.1, 127.9, 126.1, 123.2, 119.2.

**MS** (70 eV, EI), *m/z* (%): 298 (12) [$M^+$], 272 (36), 242 (47), 215 (70), 169 (92), 150 (100), 139 (68).

**IR** (KBr): $\tilde{\nu}$ = 3436 (m), 3099 (m), 3052 (w), 1598 (s), 1532 (vs), 1476 (w), 1349 (vs), 1291 (w), 1110 (w), 1078 (w), 1006 (w), 917 (w), 858 (s), 836 (m), 760 (m), 745 (m), 723 (w), 700 (m), 537 (w).

**HRMS** for $\mathbf{C_{12}H_7N_3O_6}$ (289.0335): found: 289.0339.

## Synthesis of ethyl 2',4'-dinitro-biphenyl-4-carboxylate (51c)




Prepared according to **TP 4** from 1-iodo-2,4-dinitrobenzene (**21b**) (441 mg, 1.50 mmol), mesitylmagnesium bromide (2.5 mL, 1.7 mmol, 0.72 M in THF), $ZnBr_2$ (1.7 mL, 1.7 mmol, 1.0 M in THF), $Pd(dba)_2$ (39.5 mg, 0.075 mmol), tfp (35 mg, 0.15 mmol) and ethyl 4-iodobenzoate (455 mg, 1.65 mmol). Reaction time: 3 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded biphenyl **51c** as a yellow solid (320 mg, 68%).

**mp**.: 121-122°C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.70 (d, $^4J$(H,H) = 2.4 Hz, 1 H), 8.43 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.4 Hz, 1 H), 8.08 (d, $^3J$(H,H) = 8.2 Hz, 2 H), 7.61 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.34 (d, $^3J$(H,H) = 8.2 Hz, 2 H), 4.41 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.39 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.7, 147.9, 146.3, 140.4, 138.6, 132.1, 130.5, 129.2, 126.8, 125.7, 118.9, 60.4, 13.3.

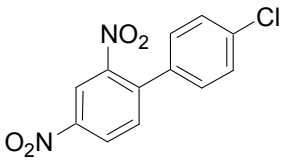
**MS** (70 eV, EI), *m/z* (%): 316 (2) [$M^+$], 288 (50), 271 (100), 260 (22), 242 (12), 225 (32), 215 (20), 179 (53), 169 (16), 151 (33), 139 (20).

**IR** (KBr): $\tilde{\nu}$ = 3106 (w), 2988 (w), 1717 (vs), 1602 (m), 1530 (vs), 1416 (w), 1352 (s), 1298 (m), 1286 (s), 1189 (w), 1134 (w), 1106 (m), 1077 (w), 1025 (w), 1007 (w), 910 (w), 846 (w), 836 (w), 776 (w), 763 (w), 741 (m), 705 (w).

**HRMS** for $\mathbf{C_{15}H_{12}N_2O_6}$ (316.0695): found: 316.0685.

| | | |
|---|---|---|
| $\mathbf{C_{15}H_{12}N_2O_6}$: | required: | C: 56.96; H: 3.82; N: 8.86; |
| | found: | C: 56.66; H: 3.92; N: 8.69. |

## Synthesis of 4'-chlor-2,4-dinitro-biphenyl (51d)




Prepared according to **TP 4** from 1-iodo-2,4-dinitrobenzene (**21b**) (441 mg, 1.50 mmol), mesitylmagnesium bromide (2.5 mL, 1.7 mmol, 0.72 M in THF), $ZnBr_2$ (1.7 mL, 1.7 mmol, 1.0 M in THF), $Pd(dba)_2$ (39.5 mg, 0.075 mmol), tfp (35 mg, 0.15 mmol) and 4-chloro-iodobenzene (536 mg, 2.25 mmol). Reaction time: 5 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded biphenyl **51d** as a pale yellow solid (228 mg, 55%).

**mp**.: 80-81 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.65 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.40 (dd, $^3J$(H,H) = 8.3 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.58 (d, $^3J$(H,H) = 8.3 Hz, 1 H), 7.59-7.33 (m, 2 H), 7.22-7-18 (m, 2 H).

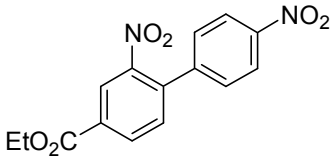
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 147.9, 146.1, 140.1, 135.0, 132.1, 128.6, 128.0, 127.4, 125.6, 118.9.

**MS** (70 eV, EI), *m/z* (%): 278 (74) [$M^+$], 250 (29), 243 (57), 233 (27), 215 (41), 186 (37), 169 (61), 151 (100), 139 (60).

**IR** (KBr): $\tilde{\nu}$ = 3103 (w), 1651 (w), 1603 (s), 1541 (vs), 1528 (vs), 1472 (m), 1351 (vs), 1192 (w), 1150 (w), 1092 (m), 1074 (m), 984 (w), 1006 (m), 909 (m), 853 (w), 834 (s), 768 (w), 747 (m), 728 (m), 716 (m), 693 (w), 549 (w), 416 (w).

**HRMS** for **$C_{12}H_7ClN_2O_4$** (278.0094): found: 278.0068.

## Synthesis of ethyl 2,4'-dinitro[1,1'-biphenyl]-4-carboxylate (51e)




Prepared according to **TP 4** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (321 mg, 1.00 mmol), mesitylmagnesium bromide (1.3 mL, 1.1 mmol, 0.85 M in THF), $ZnBr_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF), $Pd(dba)_2$ (29 mg, 0.05 mmol), tfp (23 mg, 0.10 mmol) and 4-iodonitrobenzene (374 mg, 1.50 mmol). Reaction time: 5 h at rt. Purification by flash chromatography (pentane/diethyl ether = 3:1) yielded biphenyl **51e** as a pale yellow solid (269 mg, 85%).

**mp**.: 124.5-125 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.61 (d, $^4J$(H,H) = 2.0 Hz, 1 H), 8.34-8.28 (m, 3 H), 7.54-7.47 (m, 3 H), 4.44 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.43 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 163.9, 148.6, 147.9, 143.3, 138.1, 133.4, 132.1, 131.9, 128.9, 125.6, 123.9, 62.1, 14.2.

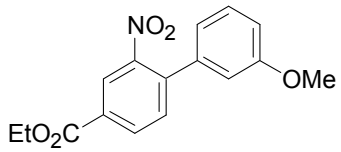
**MS** (70 eV, EI), *m/z* (%): 316 (51) [$M^+$], 299 (50), 271 (88), 255 (9), 242 (53), 225 (46), 214 (72), 195 (36), 179 (72), 168 (26), 150 (100), 139 (67), 125 (13), 115 (21), 99 (9), 75 (24), 63 (10).

**IR** (KBr): $\tilde{\nu}$ = 1722 (vs), 1530 (s), 1517 (s), 1353 (vs), 1307 (s), 1286 (s), 1242 (m), 1126 (m), 1110 (m), 857 (m), 850 (m), 749 (m).

**HRMS** for **$C_{15}H_{12}N_2O_6$** (316.0695): found: 316.0686.

**$C_{15}H_{12}N_2O_6$:** required: C: 56.96; H: 3.82; N: 8.86;
found: C: 56.69; H: 3.74; N: 8.78.

## Synthesis of ethyl 3'-methoxy-2-nitro[1,1'-biphenyl]-4-carboxylate (51f)




Prepared according to **TP 4** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (321 mg, 1.00 mmol), mesitylmagnesium bromide (1.3 mL, 1.1 mmol, 0.85 M in THF), $ZnBr_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF), $Pd(dba)_2$ (29 mg, 0.05 mmol), tfp (23 mg, 0.10 mmol) and 3-iodoanisole (468 mg, 2.00 mmol). Reaction time: 4 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded biphenyl **51f** as a colorless liquid (240 mg, 80%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.49 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.27 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.56 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.37 (t, $^3J$(H,H) = 8.4 Hz, 1 H), 6.98 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 6.93-6.87 (m, 2 H), 4.46 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.84 (s, 3 H), 1.45 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

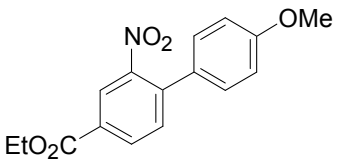
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.3, 159.8, 149.3, 140.0, 132.7, 132.0, 130.8, 129.9, 128.9, 125.0, 120.1, 114.3, 113.5, 61.8, 55.3, 14.3.

**MS** (70 eV, EI), *m/z* (%): 301 (100) [$M^+$], 284 (8), 273 (55), 256 (51), 242 (23), 230 (27), 214 (23), 202 (21), 196 (14), 183 (20), 170 (28), 152 (26), 139 (66), 127 (17), 115 (10), 101 (4), 89 (7), 76 (8), 63 (7), 55 (12).

**IR** (KBr): $\tilde{\nu}$ = 1728 (vs), 1663 (m), 1538 (vs), 1355 (s), 1318 (m), 1279 (vs), 1239 (vs), 1133 (m), 828 (m), 716 (m).

**HRMS** for **$C_{16}H_{15}NO_5$** (301.0950): found: 301.0954.

**Synthesis of ethyl 4'-methoxy-2-nitro[1,1'-biphenyl]-4-carboxylate (51g)**




Prepared according to **TP 4** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (482 mg, 1.50 mmol), mesitylmagnesium bromide (2.3 mL, 1.6 mmol, 0.70 M in THF), $ZnBr_2$ (1.6 mL, 1.6 mmol, 1.0 M in THF), $Pd(dba)_2$ (44.0 mg, 0.075 mmol), tfp (35 mg, 0.15 mmol) and 4-iodoanisole (523 mg, 2.25 mmol). Reaction time: 3 h. Purification by flash chromatography (pentane/ethyl acetate = 9:1) yielded biphenyl **51g** as a yellow oil (220 mg, 49%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.32 (d, $^4J$(H,H) = 1.8 Hz, 1H), 8.22 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1H), 7.51 (d, $^3J$(H,H) = 8.0 Hz, 1 H), 7.26 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 6.95 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 4.41 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.83 (s, 3 H), 1.42 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

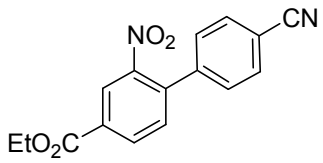
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.4, 160.2, 149.2, 139.7, 132.6, 131.9, 130.2, 129.1, 128.4, 125.1, 114.4, 61.8, 55.3, 14.3.

**MS** (70 eV, EI), *m/z* (%): 301 (100) [$M^+$], 284 (9), 271 (3), 256 (32), 241 (5), 228 (6), 218 (17), 190 (9), 182 (14), 167 (12), 156 (5), 139 (57), 127 (4), 113 (4), 89 (4).

**IR** (KBr): $\tilde{\nu}$ = 1722 (vs), 1675 (s), 1534 (s), 1352 (s), 1315 (m), 1287 (vs), 1237 (vs), 1164 (m), 764 (w), 716 (m), 687 (m).

**HRMS** for **$C_{16}H_{15}NO_5$** (301.0950): found: 301.0939.

**Synthesis of ethyl 4'-cyano-2-nitro[1,1'-biphenyl]-4-carboxylate (51h)**




Prepared according to **TP 4** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (482 mg, 1.50 mmol), mesitylmagnesium bromide (2.3 mL, 1.6 mmol, 0.70 M in THF), $ZnBr_2$ (1.6 mL, 1.6 mmol, 1.0 M in THF), $Pd(dba)_2$ (43.0 mg, 0.075 mmol), tfp (35 mg, 0.15 mmol) and 4-iodobenzonitrile (458 mg, 2.00 mmol). Reaction time: 4 h. Purification by flash chromatography (pentane/ethyl acetate = 6:1) yielded biphenyl **51h** as a yellow oil (235 mg, 53%).

**mp.:** 143-144 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.79 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.35 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.67-7.64 (m, 2 H), 7.53-7.48 (m, 1 H), 7.41-7.35 (m, 2 H), 4.41 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.38 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

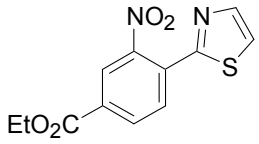
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 191.6, 162.8, 145.8, 138.7, 134.5, 133.7, 133.1, 132.1, 128.2, 128.2, 127.9, 124.5, 61.3, 13.3.

**MS** (70 eV, EI), *m/z* (%): 296 (25) [$M^+$], 279 (17), 268 (81), 251 (81), 223 (32), 207 (49), 195 (80), 177 (100), 167 (21), 150 (35).

**IR** (KBr): $\tilde{\nu}$ = 3435 (s), 2229 (m), 1721 (vs), 1619 (m), 1534 (s), 139 (w), 1369 (m), 1354 (m), 1306 (s), 1289 (s), 1241 (m), 1161 (w), 1127 (m), 1111 (m), 1022 (w), 1006 (w), 863 (w), 839 (m), 763 (m), 740 (w), 575 (m).

**$C_{16}H_{12}N_2O_4$:** required: C: 64.86; H: 4.08; N: 9.46;
found: C: 64.50; H: 4.19; N: 9.27.

## Synthesis of ethyl 3-nitro-4-(1,3-thiazol-2-yl)benzoate (51i)




Prepared according to **TP 4** from ethyl 4-iodo-3-nitrobenzoate (**21d**) (321 mg, 1.00 mmol), mesitylmagnesium bromide (1.6 mL, 1.1 mmol, 0.70 M in THF), $ZnBr_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF), $Pd(dba)_2$ (29 mg, 0.05 mmol), tfp (23 mg, 0.10 mmol) and 2-bromothiazole (328 mg, 2.00 mmol). Reaction time: 6 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) furnished title compound **51i** as a yellow solid (133 mg, 48%).

**mp**.: 140.5-143 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 8.40 (d, $^4J$(H,H) = 1.7 Hz, 1 H), 8.25 (dd, $^3J$(H,H) = 8.1 Hz, $^4J$(H,H) = 1.7 Hz, 1 H), 7.95 (d, $^3J$(H,H) = 3.2 Hz, 1 H), 7.84 (d, $^3J$(H,H) = 8.1 Hz, 1 H), 7.52 (d, $^3J$(H,H) = 3.2 Hz, 1 H), 4.44 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.42 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

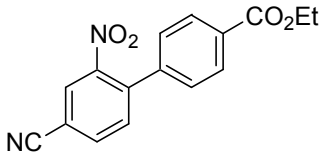
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 163.9, 160.9, 144.5, 134.1, 132.6, 131.4, 130.7, 126.0, 125.2, 121.7, 62.1, 14.2.

**MS** (70 eV, EI), *m/z* (%): 278 (9) [$M^+$], 233 (34), 206 (14), 180 (40), 176 (100), 161 (97), 152 (11), 148 (22), 135 (42), 120 (15), 103 (20), 89 (4), 75 (15), 58 (31).

**IR** (KBr): $\tilde{\nu}$ = 2963 (m), 1712 (s), 1546 (s), 1366 (m), 1288 (m), 1263 (vs), 1238 (m), 1097 (vs), 1020 (vs), 801 (vs), 766 (s).

**HRMS** for **$C_{16}H_{15}NO_5$** (278.0402): found: 278.0368.

**Synthesis of ethyl 4'-cyano-2'-nitro[1,1'-biphenyl]-4-carboxylate (51j)**




Prepared according to **TP 4** from 4-iodo-3-nitrobenzonitrile (**21e**) (411 mg, 1.50 mmol), mesitylmagnesium bromide (2.3 mL, 1.6 mmol, 0.70 M in THF), $ZnBr_2$ (1.6 mL, 1.6 mmol, 1.0 M in THF), $Pd(dba)_2$ (39.5 mg, 0.075 mmol), tfp (35 mg, 0.15 mmol) and ethyl 4-iodo-benzoate (621 mg, 2.50 mmol). Purification by flash chromatography (pentane/ethyl acetate = 6:1) yielded biphenyl **51j** as a pale yellow solid (325 mg, 73%).

**mp.**: 166-167 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 8.21 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.13 (d, $^3J$(H,H) = 8.5 Hz, 2 H), 7.93 (dd, $^3J$(H,H) = 8.5 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.60 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.38 (d, $^3J$(H,H) = 8.5 Hz, 2 H), 4.40 (q, $^3J$(H,H) = 7.2 Hz, 2 H), 1.41 (t, $^3J$(H,H) = 7.2 Hz, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 165.7, 149.1, 139.9, 135.5, 132.9, 131.4, 130.8, 130.2, 127.9, 127.8, 116.3, 113.2, 61.3, 14.3.

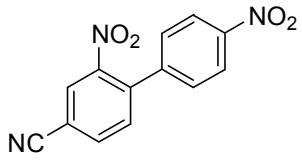
**MS** (70 eV, EI), *m/z* (%): 296 (10) [$M^+$], 269 (52), 251 (100), 228 (16), 205 (40), 177 (63), 150 (23), 126 (8), 77 (14), 63 (6), 51 (4).

**IR** (KBr): $\tilde{\nu}$ = 3436 (m), 2235 (m), 1712 (vs), 1610 (w), 1528 (vs), 1358 (s), 1286 (vs), 1110 (m), 849 (m), 761 (w), 712 (w).

**HRMS** for **$C_{16}H_{12}N_2O_4$** (296.0797): found: 296.0779.

**$C_{16}H_{12}N_2O_4$**: required: C: 64.86; H: 4.08; N: 9.46;
found: C: 64.62, H: 3.64; N: 9.40.

**Synthesis of 2,4'-dinitro[1,1'-biphenyl]-4-carbonitrile (51k)**




Prepared according to **TP 4** from 4-iodo-3-nitrobenzonitrile (**21e**) (411 mg, 1.50 mmol), mesitylmagnesium bromide (2.3 mL, 1.65 mmol, 0.70 M in THF), $ZnBr_2$ (1.6 mL, 1.6 mmol, 1.0 M in THF), $Pd(dba)_2$ (39.5 mg, 0.075 mmol), tfp (35 mg, 0.15 mmol) and ethyl 4-iodo-benzoate (621 mg, 2.50 mmol). Purification by flash chromatography (pentane/ethyl acetate = 6:1) yielded biphenyl **51k** as a pale yellow solid (325 mg, 73%).

**mp.**: 142-143 °C.

**$^1$H-NMR** (300 MHz, DMSO-$d_6$, 25 °C): δ = 8.71 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.36-8.30 (m, 3 H), 7.83 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.71 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.40 (q, $^3J$(H,H) = 7.5 Hz, 2 H), 1.41 (t, $^3J$(H,H) = 7.5 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, DMSO-$d_6$, 25 °C): δ = 148.7, 148.1, 142.8, 138.1, 137.1, 133.5, 129.8, 129.0, 124.2, 117.0, 113.1.

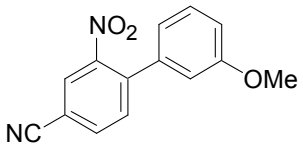
**MS** (70 eV, EI), *m/z* (%): 269 (31) [$M^+$], 252 (26), 239 (5), 222 (28), 206 (7), 195 (100), 177 (39), 164 (73 ), 150 (42), 140 (75), 126 (8), 114 (9), 99 (9), 87 (8), 75 (14), 63 (9), 51 (5).

**IR** (KBr): $\tilde{\nu}$ = 2237 (m), 1618 (w), 1600 (m), 1527 (vs), 1509 (s), 1352 (vs), 1300 (w), 1112 (w), 858 (w), 845 (m), 755 (w), 711 (w).

**HRMS** for **$C_{13}H_7N_3O_4$** (269.0437): found: 269.0425.

**$C_{13}H_7N_3O_4$**: required: C: 58.00, H: 2.62, N: 15.61;
found: C: 57.94, H: 2.31, N: 15.39.

## Synthesis of 3'-methoxy-2-nitro[1,1'-biphenyl]-4-carbonitrile (51l)




Prepared according to **TP 4** from 4-iodo-3-nitrobenzonitrile (**21e**) (273 mg, 1.00 mmol), mesitylmagnesium bromide (1.3 mL, 1.1 mmol, 0.85 M in THF), $ZnBr_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF), $Pd(dba)_2$ (29 mg, 0.05 mmol), tfp (23 mg, 0.10 mmol)and 3-iodoanisole (468 mg, 2.00 mmol). Reaction time: 5 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded biphenyl **51l** as a yellow solid (190 mg, 75%).

**mp**.: 115-115.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.10 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.87 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.60 (d, $^3J$(H,H) = 8.0 Hz, 1 H), 7.36 (t, $^3J$(H,H) = 8.0 Hz, 1 H), 6.99 (dd, $^3J$(H,H) = 8.5 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 6.88-6.82 (m, 2 H), 3.82 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 159.9, 149.4, 140.5, 136.7, 135.1, 133.0, 130.2, 127.6, 119.9, 116.5, 114.7, 113.5, 112.5, 55.4.

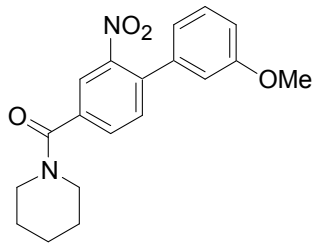
**MS** (70 eV, EI), *m/z* (%): 254 (100) [$M^+$], 237 (11), 226 (40), 209 (32), 195 (46), 183 (31), 177 (30), 164 (90), 153 (44), 140 (36), 127 (17), 114 (9), 101 (9), 87 (8), 75 (11), 63 (12), 55 (15).

**IR** (KBr): $\tilde{\nu}$ = 2234 (s), 1604 (m), 1527 (vs), 1442 (w), 1354 (vs), 1238 (vs), 1112 (m), 842 (m), 789 (w), 771 (m), 714 (m), 632 (w).

**HRMS** for **$C_{14}H_{10}N_2O_3$** (254.0691): found: 254.0705.

$C_{14}H_{10}N_2O_3$ : required: C: 66.14; H: 3.96; N: 11.02;
found: C: 65.97; H: 3.96; N: 11.03.

## Synthesis of 1-[(3'-methoxy-2-nitro[1,1'-biphenyl]-4-yl)carbonyl]piperidine (51m)




Prepared according to **TP 4** from 1-(4-iodo-3-nitrobenzoyl)piperidine (**21f**) (360 mg, 1.00 mmol), mesitylmagnesium bromide (1.3 mL, 1.1 mmol, 0.85 M in THF), $ZnBr_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF), $Pd(dba)_2$ (29 mg, 0.05 mmol), tfp (23 mg, 0.10 mmol) and 3-iodoanisole (351 mg, 1.50 mmol). Reaction time: 4 h. Purification by flash chromatography (pentane/diethyl ether = 1:1) yielded biphenyl **51m** as a light yellow solid (228 mg, 67%).

**mp**.: 90-91 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.86 (d, $^4J$(H,H) = 1.8 Hz, 2 H), 7.61 (dd, $^3J$(H,H) = 7.8 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.47 (d, $^3J$(H,H) = 7.8 Hz, 1 H), 7.32 (t, $^3J$(H,H) = 7.9 Hz, 1 H), 6.95-6.92 (m, 1 H), 6.88-6.83 (m, 2 H), 3.80 (s, 3 H), 3.72 (s_br, 2 H), 3.40 (s_br, 2 H), 1.84-1.50 (m, 6 H).

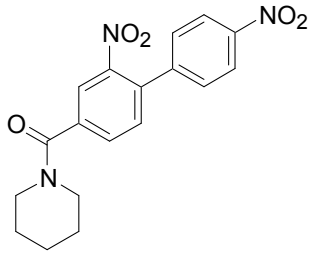
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 167.3, 159.7, 149.0, 137.9, 137.0, 126.7, 132.1, 130.5, 129.8, 122.6, 120.1, 114.0, 113.6, 55.3, 48.8, 43.4, 26.5, 25.5, 24.4.

**MS** (70 eV, EI), *m/z* (%): 339 (100) [$M^+$], 323 (10), 306 (13), 294 (21), 256 (54), 228 (10), 209 m(44), 180 (19), 152 (19), 139 (27), 127 (4), 84 (5).

**IR** (KBr): $\tilde{\nu}$ = 2857 (m), 1631 (vs), 1601 (s), 1530 (s), 1445 (s), 1350 (s), 1321 (m ), 1286 (s), 1260 (m), 1220 (s), 1179 (m), 1022 (m), 855 (m), 847 (m), 795 (m).

**HRMS** for $C_{19}H_{20}N_2O_4$ (340.1423): found: 340.1428.

## Synthesis of 1-[(2,4'-dinitro[1,1'-biphenyl]-4-yl)carbonyl]piperidine (51n)




Prepared according to **TP 4** from 1-(4-iodo-3-nitrobenzoyl)piperidine (**21f**) (360 mg, 1.00 mmol), mesitylmagnesium bromide (1.3 mL, 1.1 mmol, 0.85 M in THF), $ZnBr_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF), $Pd(dba)_2$ (29 mg, 0.05 mmol), tfp (23 mg, 0.10 mmol)and 4-iodonitrobenzene (498 mg, 2.00 mmol). Reaction time: 3 h. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded biphenyl **51n** as a pale yellow solid (345 mg, 77%).

**mp**.: 152.5-153 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.27 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 8.01 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.70 (dd, $^3J$(H,H) = 7.9 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.49-7.44 (m, 3 H), 3.72 (s_br, 2 H), 3.40 (s_br, 2 H), 1.75-1.52 (m, 6 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.8, 148.3, 147.8, 143.6, 138.1, 135.2, 131.9, 131.1, 128.9, 123.9, 123.3, 48.9, 43.3, 26.5, 25.4, 24.3.

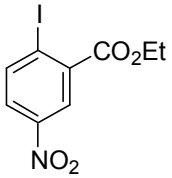
**MS** (70 eV, EI), *m/z* (%): 354 (100) $[M-H]^+$, 338 (19), 320 (9), 309 (17), 271 (54), 225 (26), 179 (47), 167 (3), 150 (28), 139 (11), 84 (8).

**IR** (KBr): $\tilde{\nu}$ = 2940 (w), 1632 (vs), 1599 (m), 1523 (vs), 1466 (w), 1444 (s), 1348 (vs), 1284 (m), 1113 (w), 1006 (w), 911 (w), 854 (m), 847 (m), 744 (m), 694 (w).

**HRMS** for **$C_{18}H_{17}N_3O_5$** (355.1168): found: 355.1162.

**$C_{18}H_{17}N_3O_5$**: required: C: 60.84; H: 4.82; N: 11.83;
found: C: 60.47; H: 4.87; N: 11.71.

## Synthesis of ethyl 2-iodo-5-nitrobenzoate (65a)




Prepared according to **TP 1** from $HNO_3$ (100%, 3.8 mL), $H_2SO_4$ (100%, 5.2 mL) ethyl 2-iodobenzoate (11.0 g, 40.0 mmol) at 75 °C. Reaction time: 12 h. Recrystallization from ethanol furnished product **65a** as pale yellow needles (10.8 g, 84%).

**mp.:** 100-101.3 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.52 (d, $^3J$(H,H) = 8.7 Hz, 1 H), 8.14 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 7.90 (dd, $^3J$(H,H) = 8.7 Hz, $^4J$(H,H) = 2.7 Hz, 1 H), 4.39 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.38 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

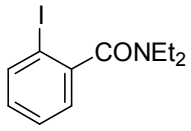
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 165.0, 148.1, 143.1, 137.1, 126.6, 125.8, 102.9, 63.0, 14.6.

**MS** (70 eV, EI), *m/z* (%): 321 (84) [$M^+$], 293 (79), 276 (100), 260 (10), 247 (11), 230 (31), 202 (14), 176 (2), 136 (2), 120 (5), 103 (5), 92 (9), 75 (23), 63 (3).

**IR** (KBr): $\tilde{\nu}$ = 1731 (vs), 1601 (s), 1565 (m), 1526 (vs), 1474 (m), 1459 (m), 1445 (m), 1384 (m), 1341 (vs), 1303 (vs), 1253 (vs), 1150 (s), 1127 (s), 1112 (m), 1091 (s), 1021 (vs), 969 (w), 919 (s), 869 (m), 837 (s), 781 (m), 734 (s).

**$C_9H_8INO_4$**: required: C: 33.67; H: 2.51; N: 4.36; I: 39.53;
found: C: 33.57; H: 2.44; N: 4.29; I: 39.52.

## Synthesis of *N*, *N*-diethyl-2-iodobenzamide (63)




A dry and nitrogen flushed 100 mL two neck round-bottom flask, equipped with a magnetic stirring bar and a dropping funnel, was charged with 2-iodobenzoyl chloride (10.7 g, 40.0 mmol) and $CH_2Cl_2$ (50 mL) was added. The reaction mixture was cooled to 0 °C and diethylamine (12.5 mL, 120 mmol) was added slowly with vigorous stirring. On completion of the addition, the cooling bath was removed, the reaction mixture stirred for additional 30 min and poured into water. After extraction with $CH_2Cl_2$ (3 x 100 mL), the combined organic fractions were washed with water, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Analytically pure *N*,*N*-diethyl-2-iodobenzamide (**63**) was obtained without further purification as a yellow oil (11.6 g, 95%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 7.73 (dd, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 7.38 (dt, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 1.4 Hz 1 H), 7.21 (dd, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 7.06 (dt, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 1.4 Hz 1 H), 3.90-3.75 (m, 1 H), 3.35-3.09 (m, 3 H), 1.30 (t, $^3J$(H,H) = 7.1 Hz, 3 H), 1.07 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

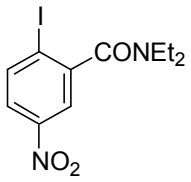
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 170.0, 142.9, 139.1, 129.8, 128.2, 126.8, 92.8, 42.8, 38.9, 13.9, 11.5.

**MS** (70 eV, EI), *m/z* (%): 302 (98) [$M^+$], 274 (3), 231 (100), 203 (37), 176 (42), 105 (7), 76 (11).

**IR** (KBr): $\tilde{\nu}$ = 2973 (m), 2933 (m), 1633 (vs), 1584 (m), 1479 (m), 1457 (s), 1427 (s), 1380 (m), 1363 (m), 1314 (m), 1290 (s), 1221 (m), 1101 (m), 1015 (m), 768 (m), 750 (m), 733 (m).

**$C_{11}H_{14}INO$:** required: C: 43.58; H: 4.66; N: 4.62; I: 41.86;
found: C: 43.39; H: 4.87; N: 4.77; I: 41.82.

## Synthesis of *N*, *N*-diethyl-2-iod-5-nitrobenzamide (65b)




Prepared according to **TP 1** from $HNO_3$ (100%, 3.8 mL), $H_2SO_4$ (100%, 5.2 mL) *N*, *N*-diethyl-2-iodobenzamide (63) (11.2 g, 37.0 mmol) at 75 °C. Reaction time: 12 h. Purification by flash-chromatography (pentane/diethyl ether = 1:1) yielded product **65b** as pale yellow solid (6.30 g, 49%).

**mp.:** 87-88 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.04-8.00 (m, 2 H), 7.87 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.6 Hz, 1 H), 3.92-3.70 (m, 1 H), 4.42-3.98 (m, 3 H), 1.30 (t, $^3J$(H,H) = 7.1 Hz, 3 H), 1.10 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

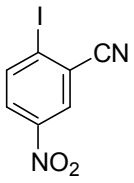
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 169.9, 148.0, 144.4, 140.6, 124.1, 121.5, 101.3, 43.0, 39.3, 14.0, 12.4.

**MS** (70 eV, EI), *m/z* (%): 347 (36) [$M^+$], 331 (21), 319 (2), 305 (6), 276 (100), 260 (5), 248 (2), 230 (34), 218 (4), 202 (15), 175 (15), 150 (6), 131 (1), 118 (1), 104 (5), 90 (1), 75 (15), 56 (3).

**IR** (KBr): $\tilde{\nu}$ = 3280 (s), 1642 (vs), 1602 (m), 1550 (s), 1522 (vs), 1450 (m), 1341 (vs), 1309 (s), 1253 (w), 1160 (w), 1150 (w), 1125 (w), 1099 (w), 1047 (w), 1019 (m), 843 (m), 827 (w), 778 (w), 735 (m).

**HRMS** for **$C_{11}H_{13}IN_2O_3$** (347.9971): found: 347.9985.

## Synthesis of 2-iodo-5-nitrobenzonitrile (65c)



Prepared according to **TP 1** from $HNO_3$ (100%, 2.8 mL), $H_2SO_4$ (100%, 3.9 mL) and 2-iodobenzonitrile (**64**) (6.87 g, 30.0 mmol) at 75 °C. Reaction time: 12 h. Recrystallization from ethanol furnished product **65c** as pale yellow solid (5.01 g, 59%).

**mp.:** 124-125.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.42 (d, $^4J$(H,H) = 2.6 Hz, 1 H), 8.17 (d, $^3J$(H,H) = 8.6 Hz, 1 H), 8.09 (dd, $^3J$(H,H) = 8.6 Hz, $^4J$(H,H) = 2.6 Hz, 1 H).

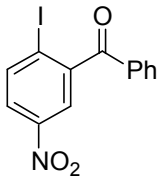
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 147.7, 141.1, 128.7, 127.7, 122.4, 117.5, 106.9.

**MS** (70 eV, EI), *m/z* (%): 274 (100) [$M^+$], 258 (2), 244 (19), 228 (35), 216 (24), 152 (1), 127 (5), 117 (11), 101 (47), 88 (2), 75 (18), 50 (12).

**IR** (KBr): $\tilde{\nu}$ = 1597 (m), 1566 (m), 1526 (vs), 1452 (m), 1351 (vs), 1253 (m), 1126 (w), 1025 (m), 925 (w), 912 (m), 852 (w), 841 (w), 790 (m), 739 (m).

**$C_7H_3IN_2O_2$:** required: C: 30.68; H: 1.10; N: 10.22; I: 46.31;
found: C: 30.70; H: 1.12; N: 9.99; I: 46.36.

## Synthesis of 2-iodo-5-nitrobenzophenone (65d)




Prepared according to the procedure of Baik and Wong[63] from 2-amino-5-nitrobenzophenone (726 mg, 3.00 mmol), $NaNO_2$ (417 mg, 6.00 mmol), HI (2.8 mL, 15 mmol, 50%$_{(aq)}$), CuI (570 mg, 3.00 mmol) and DMSO (20 mL) at 60 °C. Recrystallization from ethanol yielded compound **65d** as yellow solid (650 mg, 62%).

**mp.:** 141.5-143 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.14 (d, $^3J$(H,H) = 8.8 Hz, 1 H), 8.10 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.00 (d, $^3J$(H,H) = 8.8 Hz, $^4J$(H,H) = 2.7 Hz, 1 H), 7.81-7.76 (m, 2 H), 7.69-7.63 (m, 1 H), 7.53-7.46 (m, 2 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 194.9, 147.7, 145.9, 141.1, 134.5, 134.5, 130.4, 129.0, 125.1, 122.8, 100.6.

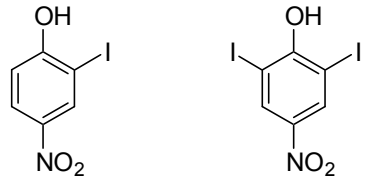
**MS** (70 eV, EI), *m/z* (%): 353 (60) [$M^+$], 275 (9), 229 (5), 201 (3), 180 (3), 151 (6), 105 (100), 77 (43), 51 (9).

**IR** (KBr): $\tilde{\nu}$ = 1662 (vs), 1593 (s), 1523 (vs), 1449 (m), 1350 (vs), 1315 (m), 1279 (vs), 1160 (m), 1023 (m), 967 (m), 858 (m), 850 (m), 798 (m), 761 (m), 740 (m), 728 (m), 705 (m), 688 (m), 638 (m).

**HRMS** for **$C_{13}H_8INO_3$** (352.9549): found: 352.9579.

**$C_{13}H_8INO_3$:** required: C: 44.22; H: 2.28; N: 3.97;
found: C: 44.70; H: 2.32; N: 4.03.

## Synthesis of 2-iodo-4-nitrophenol (69) and 2,6-diiodo-4-nitrophenol (70)




Prepared according to **TP 2** from 4-nitrophenol (1.39 g, 10.0 mmol), iodine (2.79 g, 11.0 mmol) and $Ag_2SO_4$ (3.43 g, 11.0 mmol) in ethanol (100 mL). Purification by flash-chromatography furnished products **69** and **70** as light yellow solids; (1.33 g, 50%) and (858 mg, 22%).

**Compound 69**

**mp.:** 78-79 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.57 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.15 (dd, $^3J$(H,H) = 8.8 Hz, $^4J$(H,H) = 2.7 Hz, 1 H), 7.05 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 6.00 (s_br, 1 OH).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 136.4, 134.4, 126.1, 115.7, 114.6, 84.4.

**MS** (70 eV, EI), *m/z* (%): 265 (100) [$M^+$], 235 (61), 92 (44), 42 (37), 63 (23), 64 (21), 53 (17).

**IR** (KBr): $\tilde{\nu}$ = 3550 (w), 1581 (s), 1510 (vs), 1487 (s), 1414 (w), 1342 (vs), 1290 (vs), 1212 (w), 1130 (w), 1117 (s), 747 (s), 683 (m), 638 (w), 552 (w), 521 (w), 466 (w), 435 (w).

**HRMS** for **$C_6H_4INO_3$** (264.9236): found: 264.9243.

**$C_6H_4INO_3$:** calc.: C: 27.19; H: 1.52; N: 5.29;
found: C: 27.53; H: 1.82; N: 5.22.

**Compound 70**

**mp.:** 155-156 °C.

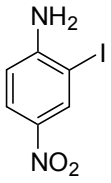
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.42 (s, 2 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 160.9, 141.2, 134.5, 82.2.

**MS** (70 eV, EI), *m/z* (%): 391 (100), 361 (22), 345 (3), 218 (24), 127 (11), 91 (14).

Spectral data match those of the commercially available sample.

**Synthesis of 2-iodo-5-nitroaniline (71)**




Prepared according to **TP 2** from 4-nitroaniline (1.38 mg, 10.0 mmol), iodine (2.79 g, 11.0 mmol) and $Ag_2SO_4$ (3.43 g, 11.0 mmol) in ethanol (100 mL). Recrystallization from ethanol furnished compound **71** as yellow solid (2.38 mg, 90%)

**mp.:** 105-107 °C.

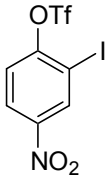
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.49 (d, $^4J$(H,H) = 2.5 Hz, 1 H), 7.99 (dd, $^3J$(H,H) = 8.8 Hz, $^4J$(H,H) = 2.5 Hz, 1 H), 6.77 (d, $^3J$(H,H) = 8.8 Hz, 1 H), 4.75 (s_br, 2 NH).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 162.3, 150.3, 132.0, 124.3, 117.8, 88.7

**MS** (70 eV, EI), *m/z* (%): 264 (100) [$M^+$], 234 (45), 218 (14), 91 (55).

Spectral data match those of the literature.[119]

**Synthesis of 2-iodo-4-nitro-1-[(trifluoromethyl)sulfonyl]benzene (72a)**




Prepared according to **TP 14** from 2-iodo-4-nitrophenol **69** (2.31 g, 8.70 mmol) and trifluomethylsulfonicacid anhydride (1.76 mL, 10.4 mmol). Purification by flash chromatography (pentane/diethyl ether = 19:1) furnished title compound **72a** as a yellow oil (2.90 g, 84%).

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.76 (d, $^4J$(H,H) = 2.6 Hz, 1 H), 8.35 (dd, $^3J$(H,H) = 9.0 Hz, $^4J$(H,H) = 2.6 Hz, 1 H), 7.50 (d, $^3J$(H,H) = 9.0 Hz, 1 H).

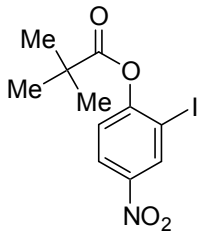
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): $\delta$ = 154.1, 136.2, 135.9, 125.3, 122.3, 118.6 (q, $^1J$(C,F) = 320 Hz), 89.2.

**MS** (70 eV, EI), *m/z* (%): 397 (100) [$M^+$], 303 (8), 287 (15), 275 (13), 264 (27), 221 (34), 176 (15), 94 (13), 63 (22).

**IR** (KBr): $\tilde{\nu}$ = 1532 (vs), 1462 (m), 1432 (vs), 1350 (vs), 1247 (vs), 1217 (vs), 1177 (s), 1135 (vs), 1033 (m), 890 (vs), 862 (m), 779 (m), 755 (s), 742 (m), 660 (w), 610 (s).

**HRMS** for $C_7H_3F_3INO_5S$ (396.8729): found: 396.8730.

## Synthesis of 2-iodo-4-nitrophenyl pivalate (72b)




A dry and nitrogen flushed 50 mL Schlenk flask, equipped with a magnetic stirring bar, was charged with 2-iodo-4-nitrophenol (**69**) (1.22 g, 4.60 mmol) and $CH_2Cl_2$ (15 mL), cooled to 0 °C and triethylamine (0.77 mL, 5.5 mmol) and DMAP (60 mg, 0.50 mmol) were added. Subsequently, pivaloyl chloride (680 mg, 5.60 mmol) was added slowly with vigorous stirring. On completion of the addition, the cooling bath was removed, the reaction mixture stirred for additional 4 h and poured into water. After extraction with $CH_2Cl_2$ (3 x 100 mL), the combined organic fractions were washed with water, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 29:1) furnished title compound **72b** as colourless solid (850 mg, 52%).

**mp.:** 71-72.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.70 (d, $^4J$(H,H) = 2.6 Hz, 1 H), 8.25 (dd, $^3J$(H,H) = 8.9 Hz, $^4J$(H,H) = 2.6 Hz, 1 H), 7.27 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 1.35 (s, 9 H).

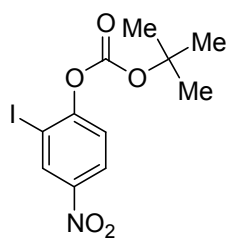
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 175.2, 156.4, 145.4, 134.8, 124.6, 123.0, 90.0, 39.5, 27.1.

**MS** (70 eV, EI), *m/z* (%): 349 (8) [$M^+$], 306 (2), 265 (49), 249 (5), 235 (9), 219 (3), 85 (39), 57 (100).

**IR** (KBr): $\tilde{\nu}$ = 1764 (vs), 1523 (vs), 1464 (s), 1345 (vs), 1212 (m), 1081 (vs), 1027 (s), 902 (m), 891 (m), 739 (w), 698 (w).

**HRMS** for $C_{11}H_{12}INO_4$ (348.9811): found: 348.9830.

## Synthesis of *tert*-butyl 2-iodo-4-nitrophenyl carbonate (72c)



A dry and nitrogen flushed 50 mL Schlenk flask, equipped with a magnetic stirring bar, was charged with 2-iodo-4-nitrophenol (**69**) (1.41 g, 5.30 mmol) and acetonitrile (15 mL), cooled to 0 °C and DMAP (60 mg, 0.50 mmol) was added. Subsequently, a solution of $Boc_2O$ (1.38 g, 6.30 mmol) dissolved in acetonitrile (5 mL) was added dropwise. On completion of the addition, the cooling bath was removed, the reaction mixture stirred for 24 h and poured into water. After extraction with ethyl acetate (3 x 30 mL), the combined organic fractions were washed with $KHSO_{4(aq)}$ (30 mL, 1 M), brine (30 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 9:1) furnished title compound **72c** as colourless oil (1.45 g, 75%).

**mp.:** 74.5-75.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.67 (d, $^4J$(H,H) = 2.6 Hz, 1 H), 8.23 (d, $^3J$(H,H) = 8.9 Hz, $^4J$(H,H) = 2.6 Hz, 1 H), 7.33 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 1.57 (s, 9 H).

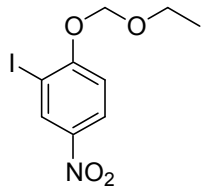
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 156.2, 149.7, 145.6, 134.8, 124.8, 123.0, 90.4, 85.4, 27.6.

**MS** (70 eV, EI), *m/z* (%): 350 (19) $[M-CH_3]^+$, 265 (22), 234 (9), 218 (2), 92 (8), 63 (11), 57 (100).

**IR** (KBr): $\tilde{\nu}$ = 2980 (w), 1765 (vs), 1526 (vs), 1372 (s), 1347 (vs), 1279 (s), 1223 (s), 1146 (vs), 1035 (m), 903 (m), 867 (m), 730 (m), 681 (w).

**HRMS** for **$C_{11}H_{12}INO_5$** (364.9760): found: 349.9502 $[M-CH_3]^+$.

## Synthesis of 1-(ethoxymethoxy)-2-iodo-4-nitrobenzene (72d)




A dry and argon flushed 50 mL Schlenk-flask, equipped with a magnetic stirring bar and a septum, was charged with 2-iodo-4-nitrophenol (**69**) (1.20 g, 4.70 mmol), dry DMF (25 mL) was added and the mixture cooled to 0 °C. NaH (120 mg, 5.00 mmol) was added portionwise and the suspension was stirred for further 10 min at 0 °C and additional 30 min at rt. Then, chloromethyl-ethyl ether (489 mg, 5.20 mmol) was added dropwise and the reaction mixture was stirred at rt for 2 h and poured into water. After extraction with ethyl acetate (3 x 30 mL), the combined organic fractions were washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 2:1) furnished title compound **72d** as colourless solid (1.40 g, 92%).

**mp.:** 63-64 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.67 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.21 (dd, $^3J$(H,H)= 8.8 Hz, $^4J$(H,H)= 2.7 Hz, 1 H), 7.16 (d, $^3J$(H,H)= 8.8 Hz, 1 H), 5.39 (s, 2 H), 3.77 (q, $^3J$(H,H)= 7.1 Hz, 2 H), 1.23 (t, $^3J$(H,H)= 7.1 Hz, 3H)

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 161.1, 142.4, 135.1, 125.4, 113.1, 93.8, 85.9, 65.4, 15.0

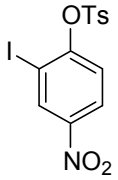
**MS** (70 eV, EI), *m/z* (%): 323.0 (6) [$M^+$], 264.9 (4), 92.0 (3), 59.0 (100).

**IR** (KBr): $\tilde{\nu}$ = 2981 (s), 2917 (m), 1593 (s), 1578 (vs), 1514 (vs), 1468 (vs), 1418 (w), 1392 (w), 1344 (vs), 1280 (w), 1256 (vs), 1241 (vs), 1171 (s), 1157 (s), 1116 (vs), 1088 (s), 1032 (s), 954 (vs), 898 (s), 838 (w), 788 (w), 743 (s), 669 (m), 625 (w).

**HRMS** for **$C_9H_{10}INO_4$** (322.9655): found: 322.9668.

**$C_9H_{10}INO_4$:** required: C: 33.46; H: 3.12; N: 4.34;
found: C: 33.47; H: 3.09; N: 4.28.

## Synthesis of 2-iodo-4-nitrophenyl 4-methylbenzenesulfonate (72e)




Prepared according to **TP 14** from 2-iodo-4-nitrophenol (**69**) (2.85 g, 10.0 mmol) and *p*-toluenesulfonicacid chloride (2.52 g, 12.0 mmol). Recrystallization from ethanol furnished title compound **72e** as light yellow solid (3.85 g, 92%).

**mp.:** 101-101.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.60 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.21 (dd, $^3J$(H,H)= 9.3 Hz, $^4J$(H,H)= 2.7 Hz, 1 H), 7.81 (d, $^3J$(H,H)= 8.4 Hz, 1 H), 7.51 (d, $^3J$(H,H)= 9.3 Hz, 1 H), 7.36 (d, $^3J$(H,H)= 8.4 Hz, 1 H), 2.46 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 154.6, 146.6, 145.9, 135.3, 132.3, 130.1, 128.8, 124.8, 122.8, 90.1, 21.8.

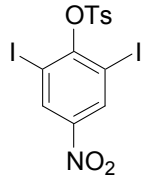
**MS** (70 eV, EI), *m/z* (%): 418 (21) [$M^+$], 264 (3), 1881 (2), 155 (100), 91 (47), 63 (23).

**IR** (KBr): $\tilde{\nu}$ = 3073 (m), 1595 (m), 1530 (vs), 1459 (s), 1381 (vs), 1348 (vs), 1291 (m), 1208 (m), 1178 (vs), 1188 (vs), 1129 (m), 1088 (m), 1035 (m), 920 (m), 877 (s), 844 (vs), 830 (m), 815 (s), 754 (vs), 733 (vs), 709 (m), 673 (vs), 650 (m), 571 (vs), 552 (m), 543 (m).

**HRMS** for **$C_{13}H_{10}INO_5S$** (418.9324): found: 418.9285.

**$C_{13}H_{10}INO_5S$:** required: C: 37.25; H: 2.40; N: 3.34; S: 7.65;
found: C: 37.25; H: 2.38; N: 3.37; S: 7.51.

## Synthesis of 2,6-diiodo-4-nitrophenyl 4-methylbenzenesulfonate (72f)




Prepared according to **TP 14** from 2,6-diiodo-4-nitrophenol (70) (3.91 g, 10.0 mmol) and *p*-toluenesulfonicacid chloride (2.15 g, 11.0 mmol). Recrystallization from ethanol furnished title compound **72f** as light yellow solid (4.76 g, 90%).

**mp.:** 189.5-190 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.57 (s, 2 H), 7.90 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.41 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 2.42 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 156.9, 147.0, 146.1, 136.0, 135.1, 130.6, 129.5, 129.2, 90.7, 22.3.

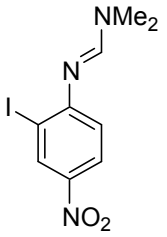
**MS** (70 eV, EI), *m/z* (%): 544 (10) [$M^+$], 390 (11), 216 (4), 188 (9), 155 (100), 91 (43), 65 (8).

**IR** (KBr): $\tilde{\nu}$ = 3088 (w), 1595 (m), 1522 (vs), 1450 (w),1405 (m), 1381 (vs), 1339 (vs), 1306 (m), 1271 (w), 1216 (s), 1189 (s), 1175 (vs), 1090 (s), 1047 (m), 892 (vs), 839 (vs), 816 (s), 751 (vs), 736 (m), 723 (vs), 707 (m), 668 (vs), 631 (s), 567 (s), 544 (vs).

**HRMS** for **$C_{13}H_9I_2NO_5S$** (544.8291): found: 544.8316.

| | | |
|---|---|---|
| **$C_{13}H_9I_2NO_5S$:** | required: | C: 28.64; H: 1.66; N: 2.57; |
| | found: | C: 28.55; H: 1.65; N: 2.61. |

## Synthesis of *N*'-(2-iodo-4-nitrophenyl)-*N*,*N*-dimethylimidoformamide (72g)




A 100 mL round bottom flask was charged with 2-iodo-4-nitroaniline (**71**) (2.63 g, 10.0 mmol), toluene (50 mL) and *N*,*N*-dimethylformamide-dimethyl-acetal (3.5 mL, 20 mmol) were added and the reaction mixture was heated then to reflux for 12 h. After cooling to room temperature the solvents were removed *in vacuo* and the resulting oil was triturated with pentane/diethyl ether 2:1 (20 mL) and the precipitate collected by filtration to give title compound **72g** after recrystallization from methanol as yellow solid (2.48 g, 78%).

**mp.:** 103.5-104.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.63 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.06 (dd, $^3J$(H,H)= 8.9 Hz, $^4J$(H,H)= 2.7 Hz, 1 H), 7.52 (s, 1 H), 6.79 (d, $^3J$(H,H)= 8.9 Hz, 1 H), 3.12 (s, 3 H), 3.10 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 158.3, 153.2, 142.4, 134.5, 124.8, 116.6, 95.7, 40.4, 34.8.

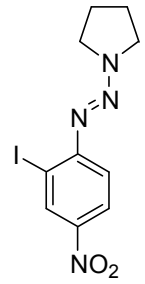
**MS** (70 eV, EI), *m/z* (%): 319 (85) [$M^+$], 303 (12), 289 (10), 276 (14), 258 (6), 192 (100), 190 (8), 176 (6), 165 (7), 146 (88), 127 (17), 115 (11), 104 (13), 91 (11), 77 (10).

**IR** (KBr): $\tilde{\nu}$ = 1629 (vs), 1559 (vs), 1489 (s), 1464 (s), 1370 (m), 1316 (vs), 1300 (s), 1271 (s), 1241 (m), 1108 (s), 976 (w), 867 (w), 818 (w), 749 (w).

**HRMS** for **$C_9H_{10}IN_3O_2$** (318.9818): found: 318.9808.

**$C_9H_{10}IN_3O_2$:** required: C: 33.88; H: 3.16; N: 13.17;
found: C: 33.85; H: 3.36; N: 13.26.

## Synthesis of 1-[(*E*)-(2-iodo-4-nitrophenyl)diazenyl]pyrrolidine (72h)




A 50 mL round-bottom flask, equipped with a magnetic stirring bar and a dropping funnel was charged with water (5 mL), conc. HCl (0.6 mL) and 2-iodo-4-nitroaniline (**71**) (2.64 g, 10.0 mmol) were added at 0 °C. Afterwards, a solution of $NaNO_2$ (825 mg, 12.0 mmol, in 10 mL $H_2O$) was added dropwise over a period of 30 min. On completion of the addition the mixture was stirred for 30 min and was poured into a solution of pyrrolidine (1.06 g, 15.0 mmol, in 9 mL $H_2O$) and $K_2CO_3$ (2.49 g, 18.0 mmol) with a strong evolution of gas. The sticky mixture was stirred for an additional 1 h at rt and the reaction mixture was poured into saturated $NaHCO_{3(aq)}$ solution (30 mL) in a separatory funnel. After extraction with ethyl acetate (2x 30 ml) the organic phases were washed with brine, dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. The residue was recrystallized from ethanol furnishing compound **72h** as an orange powder (2.69 g, 78%).

**mp.:** 156-157 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.69 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.12 (dd, $^3J$(H,H)= 8.9 Hz, $^4J$(H,H)= 2.7 Hz, 1 H), 7.38 (d, $^4J$(H,H) = 8.9 Hz, 1 H), 4.00 (br_t, $^3J$(H,H)= 6.6 Hz, 2 H), 3.79 (br_t, $^3J$(H,H)= 6.6 Hz, 2 H), 2.14-2.05 (m, 4 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 155.4, 144.5, 134.9, 124.2, 116.2, 94.8, 51.7, 48.0, 24.0, 23.4.

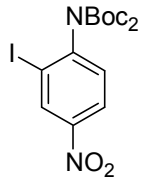
**MS** (70 eV, EI), *m/z* (%): 346 (24) [$M^+$], 275 (64), 247 (100), 217 (11), 201 (15), 75 (37), 70 (15).

**IR** (KBr): $\tilde{\nu}$ = 1505 (s), 1406 (m), 1375 (m), 1331 (vs), 1299 (vs), 1270 (vs), 1245 (m), 1112 (m), 866 (w), 854 (w), 826 (w), 748 (w).

**HRMS** for **$C_{10}H_{11}IN_4O_2$** (345.9927): found: 345.9892.

| | | |
|---|---|---|
| **$C_{10}H_{11}IN_4O_2$:** | required: | C: 34.70; H: 3.20; N: 16.19; |
| | found: | C: 34.59; H: 3.22; N: 16.09. |

## Synthesis of di(*tert*-butyl) 2-iodo-4-nitrophenylimidodicarbonate (72i)[127]




A dry and nitrogen flushed 50 mL Schlenk flask, equipped with a magnetic stirring bar, was charged with 2-iodo-4-nitroaniline (**71**) (2.64 g, 10.0 mmol) and acetonitrile (25 mL), cooled to 0 °C and DMAP (125 mg, 1.00 mmol) was added. Subsequently, a solution of $Boc_2O$ (5.23 g, 24.0 mmol) dissolved in acetonitrile (15 mL) was added dropwise. On completion of the addition, the cooling bath was removed, the reaction mixture stirred for 24 h at 60 °C and poured into water. After extraction with ethyl acetate (3 x 30 mL), the combined organic fractions were washed with $KHSO_{4(aq)}$ (30 mL, 1 M), brine (30 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 9:1) furnished title compound **72i** as colourless oil (3.41 g, 70%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.68 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.22 (dd, $^3J$(H,H)= 8.4 Hz, $^4J$(H,H)= 2.7 Hz, 1 H), 7.36 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 1.40 (s, 18 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.2, 148.0, 146.7, 134.1, 129.4, 123.9, 99.7, 84.0, 41.8, 27.9.

**MS** (FAB, NBA): m/z (%): 487 [M+Na]$^+$.

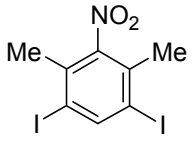
**MS** (70 eV, EI), *m/z* (%): 363 (11) [M-Boc]$^+$, 307 (17), 263 (6), 233 (4), 181 (4), 91 (3.6, 57 (100).

**IR** (KBr): $\tilde{\nu}$ = 3435 (m), 1797 (m), 1756 (vs), 1725 (s), 1524 (vs), 1372 (m), 1346 (vs), 1315 (m), 1280 (vs), 1252 (s), 1153 (s), 1115 (vs), 860 (w), 772 (w).

**HRMS** for **$C_{16}H_{21}IN_2O_6$** (487.0342 [M+Na]$^+$): found: 487.0351 [M+Na]$^+$.

| | | |
|---|---|---|
| **$C_{16}H_{21}IN_2O_6$:** | required: | C: 41.39; H: 4.56; N: 6.03; |
| | found: | C: 41.17; H: 4.58; N: 6.01. |

## Synthesis of 3,5-diiodo-2,6-dimethylnitrobenzene (74)[59]




A suspension of $Ag_2SO_4$ (3.12 g, 10.0 mmol) in $H_2SO_4$ (50 mL, 90%$_{(aq)}$) was stirred at rt for 15 min, ICl (3.25 g, 20.0 mmol) was added and stirring was continued at rt for 1 h. The precipitated AgCl was removed by filtration and the resulting dark brown solution was added over a period of 1 h to a solution of 1,3-dimethyl-2-nitrobenzene (1.41 g, 9.00 mmol), dissolved in $H_2SO_4$ (10 mL, 90%$_{(aq)}$) at 0 °C. On completion of the addition, the reaction mixture was stirred for 1 h at rt and the mixture was poured into $H_2O$ (100 mL). Filtration and subsequent recrystallization from ethanol furnished compound **74** as white solid (2.73 g, 68%).

**mp.:** 137.5-139 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.31 (s, 2 H), 2.24 (s, 6 H).

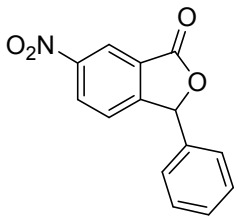
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 148.5, 138.1, 130.4, 97.1, 21.3.

**MS** (70 eV, EI), *m/z* (%): 402 (74) [$M^+$], 385 (95), 357 (21), 293 (9), 258 (28), 230 (36), 132 (19), 103 (100).

**IR** (KBr): $\tilde{\nu}$ = 1528 (vs), 1422 (m), 1381 (s), 1346 (m), 942 (w), 879 (m), 739 (s).

**HRMS** for **$C_8H_7I_2NO_2$** (402.8566): found: 402.8575.

## Synthesis of 6-nitro-3-phenyl-2-benzofuran-1(3*H*)-one (75a)




Prepared according to **TP 5** from ethyl 2-iodo-5-nitrobenzoate (**65a**) (321 mg, 1 mmol), PhMgCl (0.55 mL, 1.1 mmol, 2.0 M in THF) and benzaldehyde (212 mg, 2 mmol). Reaction time: 2 h at −78 °C. Purification by flash chromatography (pentane/diethyl ether = 19:1) furnished the title compound **75a** as a pale yellow oil (199 mg, 78%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.75 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.51 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.56 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.45-7.37 (m, 5 H), 6.53 (s, 1 H).

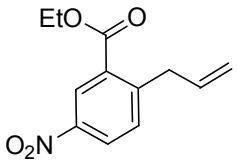
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 167.1, 155.2, 149.6, 135.2, 130.4, 129.7, 129.6, 127.7, 127.3, 124.9, 121.7, 83.2.

**MS** (70 eV, EI), *m/z* (%): 255 (100) [$M^+$], 226 (4), 180 (12), 165 (28), 149 (40), 139 (8), 132 (9), 105 (85), 87 (3), 77 (23).

**IR** (KBr): $\tilde{\nu}$ = 1778 (vs), 1615 (m), 1537 (vs), 1455 (m), 1347 (vs), 1303 (m), 1254 (m), 1097 (vs), 797 (w), 763 (w), 739 (m), 700 (m), 620 (w).

**HRMS** for **$C_{14}H_9NO_4$** (255.0532): found: 255.0504.

## Synthesis of ethyl 2-allyl-5-nitrobenzoate (75b)




Prepared according to **TP 5** from ethyl 2-iodo-5-nitrobenzoate (**65a**) (321 mg, 1.00 mmol), PhMgCl (0.66 mL, 1.1 mmol, 1.6 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and allyl bromide (240 mg, 2.00 mmol). Reaction time: 2 h at −78 °C. Purification by flash chromatography (pentane/diethyl ether = 29:1) furnished title compound **75b** as a yellow oil (204 mg, 87%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.70 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.24 (dd, $^3J$(H,H) = 8.9 Hz, $^4J$(H,H) = 2.7 Hz, 1 H), 7.46 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 6.03-5.89 (m, 1 H), 5.12-5.00 (m, 2 H), 4.39 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.84 (d, $^3J$(H,H) = 6.6 Hz, 2 H), 1.40 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

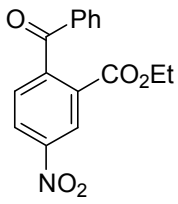
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.5, 148.9, 146.2, 135.6, 132.0, 131.2, 126.1, 125.7, 117.1, 61.8, 38.2, 14.2.

**MS** (70 eV, EI), *m/z* (%): 235 (23) [$M^+$], 220 (35), 207 (34), 192 (100), 179 (11), 160 (12), 144 (8), 115 (42), 89 (5).

**IR** (KBr): $\tilde{\nu}$ = 2983 (w), 1727 (vs), 1613 (m), 1525 (vs), 1479 (m), 1445 (m), 1350 (vs), 1252 (s), 1127 (s), 1067 (m), 1018 (m), 921 (m), 837 (w), 745 (w), 716 (w), 604 (w).

**HRMS** for **$C_{12}H_{13}NO_4$** (235.0845): found: 235.0845.

## Synthesis of ethyl 2-benzoyl-5-nitrobenzoate (75c)



Prepared according to **TP 5** from ethyl 2-iodo-5-nitrobenzoate (**65a**) (642 mg, 2 mmol), PhMgCl (1.1 mL, 2.2 mmol, 2.0 M in THF), CuCN·2LiCl (2.2 mL, 2.2 mmol, 1.0 M in THF) and benzoyl bromide (648 mg, 3.50 mmol). Reaction time: 1 h at −78 °C. Purification by flash chromatography (pentane/diethyl ether = 9:1) furnished title compound **75c** as a yellow solid (570 mg, 94%).

**mp.:** 88-89.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.83 (d, $^4J$(H,H) = 2.8 Hz, 1 H), 8.40 (dd, $^3J$(H,H) = 8.8 Hz, $^4J$(H,H) = 2.8 Hz, 1 H), 7.67–7.64 (m, 2 H), 7.53–7.51 (m, 1 H), 7.51–7.49 (m, 2 H), 7.42–7.36 (m, 1 H), 4.10 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.07–1.03 (m, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 194.8, 163.7, 148.2, 147.3, 136.1, 133.9, 130.9, 129.3, 128.9, 128.8, 126.9, 125.4, 62.4, 13.6.

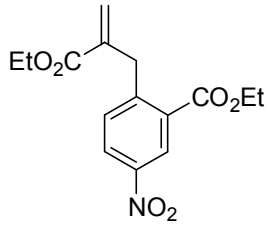
**MS** (70 eV, EI), *m/z* (%): 299 (22) [$M^+$], 270 (4), 254 (14), 222 (15), 194 (51), 180 (3), 152 (7), 105 (100), 77 (28).

**IR** (KBr): $\tilde{\nu}$ = 1723 (vs), 1672 (vs), 1606 (s), 1596 (s), 1582 (m), 1528 (vs), 1450 (s), 1367 (m), 1353 (vs), 1313 (vs), 1278 (vs), 1250 (s), 1017 (m), 908 (m), 863 (w), 848 (m), 838 (w), 792 (w), 742 (m), 714 (s), 698 (s), 690 (m).

**HRMS** for **$C_{16}H_{13}NO_5$** (299.0794): found: 299.0801.

| | | |
|---|---|---|
| **$C_{16}H_{13}NO_5$:** | required: | C: 64.21; H: 4.38; N: 4.68; |
| | found: | C: 63.98; H: 4.76; N: 4.67. |

## Synthesis of ethyl 2-[2-(ethoxycarbonyl)-2-propenyl]-5-nitrobenzoate (75d)




Prepared according to **TP 5** from ethyl 2-iodo-5-nitrobenzoate (**65a**) (642 mg, 2.00 mmol), PhMgCl (1.1 mL, 2.2 mmol, 2.0 M in THF), CuCN·2LiCl (2.2 mL, 2.2 mmol, 1.0 M in THF) and ethyl (2-bromomethyl) acrylate (580 mg, 3.00 mmol). Reaction time: 1 h at −78 °C. Purification by flash chromatography (pentane/diethyl ether = 4:1) furnished title compound **75d** as an orange oil (411 mg, 67%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.66 (d, 1 H), 8.19 (dd, $^4J$(H,H) = 2.7 Hz, $^3J$(H,H) = 8.6 Hz, 1 H), 7.40 (d, 1 H), 6.20 (d, 1 H), 5.29–5.28 (m, 1 H), 4.30 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 4.15-4.11 (m, 2 H), 4.08-4.06 (m, 2 H), 1.33 (t, $^3J$(H,H) = 7.1 Hz, 3 H), 1.21-1.13 (m, 3 H).

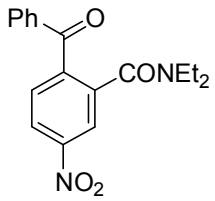
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.4, 164.4, 146.7, 145.4, 137.9, 131.4, 130.6, 125.8, 125.0, 124.8, 60.8, 60.0, 34.8, 13.2, 13.1.

**MS** (70 eV, EI), *m/z* (%): 307 (1) [$M^+$], 261 (41), 233 (100), 216 (3), 205 (43), 189 (24), 175 (11), 159 (9), 142 (6), 131 (12), 115 (29), 103 (4), 89 (3), 77 (4).

**IR** (KBr): $\tilde{\nu}$ = 1722 (vs), 1526 (vs), 1367 (s), 1351 (vs), 1254 (vs), 1137 (s), 1070 (s), 1023 (m), 935 (w), 921 (w), 838 (w), 821 (w), 787 (w), 738 (w), 722 (w).

**HRMS** for **$C_{15}H_{17}NO_6$** (307.1056): found: 307.1058.

## Synthesis of 2-benzoyl-*N*,*N*-diethyl-5-nitrobenzamide (75e)




Prepared according to **TP 5** from *N*,*N*-diethyl-2-iodo-5-nitrobenzamide (**65b**) (694 mg, 2.00 mmol), PhMgCl (1.1 mL, 2.2 mmol, 2.0 M in THF), CuCN·2LiCl (2.2 mL, 2.2 mmol, 1.0 M in THF) and benzoyl bromide (648 mg, 3.50 mmol). Reaction time: 1 h at −78 °C. Purification by flash chromatography (pentane/ethyl acetate = 9:1) furnished title compound **75e** as a yellow oil (313 mg, 68%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.28 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 8.24-8.21 (m, 1 H), 7.77-7.72 (m, 2 H), 7.64 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.62-7.56 (m, 1 H), 7.47-7.41 (m, 2 H), 3.40 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.25 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.15 (t, $^3J$(H,H) = 7.1 Hz, 3 H), 1.02 (t, $^3J$(H,H) = 7.1 Hz, 2 H),.

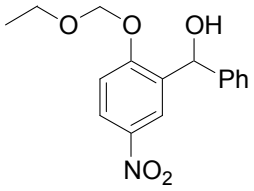
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 194.9, 167.3, 148.4, 143.0, 139.5, 136.0, 134.0, 130.3, 129.2, 128.6, 123.2, 121.7, 43.0, 39.2, 13.7, 12.1.

**MS** (70 eV, EI), *m/z* (%): 325 (1) $[M]^+$, 254 (73), 238 (3), 208 (29), 196 (6), 180 (21), 152 (43), 105 (4), 72 (100).

**IR** (KBr): $\tilde{\nu}$ = 1671 (s), 1634 (vs), 1528 (vs), 1448 (s), 1349 (vs), 1316 (s), 1278 (vs), 1218 (m), 1113 (m), 940 (m), 901 (m), 851 (m), 733 (m), 705 (m).

**HRMS** for **$C_{18}H_{18}N_2O_4$** (326.1267): found: 326.1277.

## Synthesis of (2-ethoxymethoxy-5-nitro-phenyl)-phenyl-methanol (76a)




Prepared according to **TP 5** from 1-(ethoxymethoxy)-2-iodo-4-nitrobenzene (**72d**) (323 mg, 1.00 mmol), PhMgCl (0.62 mL, 1.1 mmol, 1.7 M in THF), and benzaldehyde (127 mg, 1.20 mmol). Reaction time: 4 h at −78 °C. Purification by flash chromatography (pentane/ethyl acetate = 2:1) furnished title compound **76a** as a colourless oil (85 mg, 28%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.41 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 8.05 (dd, $^3J$(H,H) = 8.8 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.22 (m, 5 H), 7.05 (d, $^3J$(H,H) = 8.8 Hz, 1 H), 5.97 (s, 1 H), 5.16 (m, 2 H), 3.33 (m, 2 H), 2.79 (s, 1 H), 0.99 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

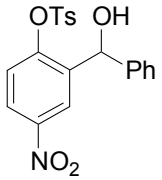
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 158.5, 142.3, 142.0, 133.7, 128.4, 127.8, 127.5, 126.9, 126.7, 124.6, 122.7, 113.3, 92.6, 70.9, 64.8, 14.8.

**MS** (70 eV, EI), *m/z* (%): 227.1 (100), 226.1 (62), 180.1 (19), 228.1 (19), 152.1 (13), 120.0 (7).

**IR** (KBr): $\tilde{\nu}$ = 3582 (m), 2981 (m), 1593 (s), 1576 (vs), 1522 (vs), 1474 (vs), 1347 (vs), 1256 (vs), 1241 (vs), 1121 (vs), 1088 (s), 1036 (s), 954 (vs), 898 (s), 761 (s), 743 (s), 711 (s), 672 (m).

**HRMS** for **$C_{16}H_{17}NO_5$** (303.1107): found: 303.1094.

## Synthesis of 2-[hydroxy(phenyl)methyl]-4-nitrophenyl 4-methylbenzenesulfonate (76b)




Prepared according to **TP 5** from 2-iodo-4-nitrophenyl 4-methylbenzenesulfonate (**72e**) (439 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF) and benzaldehyde (127 mg, 1.20 mmol). Purification by flash chromatography (pentane/diethyl ether = 4:1) furnished title compound **76b** as a colourless oil (320mg, 77%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.27 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.06 (dd, $^3J$(H,H) = 8.9 Hz, $^4J$(H,H) = 2.7 Hz, 1 H), 7.70 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.36-7.26 (m, 7 H), 7.21 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 6.01 (s, 1 H), 2.80 (s_br, 1 OH), 2.47 (s, 3 H).

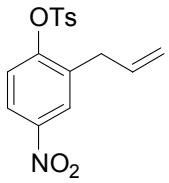
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 150.7, 146.5, 146.2, 141.1, 138.9, 131.8, 130.2, 128.6, 128.3, 128.1, 126.5, 124.0, 123.8, 122.1, 69.6, 21.7.

**MS** (70 eV, EI), *m/z* (%): 399 (0.1) [$M^+$], 382 (14), 319 (23), 301 (13), 244 (100), 226 (34), 180 (11), 166 (22), 155 (10), 91 (61), 77 (13).

**IR** (KBr): $\tilde{\nu}$ = 3541 (w), 1596 (m), 1530 (vs), 1475 (m), 1381 (s), 1350 (vs), 1209 (s), 1178 (vs), 1090 (s), 1038 (m), 856 (s), 766 (m), 717 (s), 700 (s), 670 (m), 565 (m), 550 (m).

**HRMS** for **$C_{20}H_{17}NO_6S$** (399.0777): found: 399.0812.

## Synthesis of 2-allyl-4-nitrophenyl 4-methylbenzenesulfonate (76c)




Prepared according to **TP 5** form 2-iodo-4-nitrophenyl 4-methylbenzenesulfonate (**72e**) (439 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and allyl bromide (0.17 mL, 1.6 mmol). Purification by flash chromatography (pentane/diethyl ether = 19:1) furnished title compound **76c** as a colourless oil (311mg, 93%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.08-8.02 (m, 2 H), 7.77 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.38-7.35 (m, 1 H), 7.27 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 5.81-5.67 (m, 1 H), 5.13 (ddt, $^3J$(H,H) = 9.7 Hz, $^2J$(H,H), $^4J$(H,H) = 1.8 Hz, 1 H), 5.04 (ddt, $^3J$(H,H) = 16.8 Hz, $^2J$(H,H), $^4J$(H,H) = 1.8 Hz, 1 H), 3.27 (d, $^3J$(H,H) = 6.6 Hz, 1 H), 2.47 (s, 3 H).

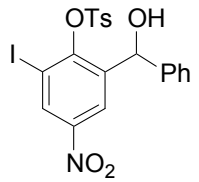
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 152.0, 146.2, 146.0, 135.4, 133.7, 132.4, 130.1, 128.4, 125.9, 122.9, 118.4, 112.6, 33.8, 21.7.

**MS** (70 eV, EI), *m/z* (%): 334 (17) [M+H]$^+$, 317 (19), 178 (48), 155 (68), 132 (12), 103 (7), 91 (100), 77 (4), 65 (8).

**IR** (KBr): $\tilde{\nu}$ = 3081 (w), 1596 (w), 1585 (w), 1528 (vs), 1479 (m), 1381 (vs), 1350 (vs), 1218 (s), 1191 (vs), 1179 (vs), 1159 (s), 1091 (s), 1074 (s), 922 (m), 850 (vs), 809 (s), 761 (s), 735 (s), 708 (s), 669 (m), 577 (m), 550 (m).

**HRMS** for **$C_{16}H_{15}NO_5S$** (333.0671): found: 334.0751 [M+H]$^+$.

## Synthesis of 2-[hydroxy(phenyl)methyl]-6-iodo-4-nitrophenyl 4-methylbenzenesulfonate (76d)




Prepared according to **TP 5** form 2,6-diiodo-4-nitrophenyl 4-methylbenzenesulfonate (**72f**) (529 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF) and benzaldehyde (127 mg, 1.20 mmol). Purification by flash chromatography (pentane/diethyl ether = 4:1) furnished title compound **76d** as a light yellow solid (445 mg, 85%).

**mp.:** 156-158 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.51 (d, $^3J$(H,H) = 2.8 Hz, 1 H), 8.37 (d, $^3J$(H,H) = 2.8 Hz, 1 H), 7.94 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.43 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.38-7.27 (m, 5 H), 6.42 (s_br, 1 H), 3.12 (s_br, 1 OH), 2.50 (s, 3 H).

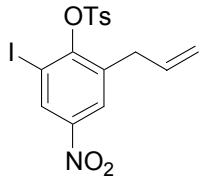
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 151.5, 146.8, 146.6, 142.3, 141.3, 134.3, 133.0, 130.2, 129.0, 128.7, 128.0, 126.1, 125.1, 91.1, 70.0, 21.9.

**MS** (70 eV, EI), *m/z* (%): 525 (0.6) [$M^+$], 508 (9), 443 (15), 428 (35), 415 (29), 370 (100), 369 (14), 352 (52), 321 (9), 305 (9), 292 (10), 155 (14), 139 (18), 105 (29), 91 (81), 77 (28).

**IR** (KBr): $\tilde{\nu}$ = 3436 (m), 1526 (vs), 1367 (s), 1352 (vs), 1179 (s), 1088 (s), 846 (m), 728 (vs), 701 (m), 570 (m).

**HRMS** for **$C_{20}H_{16}INO_6S$** (524.9743): found: 524.9745.

## Synthesis of 2-allyl-6-iodo-4-nitrophenyl 4-methylbenzenesulfonate (76e)




Prepared according to **TP 5** form 2,6-diiodo-4-nitrophenyl 4-methylbenzenesulfonate (**72f**) (545 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and allyl bromide (0.17 mL, 1.6 mmol). Purification by flash chromatography (pentane/diethyl ether = 19:1) furnished title compound **76e** as a colourless oil (401 mg, 87%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.50 (d, $^4J$(H,H) = 2.8 Hz, 1 H), 8.13 (d, $^4J$(H,H) = 2.8 Hz, 1 H), 7.92 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.40 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 5.92-5.79 (m, 1 H), 5.25-5.16 (m, 2 H), 3.60 (d, $^3J$(H,H) = 6.6 Hz, 1 H), 2.49 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 153.4, 146.4, 146.1, 137.9, 134.0, 133.8, 133.3, 130.1, 128.4, 125.9, 119.0, 91.7, 35.8, 21.8.

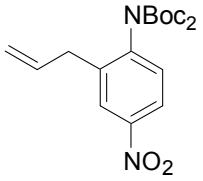
**MS** (70 eV, EI), *m/z* (%): 459 (6) [$M^+$], 304 (31), 287 (31), 258 (9), 177 (1), 155 (100), 139 (4), 91 (99), 77 (11), 65 (14).

**IR** (KBr): $\tilde{\nu}$ = 3081 (w), 1596 (w), 1528 (vs), 1425 (m), 1369 (s), 1345 (vs), 1311 (w), 1238 (w), 1200 (s), 1181 (s), 1178 (vs), 1145 (w), 1090 (m), 1076 (s), 924 (m), 841 (vs), 814 (w), 759 (s), 730 (vs), 669 (s), 573 (m), 545 (m).

**HRMS** for **$C_{16}H_{14}I_2NO_5S$** (458.9637): found: 458.9626.

**$C_{16}H_{14}I_2NO_5S$:** required: C: 41.84; H: 3.07; N: 3.05;
found: C: 42.12; H: 3.42; N: 3.04.

## Synthesis of di(*tert*-butyl) 2-allyl-4-nitrophenylimidodicarbonate (76f)




Prepared according to **TP 5** form di(*tert*-butyl) 2-iodo-4-nitrophenylimidodicarbonate (**72i**) (446 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and allyl bromide (0.17 mL, 1.6 mmol). Purification by flash chromatography (pentane/diethyl ether = 9:1) furnished title compound **76f** as a colourless oil (220 mg, 61%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.14 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.08 (dd, $^3J$(H,H)= 8.4 Hz, $^4J$(H,H)= 2.7 Hz, 1 H), 7.25 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 5.91-5.80 (m, 1 H), 5.22-5.14 (m, 2 H), 3.35 (d, $^3J$(H,H) = 6.6 Hz, 2 H), 1.39 (s, 18 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 150.8, 147.6, 144.1, 140.0, 134.3, 130.1, 125.2, 122.5, 118.7, 89.1, 84.0, 35.7, 28.3.

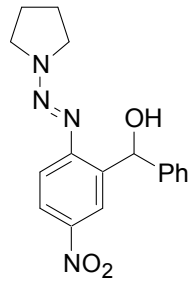
**MS** (FAB, NBA): m/z (%): 401 (32) [M+Na]$^+$, 379 (8) [M+Na]$^+$

**MS** (70 eV, EI), *m/z* (%): 278 (0.1) [M−Boc]$^+$, 269 (1), 222 (11), 207 (8), 178 (7), 153 (14), 136 (20), 107 (21), 89 (30), 77 (63), 57 (100).

**IR** (KBr): $\tilde{\nu}$ = 2981 (m), 1796 (vs), 1759 (s), 1723 (s), 1527 (vs), 1480 (m), 1394 (m), 1369 (vs), 1349 (vs), 1315 (s), 1276 (vs), 1251 (vs), 1154 (vs), 1116 (vs), 1099 (vs), 1006 (m), 869 (w), 851 (w), 832 (w), 812 (w), 778 (w).

**HRMS** for **$C_{19}H_{26}N_2O_6$** (401.1688 [M+Na]$^+$): found: 401.1692 [M+Na]$^+$.

## Synthesis of {5-nitro-2-[(*E*)-1-pyrrolidinyldiazenyl]phenyl}(phenyl)methanol (76g)



Prepared according to **TP 5** from 1-[(*E*)-(2-iodo-4-nitrophenyl)diazenyl]pyrrolidine (**72h**) (346 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF), and benzaldehyde (168 mg, 1.50 mmol) in a THF/NMP-mixture 3:1 at −55 °C. Purification by flash chromatography (pentane/diethyl ether = 2:1) furnished title compound **76g** as a yellow solid (159 mg, 58%).

**mp.:** 171-171.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.22 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 7.94 (dd, $^3J$(H,H)= 8.9 Hz, $^4J$(H,H)= 2.7 Hz, 1 H), 7.46 (d, $^4J$(H,H) = 8.9 Hz, 1 H), 7.29-7.08 (m, 5 H), 6.31 (s, 1 H), 3.86 (br_t, $^3J$(H,H)= 6.6 Hz, 2 H), 3.49 (br_t, $^3J$(H,H)= 6.6 Hz, 2 H), 2.00-1.91 (m, 4 H).

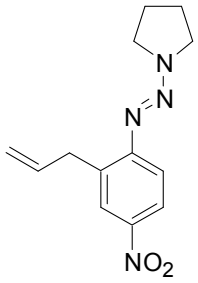
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 152.4, 144.0, 143.4, 137.8, 127.9, 126.8, 126.4, 123.1, 123.0, 116.1, 72.5, 51.4, 47.1, 23.5, 23.1.

**MS** (70 eV, EI), *m/z* (%): 326 (1) [$M^+$], 308 (8), 256 (7), 242 (41), 210 (56), 181 (544), 164 (44), 152 (30), 105 (8), 85 (100), 79 (12).

**IR** (KBr): $\tilde{\nu}$ = 3400 (m), 1599 (w), 1581 (m), 1506 (vs), 1396 (vs), 1326 (vs), 1300 (vs), 1289 (vs), 1267 (vs), 1233 (s), 1084 (m), 1036 (m), 913 (w), 843 (m), 739 (w), 702 (w).

**HRMS** for **$C_{17}H_{18}N_4O_3$** (326.1379): found: 326.1397.

## Synthesis of 1-[(*E*)-(2-allyl-4-nitrophenyl)diazenyl]pyrrolidine (76h)



Prepared according to **TP 5** from 1-[(*E*)-(2-allyl-4-nitrophenyl)diazenyl]pyrrolidine (**72h**) (346 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and allyl bromide (0.17 mL, 1.6 mmol) in a THF/NMP-mixture 3:1 at −55 °C. Purification by flash chromatography (pentane/diethyl ether = 4:1) furnished title compound **76h** as a yellow solid (159 mg, 61%).

**mp.:** 88.5-89 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.06 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.00 (dd, $^3J$(H,H)= 8.9 Hz, $^4J$(H,H)= 2.7 Hz, 1 H), 7.49 (d, $^4J$(H,H) = 8.9 Hz, 1 H), 6.06-5.93 (m, 1 H), 5.13-5.04 (m, 2 H), 3.98 (br_t, 2 H), 3.69 (br_t, 2 H), 3.63 (d, $^3J$(H,H) = 6.6 Hz, 2 H), 2.10-2.03 (m, 4 H).

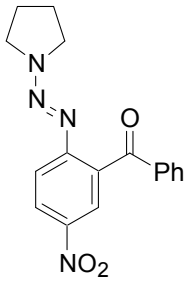
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 153.7, 144.4, 136.4, 135.1, 125.3, 122.6, 116.3, 116.2, 51.4, 47.0, 35.5, 23.9, 23.4.

**MS** (70 eV, EI), *m/z* (%): 259 (4) [$M^+$], 231 (3), 217 (3), 190 (18), 145 (12), 131 (7), 115 (100),104 (7), 89 (7), 70 (7).

**IR** (KBr): $\tilde{\nu}$ = 2975 (w), 1636 (w), 1582 (m), 1503 (vs), 1455 (m), 1389 (vs), 1325 (vs), 1305 (vs), 1268 (vs), 1231 (s), 1101 (m), 915 (m), 898 (m), 832 (w), 757 (w).

**HRMS** for **$C_{13}H_{16}N_4O_2$** (260.1273): found: 260.1297.

## Synthesis of {5-nitro-2-[1-pyrrolidinyldiazenyl]phenyl}(phenyl)methanone (76i)




Prepared according to **TP 5** from 1-[(*E*)-(2-allyl-4-nitrophenyl)diazenyl]pyrrolidine (**72h**) (346 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and benzoyl bromide (370 mg, 2.00 mmol) in a THF/NMP-mixture 3:1 at −55 °C. Purification by flash chromatography (pentane/diethyl ether = 3:1) furnished title compound **76i** as a yellow solid (159 mg, 75%).

**mp.:** 172.5-173 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 8.30-8.26 (m, 2 H), 7.73-7.69 (m, 2 H), 7.62 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 7.51 (tt, $^3J$(H,H)= 7.5 Hz, $^4J$(H,H)= 2.0 Hz, 1 H), 7.40-7.36 (m, 2 H), 3.74 (br_t, 2 H), 3.09 (br_t, 2 H), 1.87-1.81 (m, 4 H).

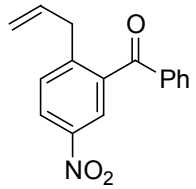
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 195.9, 154.3, 144.2, 137.7, 133.5, 132.7, 129.3, 128.3, 125.9, 124.8, 119.1, 51.3, 46.9, 23.7, 23.1.

**MS** (70 eV, EI), *m/z* (%): 324 (3) [$M^+$], 254 (36), 226 (12), 195 (7), 180 (100), 152 (37), 139 (6), 105 (41), 77 (40).

**IR** (KBr): $\tilde{\nu}$ = 1667 (vs), 1597 (m), 1578 (w), 1511 (s), 1398 (vs), 1333 (vs), 1306 (vs), 1270 (vs), 1147 (m), 970 (m), 862 (w), 713 (m).

**HRMS** for $\mathbf{C_{17}H_{16}N_4O_3}$ (324.1222): found: 324.1226.

## Synthesis of 1-allyl-5-nitrobenzophenone (76j)




Prepared according to **TP 5** from 3,5-diiodo-2,6-dimethyl-nitrobenzene (**65d**) (352 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF), CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and allyl bromide (0.17 mL, 1.50 mmol) at −78 °C. Reaction time 1 h. Purification by flash chromatography (pentane/diethyl ether = 19:1) furnished title compound **76j** as a yellow oil (144 mg, 54%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.25 (dd, $^3J$(H,H)= 8.4 Hz, $^4J$(H,H)= 2.2 Hz, 1 H), 8.15 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.79-7.75 (m, 2 H), 7.51 (tt, $^3J$(H,H)= 7.5 Hz, $^4J$(H,H)= 1.4 Hz, 1 H), 7.54-7.46 (m, 3 H), 5.91-5.77 (m, 1 H), 5.07-4.96 (m, 2 H), 3.53-3.50 (m, 2 H).

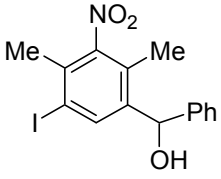
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 196.1, 146.9, 146.3, 140.1, 136.9, 135.3, 134.5, 131.8, 130.5, 129.2, 125.2, 123.7, 118.3, 37.7.

**MS** (70 eV, EI), *m/z* (%): 267 (30) [$M^+$], 252 (100), 237 (15), 220 (18), 206 (29), 202 (16), 189 (19), 165 (32), 115 (53), 105 (56), 77 (90), 51 (21).

**IR** (KBr): $\tilde{\nu}$ = 1669 (vs), 1610 (w), 1596 (w), 1581 (w), 1525 (vs), 1449 (m), 1350 (vs), 1316 (m), 1261 (s), 1075 (w), 999 (w), 962 (w), 920 (m), 869 (m), 796 (m), 740 (m), 703 (m), 642 (m).

**HRMS** for $\mathbf{C_{16}H_{13}NO_3}$ (267.0895): found: 267.0899.

## Synthesis of (5-iodo-2,4-dimethyl-3-nitrophenyl)(phenyl)methanol (76k)



Prepared according to **TP 5** from 3,5-diiodo-2,6-dimethyl-nitrobenzene (**74)** (402 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF), and benzaldehyde (168 mg, 1.50 mmol) at −40 °C. Exchange was finished after 30 min. Reaction time 1 h. Purification by flash chromatography (pentane/diethyl ether = 19:1) furnished title compound **76k** as a yellow oil (159 mg, 58%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.15 (s, 1 H), 7.30-7.13 (m, 5 H), 5.75 (s, 1 H), 2.46 (s, 1 OH), 2.27 (s, 3 H), 1.88 (s, 3 H).

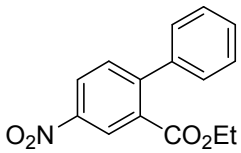
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 152.6, 142.2, 141.1, 138.0, 131.1, 128.9, 128.4, 127.1, 126.4, 98.7, 72.7, 23.2, 13.6.

**MS** (70 eV, EI), *m/z* (%): 383 (81) [$M^+$], 348 (62), 303 (44), 288 (12), 221 (12), 193 (36), 165 (30), 127 (18), 105 (100), 77 (56).

**IR** (KBr): $\tilde{\nu}$ = 3350 (m), 1531 (vs), 1454 (s), 1382 (s), 1359 (vs), 1164 (m), 1059 (m), 1016 (m), 891 (w), 767 (m), 742 (s), 700 (s).

**HRMS** for **$C_{15}H_{14}INO_3$** (383.0018): found: 383.0018.

## Synthesis of ethyl 4-nitro[1,1'-biphenyl]-2-carboxylate (78a)




Prepared according to **TP 6** from ethyl 2-iodo-5-nitrobenzoate (**65a**) (321 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.7 M in THF), $ZnBr_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF), $Pd(dba)_2$ (29 mg, 0.05 mmol) and tfp (23 mg, 0.10 mmol). Reaction time: 4 h at 20 °C. Purification by flash chromatography (pentane/diethyl ether = 19:1) furnished biphenyl **78a** as a colourless solid (184 mg, 68%).

**mp**.: 64.8-66.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.60 (d, 1 H), 8.27 (dd, $^4J$(H,H) = 2.7 Hz, $^3J$(H,H) = 8.7 Hz, 1 H), 7.48 (d, 1 H), 7.37-7.36 (m, 2 H), 7.35-7.34 (m, 2 H), 7.26-7.23 (m, 1 H), 4.07 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 0.97 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

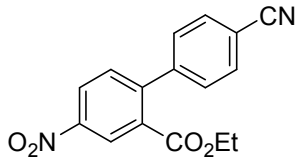
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.6, 147.6, 145.8, 138.3, 131.6, 130.8, 127.4, 127.3, 127.1, 124.5, 124.0, 60.8, 12.6.

**MS** (70 eV, EI), *m/z* (%): 271 (61) [$M^+$], 243 (18), 226 (100), 210 (3), 196 (2), 180 (39), 168 (2), 152 (37), 139 (12), 126 (4), 115 (3).

**IR** (KBr): $\tilde{\nu}$ = 1720 (vs), 1609(w), 1575 (w), 1524 (s), 1349 (s), 1283 (s), 1236 (w), 1143 (m), 1115 (w), 777 (m), 759 (w), 742 (m), 699 (m).

**$C_{15}H_{13}NO_4$:** required: C: 66.41; H: 4.83; N: 5.16;
found: C: 66.57; H: 4.89; N: 5.24.

**Synthesis of ethyl 4'-cyano-4-nitro[1,1'-biphenyl]-2-carboxylate (78b)**




Prepared according to **TP 6** from ethyl 2-iodo-5-nitrobenzoate (**65a**) (321 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.7 M in THF), $ZnBr_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF), $Pd(dba)_2$ (29 mg, 0.05 mmol), tfp (23 mg, 0.10 mmol) and 4-iodobenzonitrile (**25**) (458 mg, 2.00 mmol). Reaction time: 2 h at 20 °C. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded biphenyl **78b** as a pale yellow solid (245 mg, 83%).

**mp**.: 105-106 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.77 (d, $^4J$(H,H) = 2.8 Hz, 1 H), 8.40 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.8 Hz, 1 H), 7.72 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 7.53 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.40 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 4.20 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.12 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.7, 147.6, 144.5, 132.4, 132.1, 128.9, 126.9, 124.9, 118.8, 114.0, 112.9, 89.1, 62.5, 14.3.

**MS** (70 eV, EI), *m/z* (%): 296 (51) [$M^+$], 268 (53), 251 (100), 205 (32), 177 (28), 150 (12), 140 (8).

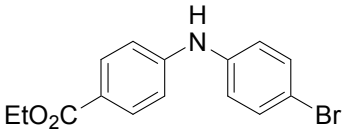
**IR** (KBr): $\tilde{\nu}$ = 2228 (s), 1710 (vs), 1609 (s), 1525 (vs), 1474 (s), 1419 (m), 1353 (vs), 1304 (s), 1283 (vs), 1262 (m), 1153 (s), 1143 (s), 1006 (s), 837 (m), 733 (m).

**HRMS** for **$C_{16}H_{12}N_2O_4$** (296.0797): found: 296.0865.

**$C_{16}H_{12}N_2O_4$:** required: C: 64.86; H: 4.08; N: 9.20;
found: C: 65.14; H: 4.09; N: 9.20.

# 11. Preparation of Polyfunctionalized Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Nitroarenes

### Synthesis of ethyl 4-(4-bromoanilino)benzoate (85a)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 4-bromonitrobenzene **84a** (303 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 12:1) yielded amine **85a** as a colourless solid (351 mg, 73%).

**mp**.: 154.5-155 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.92 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 7.42 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.03 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 6.98 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 4.33 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.37 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.8, 147.7, 140.6, 132.8, 131.9, 122.5, 122.0, 115.4, 114.9, 60.9, 14.8.

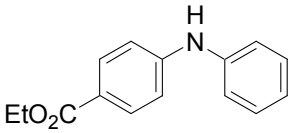
**MS** (70 eV, EI), *m/z* (%): 319 (100) [$M^+$], 292 (33), 273 (62), 167 (65), 139 (12), 83 (12).

**IR** (KBr): $\tilde{\nu}$ = 3340 (s), 1686 (vs), 1612 (vs), 1588 (vs), 1532 (vs), 1490 (vs), 1368 (s), 1352 (vs), 1308 (s), 1289 (vs), 1192 (s), 1174 (vs), 1129(s), 825 (m), 766 (s), 502 (m).

**HRMS** for **$C_{15}H_{14}BrNO_2$** (319.0208): found: 319.0200.

**$C_{15}H_{14}BrNO_2$:** required: C: 56.27; H: 4.41; N: 4.37;
found: C: 56.24; H: 4.07; N: 4.27.

### Synthesis of ethyl 4-anilinobenzoate (85b)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.5 mmol, 0.85 M in THF) and nitrobenzene **84b** (185 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 12:1) yielded amine **85b** as a colourless solid (340 mg, 85%).

**mp.:** 111.5-112.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.92 (d, $^3J$(H,H) = 8.8 Hz, 1 H), 7.35-7.23 (m, 2 H), 7.18-7.14 (m, 2 H), 7.05 (t, $^3J$(H,H) = 7.5 Hz, 1 H), 6.98 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 5.90 (s_br, 1 NH), 4.33 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.37 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.5, 147.9, 140.9, 131.4, 129.5, 123.0, 121.5, 120.3, 114.6, 60.4, 14.4.

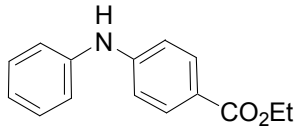
**MS** (70 eV, EI), *m/z* (%): 241 (100) [$M^+$], 213 (41), 196 (87), 167 (51), 139 (6), 115 (3), 98 (2), 83 (7). 65 (3).

**IR** (KBr): $\tilde{\nu}$ = 3360 (s), 3336 (s), 2559 (w), 1689 (vs), 1678 (vs), 1589 (vs), 1529 (s), 1496 (s), 1475 (s), 1447 (w), 1412 (m), 1366 (s), 1338 (vs), 1280 (vs), 1250 (s), 1177 (vs), 1154 (m), 1121 (vs), 1021 (m), 846 (m), 769 (s), 753 (s), 695 (m).

**HRMS** for **$C_{15}H_{15}NO_2$** (241.1103): found: 241.1090.

**$C_{15}H_{15}NO_2$**: required: C: 74.67; H: 6.27; N: 5.81;
found: C: 74.35; H: 6.41; N: 5.69.

## Synthesis of ethyl 4-anilinobenzoate (85b)




Prepared according to **TP 7** from PhMgCl (1.8 mL, 3.5 mmol, 2.0 M in THF) and ethyl 4-nitrobenzoate (293 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 29:1) yielded amine **85b** as a colourless solid (340 mg, 72%).

**mp.:** 112-113 °C.

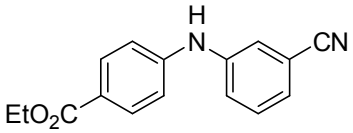
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.90 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 7.36-7.25 (m, 2 H), 7.18-7.04 (m, 3 H), 6.97 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.90 (s_br, 1 NH), 4.32 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.39 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.4, 147.7, 140.9, 131.4, 129.4, 123.1, 121.4, 120.3, 114.5, 60.5, 14.4.

**MS** (70 eV, EI), *m/z* (%): 241 (100) [$M^+$], 213 (39), 196 (88), 167 (51), 139 (5), 115 (4), 98 (3), 83 (8). 65 (3).

Spectral data are in accordance with those reported for the compound mentioned above.

**Synthesis of ethyl 4-(3-cyanoanilino)benzoate (85c)**




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 3-nitrobenzonitrile (**84c**) (222 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/$CH_2Cl_2$ = 1:2) yielded amine **85c** as a colourless solid (300 mg, 75%).

**mp**.: 191-192 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.62 (d, $^3J$(H,H) = 9.3 Hz, 2 H), 7.14-7.05 (m, 3 H), 6.90-6.87 (m, 1 H), 6.81 (d, $^3J$(H,H) = 9.3 Hz, 2 H), 4.02 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.08 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.5, 146.2, 142.5, 130.6, 129.6, 123.7, 121.9, 121.4, 120.3, 118.2, 115.1, 112.2, 59.7, 13.7.

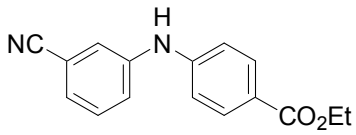
**MS** (70 eV, EI), *m/z* (%): 266 (77) [$M^+$], 238 (29), 221 (100), 192 (37), 166 (7), 139 (4), 110 (4), 83 (3).

**IR** (KBr): $\tilde{\nu}$ = 3332 (s), 2228 (s), 1684 (vs), 1602(vs), 1587 (s), 1580 (s), 1541 (s), 1508 (s), 1488 (m), 1368 (m), 1343 (vs), 1323 (m), 1311 (m), 1288 (vs), 1249 (m), 1167 (s), 851 (m), 796 (m), 773 (m), 688 (m).

**HRMS** for **$C_{16}H_{14}N_2O_2$** (266.1055): found: 266.1048.

**$C_{16}H_{14}N_2O_2$**: required: C: 72.16; H: 5.30; N: 10.52;
found: C: 71.94; H: 5.46; N: 10.50.

**Synthesis of ethyl 4-(3-cyanoanilino)benzoate (85c)**




Prepared according to **TP 7** from 3-iodobenzonitrile (790 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and ethyl 4-nitrobenzoate (293 mg, 1.50 mmol). Reaction time: 3 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography ($CH_2Cl_2$) yielded the amine **85c** as a colourless solid (252 mg, 63%).

**mp**.: 192-193 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.01 (s, 1 NH), 7.66 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.15-7.06 (m, 3 H), 6.91-6.88 (m, 1 H), 6.82 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.03 (q, $^3J$(H,H) = 7.3 Hz, 2 H), 1.10 (t, $^3J$(H,H) = 7.3 Hz, 3 H).

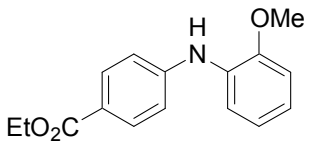
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.5, 146.2, 142.5, 130.5, 129.5, 123.7, 121.9, 121.5, 120.3, 118.2, 115.1, 112.2, 59.7, 13.7.

**MS** (70 eV, EI), *m/z* (%): 266 (76) [$M^+$], 238 (27), 221 (100), 192 (39), 166 (9), 139 (6), 110 (5), 83 (3).

**HRMS** for **$C_{16}H_{14}N_2O_2$** (266.1055): found: 266.1082.

Spectral data are in accordance with those reported for the compound mentioned above.

## Synthesis of ethyl 4-(2-methoxyanilino)benzoate (85d)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 2-nitroanisole (**84d**) (230 mg, 1.50 mmol). Reaction time: 8 h at 0 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 15:1) yielded amine **85d** as a colourless liquid (345 mg, 85%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.94 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.42-7.37 (m, 1 H), 7.08 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.99-6.90 (m, 3 H), 4.43 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.88 (s, 3 H), 1.38 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.5, 148.4, 146.4, 130.3, 129.6, 121.1, 120.6, 119.7, 116.6, 114.2, 109.9, 59.4, 54.6, 13.4.

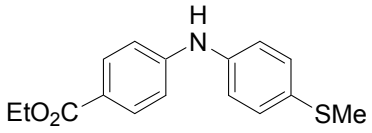
**MS** (70 eV, EI), *m/z* (%): 271 (100) [$M^+$], 243 (9), 226 (22), 183 (37), 167 (5), 154 (15), 128 (4), 92 (8).

**IR** (KBr): $\tilde{\nu}$ = 3354 (s), 2979 (s), 1703 (vs), 1610 (vs), 1592 (vs), 1525 (vs), 1505 (vs), 1485 (s), 1462 (vs), 1439 (s), 1409 (s), 1366 (s), 1311 (s), 1278 (vs), 1247 (vs), 1174 (vs), 1105 (vs), 1026 (s), 842 (m), 768 (s), 746 (s), 699 (m).

**HRMS** for **$C_{16}H_{17}NO_3$** (271.1208): found: 271.1202.

**$C_{16}H_{17}NO_3$**: required: C: 70.83; H: 6.32; N: 5.16;
found: C: 70.76; H: 6.66; N: 5.14.

## Synthesis of ethyl 4-[4-(methylsulfanyl)anilino]benzoate (85e)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.50 mmol), *i*PrMgCl (5.2 mL, 3.5 mmol, 0.70 M in THF), and 4-nitrothioanisole (253 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded amine **85e** as a pale yellow solid (310 mg, 72%).

**mp**.: 97.5-98.3 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.83 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.18 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.02 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.86 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.10 (s_br, 1 NH), 4.26 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 2.40 (s, 3 H), 1.29 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.5, 147.9, 138.7, 132.0, 131.4, 129.0, 121.5, 121.2, 114.5, 60.4, 17.1, 14.4.

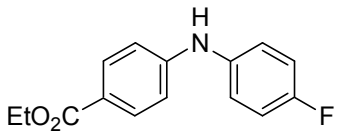
**MS** (70 eV, EI), *m/z* (%): 287 (100) [$M^+$], 272 (38), 244 (41), 199 (7), 167 (9), 121 (8).

**IR** (KBr): $\tilde{\nu}$ = 3347 (vs), 2978 (w), 1676 (vs), 1605 (vs), 1591 (vs), 1520 (vs), 1497 (s), 1488 (s), 1422 (m), 1367 (s), 1331 (s), 1277 (vs), 1174 (vs), 1131 (m), 1110 (m), 1024 (m), 837 (w), 796 (w), 770 (s), 698 (w), 523 (m), 508 (m).

**HRMS** for **$C_{16}H_{17}NO_2S$** (287.0980): found: 287.1014.

**$C_{16}H_{17}NO_2S$**: required: C: 66.87; H: 5.96; N: 4.87; S: 11.16;
found: C: 66.85; H: 5.92; N: 4.89; S: 11.37.

## Synthesis of ethyl 4-(4-fluoroanilino)benzoate (85f)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (5.2 mL, 3.6 mmol, 0.70 M in THF) and 4-fluoronitrobenzene (212 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 12:1) yielded amine **85f** as a white solid (285 mg, 73 %).

**mp:** 135.2-136.7 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.85 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.15-7.07 (m, 2 H), 7.06-6.99 (m, 2 H), 6.85 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.00 (s_br, 1 NH), 4.32 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.36 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.9, 159.1 (d, $^1J$(C,F) = 243 Hz), 149.1, 137.2 (d, $^4J$(C,F) = 3 Hz), 131.9, 123.6 (d, $^3J$(C,F) = 8 Hz), 121.6, 116.5 (d, $^2J$(C,F) = 22 Hz), 114.3, 60.8, 14.8.

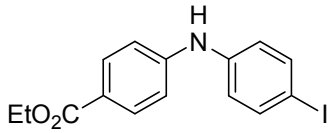
**MS** (70 eV, EI), *m/z* (%): 259 (100) [$M^+$], 231 (49), 214 (71), 185 (52), 157 (6), 133 (8), 107 (16), 92 (18), 83 (9), 65 (13).

**IR** (KBr): $\tilde{\nu}$ = 3350 (vs), 1686 (vs), 1608 (s), 1597 (vs), 1530 (s), 1509 (vs), 1430 (w), 1365 (m), 1343 (m), 1311 (m), 1279 (vs), 1211 (m), 1174 (s), 1109 (m), 837 (w), 768 (m), 697 (w), 577 (w), 557 (w), 502 (w).

**HRMS** for **$C_{15}H_{14}FNO_2$** (259.1009): found: 259.0993.

**$C_{15}H_{14}FNO_2$**: required: C: 69.49; H: 5.44; N: 5.40;
found: C: 69.34; H: 5.58; N: 5.30.

## Synthesis of ethyl 4-(4-iodoanilino)benzoate (85g)




Prepared according to **TP** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (5.2 mL, 3.6 mmol, 0.70 M in THF) and 4-iodonitrobenzene (373 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 19:1) yielded amine **85g** as a colourless solid (352 mg, 64%).

**mp**.: 156-157 °C.

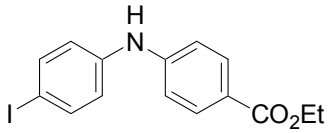
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.92 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.53 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.91 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.83 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.05 (s_br, 1 NH), 4.28 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.35 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.3, 146.0, 139.9, 137.3, 130.4, 121.2, 120.7, 114.2, 83.9, 59.5, 13.4.

**MS** (70 eV, EI), *m/z* (%): 367 (100) [$M^+$], 339 (21), 322 (32), 167 (24), 139 (7), 83 (5).

Spectral data are in accordance with those reported for the compound mentioned below.

## Synthesis of ethyl 4-(4-iodoanilino)benzoate (85g)




Prepared according to **TP 7** from 1,4-diiodobenzene (1.14 g, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and ethyl 4-nitrobenzoate (293 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 19:1) yielded amine **85g** as a colourless solid (389 mg, 71%).

**mp**.: 157-157.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.93 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.59 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.98 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.92 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.09 (s, 1 NH), 4.34 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.37 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.4, 146.0, 139.9, 137.3, 130.4, 121.2, 120.7, 114.2, 83.9, 59.6, 13.4.

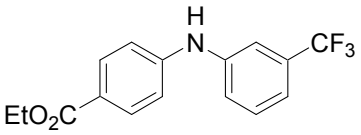
**MS** (70 eV, EI), *m/z* (%): 367 (100) [$M^+$], 339 (26), 322 (42), 167 (28), 139 (9), 82 (5).

**IR** (KBr): $\tilde{\nu}$ = 3337 (s), 1681 (vs), 1610 (vs), 1583 (vs), 1529 (vs), 1486 (vs), 1349 (s), 1309 (s), 1286 (vs), 1175 (s), 1129 (m), 1023 (m), 823 (m), 801 (m), 765 (m), 694 (w), 503 (m).

**HRMS** for **$C_{15}H_{14}INO_2$** (367.0069): found: 367.0034.

**$C_{15}H_{14}INO_2$**: required: C: 49.07; H: 3.84; N: 3.81;
found: C: 49.04; H: 3.89; N: 3.74.

## Synthesis of ethyl 4-[3-(trifluoromethyl)anilino]benzoate (85h)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.50 mmol), *i*PrMgCl (5.3 mL, 3.6 mmol, 0.70 M in THF), and 1-nitro-3-(trifluoromethyl)benzene (287 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded amine **85h** as a colourless solid (330 mg, 71%).

**mp**.: 114.5-115 °C.

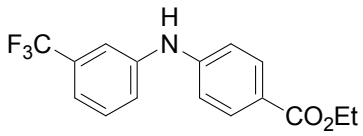
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.88 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 7.33-7.18 (m, 4 H), 6.94 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 6.25 (s_br, 1 NH), 4.26 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.30 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.4, 146.7, 141.9, 132.3 (q, $^2J$(C,F) = 32 Hz), 131.5, 130.0, 124.2 (q, $^1J$(C,F) = 273 Hz), 122.6, 122.2 (q, $^4J$(C,F) = 1 Hz), 118.8 (q, $^3J$(C,F) = 4 Hz), 115.8 (q, $^3J$(C,F) = 4 Hz), 115.6, 60.6, 14.4.

**MS** (70 eV, EI), m/z (%): 309 (90) [$M^+$], 281 (40), 264 (100), 235 (13), 216 (13), 167 (33), 132 (8).

Spectral data are in accordance with those reported for the compound mentioned below.

## Synthesis of ethyl 4-[4-(trifluoromethyl)anilino]benzoate (85h)




Prepared according to **TP 7** from 3-iodobenzotrifluoride (925 mg, 3.50 mmol), *i*PrMgCl (4.7 mL, 3.5 mmol, 0.75 M in THF) and ethyl 4-nitrobenzoate (292 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded amine **85h** as a colourless solid (282 mg, 61%).

**mp**.: 115-115.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.87 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.32-7.18 (m, 4 H), 6.94 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.24 (s_br, 1 NH), 4.26 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.29 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.5, 146.7, 141.9, 132.4 (q, $^2J$(C,F) = 32 Hz), 131.5, 129.9, 124.2 (q, $^1J$(C,F) = 273 Hz), 122.6, 122.2 (q, $^4J$(C,F) = 1 Hz), 118.9 (q, $^3J$(C,F) = 4 Hz), 115.8 (q, $^3J$(C,F) = 4 Hz), 115.5, 60.6, 14.3.

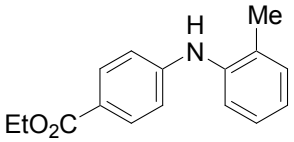
**MS** (70 eV, EI), *m/z* (%): 309 (79) [$M^+$], 281 (35), 264 (100), 235 (12), 216 (12), 167 (33), 132 (7), 65 (3).

**IR** (KBr): $\tilde{\nu}$ = 3337 (s), 2984 (w), 1686 (vs), 1597 (vs), 1540 (s), 1509 (s), 1495 (s),1479 (m), 1444 (s), 1369 (w), 1344 (vs), 1322 (s), 1286 (vs), 1251 (s), 1223 (m), 1166 (vs), 1123 (vs), 1072 (s), 1021 (m), 924 (m), 884 (w), 853 (m), 789 (m), 776 (m), 762 (m), 697 (s) 568 (m).

**HRMS** for **$C_{16}H_{14}F_3NO_2$** (309.0977): found: 309.0969.

| | | |
|---|---|---|
| **$C_{16}H_{14}F_3NO_2$**: | required: | C: 62.13; H: 4.56; N: 4.53; |
| | found: | C: 62.06; H: 4.33; N: 4.51. |

## Synthesis of ethyl 4-(2-methylanilino)benzoate (85i)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.5 mmol, 0.85 M in THF) and 2-nitrotoluene (206 mg, 1.50 mmol). Reaction time: 8 h at −5 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 19:1) yielded amine **85i** as a colourless oil (255 mg, 67%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.92 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 7.32-7.20 (m, 3 H), 7.11 (td, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 1.3 Hz, 1 H), 6.82 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.7 (s_br, 1 H), 4.35 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 2.27 (s, 3 H), 1.39 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

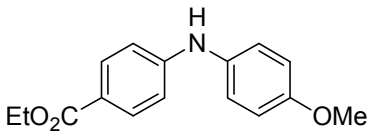
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.5, 149.1, 138.9, 131.8, 131.5, 131.4, 131.2, 125.9, 124.5, 122.8, 120.8, 114.0, 60.3, 17.9, 14.4.

**MS** (70 eV, EI), *m/z* (%): 255 (100) [$M^+$], 227 (20), 210 (63), 180 (21), 167 (27), 152 (2), 140 (1), 129 (1), 105 (3), 91 (3), 77 (3), 65 (4).

**IR** (KBr): $\tilde{\nu}$ = 3351 (s), 2979 (m), 1689 (vs), 1599 (vs), 1519 (vs), 1481 (s), 1461 (s), 1408 (w), 1367 (s), 1329 (vs), 1279 (vs), 1173 (vs), 1106 (vs), 1021 (m), 844 (m), 769 (s), 748 (s), 699 (m).

**HRMS** for **$C_{16}H_{17}NO_2$** (255.1259): found: 255.1245.

## Synthesis of ethyl 4-(4-methoxyanilino)benzoate (85j)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.5 mmol, 0.85 M in THF) and 4-nitroanisole (230 mg, 1.50 mmol). Reaction time: 4 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 19:1) yielded amine **85j** as a colourless solid (317 mg, 78%).

**mp**.: 77-78 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.90 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.15 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.91 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.83 (d, $^3J$(H,H) = 8.9 Hz, 2 H),

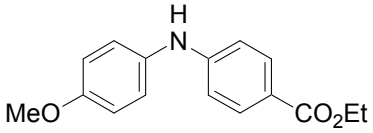
5.80 (s_br, 1 H), 4.35 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.83 (s, 3 H), 1.38 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.8, 156.9, 150.0, 133.9, 131.9, 124.5, 121.2, 115.1, 113.6, 60.5, 55.7, 14.8.

**MS** (70 eV, EI), *m/z* (%): 271 (100) [$M^+$], 228 (63), 183 (6), 167 (7), 154 (18), 128 (5), 113 (2), 77 (2).

Spectral data are in accordance with those reported for the compound mentioned below.

### Synthesis of ethyl 4-(2-methoxyanilino)benzoate (85j)




Prepared according to **TP 7** from 4-methoxyphenylmagnesium bromide (4.1 mL, 3.5 mmol, 0.85 M in THF) and ethyl 4-nitrobenzoate (298 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 9:1) yielded amine **85j** as a yellow solid (300 mg, 74%).

**mp**.: 76.5-78 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.88 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.13 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.89 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.81 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.88 (s, 1 NH), 4.32 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.81 (s, 3 H), 1.36 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

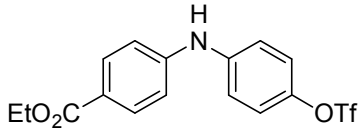
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 167.1, 156.9, 150.1, 133.9, 131.9, 124.7, 120.8, 115.2, 113.6, 60.7, 55.9, 14.8.

**MS** (70 eV, EI), *m/z* (%): 271 (100) [$M^+$], 228 (48), 183 (6), 154 (14), 113 (5), 77 (4).

**IR** (KBr): $\tilde{\nu}$ = 3357 (vs), 1696 (vs), 1595 (vs), 1530 (s), 1513 (vs), 1344 (m), 1282 (s), 1257 (s), 1167 (s), 1104 (s), 1032 (m), 833 (m), 818 (m), 761 (m).

**HRMS** for **$C_{16}H_{17}NO_3$** (271.1208): found: 271.1192.

### Synthesis of ethyl 4-(4-{[(trifluoromethyl)sulfonyl]oxy}anilino)benzoate (85k)



Prepared according to **TP 7** from ethyl 4-iodobenzoate (635 mg, 2.30 mmol), *i*PrMgCl (3.0 mL, 2.4 mmol, 0.80 M in THF) and 4-nitrophenyl trifluoromethanesulfonate (271 mg, 1.00 mmol). Reaction time: 1 h. Addition of ethanol (1 mL), $FeCl_2$ (252 mg, 2.00 mmol) and $NaBH_4$ (39 mg, 1.00 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 9:1) yielded amine **85k** as a colourless solid (330 mg, 85%).

**mp**.: 132-132.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.97 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.22-7.15 (m, 4 H), 7.04 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.12 (s, 1 NH), 4.33 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.37 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.7, 146.9, 144.4, 141.9, 131.9, 123.4, 122.9, 120.5, 118.7 (quart, $^1J$(C,F) = 320 Hz), 116.2, 61.0, 14.8.

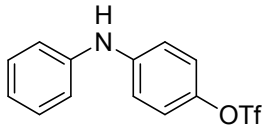
**MS** (70 eV, EI), *m/z* (%): 389 [$M^+$] (12), 344 (7), 290 (3), 256 (100), 228 (30), 212 (4), 183 (13), 154 (11), 128 (4), 69 (6).

**IR** (KBr): $\tilde{\nu}$ = 3337 (vs), 1683 (vs), 1610 (s), 1592 (vs), 1535 (s), 1502 (vs), 1477 (w), 1425 (s), 1402 (m), 1368 (s), 1348 (vs), 1310 (m), 1284 (vs), 1248 (m), 1220 (s), 1199 (vs), 1171 (s), 1135 (vs), 1105 (m), 1015 (m), 879 (vs), 841 (s), 811 (m), 772 (m), 601 (s).

**HRMS** for **$C_{16}H_{14}F_3NO_5S$** (389,0545): found: 389.0562.

**$C_{16}H_{14}F_3NO_5S$**: required: C: 49.36; H: 3.62; N: 3.60;
found: C: 49.38; H: 3.43; N: 3.50.

## Synthesis of 4-anilinophenyl trifluoromethanesulfonate (85l)




Prepared according to **TP 7** from PhMgCl (1.2 mL, 2.3 mmol, 1.9 M in THF) and 4-nitrophenyl trifluoromethanesulfonate (271 mg, 1.00 mmol). Reaction time: 2 h. Addition of ethanol (1 mL), $FeCl_2$ (252 mg, 2.00 mmol) and $NaBH_4$ (39 mg, 1.00 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 49:1) yielded amine **85l** as a colourless oil (270 mg, 85%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.34-7.28 (m, 2 H), 7.16-7.07 (m, 4 H), 7.05-7.00 (m, 2 H), 5.80 (s, 1 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 143.8, 142.6, 141.7, 129.5, 122.5, 122.3, 119.3, 118.7 (quart, $^1J$(C,F) 320 Hz), 117.3.

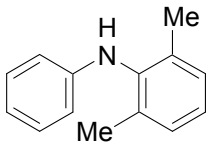
**MS** (70 eV, EI), *m/z* (%): 317 (28) [$M^+$], 184 (100), 167 (2), 154 (11), 128 (14), 103 (3), 91 (8), 77 (10), 69 (9).

**IR** (KBr): $\tilde{\nu}$ = 3420 (m), 1594 (s), 1501 (vs), 1420 (vs), 1322 (m), 1248 (s), 1213 (vs), 1174 (s), 1140 (vs), 886 (S), 834 (w), 753 (m), 694 (m), 608 (m), 517 (m), 498 (w).

**HRMS** for **$C_{13}H_{10}F_3NO_3S$** (317.0333): found: 317.0338.

**$C_{16}H_{14}F_3NO_5S$**: required: C: 49.21; H: 3.18; N: 4.41;
found: C: 49.06; H: 3.28; N: 4.29.

## Synthesis of 2,6-dimethyl-*N*-phenylaniline (85m)




Prepared according to **TP 7** from PhMgCl (1.9 mL, 3.6 mmol, 1.8 M in THF) and 2,6-dimethylnitrobenzene (226 mg, 1.50 mmol). Reaction time: 24 h at −5 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 99:1) yielded amine **85m** as a pale orange solid (220 mg, 76%).

**mp**.: 53.7-55.1 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.20-7.09 (m, 5 H), 6.77 (tt, $^3J$(H,H) = 7.1 Hz and $^4J$(H,H) = 0.9 Hz, 1 H), 6.55-6.50 (m, 2 H), 5.22 (1 NH), 2.24 (s, 6 H).

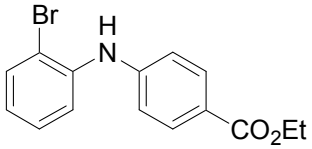
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 146.3, 138.2, 135.9, 129.2, 128.5, 125.7, 118.1, 113.5, 18.3.

**MS** (70 eV, EI), *m/z* (%): 197 (100) [$M^+$], 182 (35), 167 (12), 120 (18), 91 (8), 77 (9).

**IR** (KBr): $\tilde{\nu}$ = 3396 (s), 1604 (s), 1503 (vs), 1469 (s), 1310 (s), 1248 (w), 1207 (m), 1175 (m), 1147 (w), 1089 (m), 1075 (m), 1026 (w), 867 (m), 780 (s), 745 (vs), 690 (vs), 612 (w), 499 (m).

**HRMS** for **$C_{14}H_{15}N$** (197.1204): found: 197.1213.

## Synthesis of ethyl 4-(2-bromoanilino)benzoate (85n)




Prepared according to **TP 7** from 1-bromo-2-iodobenzene (976 mg, 3.45 mmol), *i*PrMgCl (4.7 mL, 3.5 mmol, 0.75 M in THF) and ethyl 4-nitrobenzoate (293 mg, 1.50 mmol). Reaction time: 48 h at −5 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and

$NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded amine **85n** as a colourless oil (240 mg, 50%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.96 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 7.58 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.41 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.25 (dt, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.09 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 6.88 (dt, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 6.27 (s_br, 1 NH), 4.36 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.39 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

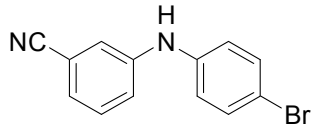
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 145.4, 138.3, 132.3, 130.4, 127.2, 122.1, 122.0, 117.8, 115.4, 113.5, 87.7, 59.6, 13.4.

**MS** (70 eV, EI), *m/z* (%): 319 (100) [$M^+$], 291 (22), 274 (83), 194 (21), 167 (99), 139 (21), 83 (16).

**IR** (KBr): $\tilde{\nu}$ = 3394 (m), 3346 (m), 2980 (w), 1704 (vs), 1608 (vs), 1591 (vs), 1520 (vs), 1462 (s), 1366 (m), 1276 (vs), 1175 (vs), 1105 (vs), 1023 (m), 768 (m), 748 (m), 697 (w).

**HRMS** for **$C_{15}H_{14}BrNO_2$** (319.0208): found: 319.0189.

## Synthesis of 3-(4-bromoanilino)benzonitrile (85o)




Prepared according to **TP 7** from 3-iodobenzonitrile (790 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 4-bromonitrobenzene (303 mg, 1.50 mmol). Reaction time: 3 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/$CH_2Cl_2$ = 1:1) yielded amine **85o** as a colourless solid (389 mg, 78%).

**mp**.: 135-135.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.31 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.23-7.16 (m, 3 H), 7.13 (s, 1 NH), 7.04 (d, $^3J$(H,H) = 7.8 Hz, 1 H), 6.93 (d, $^3J$(H,H) = 8.9 Hz, 2 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 143.4, 140.0, 131.3, 129.1, 122.4, 119.5, 118.1, 118.0, 113.0, 112.0.

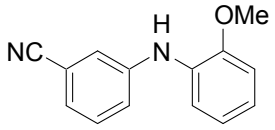
**MS** (70 eV, EI), *m/z* (%): 272 (100) [$M^+$], 192 (65), 166 (17), 139 (5), 96 (11), 75 (7).

**IR** (KBr): $\tilde{\nu}$ = 3378 (vs), 2228 (s), 1585 (vs), 1520 (s), 1491 (s), 1334 (m), 1304 (m), 1075 (w), 822 (w), 812 (w), 776 (m), 680 (m).

**HRMS** for **$C_{13}H_9BrN_2$** (271.9949): found: 271.9955.

**$C_{13}H_9BrN_2$**: required: C: 57.17; H: 3.32; N: 10.26;
found: C: 56.93; H: 3.10; N: 10.13.

## Synthesis of 3-(2-methoxyanilino)benzonitrile (85p)




Prepared according to **TP 7** from 3-iodobenzonitrile (790 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 2-nitroanisole (230 mg, 1.50 mmol). Reaction time: 8 h at 0 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 9:1) yielded amine **85p** as a pale yellow oil (250 mg, 74%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.39-7.26 (m, 4 H), 7.19-7.14 (m, 1 H), 7.02-6.90 (m, 3 H), 6.12 (s_br, 1 NH), 3.89 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.3, 144.3, 130.7, 130.1, 127.7, 122.2, 121.3, 120.8, 119.4, 117.0, 115.6, 112.1, 111.0, 55.6.

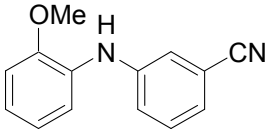
**MS** (70 eV, EI), *m/z* (%): 224 (100) [$M^+$], 209 (65), 192 (7), 181 (41), 154 (25), 127 (11), 102 (5).

**IR** (KBr): $\tilde{\nu}$ = 3394 (s), 2228 (s), 1593 (vs), 1580 (vs), 1525 (vs), 1493 (vs), 1413 (s), 1339 (s), 1294 (s), 1247 (vs), 1117 (s), 1028 (s), 872 (w), 789 (m), 745 (s), 683 (m).

**HRMS** for **$C_{14}H_{12}N_2O$** (224.0950): found: 224.0936.

Spectral data are in accordance with those reported for the compound mentioned below.

## Synthesis of 3-(2-methoxyanilino)benzonitrile (85p)




Prepared according to **TP 7** from 2-methoxyphenylmagnesium bromide (5.8 mL, 3.5 mmol, 0.60 M in THF) and 3-nitrobenzonitrile (222 mg, 1.50 mmol). Reaction time: 12 h at −10 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 7:1) yielded amine **85p** as a colourless oil (318 mg, 95%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.38-7.26 (m, 4 H), 7.17 (dt, $^3J$(H,H) = 7.1 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.03-6.93 (m, 3 H), 6.20 (s_br, 1 NH), 3.91 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.3, 144.2, 130.7, 130.1, 123.7, 122.2, 121.3, 120.8, 119.4, 117.0, 115.6, 113.1, 111.0, 55.6.

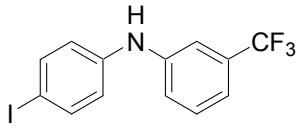
**MS** (70 eV, EI), *m/z* (%): 224 (100) [$M^+$], 209 (63), 192 (7), 181 (42), 166 (2), 154 (25), 127 (10), 102 (5), 76 (3), 63 (2), 52 (3).

**IR** (KBr): $\tilde{\nu}$ = 3339 (s), 2228 (s), 1593 (vs), 1580 (vs), 1526 (vs), 1493 (vs), 1462 (vs), 1440 (m), 1413 (m), 1338 (m), 1294 (s), 1247 (vs), 1177 (m), 1159 (w), 1117 (s), 1048 (m), 1028 (s), 872 (w), 788 (m), 745 (s), 683 (m).

**HRMS** for **$C_{14}H_{12}N_2O$** (224.0950): found: 224.0956.

**$C_{14}H_{12}N_2O$**: required: C: 74.98; H: 5.39; N: 12.49;
found: C: 74.79; H: 5.45; N: 12.29.

## Synthesis of *N*-(4-iodophenyl)-3-(trifluoromethyl)aniline (85q)




Prepared according to **TP 7** from 1,4 diiodobenzene (1.14 g, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 1-nitro-3-(trifluoromethyl)benzene (287 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 50:1) yielded amine **85q** as a pale yellow oil (325 mg, 60%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.63-7.60 (m, 2 H), 7.42-7.37 (m, 1 H), 7.29 (br_s, 1 H), 7.24-7.20 (m, 2 H), 6.90-6.86 (m, 2 H), 5.82 (s_br, 1 NH).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 143.0, 141.7, 138.3, 131.7 (q, $^2J$(C,F) = 32 Hz), 129.9, 123.8 (q, $^1J$(C,F) = 273 Hz), 120.3, 120.3 (m), 117.6 (q, $^3J$(C,F) = 4 Hz), 113.7 (q, $^3J$(C,F) = 4 Hz), 83.9.

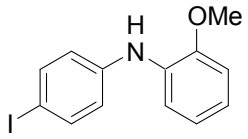
**MS** (70 eV, EI), *m/z* (%): 363 (100) [$M^+$], 235 (19), 216 (16), 185 (3), 167 (59), 127 (10), 91 (4), 75 (5), 63 (8), 58 (8), 43 (37).

**IR** (KBr): $\tilde{\nu}$ = 3393 (s), 1616 (m), 1583 (s), 1516 (m), 1491 (s), 1337 (vs), 1217 (m), 1164 (s), 1120 (s), 1068 (m), 921 (w), 789 (m), 698 (m).

**HRMS** for **$C_{13}H_9F_2IN$** (362.9732): found: 362.9734.

**$C_{13}H_9F_2IN$**: required: C: 43.00; H: 2.50; N: 3.86;
found: C: 42.93; H: 2.16; N: 3.74.

## Synthesis of *N*-(4-iodophenyl)-2-methoxyaniline (85r)




Prepared according to **TP 7** from 1,4-diiodobenzene (1.14 g, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 2-nitroanisole (230 mg, 1.50 mmol). Reaction time: 8 h at 0 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 50:1) yielded amine **85r** as a colourless solid (430 mg, 86%).

**mp**.: 59-60 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.42 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.18-7.14 (m, 1 H), 6.81-6.77 (m, 5 H), 6.01 (s, 1 NH), 3.78 (s, 3 H).

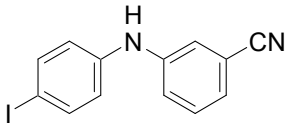
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.1, 143.1, 138.4, 132.4, 121.2, 120.4, 119.7, 115.9, 111.1, 82.7, 56.0.

**MS** (70 eV, EI), *m/z* (%): 325 (100) [$M^+$], 183 (85), 154 (29), 127 (6), 77 (5).

**IR** (KBr): $\tilde{\nu}$ = 3408 (vs), 2960 (m), 1579 (vs), 1517 (vs), 1487 (vs), 1455 (vs), 1430 (vs), 1338 (s), 1298 (s), 1244 (vs), 1176 (s), 1117 (s), 1029 (s), 999 (s), 829 (m), 802 (m), 742 (vs), 700 (m), 487 (m).

**HRMS** for **$C_{13}H_{12}INO$** (324.9964): found: 324.9957.

## Synthesis of 3-(4-iodoanilino)benzonitrile (85s)




Prepared according to **TP 7** from 1,4-diiodobenzene (1.14 g, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 3-nitrobenzonitrile (222 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/$CH_2Cl_2$ = 2:3) yielded amine **85s** as a pale yellow solid (340 mg, 71%).

**mp**.: 114-115.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.50 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 7.23-7.20 (m, 1 H), 7.17-7.05 (m, 3 H), 6.76 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 5.83 (s, 1 NH).

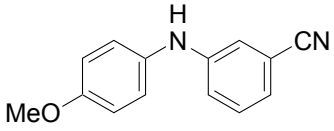
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 142.7, 140.1, 137.4, 129.3, 123.2, 120.2, 120.0, 118.5, 117.8, 112.2, 83.8.

**MS** (70 eV, EI), *m/z* (%): 320 (100) [$M^+$], 243 (9), 192 (33), 166 (7), 139 (3), 97 (2).

**IR** (KBr): $\tilde{\nu}$ = 3388 (s), 2224 (s), 1601 (vs), 1580 (vs), 1514 (s), 1487 (s), 1333 (s), 821 (s), 812 (m), 775 (s), 679 (m).

**HRMS** for **$C_{13}H_9IN_2$** (319.9810): found: 319.9812.

## Synthesis of 3-(4-methoxyanilino)benzonitrile (85t)




Prepared according to **TP 7** from 4-methoxyphenylmagnesium bromide (4.1 mL, 3.5 mmol, 0.85 M in THD) and 3-nitrobenzonitrile (222 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 17:1) yielded amine **85t** as a yellow solid (238 mg, 72%).

**mp**.: 86-87.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.18-7.13 (m, 1 H), 7.01 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.98-6.91 (m, 3 H), 6.81 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.60 (s, 1 NH), 3.74 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 155.6, 145.5, 132.5, 129.0, 123.1, 121.3, 118.2, 118.0, 116.0, 113.9, 112.0, 54.5.

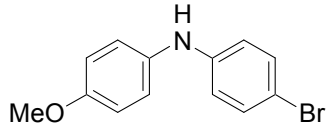
**MS** (70 eV, EI), *m/z* (%): 224 (64) [$M^+$], 209 (100), 192 (6), 179 (8), 154 (10),127 (7), 102 (5).

**IR** (KBr): $\tilde{\nu}$ = 3380 (s), 2226 (s), 1604 (s), 1536 (vs), 1509 (vs), 1487 (s), 1340 (s), 1246 (vs), 1183 (vs), 1033 (s), 855 (m), 838 (m), 822 (m), 774 (m), 681 (w).

**HRMS** for **$C_{14}H_{12}N_2O$** (224.0950): found: 224.0948.

**$C_{14}H_{12}N_2O$**: required: C: 74.98; H: 5.39; N: 12.49;
found: C: 75.16; H: 5.59; N: 12.50.

## Synthesis of 4-bromo-*N*-(4-methoxyphenyl)aniline (85u)




Prepared according to **TP 7** from 4-methoxyphenylmagnesium bromide (4.1 mL, 3.5 mmol, 0.85 M in THD) and 4-bromonitrobenzene (303 mg, 1.50 mmol). Reaction time: 2 h.

Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 19:1) yielded amine **85u** as a colourless solid (352 mg, 84%).

**mp**.: 87-88 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.19 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.96 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.78 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.67 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.38 (s_br, 1 NH), 3.71 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 156.1, 144.9, 135.4, 132.5, 123.2, 117.4, 115.2, 111.4, 56.0.

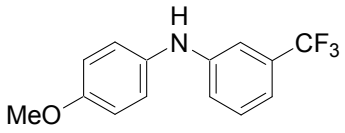
**MS** (70 eV, EI), *m/z* (%): 277 (84) [$M^+$], 262 (100), 183 (10), 154 (34), 128 (6).

**IR** (KBr): $\tilde{\nu}$ = 3419 (m), 1596 (m), 1515 (vs), 1493 (vs), 1298 (m), 1250 (vs), 1177 (m), 1032 (s), 8.24 (s), 817 (s), 770 (w).

**HRMS** for **$C_{13}H_{12}BrNO$** (277.0102): found: 277.0117.

**$C_{13}H_{12}BrNO$**: required: C: 56.14; H: 4.35; N: 5.04;
found: C: 56.22; H: 4.09; N: 4.89.

## Synthesis of *N*-(4-methoxyphenyl)-3-(trifluoromethyl)aniline (85v)




Prepared according to **TP 7** from 4-methoxyphenylmagnesium bromide (4.3 mL, 3.45 mmol, 0.80 M in THF) and 1-nitro-3-(trifluoromethyl)benzene (287 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 19:1) yielded amine **85v** as a colourless oil (340 mg, 85%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.31 (t, $^3J$(H,H) = 8.9 Hz, 1 H), 7.14-7.01 (m, 5 H), 6.94 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.62 (s_br, 1 NH), 3.72 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 156.1, 146.0, 134.6, 131.4 (q, $^2J$(C,F) = 32 Hz), 129.7, 124.2 (q, $^1J$(C,F) = 272 Hz), 123.5, 122.2 (q, $^4J$(C,F) = 1 Hz), 115.5 (q, $^3J$(C,F) = 4 Hz), 114.9, 112.4 (q, $^3J$(C,F) = 4 Hz), 55.5.

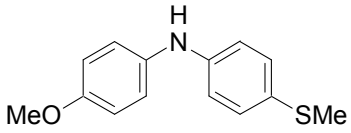
**MS** (70 eV, EI), *m/z* (%): 267 (94) [$M^+$], 252 (100), 224 (3), 177 (2), 154 (5), 145 (2), 128 (2), 95 (1), 63 (2).

**IR** (KBr): $\tilde{\nu}$ = 3398 (w), 2956 (w), 2837 (w), 1616 (s), 1597 (s), 1512 (vs), 1492 (s), 1475 (s), 1453 (m), 1340 (vs), 1321 (s), 1238 (vs), 1218 (s), 1164 (vs), 1123 (vs), 1097 (s), 1069 (s), 1036 (s), 995 (m), 922 (m), 825 (m), 787 (m), 757 (w), 698 (s), 662 (w), 514 (m).

**HRMS** for **$C_{14}H_{12}F_3NO$** (267.0871): found: 267.0878.

**$C_{14}H_{12}F_3NO$**: required: C: 62.92; H: 4.53; N: 5.24;
found: C: 62.80; H: 4.63; N: 5.18.

### Synthesis of *N*-(4-methoxyphenyl)-4-(methylsulfanyl)aniline (85w)




Prepared according to **TP** from 4-methoxyphenylmagnesium bromide (4.3 mL, 3.5 mmol, 0.80 M in THF) and 4-nitrothioanisole (254 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded amine **85w** as a colourless solid (292 mg, 79%).

**mp**.: 45.2-46.3 °C.

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 7.22 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.82 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.73 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.65 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.83 (s_br, 1 NH), 3.35 (s, 3 H), 2.12 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 155.8, 144.1, 135.9, 130.9, 127.8, 122.4, 116.7, 114.9, 55.1, 18.2.

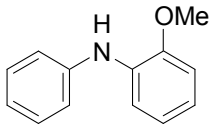
**MS** (70 eV, EI), *m/z* (%): 245 (94) [$M^+$], 230 (100), 215 (23), 186 (5), 167 (2), 154 (12), 122 (3), 115 (2), 77 (2).

**IR** (KBr): $\tilde{\nu}$ = 3416 (m), 2919 (w), 1599 (m), 1516 (vs), 1498 (vs), 1440 (m), 1316 (m), 1298 (m), 1283 (m), 1247 (vs), 1181 (m), 1108 (m), 1033 (vs), 966 (w), 816 (vs), 768 (w), 504 (m), 519 (w).

**HRMS** for **$C_{14}H_{15}NOS$** (245.0874): found: 245.0867.

**$C_{14}H_{15}NOS$**: required: C: 68.54; H: 4.16; N: 5.71;
found: C: 68.41; H: 6.10; N: 5.64.

### Synthesis of *N*-(2-methoxyphenyl)-*N*-phenylamine (85x)




Prepared according to **TP 7** from PhMgCl (1.9 mL, 3.5 mmol, 1.8 M in THF) and 2-nitroanisole (230 mg, 1.50 mmol). Reaction time: 2 h at −20 °C and 8 h at 0 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h

at rt. Purification by flash chromatography (pentane/diethyl ether = 49:1) yielded amine **85x** as a colourless oil (290 mg, 97%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.37-7.29 (m, 3 H), 7.22-7.18 (m, 2 H), 7.01-6.89 (m, 4 H), 3.92 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 148.2, 142.7, 132.9, 129.2, 121.1, 120.8, 119.9, 118.5, 114.7, 110.5, 55.5.

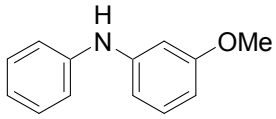
**MS** (70 eV, EI), *m/z* (%): 199 (100) [$M^+$], 184 (78), 167 (11), 156 (19), 129 (23), 77 (11), 51 (7).

**IR** (KBr): $\tilde{\nu}$ = 3409 (s), 3047 (m), 1592 (vs), 1518 (vs), 1496 (vs), 1464 (s), 1420 (s), 1344 (m), 1296 (s), 1245 (vs), 1177 (m), 1116 (s), 1048 (m), 1027 (s), 881 (w), 782 (m), 741 (vs), 694 (s), 499 (w).

**HRMS** for **$C_{13}H_{13}NO$** (199.0997): found: 199.1000.

**$C_{13}H_{13}NO$**: required: C: 78.36; H: 6.58; N: 7.03;
found: C: 78.15; H: 6.54; N: 7.05.

## Synthesis of *N*-(3-methoxyphenyl)-*N*-phenylamine (85y)




Prepared according to **TP 7** from PhMgCl (1.9 mL, 3.5 mmol, 1.8 M in THF) and 3-nitroanisole (230 mg, 1.50 mmol). Reaction time: 2 h at −20 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded amine **85y** as a colourless solid (275 mg, 92%).

**mp**.: 72-73 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.36-7.30 (m, 2 H), 7.23 (t, $^3J$(H,H) = 8 Hz, 1 H), 7.16-7.13 (m, 2 H), 7.03-6.98 (m, 1 H), 6.73-6.68 (m, 2 H), 6.58-6.53 (m, 1 H), 5.75 (s_br, 1 NH), 3.83 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 160.6, 144.5, 142.8, 130.0, 129.3, 121.2, 118.3, 110.1, 106.1, 103.3, 55.1.

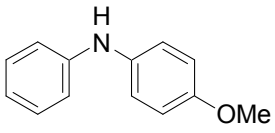
**MS** (70 eV, EI), *m/z* (%): 199 (100) [$M^+$], 183 (9), 167 (11), 154 (10), 128 (8), 92 (5), 77 (8).

**IR** (KBr): $\tilde{\nu}$ = 3385 (s), 2997 (w), 1598 (vs), 1587 (vs), 1497 (vs), 1453 (m), 1340 (w), 1267 (vs), 1238 (w), 1200 (m), 1177 (m), 1159 (m), 1036 (m), 953 (w), 837 (w), 782 (m), 739 (w), 691 (m).

**HRMS** for **$C_{13}H_{13}NO$** (199.0997): found: 199.0998.

**$C_{13}H_{13}NO$**: required: C: 78.36; H: 6.58; N: 7.03;
found: C: 78.14; H: 6.61; N: 7.01.

### Synthesis of *N*-(4-methoxyphenyl)-*N*-phenylamine (85z)




Prepared according to **TP 7** from PhMgCl (1.9 mL, 3.5 mmol, 1.8 M in THF) and 4-nitroanisole (230 mg, 1.50 mmol). Reaction time: 2 h at −20 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded amine **85z** as a colourless solid (280 mg, 94 %).

**mp**.: 106.8-107.8 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.32-7.27 (m, 2 H), 7.14 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.01-6.89 (m, 5 H), 5.55 (s_br, 1 NH), 3.87 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 155.1, 145.1, 135.7, 129.2, 122.1, 119.5, 115.6, 114.6, 55.5.

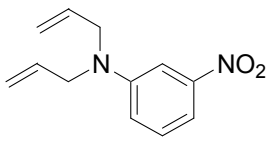
**MS** (70 eV, EI), *m/z* (%): 199 (76) [$M^+$], 184 (100), 167 (7), 154 (11), 128 (13), 77 (9).

**IR** (KBr): $\tilde{\nu}$ = 3365 (vs), 3030 (w), 1598 (vs), 1514 (vs), 1493 (vs), 1466 (s), 1323 (s), 1293 (s), 1260 (s), 1232 (vs), 1185 (m), 1173 (m), 1108 (w), 1031 (s), 945 (w), 828 (m),761 (s), 747 (vs), 693 (s), 616 (w), 511 (m).

**HRMS** for **$C_{13}H_{13}NO$** (199.0997): found: 199.1014.

**$C_{13}H_{13}NO$**: required: C: 78.36; H: 6.58; N: 7.03;
found: C: 78.08; H: 6.61; N: 6.98.

### Synthesis of *N*,*N*-diallyl-3-nitroaniline (84o)




3-Nitroaniline (1.38 g, 10.0 mmol) was dissolved in DMF (80 mL). Allyl bromide (8.0 mL, 90 mmol) and $K_2CO_3$ (4.14 g, 30.0 mmol) were added and the mixture was heated to 100 °C for 24 h. The solution was filtered after cooling to rt, the filter cake was washed with diethyl ether and the combined organic fractions were poured into water (200 mL). The aqueous

phase was washed three times with diethyl ether (3 x 100 mL) and the combined organic layers were washed with brine (200 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded **84o** as an orange oil (1.66 g, 76%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.49-7.45 (m, 2 H), 7.14 (t, $^3J$(H,H) = 8.4 Hz, 1 H), 7.94-6.90 (m, 1 H), 5.90-5.78 (m, 2 H), 5.22-5.13 (m, 4 H), 3.99-3.96 (m, 4 H).

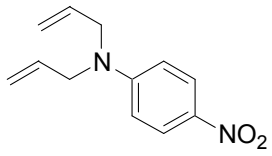
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 148.4, 148.2, 131.6, 128.5, 116.7, 115.6, 109.8, 105.3, 51.9.

**MS** (70 eV, EI), *m/z* (%): 218 (82) [$M^+$], 191 (100), 171 (46),157 (17), 149 (26), 143 (17), 130 (57), 117 (17), 103 (32), 91 (13), 77 (39), 63 (11).

**IR** (KBr): $\tilde{\nu}$ = 1619 (m), 1526 (vs), 1495 (m), 1391 (m), 1347 (vs), 1238 (s), 1181 (m), 988 (m), 923 (m), 848 (m), 784 (m), 734 (s), 671 (m).

**$C_{12}H_{14}N_2O_2$:** required: C: 66.04; H: 6.47; N: 12.84;
found: C: 65.83; H: 6.46; N: 12.77.

## Synthesis of *N*,*N*-diallyl-3-nitroaniline (84p)




4-Nitroaniline (1.38 g, 10.0 mmol) was dissolved in DMF (80 mL). Allyl bromide (8.0 mL, 90 mmol) and $K_2CO_3$ (4.14 g, 30.0 mmol) were added and the mixture was heated to 100 °C for 24 h. The solution was filtered after cooling to rt, the filter cake was washed with diethyl ether and the combined organic fractions were poured into water (200 mL). The aqueous phase was washed three times with diethyl ether (3 x 100 mL) and the combined organic layers were washed with brine (200 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded **84p** as an orange oil (1.57 g, 72%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.06 (d, $^3J$(H,H) = 9.3 Hz, 2 H), 6.61 (d, $^3J$(H,H) = 9.3 Hz, 2 H), 5.89-5.76 (m, 2 H), 5.24-5.10 (m, 4 H), 4.02-3.99 (m, 4 H).

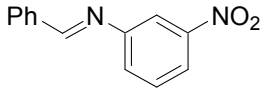
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 153.1, 137.2, 131.7, 126.0, 116.8, 110.6, 53.1

**MS** (70 eV, EI), *m/z* (%): 218 (100) [$M^+$], 191 (75), 177 (7), 171 (8), 157 (7), 149 (16), 145 (31), 130 (36), 117 (16), 103 (20), 91 (6), 77 (17), 63 (5).

**IR** (KBr): $\tilde{\nu}$ = 1596 (vs), 1516 (vs), 1487 (vs), 1450 (s), 1433 (s), 1402 (s), 1315 (vs), 1241 (vs), 1201 (vs), 1177 (s), 1113 (vs), 995 (s), 943 (s), 927 (s), 826 (s),753 (s).

**$C_{12}H_{14}N_2O_2$:** required: C: 66.04; H: 6.47; N: 12.84;
found: C: 65.99; H: 6.45; N: 12.80.

## Synthesis of 3-nitro-*N*-[phenylmethylidene]aniline (84q)




3-Nitroaniline (1.38 g, 10.0 mmol) was dissolved in dry toluene (30 mL), then benzaldehyde (1.27 g, 12.0 mmol), $H_2SO_4$ (100%, a few drops) and molecular sieves (4Å, 500 mg) were added and the mixture was heated to reflux for 2 h. The solution was filtered after cooling to rt and concentrated *in vacuo*. The resulting yellow oil crystallized upon addition of diethyl ether. Recrystallization from ethanol yielded compound **84q** as pale yellow solid (1.92 g, 85%).

**mp.:** 71-73 °C.

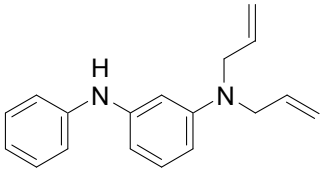
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.86-8.83 (m, 2 H), 7.76-7.70 (m, 2 H), 7.16-7.13 (m, 3 H), 7.03-7.00 (m, 1 H), 6.77 (t, $^4J$(H,H) = 8.0 Hz, 2 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 162.1, 153.2, 136.1, 132.0, 129.6, 129.4, 128.9, 127.6, 120.3, 115.2.

**MS** (70 eV, EI), *m/z* (%): 226 (100) [$M^+$], 196 (11), 179 (9), 167 (3), 152 (7), 76 (5).

Spectral data are in accordance with those reported in the literature[128]

## Synthesis of $N^3$,$N^3$-Diallyl-$N^1$-phenyl-benzene-1,3-diamine (85aa)




Prepared according to **TP 7** from PhMgCl (2.4 mL, 4.6 mmol, 1.9 M in THF) and diallyl-3-nitroaniline (252 mg, 1.50 mmol). Reaction time: 2 h at rt. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded amine **85aa** as colourless oil (290 mg, 73%).

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 7.32-7.23 (m, 5 H), 7.07-7.04 (m, 2 H), 7.08-7.04 (m, 2 H), 6.94 (tt, $^3J$(H,H) = 7.8 Hz, $^4J$(H,H) = 0.9 Hz, 1 H), 6.56-6.50 (m, 2 H), 6.47-6.40 (m, 1 H), 5.80-5.68 (m, 2 H) 5.18-5.08 (m, 4 H) 3.78-3.72 (m, 4 H).

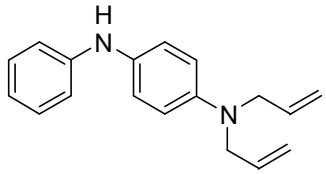
**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 150.1, 144.1, 134.6, 130.1, 129.4, 120.6, 117.9, 115.7, 107.5, 106.4, 102.9, 52.9.

**MS** (70 eV, EI), *m/z* (%): 264 (100) [$M^+$], 249 (31), 223 (29), 196 (65), 182 (5), 167 (53), 130 (18), 92 (5), 77 (11).

**IR** (KBr): $\tilde{\nu}$ = 3382 (s), 1622 (m), 1591 (m), 1518 (vs), 1491 (s), 1243 (m), 1176 (m), 985 (m), 948 (m), 914 (m), 863 (m), 821 (m), 808 (m), 780 (m), 746 (s), 692 (s), 668 (m), 518 (w).

**HRMS** for $\mathbf{C_{18}H_{20}N_2}$ (264.1626): found: 264.1644.

## Synthesis of $N^4$,$N^4$-Diallyl-$N^1$-phenyl-benzene-1,3-diamine (85ab)



Prepared according to **TP 7** from PhMgCl (2.4 mL, 4.6 mmol, 1.9 M in THF) and diallyl-4-nitroaniline (327 mg, 1.50 mmol). Reaction time: 2h at rt. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded the amine **85ab** as yellow oil (230 mg, 58%).

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 7.16-7.10 (m, 2 H), 6.98 (d, $^3J$(H,H) = 7.8 Hz, 2 H), 6.80-6.74 (m, 3 H), 6.63 (d, $^3J$(H,H) = 7.8 Hz, 2 H), 5.71-5.60 (m, 2 H) 5.09-4.98 (m, 4 H) 4.87 (s_br, 1 NH), 3.64-3.62 (m, 4 H).

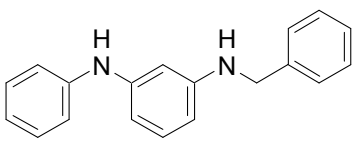
**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 146.7, 145.5, 134.7, 129.5, 123.9, 118.9, 115.8, 115.3, 114.1, 112.8, 53.3.

**MS** (70 eV, EI), *m/z* (%): 264 (100) [$M^+$], 223 (20), 195 (22), 182 (5), 167 (33), 130 (58), 92 (5), 77 (8).

**IR** (KBr): $\tilde{\nu}$ = 3349 (s), 1526 (vs), 1481 (s), 1445 (m), 1412 (m), 1333 (m), 1241 (s), 1211 (vs), 1172 (s), 1110 (s), 950 (m), 946 (m), 826 (m), 800 (m), 770 (m), 744 (s), 657 (w), 634 (w), 562 (w).

**HRMS** for $\mathbf{C_{18}H_{20}N_2}$ (264.1626): found: 264.1639.

## Synthesis of $N^1$-benzyl-$N^3$-phenyl-1,3-benzenediamine (85ac)



Prepared according to **TP 7** from PhMgCl (5.1 mL, 9.2 mmol, 1.9 M in THF) and 3-nitro-*N*-[phenylmethylidene]aniline (904 mg, 4.00 mmol). Reaction time: 2 h at rt. Addition of ethanol (5 mL), $FeCl_2$ (1.1 g, 8.00 mmol) and $NaBH_4$ (270 mg, 8.00 mmol) stirring

overnight at rt. Purification by flash chromatography (pentane/diethyl ether = 7:1) yielded amine **85ac** as a pale yellow oil (820 mg, 75%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.41-7.33 (m, 5 H), 7.29-7.24 (m, 2 H), 7.11 (t, $^3J$(H,H) = 7.8 Hz, 1 H), 7.08-7.04 (m, 2 H), 6.94 (m, 1 H), 6.49-6.45 (m, 1 H), 6.39 (t, $^4J$(H,H) = 2.5 Hz, 1 H), 6.31-6.27 (m, 1 H), 5.64 (s_br, 1 NH), 4.34 (s, 2 H), 4.09 (s_br, 1 NH).

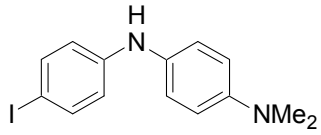
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.1, 144.1, 143.1, 139.3, 130.0, 129.2, 128.6, 127.4, 127.1, 120.7, 117.9, 107.4, 106.2, 101.8, 48.2.

**MS** (70 eV, EI), *m/z* (%): 274 (100) [$M^+$], 197 (10), 167 (13), 154 (3), 91 (27), 65 (4).

**IR** (KBr): $\tilde{\nu}$ = 3398 (s), 3028 (m), 1591 (vs), 1513 (vs), 1494 (vs), 1452 (s), 1419 (s), 1401 (m), 1344 (m), 1308 (s), 1253 (m), 1203 (m), 1187 (m), 1165 (s), 1103 (w), 1077 (w), 1027 (m), 990 (m), 948 (w), 844 (m), 826 (m), 746 (s), 689 (vs), 451 (m).

**HRMS** for **$C_{19}H_{18}N_2$** (274.1470): found: 274.1482.

## Synthesis of $N^4$,$N^4$-dimethyl-$N^1$-[4-iodophenyl]-benzene-1,3-diamine (85ad)




Prepared according to **TP 7** from 1,4-diiodobenzene (1.14 g, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and *N,N*-dimethyl-4-nitroaniline (249 mg, 1.50 mmol). Reaction time: overnight from −20 °C to rt. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded amine **85ad** as pale yellow solid (352 mg, 67%).

**mp.:** 125.5-126.5 °C (decomp.).

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 7.38 (d, $^3J$(H,H) = 8 Hz, 2H), 6.89 (d, $^3J$(H,H) = 7 Hz, 2H), 6.55 (d, $^3J$(H,H) = 8 Hz, 2H), 6.34 (d, $^3J$(H,H) = 7 Hz, 2H), 4.71 (s_br, 1NH), 2.53 (s_br, 6H).

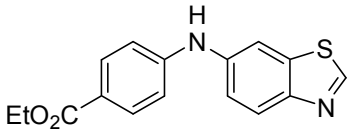
**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 147.9, 138.1, 131.5, 127.8, 124.3, 117.03, 113.9, 40.7.

**MS** (70 eV, EI), *m/z* (%): 338 (100) [$M^+$], 322 (19), 211 (10), 195 (7), 167 (20), 154 (2), 105 (3), 91 (2), 83 (2), 76 (4), 65 (2).

**IR** (KBr): $\tilde{\nu}$ = 3407 (m), 1590 (s), 1524 (vs), 1488 (s), 1311 (m), 1222 (m), 1114 (m), 1060 (w), 949 (w), 809 (vs), 628 (w).

**$C_{14}H_{15}N_2I$:** required: C: 49.72; H: 4.47; N: 8.28;
found: C: 50.01; H: 4.33; N: 8.33.

## Synthesis of ethyl 4-(1,3-benzothiazol-5-ylamino)benzoate (87a)



Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 6-nitro-benzothiazole (270 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 2:1) yielded amine **87a** as a pale yellow solid (345 mg, 77%).

**mp**.: 147-148 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.86 (s, 1 H), 8.03 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 7.95 (d, $^3J$(H,H) = 8.9 Hz, 2 H) 7.74 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.28 (dd, $^3J$(H,H) = 8.9 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.04 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.42 (s, 1 NH), 4.34 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.37 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.4, 151.3, 148.3, 146.6, 138.3, 134.2, 130.5, 123.2, 121.1, 119.2, 114.0, 110.7, 59.5, 13.4.

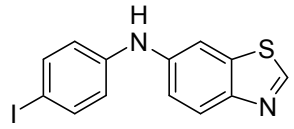
**MS** (70 eV, EI), *m/z* (%): 298 (100) [$M^+$], 270 (35), 253 (56), 225 (11), 192 (12), 154 (5), 126 (8) 98 (4).

**IR** (KBr): $\tilde{\nu}$ = 3322 (w), 1690 (s), 1595 (vs), 1477(m), 1341 (m), 1284 (vs), 1175 (vs), 1107 (m), 841 (w), 769 (w).

**HRMS** for **$C_{16}H_{14}N_2O_2S$** (298.0776): found: 298.0770.

**$C_{16}H_{14}N_2O_2S$**: required: C: 64.41; H: 4.73; N: 9.39;
found: C: 64.10; H: 4.48; N: 9.40.

## Synthesis of *N*-(4-iodophenyl)-1,3-benzothiazol-5-amine (87b)



Prepared according to **TP 7** from 1,4 diiodobenzene (1.14 g, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 6-nitro-benzothiazole (270 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 2:1) yielded amine **87b** as a yellow solid (337 mg, 64%).

**mp**.: 119-121 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.81 (s, 1 H), 7.99 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 7.60-7.53 (m, 3 H), 7.18 (dd, $^3J$(H,H) = 8.9 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 6.87 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.93 (s, 1 NH).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 150.6, 147.5, 141.7, 139.7, 137.3, 134.3, 123.1, 118.9, 117.8, 108.3, 82.1.

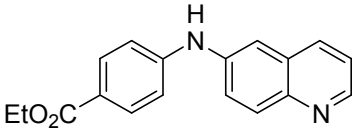
**MS** (70 eV, EI), *m/z* (%): 352 (100) [$M^+$], 224 (12), 192 (14), 154 (3), 112 (8).

**IR** (KBr): $\tilde{\nu}$ = 3306 (w), 1581 (s), 1486 (vs), 1345 (s), 1108 (m), 1043 (m), 807 (s).

**HRMS** for **$C_{13}H_9IN_2S$** (351.9531): found: 351.9506.

**$C_{13}H_9IN_2S$:** required: C: 44.33; H: 2.58; N: 7.95;
found: C: 44.67; H: 2.39; N: 8.06.

## Synthesis of ethyl 4-(6-quinolinylamino)benzoate (87c)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 6-nitro-chinoline (261 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 1:2) yielded amine **87c** as a yellow solid (255 mg, 57%).

**mp**.: 180-180.5°C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.53 (dd, $^3J$(H,H) = 4.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.87 (s, 1 H), 7.82-7.73 (m, 4 H), 7.38-7.34 (m, 2 H), 7.16-7.13 (dd, $^3J$(H,H) = 8.4 Hz, $^3J$(H,H) = 4.4 Hz, 1 H), 7.00 (d, $^3J$(H,H) = 8.9 Hz, 2 H) 4.14 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.18 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.6, 148.3, 147.9, 144.9, 140.4, 134.9, 131.5, 130.5, 129.6, 124.6, 121.9, 121.8, 115.7, 112.6, 60.6, 14.7.

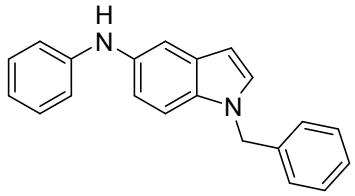
**MS** (70 eV, EI), *m/z* (%): 292 (100) [$M^+$], 264 (32), 247 (46), 218 (22), 124 (5), 96 (6).

**IR** (KBr): $\tilde{\nu}$ = 1697 (s), 1602 (vs), 1549 (m), 1495 (m), 1379 (m), 1365 (m), 1347 (m), 1284 (vs), 1264 (s), 1177 (m), 1106 (m), 843 (w), 829 (w), 769 (m).

**HRMS** for **$C_{18}H_{16}N_2O_2$** (292.1212): found: 292.1192.

**$C_{18}H_{16}N_2O_2$**: required: C: 73.35; H: 5.52; N: 9.58;
found: C: 73.51; H: 5.92; N: 9.52.

**Synthesis of *N*-(1-benzyl-1*H*-indol-5-yl)-*N*-phenylamine (87d)**



Prepared according to **TP 7** from PhMgCl (1.2 mL, 2.3 mmol, 1.9 M in THF) and 1-benzyl-5-nitro-1*H*-indole (252 mg, 1.00 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (252 mg, 2.00 mmol) and $NaBH_4$ (39 mg, 1.00 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 19:1) yielded amine **87d** as colourless solid (262 mg, 88%).

**mp**.: 83.6-84.9 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.51 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.43-7.19 (m, 8 H), 7.08 (dd, $^3J$(H,H) = 8.8 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.03-6.99 (m, 2 H), 6.93-6.87 (m, 1 H), 5.35 (s, 2 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 146.1, 137.5, 134.9, 133.2, 129.3, 129.2, 128.9, 128.7, 127.6, 126.7, 119.0, 117.8, 115.3, 113.2, 110.3, 101.2, 50.2.

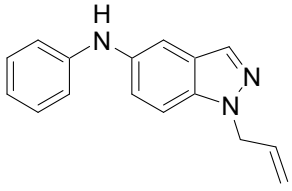
**MS** (70 eV, EI), *m/z* (%): 298 (100) [$M^+$], 207 (45), 180 (13), 154 (4), 91 (20), 77 (4), 65 (5).

**IR** (KBr): $\tilde{\nu}$ = 3395 (w), 1598 (s), 1504 (vs), 1474 (vs), 1450 (s), 1439 (m), 1359 (m), 1312 (vs), 1259 (m), 1231 (m), 1199 (w), 1181 (m), 1151 (w) 1074 (w), 992 (w), 854 (m), 745 (s), 712 (vs), 694 (s), 662 (w).

**HRMS** for **$C_{21}H_{18}N_2$** (298.1470): found: 298.1462.

**$C_{21}H_{18}N_2$**: required: C: 84.53; H: 6.08; N: 9.39;
found: C: 84.44; H: 6.20; N: 9.12.

**Synthesis of 1-allyl-*N*-phenyl-1*H*-indazol-5-amine (87f)**



Prepared according to **TP 7** from PhMgCl (1.2 mL, 2.3 mmol, 1.9 M in THF) and 1-allyl-5-nitro-1*H*-indazole (203 mg, 1 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (252 mg, 2 mmol) and $NaBH_4$ (39 mg, 1 mmol) stirring for 2 h at rt. Purification by flash

chromatography (pentane/ethyl acetate = 4:1) yielded amine **87f** as colourless solid (199 mg, 80%).

**mp**.: 101-102.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.82 (s, 1 H), 7.37-7.35 (m, 1 H), 7.23-7.17 (m, 4 H), 6.96-6.85 (m, 3 H), 5.99-5.87 (m, 1 H), 5.18-5.12 (m, 2 H), 5.00-4.93 (m, 2 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 144.0, 135.5, 135.2, 131.8, 131.4, 128.3, 123.9, 121.6, 119.0, 116.7, 115.1, 109.5, 109.1, 50.9.

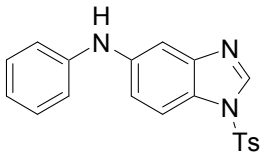
**MS** (70 eV, EI), *m/z* (%): 249 (100) [$M^+$], 222 (6), 208 (20), 180 (2), 154 (2), 77 (3).

**IR** (KBr): $\tilde{\nu}$ = 3395 (w), 1599 (s), 1516 (vs), 1498 (vs), 1482 (m), 1438 (m), 1418 (m), 1312 (s), 1291 (m), 1248 (m), 1176 (m), 1076 (w), 994 (m), 928 (m), 890 (m), 870 (m), 805 (m).

**HRMS** for **$C_{21}H_{18}N_2$** (249.1266): found: 249.1244.

**$C_{16}H_{15}N_3$**: required: C: 77.08; H: 6.06; N: 16.85;
found: C: 77.19; H: 6.08; N: 16.68.

## Synthesis of *N*-{1-[(4-methylphenyl)sulfonyl]-1*H*-benzimidazol-5-yl}-*N*-phenylamine (87g)




Prepared according to **TP 7** from PhMgCl (1.2 mL, 2.3 mmol, 1.9 M in THF) and 1-[(4-methylphenyl)sulfonyl]-5-nitro-1*H*-benzimidazole (317 mg, 1.00 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (252 mg, 2.00 mmol) and $NaBH_4$ (39 mg, 1.00 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 3:1) yielded amine **87g** as colourless solid (272 mg, 75%).

**mp**.: 172.2-172.9 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.33 (s, 1 H), 7.88 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.73 (d, $^3J$(H,H) = 8.6 Hz, 2 H), 7.49 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.34-7.22 (m, 4 H), 7.14-7.04 (m, 3 H), 6.97-6.92 (m, 1 H), 5.82 (s_br, 1 NH), 2.41 (s, 3 H).

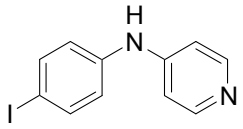
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 146.5, 145.7, 143.3, 142.2, 141.3, 135.0, 130.7, 129.8, 127.8, 126.0, 121.6, 118.3, 117.9, 113.4, 109.6, 22.1.

**MS** (70 eV, EI), *m/z* (%): 363 (49), 208 (100), 181 (8), 154 (9), 127 (2), 91 (11), 77 (7), 65 (4).

**IR** (KBr): $\tilde{\nu}$ = 3402 (m), 1600 (vs), 1484 (vs), 1447 (s), 1371 (vs), 1174 (vs), 1147 (vs), 1090 (s), 812 (m), 748 (m), 704 (s), 676 (vs), 591 (vs), 539 (s).

**HRMS** for $C_{21}H_{18}N_2$ (363.1041): found: 363.1027.

## Synthesis of 4-iodophenyl-4-pyridylamine (87h)




Prepared according to **TP 7** from 1,4-diiodobenzene (1.14 g, 3.45 mmol), *i*PrMgCl (4.8 mL, 3.6 mmol, 0.75 M in THF) and 4-nitropyridine (186 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification of the crude product by crystallization from aqueous ethanol (ethanol/water 2:1) afforded amine **87h** as a light yellow solid (196 mg, 44%).

**mp**.: 232-234 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 8.21 (s_br, 1 NH), 8.16-8.14 (m, 2 H), 7.52-7.49 (m, 2 H), 6.91 (d, $^3J$(H,H) = 8.7 Hz, 2 H), 6.81-6.79 (m, 2 H).

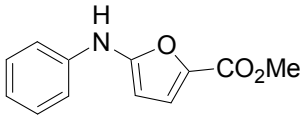
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 149.6, 149.5, 140.0, 137.4, 121.7, 109.2, 84.4.

**MS** (70 eV, EI), *m/z* (%): 296 (100) [$M^+$], 168 (29), 141 (5), 115 (13), 85 (6), 51 (8).

**IR** (KBr): $\tilde{\nu}$ = 2939 (w), 2839 (w), 1607 (vs), 1575 (vs), 1522 (s), 1483 (s), 1347 (s), 1217 (m), 997 (m), 811 (m).

**HRMS** for $C_{11}H_9IN_2$ (295.9810): found: 295.9818.

## Synthesis of methyl 5-anilino-2-furoate (87i)




Prepared according to **TP 7** from PhMgCl (1.2 mL, 2.3 mmol, 1.9 M in THF) and methyl 5-nitrofuroate (171 mg, 1.00 mmol). Reaction time: 1 h at −78 °C. Addition of ethanol (1 mL), $FeCl_2$ (252 mg, 2.00 mmol) and $NaBH_4$ (39 mg, 1.00 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 19:1) yielded amine **87i** as pale yellow solid (69 mg, 32%).

**mp**.: 67-68.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.33-7.26 (m, 2 H), 7.18 (d, $^3J$(H,H) = 3.5 Hz, 1 H), 7.08-6.96 (m, 3 H), 6.57 (br_s, 1 NH), 5.75 (d, $^3J$(H,H) = 3.5 Hz, 1 H), 3.85 (s, 3 H).

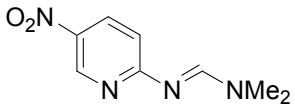
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 159.0, 154.7, 139.8, 135.5, 129.5, 122.2, 121.9, 116.9, 89.6, 51.5.

**MS** (70 eV, EI), *m/z* (%): 217 (100) [$M^+$], 186 (14), 174 (11), 159 (20), 130 (39), 103 (15), 77 (18).

**IR** (KBr): $\tilde{\nu}$ = 3280 (m), 1698 (vs), 1598 (vs), 1545 (vs), 1498 (s), 1445 (m), 1331 (s), 1226 (m), 1209 (m), 1151 (s), 747 (s), 695 (w).

**HRMS** for $\mathbf{C_{12}H_{11}NO_3}$ (217.0739): found: 217.0734.

## Synthesis of *N*,*N*-dimethyl-*N*'-(5-nitro-2-pyridinyl)imidoformamide (88)




5-Nitro-2-aminopyridine (2.78 g, 20.0 mmol) was suspended in toluene (100 mL), *N*,*N*-dimethylformamide-dimethyl acetale (7.14 g, 60.0 mmol) was added and the mixture was heated to reflux for 2 h. The reaction mixture was allowed to cool to rt, the crystals were removed by filtration and washed with toluene to give compound **88** as yellow solid (3.45 g, 89%)

**mp**.: 161.5-162.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 9.04 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 8.62 (s, 1 H), 8.02 (dd, $^3J$(H,H) = 8.9 Hz, $^4J$(H,H) = 2.7 Hz, 1 H), 6.88 (d, $^3J$(H,H) = 8.9 Hz, 1 H), 3.16 (s, 3 H), 3.13 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.7, 157.6, 145.8, 139.7, 133.2, 117.9, 41.6, 35.4.

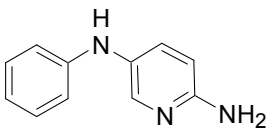
**MS** (70 eV, EI), *m/z* (%): 194 (85) [$M^+$], 177 (100), 147 (24), 134 (27), 120 (32), 106 (8), 92 (5), 78 (17), 72 (14), 44 (79).

**IR** (KBr): $\tilde{\nu}$ = 1629 (vs), 1584 (vs), 1563 (vs), 1503 (s), 1465 (vs), 1422 (s), 1384 (s) 1321 (vs), 1302 (s), 1276 (s), 1115 (s), 1105 (s), 995 (m), 859 (m), 848 (m), 773 (m).

**HRMS** for $\mathbf{C_8H_{10}N_4O_2}$ (194.0804): found: 194.0813.

$\mathbf{C_8H_{10}N_4O_2}$: required: C: 49.48; H: 5.19; N: 28.85;
found: C: 49.41; H: 5.26; N: 29.10

## Synthesis of $N^5$-phenyl-2,5-pyridinediamine (87k)



Prepared according to **TP 7** from PhMgCl (7.20 mL, 11.5 mmol, 1.60 M in THF) and *N*,*N*-dimethyl-*N*'-(5-nitro-2-pyridinyl)imidoformamide (**88**) (970 mg, 5.00 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (1.26 g, 10.0 mmol) and $NaBH_4$ (195 mg, 5.00 mmol) stirring for 3 h at rt and afterwards stirring for additional 30 min after addition of conc. HCl (2 mL). Purification by flash chromatography (ethyl acetate) yielded pyridineamine **87k** as pale yellow solid (565 mg, 61%).

**mp**.: 132-140 °C.

**$^1$H-NMR** (300 MHz, acetone-$d_6$ , 25 °C): δ = 7.82 (d, $^4J$(H,H) = 2.7 Hz, 1 H), 7.33 (d, $^4J$(H,H) = 8.4 Hz and $^4J$(H,H) = 2.7 Hz, 1 H), 7.15-7.10 (m, 2 H), 6.83-6.79 (m, 2 H), 6.71-6.65 (m, 1 H), 6.60-6.57 (m, 1 H), 1.93 (s_br, 2 H).

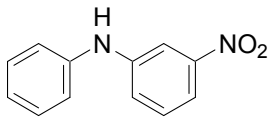
**$^{13}$C-NMR** (75 MHz, acetone-$d_6$, 25 °C): δ = 173.3, 157.3, 148.1, 142.7, 134.6, 130.9, 119.4, 115.4, 110.1.

**MS** (70 eV, EI), *m/z* (%):185 (100), 169 (8), 157 (6), 130 (6), 104 (3), 81 (5), 77 (8), 54 (5).

**IR** (KBr): $\tilde{\nu}$ = 3049 (m), 1678 (m), 1645 (m), 1603 (m), 1564 (m), 1545 (m), 1498 (vs), 1398 (m), 1338 (m), 992 (w), 871 (m), 732 (s), 687 (s), 665 (s).

**HRMS** for **$C_{11}H_{11}N_3$** (185.0953): found: 185.0967.

## Synthesis of (3-nitro-phenyl)-phenyl-amine (90a)




Prepared according to **TP 7** from PhMgCl (2.4 mL, 4.6 mmol, 1.9 M in THF) and 1,3-dinitrobenzene (336 mg, 2.00 mmol). Reaction time: 2 h at −10 °C. Addition of ethanol (3 mL), $FeCl_2$ (504 mg, 4.00 mmol) and $NaBH_4$ (76 mg, 2.00 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded amine **90a** as red crystals (290 mg, 67%).

**mp.:** 104.5-106 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.75 (t, $^4J$(H,H) = 2.5 Hz, 1 H), 7.65-7.58 (m, 1 H), 7.30-7.24 (m, 2 H), 7.24-7.20 (m, 1 H), 7.18-7.02 (m, 2 H), 6.99 (tt, $^3J$(H,H) = 8.9 Hz, $^4J$(H,H) = 2.5 Hz, 1 H), 5.89 (s_br, 1 NH).

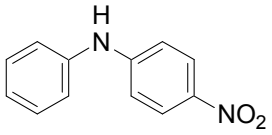
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.3, 145.1, 140.9, 129.9, 129.6, 123.1, 121.8, 119.8, 114.6, 110.2.

**MS** (70 eV, EI), *m/z* (%): 214 (100) [$M^+$], 184 (2), 167 (97), 154 (2), 139 (8), 128 (3), 115 (5), 83 (5), 77 (7), 63 (3).

**IR** (KBr): $\tilde{\nu}$ = 3380 (vs), 1691 (m), 1599 (s), 1539 (vs), 1492 (vs), 1417 (m), 1350 (vs), 1338 (vs), 1280 (s), 1250 (m), 1094 (m), 994 (m), 868 (m), 829 (m), 789 (m), 755 (m), 733 (s), 698 (s), 676 (m), 667 (m), 641 (w), 533 (m), 482 (m).

**HRMS** for $\mathbf{C_{12}H_{10}N_2O_2}$ (214.0742): found: 214.0758.

## Synthesis of (4-nitro-phenyl)-phenyl-amine (90b)




Prepared according to **TP 7** from PhMgCl (2.4 mL, 4.6 mmol, 1.9 M in THF) and 1,4-dinitrobenzene (336 mg, 2.00 mmol). Reaction time: 1 h at rt. Addition of ethanol (3 mL), $FeCl_2$ (504 mg, 4.00 mmol) and $NaBH_4$ (76 mg, 2.00 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded the amine **90b** as yellow crystals (270 mg, 63%).

**mp.:** 126.5-128 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.10 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.43 (m, 2 H), 7.03 (m, 3 H), 6.93 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.33 (s_br, 1 NH).

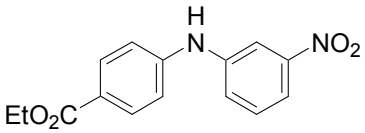
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 150.2, 139.7, 139.5, 129.7, 126.2, 124.6, 121.9, 113.6.

**MS** (70 eV, EI), *m/z* (%): 214 (100) [$M^+$], 184 (43), 167 (96), 154 (3), 139 (13), 128 (8), 115 (8), 83 (6), 77 (13), 63 (6).

**IR** (KBr): $\tilde{\nu}$ = 3391 (m), 3341 (s), 1604 (s), 1585 (vs), 1541 (m), 1525 (m), 1496 (s), 1482 (s), 1326 (vs), 1303 (vs), 1287 (vs), 1253 (s), 1230 (m), 1186 (s), 1113 (s), 843 (m), 751 (s), 692 (m), 499 (m).

**HRMS** for $\mathbf{C_{12}H_{10}N_2O_2}$ (214.0742): found: 214.0738.

## Synthesis of ethyl 4-(3-nitro-phenylamino)-benzoate (90c)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 1,3-dinitrobenzene (252 mg, 1.50 mmol). Reaction time: 1.5 h at −20 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$

(57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded amine **90c** as red crystals (245 mg, 55%).

**mp.:** 173.5-174 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.11 (s_br, 1 NH), 7.85 (t, $^4J$(H,H) = 2.5 Hz, 1 H), 7.80 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.62-7.55 (m, 1 H), 7.40-7.31 (m, 1 H), 7.03 (t, $^3J$(H,H) = 8.9 Hz, 2 H), 6.98 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.20 (q, $^3J$(H,H) = 7.2 Hz, 2 H), 1.23 (d, $^3J$(H,H) = 7.2 Hz, 3 H).

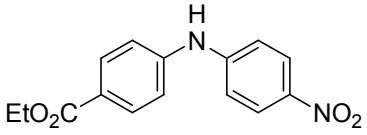
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.8, 148.7, 146.2, 143.1, 130.8, 129.6, 123.3, 122.0, 115.5, 115.1, 111.9, 60.9, 13.9.

**MS** (70 eV, EI), *m/z* (%): 286 (100) [$M^+$], 258 (22), 241 (89), 212 (4), 195 (25), 167 (50), 154 (4), 139 (12), 83 (6).

**IR** (KBr): $\tilde{\nu}$ = 3346 (s), 1687 (vs), 1600 (vs), 1523 (vs), 1483 (m), 1368 (m), 1337 (vs), 1283 (vs) 1249 (s), 1168 (m), 1121 (m), 1109 (m), 848 (w), 770 (m), 740 (m) 674 (w).

**HRMS** for **$C_{15}H_{14}N_2O_4$** (286.0954): found: 286.0968.

## Synthesis of ethyl 4-(4-nitro-phenylamino)-benzoate (90d)




Prepared according to **TP** from ethyl 4-iodobenzoate (952 mg, 3.45 mmol), *i*PrMgCl (4.2 mL, 3.6 mmol, 0.85 M in THF) and 1,4-dinitrobenzene (252 mg, 1.50 mmol). Reaction time: 1.5 h at −20 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the amine **90d** as orange crystals (245 mg, 55%).

**mp.:** 185.7-186.8 °C

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.16 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 8.05 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.18 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.10 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.35 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.39 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.9, 148.1, 144.2, 141.1, 131.5, 126.1, 118.6, 115.7, 114.9, 60.9, 14.4.

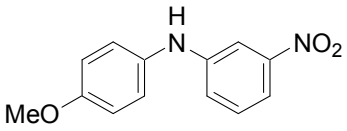
**MS** (70 eV, EI), *m/z* (%): 286 (100) [$M^+$], 241 (82), 228 (14), 195 (25), 167 (40), 139 (11), 89 (2), 76 (4), 63 (4).

**IR** (KBr): $\tilde{\nu}$ = 3329 (s), 1690 (s), 1607 (m), 1586 (vs), 1536 (m), 1500 (m), 1510 (s), 1365 (w), 1315 (vs), 1282 (vs), 1254 (m), 1173 (s), 1109 (s), 842 (m), 765 (w), 692 (w), 582 (w).

**HRMS** for **$C_{15}H_{14}N_2O_4$** (286.0954): found: 286.0934.

**$C_{15}H_{14}N_2O_4$:** required: C: 62.93; H: 4.93; N: 9.76;
found: C: 63.17; H: 4.86; N: 9.54.

### Synthesis of *N*-(4-methoxyphenyl)-3-nitroaniline (90e)




Prepared according to **TP 7** from 4-methoxyphenylmagnesium bromide (3.5 mL, 3.5 mmol, 1.0 M in THF) and 1,3-dinitrobenzene (252 mg, 1.50 mmol). Reaction time: 1 h at −20 °C. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 9:1) furnished amine **90e** as red crystals (310 mg, 64%).

**mp.:** 121.5-122 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.66 (t, $^4J$(H,H) = 2.5 Hz, 1 H), 7.64-7.58 (m, 1 H), 7.31 (t, $^3J$(H,H) = 8.8 Hz, 2 H), 7.16-7.11 (m, 3 H), 6.94 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 3.84 (s, 3 H).

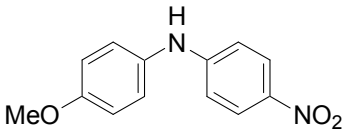
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 156.6, 149.3, 146.9, 133.4, 129.8, 124.1, 120.2, 114.9, 113.4, 108.4, 88.7, 55.5.

**MS** (70 eV, EI), *m/z* (%): 244 (100) [$M^+$], 229 (81), 198 (6), 183 (46), 167 (19), 154 (34), 127 (8), 77 (5), 64 (4).

**IR** (KBr): $\tilde{\nu}$ = 3373 (vs), 1621 (s), 1531 (vs), 1513 (vs), 1481 (s), 1464 (s), 1444 (m), 1354 (s), 1338 (vs), 1296 (s), 1259 (m), 1235 (s), 1184 (m), 1111 (m), 1033 (s), 994 (m), 835 (s), 815 (s), 789 (m), 732 (s), 682 (m), 665 (m), 611 (w), 524 (m).

**HRMS** for **$C_{13}H_{12}N_2O_3$** (244.0848): found: 244.0832.

### Synthesis of *N*-(4-methoxyphenyl)-4-nitroaniline (90f)




Prepared according to **TP 7** from 4-methoxyphenylmagnesium bromide (3.5 mL, 3.5 mmol, 1.0 M in THF) and 1,4-dinitrobenzene (252 mg, 1.50 mmol). Reaction time: 1h at rt. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded the amine **90f** as orange crystals (170 mg, 47%).

**mp.:** 111.5-112 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.05 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 7.15 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 6.93 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 6.76 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 6.14 (s_br, 1 NH), 3.82 (s, 3 H).

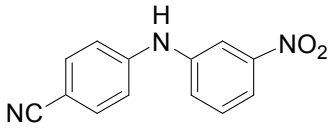
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 157.4, 151.7, 139.1, 131.9, 126.3, 125.5, 114.9, 112.6, 55.4.

**MS** (70 eV, EI), *m/z* (%): 244 (100) [$M^+$], 229 (69), 214 (5), 198 (7), 183 (41), 167 (11), 154 (29), 127 (6), 102 (2), 77 (4), 63 (4).

**IR** (KBr): $\tilde{\nu}$ = 3328 (s), 1596 (s), 1510 (s), 1480 (m), 1321 (vs), 1294 (vs), 1241 (s), 1183 (m), 1112 (s), 1030 (w), 833 (m), 750 (w), 696 (w).

**HRMS** for **$C_{13}H_{12}N_2O_3$** (244.0848): found: 244.0832.

## Synthesis of 4-(3-nitroanilino)benzonitrile (90g)




Prepared according to **TP 7** from 4-iodobenzonitrile (1.58 g, 6.90 mmol), *i*PrMgCl (8.8 mL, 7.0 mmol, 0.80 M in THF) and 1,3-dinitrobenzene (504 mg, 3.00 mmol). Reaction time: 3 h at −20 °C. Addition of ethanol (2 mL), $FeCl_2$ (756 mg, 6.00 mmol) and $NaBH_4$ (114 mg, 3.00 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 1:1) yielded amine **90g** as orange crystals (297 mg, 41%).

**mp.:** 208.5-210 °C.

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 8.43 (s_br, 1 NH), 7.91 (t, $^4J$(H,H) = 2.2 Hz, 1 H), 7.72-7.68 (m, 1 H), 7.44-7.32 (m, 5 H), 7.05 (t, $^3J$(H,H) = 8.8 Hz, 1 H).

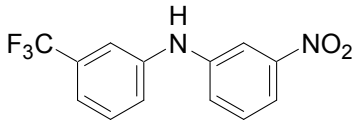
**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 148.7, 146.5, 142.5, 133.3, 129.7, 124.0, 119.3, 116.0, 115.8, 114.9, 112.9.

**MS** (70 eV, EI), *m/z* (%): 239 (100) [$M^+$], 209 (8), 192 (78), 166 (11), 140 (5), 102 (5), 65 (5).

**IR** (KBr): $\tilde{\nu}$ = 3376 (w), 2211 (s), 1599 (vs), 1530 (vs), 1481 (w), 1357 (m), 1334 (vs), 1177 (w), 833 (w), 731 (w), 544 (w).

**HRMS** for **$C_{13}H_9N_3O_2$** (239.0695): found: 239.0689.

## Synthesis of *N*-(4-nitrophenyl)-3-(trifluoromethyl)aniline (90h)



Prepared according to **TP 7** from 1-iodo-3-(trifluoromethyl)benzene (952 mg, 3.50 mmol), *i*PrMgCl (5.2 mL, 3.6 mmol, 0.70 M in THF), and 1,3-dinitrobenzene (252 mg, 1.50 mmol). Reaction time: 2 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg, 1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/diethyl ether = 29:1) yielded amine **90h** as a colourless solid (288 mg, 68 %).

**mp.:** 150-151 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.90 (t, $^4J$(H,H) = 2.5 Hz, 1 H), 7.82-7.79 (m, 1 H), 7.49-7.30 (m, 6 H), 6.12 (s_br, 1 NH).

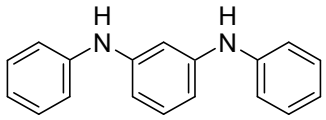
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.4, 143.8, 141.9, 132.3 (q, $^2J$(C,F) = 32 Hz), 130.3, 130.2, 123.8 (q, $^1J$(C,F) = 272 Hz), 122.8, 121.7 (q, $^4J$(C,F) = 1 Hz), 119.2 (q, $^3J$(C,F) = 4 Hz), 116.0, 115.5 (q, $^3J$(C,F) = 4 Hz), 111.6.

**MS** (70 eV, EI), *m/z* (%): 282 (100) [$M^+$], 252 (27), 235 (19), 216 (14), 167 (44), 145 (4), 95 (2), 65 (4).

**IR** (KBr): $\tilde{\nu}$ = 3382 (s), 1609 (s), 1584 (m), 1548 (vs), 1519 (s), 1482 (m), 1464 (s), 1418 (m), 1339 (vs), 1299 (m), 1275 (m), 1181 (m), 1168 (s), 1123 (vs), 1067 (s), 997 (w), 853 (m), 790 (s), 740 (m), 701 (m), 673 (w), 658 (m).

**HRMS** for **$C_{13}H_9F_3N_2O_2$** (282.0616): found: 282.0629.

## Synthesis of $N^1$,$N^3$-diphenyl-1,3-benzenediamine (91a)



Prepared according to **TP 7** from PhMgCl (5.1 mL, 9.2 mmol, 1.9 M in THF) and 1,3-dinitrobenzene (336 mg, 2.00 mmol). Reaction time: 2 h at rt. Addition of ethanol (4 mL), $FeCl_2$ (1.10 g, 8.00 mmol) and $NaBH_4$ (270 mg, 8.00 mmol) stirring overnight at rt. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded the amine **90h** as a colourless solid (478 mg, 92%).

**mp.:** 95-96 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.25-7.17 (m, 5 H), 7.11 (t, $^3J$(H,H) = 8.8 Hz, 1 H), 7.02-6.96 (m, 4 H), 6.92 (tt, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 0.9 Hz, 2 H), 6.64-6.59 (m, 3 H), 5.1 (s_br, 2 NH).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.1, 144.1, 143.1, 139.3, 130.0, 129.2, 128.6, 127.4, 127.1, 120.7, 117.9, 107.4, 106.2, 101.8, 48.2.

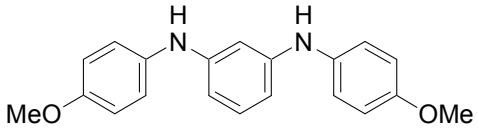
**MS** (70 eV, EI), *m/z* (%): 260 (100) [$M^+$], 167 (18), 77 (3).

**IR** (KBr): $\tilde{\nu}$ = 3366 (s), 3059 (m), 3045 (m), 1613 (vs), 1598 (vs), 1586 (vs), 1552 (m), 1521 (s), 1500 (vs), 1492 (vs), 1455 (s), 1429 (s), 1328 (vs), 1298 (vs), 1230 (s), 1179 (s), 1165 (s), 1076 (m), 1027 (m), 997 (m), 902 (m), 849 (m), 833 (m), 759 (vs), 741 (vs), 693 (vs), 688 (s), 663 (m), 486 (m).

**HRMS** for **$C_{18}H_{16}N_2$** (260.1313): found: 260.1305.

**$C_{18}H_{16}N_2$**: required: C: 83.04; H: 6.19; N: 10.76;
found: C: 83.20; H: 6.21; N: 10.75.

## Synthesis of $N^1$,$N^3$-bis(4-methoxyphenyl)-1,3-benzenediamine (91b)




Prepared according to **TP 7** from 4-methoxyphenylmagnesium bromide (14 mL, 13.8 mmol, 1.0 M in THF,) and 1,3-dinitrobenzene (504 mg, 3.00 mmol). Reaction time: 1.5 h at −20 °C. Addition of ethanol (2 mL), $FeCl_2$ (756 mg, 6.00 mmol) and $NaBH_4$ (114 mg, 3.00 mmol) stirring for 12 h at −5 °C. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the amine **90b** as white crystals (614 mg, 64%).

**mp.:** 153.6-154.6 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.86 (t, $^4J$(H,H) = 2.5 Hz, 1 H), 7.74-7.68 (m, 1 H), 7.21 (t, $^3J$(H,H) = 8.4 Hz, 4 H), 7.10-7.03 (m, 2 H), 6.74 (d, $^3J$(H,H) = 8.4 Hz, 4 H), 3.84 (s, 6 H).

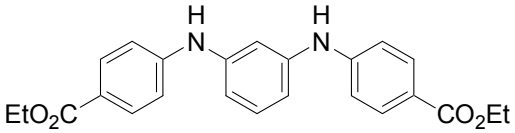
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 156.6, 149.3, 146.9, 133.4, 129.8, 124.1, 120.2, 114.9, 113.4, 108.4, 88.7, 55.5.

**MS** (70 eV, EI), *m/z* (%): 320 (100) [$M^+$], 305 (48), 289 (4), 183 (4), 167 (3), 154 (6), 145 (7), 122 (3).

**IR** (KBr): $\tilde{\nu}$ = 3361 (m), 1596 (vs), 1502 (vs), 1438 (w), 1345 (s), 1333 (m), 1295 (s), 1241 (vs), 1176 (m), 1043 (m), 835 (m), 771 (s), 754 (s), 699 (w), 674 (m).

**HRMS** for **$C_{20}H_{20}N_2O_2$** (320.1525): found: 320.1516.

## Synthesis of ethyl 4-{3-[4-(ethoxycarbonyl)anilino]anilino}benzoate (91c)




Prepared according to **TP 7** from ethyl 4-iodobenzoate (1.91 g, 6.90 mmol), *i*PrMgCl (10 mL, 7.0 mmol, 0.70 M in THF) and 1,3-dinitrobenzene (252 mg, 1.50 mmol). Reaction time: 1.5 h at −20 °C. Addition of ethanol (2 mL), $FeCl_2$ (756 mg, 6.00 mmol) and $NaBH_4$ (114 mg, 3.00 mmol) stirring for 12 h at rt. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the amine **91c** as white crystals (436 mg, 73%).

**mp.:** 172-173 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.29 (d, $^3J$(H,H) = 8.9 Hz, 4 H), 8.11 (s, 2 NH), 7.36 (m, 4 H), 7.05 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.23 (q, $^3J$(H,H) = 7.2 Hz, 4 H), 1.17 (t, $^3J$(H,H) = 7.2 Hz, 6 H).

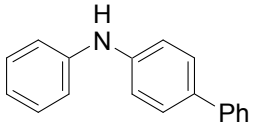
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.1, 144.1, 143.1, 139.3, 130.0, 129.2, 128.6, 127.4, 127.1, 120.7, 117.9, 107.4, 106.2, 101.8, 48.2.

**MS** (70 eV, EI), *m/z* (%): 404 (100) [$M^+$], 359 (15), 331 (5), 256 (3), 167 (9), 157 (13), 128 (3).

**IR** (KBr): $\tilde{\nu}$ = 3355 (m), 1689 (vs), 1593 (vs), 1524 (m), 1367 (m), 1279 (vs), 1175 (s), 1109 (s), 842 (w), 767 (m), 693 (w).

**HRMS** for **$C_{24}H_{24}N_2O_4$** (404.1736): found: 404.1758.

## Synthesis of 4-phenyldiphenylamine (92)



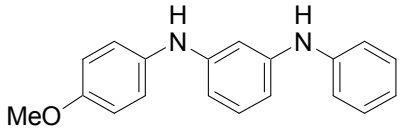

Prepared according to **TP 7** from PhMgCl (2.6 mL, 4.6 mmol, 1.9 M in THF) and 1,4-dinitrobenzene (336 mg, 2.00 mmol). Reaction time: 2 h at rt. Addition of ethanol (2 mL), $FeCl_2$ (1.10 g, 8.00 mmol) and $NaBH_4$ (270 mg, 8.00 mmol) stirring overnight at rt. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded the amine **92** as a colourless oil (180 mg, 38%).

**$^1$H-NMR** (200 MHz, $CDCl_3$, 25 °C): δ = 7.63-7.41 (m, 5 H), 7.37-7.27 (m, 4 H), 7.19-7.12 (m, 4 H), 6.99 (tt, $^3J$(H,H) = 7.1 Hz, $^4J$(H,H) = 1.1 Hz, 1 H), 5.78 (s_br, 1 NH).

**MS** (70 eV, EI), *m/z* (%): 245 (100) [$M^+$], 167 (7), 152 (5), 141 (4), 115 (5), 77 (3).

Spectral data match those of the literature.[31b]

## Synthesis of $N^1$-(4-methoxyphenyl)-$N^3$-phenyl-1,3-benzenediamine (91d)




Prepared according to **TP 7** from PhMgCl (2.5 mL, 4.2 mmol, 1.7 M in THF), 4-methoxyphenylmagnesium bromide (5.0 mL, 4.5 mmol, 0.9 M in THF) and 1,3-dinitrobenzene (336 mg, 2.00 mmol). Reaction time: 2 h at −20 °C and 3 h at rt. Addition of ethanol (5 mL), $FeCl_2$ (1.1 g, 8.00 mmol) and $NaBH_4$ (150 mg, 4.00 mmol) stirring overnight at rt. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the amine **91d** as a colourless solid (205 mg, 36%).

**mp.:** 145.9-146.8 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.41-7.36 (m, 2 H), 7.23-7.17 (m, 5 H), 7.07-6.97 (m, 3 H), 6.74 (t, $^4J$(H,H) = 2.2 Hz, 1 H), 6.71-6.67 (m, 1 H), 6.64-6.59 (m, 1 H), 5.65 (s_br, 2 NH), 3.92 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 155.4, 146.3, 144.3, 142.9, 135.4, 130.1, 129.2, 122.6, 120.9, 118.1, 114.6, 109.1, 108.5, 104.5, 55.6.

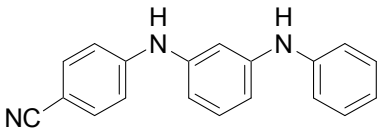
**MS** (70 eV, EI), *m/z* (%): 290 (100) [$M^+$], 275 (71), 183 (4), 167 (15), 154 (5), 145 (5), 123 (4), 110 (3), 77 (3).

**IR** (KBr): $\tilde{\nu}$ = 3361 (w), 1611 (m), 1595 (vs), 1510 (vs), 1497 (vs), 1438 (w), 1328 (m), 1295 (s), 1243 (vs), 1178 (m), 1164 (m), 1107 (w), 1036 (m), 835 (m), 766 (s), 750 (s), 690 (m).

**HRMS** for **$C_{19}H_{18}N_2O$** (290.1419): found: 290.1402.

**$C_{19}H_{18}N_2O$**: required: C: 78.59, H: 6.25, N: 9.65;
found: C: 78.78, H: 6.52, N: 9.68.

## Synthesis of 4-(3-anilinoanilino)benzonitrile (91e)




Prepared according to **TP 7** from 4-iodobenzonitrile (527 mg, 2.30 mmol), *i*PrMgCl (2.6 mL, 2.3 mmol, 0.90 M in THF), PhMgCl (1.5 mL, 2.6 mmol, 1.7 M in THF), and 1,3-dinitrobenzene (169 mg, 1.00 mmol). Reaction time: 2 h at −20 °C and 5 h at rt. Addition of ethanol (4 mL), $FeCl_2$ (512 mg, 4.00 mmol) and $NaBH_4$ (78 mg, 2.00 mmol) stirring overnight at rt. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded amine **91e** as a colourless solid (125 mg, 42%).

**mp.:** 144-146 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.47 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.34-7.28 (m, 2 H), 7.24 (t, $^3J$(H,H) = 8.0 Hz, 2 H), 7.15-7.09 (m, 2 H), 7.03-6.98 (m, 3 H), 6.87-6.79 (m, 2 H), 6.75-6.70 (m, 1 H), 6.11 (br_s, 1 NH), 5.80 (br_s, 1 NH).

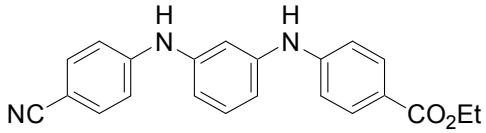
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 148.3, 145.3, 142.8, 141.6, 134.1, 130.8, 129.8, 122.2, 120.3, 119.2, 115.6, 113.4, 113.1, 109.6, 101.8.

**MS** (70 eV, EI), *m/z* (%): 285 (100) [$M^+$], 192 (8), 167 (22), 142 (3), 128 (3).

**IR** (KBr): $\tilde{\nu}$ = 3350 (s), 2215 (vs), 1591 (vs), 1517 (vs), 1495 (vs), 1319 (vs), 1173 (s), 828 (m), 771 (m), 748 (s), 689 (s), 544 (m).

**HRMS** for **$C_{19}H_{15}N_3$** (285.1266): found: 285.1265.

## Synthesis of ethyl 4-[3-(4-cyanoanilino)anilino]benzoate (91f)




Prepared according to **TP 7** from 4-iodobenzonitrile (1.58 g, 6.90 mmol), *i*PrMgCl (7.7 mL, 6.9 mmol, 0.90 M in THF), ethyl 4-iodobenzoate (1.92 g, 6.90 mmol), *i*PrMgCl (7.7 mL, 6.9 mmol, 0.90 M in THF) and 1,3-dinitrobenzene (507 mg, 3.00 mmol). Reaction time: 2 h at −20 °C and 5 h at −5 °C. Addition of ethanol (4 mL), $FeCl_2$ (768 mg, 6.00 mmol) and $NaBH_4$ (117 mg, 3.00 mmol) stirring overnight at rt. Purification by flash chromatography (pentane/diethyl ether = 1:1) yielded the amine **91f** as a colourless solid (510 mg, 47%).

**mp.:** 163-164 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.92 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.47 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.29-7.24 (m, 1 H), 7.02-6.98 (m, 4 H), 6.93 (br_s, 1 H), 6.89-6.81 (m, 2 H), 6.14 (br_s, 1 NH), 6.09 (br_s, 1 NH), 4.33 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.36 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

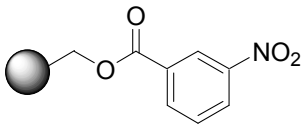
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.4, 147.6, 147.3, 142.6, 141.4, 133.8, 131.4, 130.6, 119.7, 115.4, 115.3, 115.0, 114.9, 1142, 111.6, 102.0, 60.6, 14.4.

**MS** (70 eV, EI), *m/z* (%): 357 (100) [$M^+$], 329 (7), 312 (28), 283 (7), 167 (17), 156 (3), 128 (2).

**IR** (KBr): $\tilde{\nu}$ = 3361 (m), 2212 (s), 1688 (s), 1592 (vs), 1522 (s), 1505 (s), 1282 (s), 1175 (s), 1109 (m), 767 (w).

**HRMS** for **$C_{22}H_{19}N_3O_2$** (357.1477): found: 357.1477.

## Synthesis of Wang-resin attached 3-nitrobenzoic acid (94)

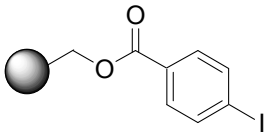



Prepared according to TP from 4-nitrobenzoic acid (2.52 g, 15.0 mmol), Wang resin (2.00 g, 1.50 mmol), DIC (947 mg, 7.50 mmol), and DMAP (183 mg, 1.50 mmol). rt: 20 h.

**HPLC purity** (UV 254 nm): $t_R$ = 8.91 min (97%).

**Loading:** 0.75 mmol/g.

## Synthesis of Wang-resin attached 4-iodobenzoic acid (93)

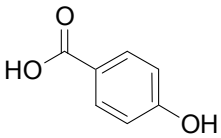



Prepared according to TP from 4-iodobenzoic acid (3.72 g, 15.0 mmol), Wang resin (2.00 g, 1.50 mmol), DIC (947 mg, 7.50 mmol), and DMAP (183 mg, 1.50 mmol). rt: 24 h.

**HPLC purity** (UV 254 nm): $t_R$ = 10.82 min (98%)

**Loading:** 0.63 mmol/g

## Synthesis of 4-hydroxybenzoic acid (96)



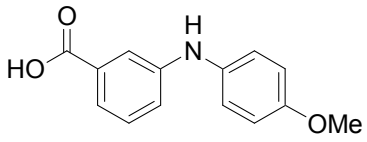

Prepared according to **TP 11** from resin **93** (100 mg, 0.063 mmol), *i*PrMgCl (1.2 mL, 0.63 mmol, 0.52 M in THF) and nitrobenzene (116 mg, 0.945 mmol) leading to **96** as a brown solid (15 mg, 94%).

**HPLC purity** (UV 254 nm): $t_R$ = 2.42 min (96%).

**$^1$H-NMR** (200 MHz, DMSO-$d_6$, 25 °C): $\delta$ = 12.4 (s_br, 1H), 10.4 (s_br, 1 OH), 7.76 (d, $^3J$(H,H) = 8.6 Hz, 2 H), 6.79 (d, $^3J$(H,H) = 8.6 Hz, 2 H).

HPLC-chromatogram and NMR data are in accordance with a sample of the commercially available substrate.

**Synthesis of 3-(4-methoxyanilino)benzoic acid (97a)**



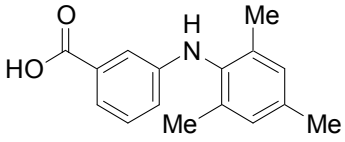

Prepared according to **TP 11** from resin **94** (100 mg, 0.075 mmol) and 4-methoxyphenylmagensium bromide (0.68 mL, 0.75 mmol, 0.90 M in THF) leading to **97a** as a red oil (15 mg, 94%)

**HPLC purity** (UV 254 nm): $t_R$ = 13.31 min (92%).

**$^1$H-NMR** (200 MHz, DMSO-$d_6$, 25 °C): δ = 8.22 (s_br, 1 H), 7.48-7.20 (m, 4 H), 6.99-6.72 (m, 4 H), 3.68 (s, 3 H).

**HRMS** for **$C_{14}H_{13}NO_3$** (243.0895): found: 243.0890.

**Synthesis of 3-(mesitylamino)benzoic acid (97b)**



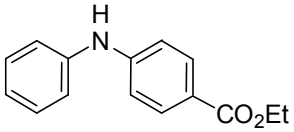

Prepared according to **TP 11** from resin **94** (100 mg, 0.075 mmol) and mesitylmagnesium bromide (1.1 mL, 0.75 mmol, 0.70 M in THF) leading to **97b** as a brown oil (19 mg, 99%)

**HPLC purity** (UV 254 nm): $t_R$ = 15.69 min (91%).

**$^1$H-NMR** (200 MHz, DMSO-$d_6$, 25 °C): δ = 8.62 (br_s, 1 H), 7.42-7.02 (m, 4 H), 6.83 (s, 2 H), 2.25 (s, 3 H), 2.12 (s, 6 H).

**HRMS** for **$C_{16}H_{17}NO_2$** (255.1259): found: 255.1274.

**Synthesis of ethyl 4-anilinobenzoate (85b)**




Prepared according to **TP 7** from ethyl 4-iodobenzoate (662 mg, 2.40 mmol), *i*PrMgCl (3.6 mL, 2.5 mmol, 0.70 M in THF) and nitrosobenzene (214 mg, 2.00 mmol). Reaction time: 1.5 h. Addition of ethanol (2 mL), $FeCl_2$ (378 mg, 3.00 mmol) and $NaBH_4$ (57 mg,

1.50 mmol) stirring for 2 h at rt. Purification by flash chromatography (pentane/ethyl acetate = 12:1) yielded amine **85b** as a colourless solid (357 mg, 74%).

**mp.:** 111-112 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.90 (d, $^{3}J$(H,H) = 8.9 Hz, 1 H), 7.36-7.25 (m, 2 H), 7.18-7.05 (m, 3 H), 6.97 (d, $^{3}J$(H,H) = 8.9 Hz, 2 H), 5.9 (s_br, 1 H), 4.32 (q, $^{3}J$(H,H) = 7.1 Hz, 2 H), 1.39 (t, $^{3}J$(H,H) = 7.1 Hz, 3 H).

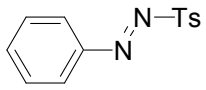
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.3, 147.4, 140.8, 131.4, 129.6, 123.1, 121.5, 120.4, 114.6, 60.5, 14.4.

**MS** (70 eV, EI), *m/z* (%): 241 (100) [$M^+$], 213 (40), 196 (87), 167 (51), 139 (5), 115 (3), 98 (3), 83 (8). 65 (3).

The spectral data match with those reported for compound **85b** prepared from nitrobenzene.

# 12. Synthesis of Polyfunctional Diarylamines by the Addition of Functionalized Arylmagnesium Reagents to Arylazosulfones

## Synthesis of phenyl-4-tolylazo sulfone (110a)




Prepared according to **TP 8** from aniline (1.86 g, 20.0 mmol). Reaction time: 15 h. Recrystallisation from ethanol (50 mL) yielded product **110a** as orange solid (2.66 g, 80%) which decomposed within 1 week on light and air (storage at −20 °C under $N_2$).

**mp**.: 95.5-96 °C (>102 °C, decomp.).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.84 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.81-7.76 (m, 2 H), 7.60-7.54 (m, 1 H), 7.50-7.44 (m, 2 H), 7.37 (d, $^3J$(H,H) = 8.0 Hz, 2 H), 2.45 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.1, 145.9, 134.7, 130.3, 129.9, 129.8, 129.4, 124.4, 21.7.

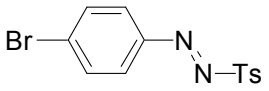
**MS** (FAB, NBA), *m/z* (%): 261 (85) $[M+H]^+$.

**IR** (KBr): $\tilde{\nu}$ = 1596 (w), 1345 (vs), 1186 (w), 1167 (vs), 1145 (s), 881 (m), 773 (m), 656 (m), 608 (s), 550 (m).

**HRMS** for **$C_{13}H_{12}N_2O_2S$** (261.0698 [M+H]): found: 261.0662 $[M+H]^+$.

| | | |
|---|---|---|
| **$C_{13}H_{12}N_2O_2S$:** | required: | C: 59.98; H: 4.65; N: 10.76; |
| | found: | C: 60.20; H: 4.81; N: 10.86. |

## Synthesis of 4-bromophenyl-4-tolylazo sulfone (110b)




Prepared according to **TP 8** from 4-bromoaniline (1.72 g, 10.0 mmol). Reaction time: 16 h. Recrystallisation from ethanol (30 mL) yielded product **110b** as orange solid (2.76 g, 82%).

**mp**.: 111-112 °C (decomp.).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.86 (d, $^3J$(H,H) = 8.4 Hz, 2H), 7.69-7.61 (m, 4 H), 7.37 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 2.40 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 148.3, 146.6, 134.5, 133.3, 132.2, 130.8, 130.3, 129.8, 129.2, 127.8, 126.2, 87.6, 27.2.

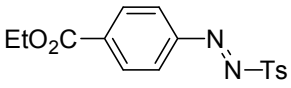
**MS** (FAB, NBA), *m/z* (%): 341 (3) $[M^+]$.

**IR** (KBr): $\tilde{\nu}$ = 1595 (w), 1480 (s), 1399 (m), 1348 (vs), 1166 (vs), 1149 (m), 1086 (m), 1063 (m), 1009 (w), 883 (w), 832 (m), 811 (m), 702 (m), 671 (vs), 621 (m), 548 (vs).

**HRMS** for **$C_{13}H_{11}BrN_2O_2S$** (338.9803 [M+1H]): found: 338.9776.

**$C_{13}H_{11}BrN_2O_2S$:** required: C: 46.03; H: 3.27; N: 8.26; S: 9.62;
found: C: 46.03; H: 3.38; N: 8.25; S: 9.45.

## Synthesis of 4-carbethoxyphenyl-4-tolylazo sulfone (110c)




Prepared according to **TP 8** from ethyl 4-aminobenzoate (1.65 g, 10.0 mmol). Reaction time: 16 h. Recrystallisation from ethanol (30 mL) yielded product **110c** as orange solid (2.66 g, 80%).

**mp**.: 102.5-104 °C (decomp.).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.15 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.86-7.81 (m, 4 H), 7.38 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.33 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 2.41 (s, 3 H), 1.30 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

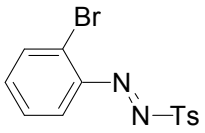
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.2, 151.4, 146.3, 135.4, 130.7, 130.5, 129.7, 129.5, 124.1, 61.7, 21.8, 14.2.

**MS** (FAB, NBA), *m/z* (%): 335 (9) [$M^+$].

**IR** (KBr): $\tilde{\nu}$ = 3430 (w), 2987 (w), 1720 (vs), 1592 (w), 1355 (vs), 1276 (vs), 1184 (s), 1171 (s), 1127 (s), 1107 (s), 1084 (s), 1023 (w), 870 (w), 850 (w), 814(w), 772 (m), 666 (vs), 627 (w), 553 (vs).

**HRMS** for **$C_{16}H_{16}N_2O_4S$** (335.1066 [M+3H]): found: 335.1106.

## Synthesis of 2-bromophenyl-4-tolylazo sulfone (110d)




Prepared according to **TP 8** from 2-bromoaniline (1.72 g, 10.0 mmol). Reaction time: 16 h. Recrystallisation from ethanol (30 mL) yielded product **110d** as orange solid (2.92 g, 86%).

**mp**.: 115-116.5 °C (decomp.).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.84 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.69 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.61 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.43-7.33 (m, 4 H), 2.46 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 141.3, 134.5, 133.4, 129.9, 128.8, 128.2, 127.3, 127.2, 117.2, 87.6, 20.8.

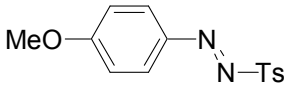
**MS** (FAB, NBA), *m/z* (%): 341 (3) [$M^+$].

**IR** (KBr): $\tilde{\nu}$ = 1595 (m), 1477 (m), 1340 (vs), 1182 (m), 1163 (vs), 1151 (vs), 1083 (m), 1045 (m), 1030 (w), 882 (m), 809 (m), 764 (vs), 667 (vs), 607 (s), 557 (s), 529 (s).

**HRMS** for **$C_{13}H_{11}BrN_2O_2S$** (338.9803 [M+1H]): found: 338.9771.

| | | |
|---|---|---|
| **$C_{13}H_{11}BrN_2O_2S$:** | required: | C: 46.03; H: 3.27; N: 8.26; |
| | found: | C: 46.29; H: 3.29; N: 8.26. |

## Synthesis of 4-methoxyphenyl-4-tolylazo sulfone (110e)




Prepared according to **TP 8** from 4-methoxyaniline (2.46 g, 20.0 mmol). Reaction time: 16 h. Recrystallisation from ethanol (50 mL) yielded product **110e** as yellow solid (5.21 g, 90%).

**mp**.: 114.5-115.5 °C (decomp.).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.79-7.72 (m, 4 H), 7.30 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 6.86 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 3.81 (s, 3 H), 2.40 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.4, 145.6, 143.4, 130.8, 130.1, 129.8, 127.3, 114.7, 55.9, 21.8.

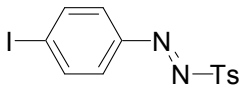
**MS** (FAB, NBA), *m/z* (%): 291 (10) [$M^+$].

**IR** (KBr): $\tilde{\nu}$ = 2950 (w), 1602 (vs), 1580 (s), 1502 (vs), 1463 (m), 1420 (m), 1341 (vs), 1300 (m), 1265 (vs), 1162 (vs), 1146 (vs), 1086 (s), 1016 (s), 888 (s), 844 (vs), 817 (s), 733 (s), 660 (s), 590 (vs), 552 (s), 526 (s).

**HRMS** for **$C_{14}H_{14}N_2O_3S$** (291.0803 [M+1H]): found: 291.0891.

| | | |
|---|---|---|
| **$C_{14}H_{14}N_2O_3S$:** | required: | C: 57.92; H: 4.86; N: 9.65; S: 11.04; |
| | found: | C: 58.06; H: 4.80; N: 9.61; S: 11.32. |

## Synthesis of 4-iodophenyl-4-tolylazo sulfone (110f)



Prepared according to **TP 8** from 4-iodoaniline (2.19 g, 10.1 mmol). Reaction time: 18 h. Recrystallisation from ethanol (30 mL) yielded product **110f** as orange solid (3.23 g, 83%).

**mp**.: 103-105 °C (decomp.).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.80-7.76 (m, 4 H), 7.45 (d, $^3J$(H,H) = 8.4 Hz, 2H), 7.30 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 2.40 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 148.4, 146.2, 138.9, 130.4, 129.9, 129.7, 125.6, 103.0, 20.8.

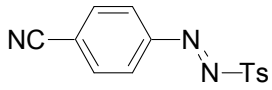
**MS** (FAB, NBA), *m/z* (%): 388 (2) [$M^+$].

**IR** (KBr): $\tilde{\nu}$ = 1593 (w), 1483 (s), 1395 (w), 1347 (vs), 1299 (w), 1174 (vs), 1146 (m), 1084 (m), 1003 (m), 882 (s), 826 (m), 760 (w), 703 (w), 657 (m), 618 (m), 543 (s).

**HRMS** for **$C_{13}H_{11}IN_2O_2S$** (386.9664 [M+1H]): found: 386.9630.

**$C_{13}H_{11}IN_2O_2S$:** required: C: 40.43; H: 2.87; N: 7.25; S: 8.30;
found: C: 40.62; H: 2.90; N: 7.27; S: 8.23.

## Synthesis of 4-cyanophenyl-4-tolylazo sulfone (110g)




Prepared according to **TP 8** from 4-aminobenzonitrile (1.18 g, 10.0 mmol). Reaction time: 16 h. Recrystallisation from ethanol (30 mL) yielded product **110g** as orange-red solid (2.42 g, 85%).

**mp**.: 138-140 °C (decomp.).

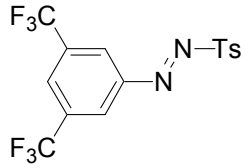
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.93-7.81 (m, 6 H), 7.45 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 2.42 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 151.3, 147.0, 133.9, 130.9, 130.5, 129.5, 129.1, 125.1, 117.9, 117.8, 22.2.

**IR** (KBr): $\tilde{\nu}$ = 2224 (s), 1593 (m), 1503 (m), 1355 (s), 1167 (vs), 1085 (s), 859 (m), 706 (m), 571 (vs), 531 (vs).

**MS** (FAB, NBA), not possible.

## Synthesis of 3,5-bis(trifluoromethyl)phenyl-4-tolylazo sulfone (110h)




Prepared according to **TP 8** from 3,5-bis(trifluoromethyl)phenylamine (1.15 g, 5.00 mmol). Reaction time: 24 h. Recrystallisation from ethanol (20 mL) yielded product **110h** as yellow solid (1.25 g, 63%).

**mp**.: 108.5-109.5 °C (decomp.).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.25 (s, 2 H), 8.08 (s, 1 H), 7.87 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.43 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 2.50 (s, 3 H).

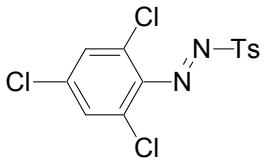
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.5, 146.9, 133.4 (q, $J$(C,F) = 35 Hz), 130.6, 130.2, 128.8, 127.2 (m), 124.3 (m), 122.2 (q, $^2J$(C,F) = 271 Hz), 23.4.

**MS** (FAB, NBA), *m/z* (%): 397 (100) $[M+H]^+$.

**IR** (KBr): $\tilde{\nu}$ = 1596 (w), 1368 (vs), 1355 (vs), 1280 (vs), 1204 (vs), 1170 (vs), 1139 (vs), 907 (s), 811 (m), 726 (m), 679 (s), 608 (m).

**$C_{15}H_{10}F_6N_2O_2S$:** required: C: 45.46; H: 2.54; N: 7.07;
found: C: 45.45; H: 2.68; N: 7.06.

## Synthesis of 2,4,6-trichlorophenyl-4-tolylazo sulfone (110i)




Prepared according to **TP 8** from ethyl 2,4,6-trichloroaniline (980 g, 5.00 mmol). Reaction time: 18 h. Recrystallisation from ethanol (20 mL) yielded product **110i** as yellow solid (1.39 g, 77%).

**mp**.: 111-112 °C (decomp.).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.83 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.40-7.37 (m, 4 H), 2.46 (s, 3 H).

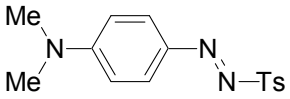
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 146.6, 141.8, 137.3, 130.8, 130.0, 129.8, 128.7, 21.8.

**IR** (KBr): $\tilde{\nu}$ = 1594 (w), 1349 (vs), 1162 (vs), 1048 (m), 894 (w), 864 (w), 815 (w), 709 (m), 583 (m), 562 (m).

**MS** (FAB, NBA), *m/z* (%): 365 (8) [$M^+$].

**HRMS** for **$C_{13}H_9Cl_3N_2O_2S$** (364.9499 [M+H($^{37}$Cl)]): found: 364.9503.

## Synthesis of 4-dimethylaminophenyl-4-tolylazo sulfone (110j)




Prepared according to **TP 8** from $N^1$,$N^1$-dimethyl-1,4-benzenediamine (1.09 g, 8 mmol). Reaction time: 16 h. Recrystallisation from ethanol (30 mL) yielded product **110j** as dark red solid (2.66 g, 80%).

**mp**.: 134.5-135.5 °C (decomp.).

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 7.98 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.75 (d, $^3J$(H,H) = 9.3 Hz, 2 H), 6.86 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 6.17 (d, $^3J$(H,H) = 9.3 Hz, 2 H), 2.28 (s, 6 H), 1.90 (s, 3 H).

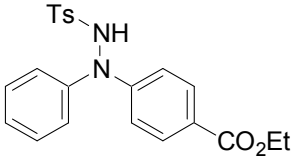
**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 155.1, 144.5, 140.3, 133.6, 130.1, 129.8, 128.7, 111.7, 40.0, 21.2.

**MS** (FAB, NBA), *m/z* (%): 304 (5) $[M+H]^+$.

**IR** (KBr): $\tilde{\nu}$ = 1611 (vs), 1358 (s), 1333 (vs), 1307 (s), 1168 (s), 1150 (vs), 1082 (s), 768 (s), 710 (s), 658 (m), 579 (s).

| | | |
|---|---|---|
| **$C_{15}H_{17}N_3O_2S$:** | required: | C: 59.38; H: 5.65; N: 13.85; |
| | found: | C: 59.39; H: 5.69; N: 13.91. |

## Synthesis of ethyl 4-{2-[(4-methylphenyl)sulfonyl]-1-phenylhydrazino} benzoate (112a)




A dry and argon flushed 25 mL round bottom flask, equipped with a magnetic stirrer and a septum, was charged with ethyl 4-iodobenzoate (303 mg, 1.10 mmol) dissolved in dry THF (5 mL) and cooled to −20 °C. *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) was added dropwise and the I/Mg exchange was checked by GC analysis of reaction aliquots until completion (30 min). Afterwards, azo sulfone **110a** (260 mg, 1.00 mmol), dissolved in THF (3 mL), was added dropwise to the Grignard reagent. The reaction mixture was stirred for 1 h at −20 °C, after which time TLC analysis indicated full conversion of the starting

material and the reaction mixture was poured into water (20 mL). The aqueous phase was extracted with diethyl ether (3 x 30 mL) and the combined organic phases were washed with saturated $NaHCO_{3(aq.)}$-solution and brine successively. The organic phases were dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. Flash chromatography on silica gel (pentane/diethyl ether = 2:1) furnished product **112a** as a colourless solid (398 mg, 97%).

**mp.:** 106.5-107 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.76 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.69 (s, 1 NH), 7.55 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.19-7.02 (m, 7 H), 6.91 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.30 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 2.30 (s, 3 H), 1.33 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.3, 151.4, 144.4, 144.0, 135.5, 130.5, 129.3, 129.3, 128.0, 126.0, 124.5, 123.3, 116.0, 60.6, 21.4, 14.3.

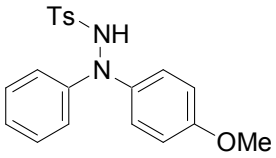
**MS** (70 eV, EI), *m/z* (%): 410 (11) [$M^+$], 365 (22), 255 (100), 241 (30), 196 (23), 167 (26), 149 (8), 105 (9), 91 (23), 77 (27).

**IR** (KBr): $\tilde{\nu}$ = 3246 (s), 1703 (vs), 1605 (vs), 1592 (s), 1511 (s), 1343 (s), 1276 (vs), 1182 (s), 1160 (vs), 1123 (m), 1106 (m), 1088 (m), 1019 (w), 848 (w), 815 (w), 768 (s), 696 (s), 668 (s), 559 (vs).

**HRMS** for **$C_{22}H_{22}N_2O_4S$** (410.1300): found: 410.1317.

| | | |
|---|---|---|
| **$C_{22}H_{22}N_2O_4S$**: | required: | C: 64.37; H: 5.40; N: 6.82; |
| | found: | C: 64.32; H: 5.17; N: 6.81. |

## Synthesis of *N*'-(4-methoxyphenyl)-4-methyl-*N*'-phenylbenzenesulfono hydrazide (112b)




A dry and argon flushed 25 mL round bottom flask, equipped with a magnetic stirrer and a septum, was charged with azo sulfone **110a** (260 mg, 1.00 mmol), dissolved in THF (5 mL) and *p*-methoxyphenylmagnesium bromide (1.4 mL, 1.1 mmol, 0.80 M in THF) was added dropwise. The reaction mixture was stirred for 1 h at −20 °C, after which time TLC-analysis indicated full conversion of the starting material and the reaction mixture was poured into water (20 mL). The aqueous phase was extracted with diethyl ether (3 x 30 mL) and the combined organic phases were washed with saturated $NaHCO_{3(aq.)}$-solution and brine successively. The organic phases were dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. Flash chromatography on silica gel (pentane/diethyl ether = 5:1) furnished product **112b** as a colourless solid (323 mg, 88%).

**mp.:** 130-131 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.64 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.14-7.07 (m, 5 H), 6.91-6.84 (m, 5 H), 6.69 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 3.74 (s, 3 H), 2.35 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 157.4, 148.5, 143.9, 139.5, 135.6, 129.3, 128.7, 128.3, 125.8, 121.9, 117.2, 114.4, 55.4, 21.5.

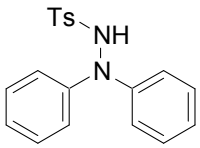
**MS** (70 eV, EI), *m/z* (%): 368 (1) [$M^+$], 213 (100), 199 (24), 184 (30), 167 (8), 154 (9), 135 (6), 107 (18), 91 (21), 77 (35).

**IR** (KBr): $\tilde{\nu}$ = 3436 (m), 1585 (m), 1508 (vs), 1491 (m), 1336 (s), 148 (s), 1160 (vs), 1091 (m), 1032 (w), 810 (w), 757 (m), 726 (w, 670 (m), 563 (s).

**HRMS** for **$C_{20}H_{20}N_2O_3S$** (368.1195): found: 368.1159.

**$C_{20}H_{20}N_2O_3S$**: required: C: 65.20; H: 5.47; N: 7.60;
found: C: 65.17; H: 5.25; N: 7.63.

## Synthesis of 4-methyl-*N*',*N*'-diphenylbenzenesulfonohydrazide (112c)




A dry and argon flushed 25 mL round bottom flask, equipped with a magnetic stirrer and a septum, was charged with azo sulfone **110a** (260 mg, 1.0 mmol), dissolved in THF (5 mL) and PhMgCl (0.65 mL, 1.1 mmol, 1.7 M in THF) was added dropwise. The reaction mixture was stirred for 1 h at −20 °C, after which time TLC-analysis indicated full conversion of the starting material and the reaction mixture was poured into water (20 mL). The aqueous phase was extracted with diethyl ether (3 x 30 mL) and the combined organic phases were washed with saturated $NaHCO_3$-solution and brine successively. The organic phases were dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. Flash chromatography on silica gel (pentane/diethyl ether = 7:1) furnished product **112c** as a colourless solid (314 mg, 93%).

**mp.:** 143.4-144 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.62 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.34 (s, 1 NH), 7.17-7.12 (m, 4 H), 7.06 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.01-6.95 (m, 6 H), 2.32 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 146.8, 143.8, 135.5, 129.2, 128.9, 128.2, 123.7, 120.7, 21.4.

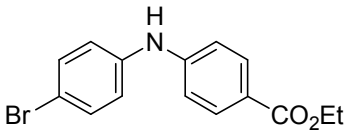
**MS** (70 eV, EI), *m/z* (%): 338 (1) [$M^+$], 183 (100), 167 (12), 105 (5), 91 (12), 77 (39).

**IR** (KBr): $\tilde{\nu}$ = 3207 (s), 1591 (s), 1493 (vs), 1334 (vs), 1271 (w), 1159 (vs), 1091 (w), 814 (w), 787 (w), 754 (s), 700 (s), 667 (m), 565 (s), 548 (s).

**HRMS** for **$C_{19}H_{18}N_2O_2S$** (338.1089): found: 338.1089.

**$C_{19}H_{18}N_2O_2S$**: required: C: 67.43; H: 5.36; N: 8.28;
found: C: 67.25; H: 5.16; N: 8.22.

## Synthesis of ethyl 4-(4-bromoanilino)benzoate (85a)




Prepared according to **TP 9** from ethyl 4-iodobenzoate (303 mg, 1.10 mmol) *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110b** (339 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 2 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded the amine (**1f**) as a colourless solid (265 mg, 83%).

**mp**.: 154.5-155 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.92 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.42 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.03 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.98 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 6.15 (s_br, 1 NH), 4.33 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.37 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.8, 147.7, 140.6, 132.8, 131.9, 122.5, 122.0, 115.4, 114.9, 60.9, 14.8.

**MS** (70 eV, EI), *m/z* (%): 319 (100) [$M^+$], 292 (33), 273 (62), 167 (65), 139 (12), 83 (12).

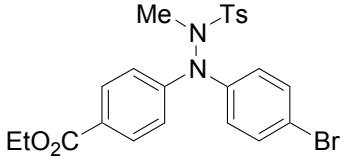
**IR** (KBr): $\tilde{\nu}$ = 3340 (s), 1686 (vs), 1613 (vs), 1587 (vs), 1531 (vs), 1489 (vs), 1368 (vs), 1352 (s), 1308 (vs), 1287 (vs), 1174 (s), 1129 (s), 825 (m), 766 (s), 694 (m), 502 (m).

**HRMS** for **$C_{15}H_{14}BrNO_2$** (319.0208): found: 319.0200.

**$C_{15}H_{14}BrNO_2$**: required: C: 56.27; H: 4.41; N: 4.37;
found: C: 56.24; H: 4.07; N: 4.27.

Spectral data are in accordance with those reported for compound **85a** in chapter 11

## Synthesis of ethyl 4-{2-[(4-methylphenyl)sulfonyl]-1-phenylhydrazino} benzoate (113a)



A dry and argon flushed 50 mL round bottom flask, equipped with a magnetic stirrer and a septum, was charged with ethyl 4-iodobenzoate (1.52 g, 5.50 mmol) dissolved in dry THF (20 mL) and cooled to −20 °C. *i*PrMgCl (5.7 mL, 5.4 mmol, 0.95 M in THF) was added dropwise and the I/Mg-exchange was checked by GC analysis of reaction aliquots until completion (30 min). Afterwards, azo sulfone **110b** (1.70 g, 5.00 mmol), dissolved in THF (10 mL), was added dropwise to the Grignard reagent. After 1 h of stirring at −20 °C, no starting material was observed by TLC-analysis and methyl iodide (3.56 g, 25.0 mmol) and NMP (5 mL) were added and the reaction mixture was stirred for additional 2 h at rt. The reaction mixture was poured into water (100 mL), the aqueous phase was extracted with diethyl ether (3 x 100 mL) and the combined organic phases were washed with saturated $NaHCO_{3(aq.)}$-solution (50 mL) and brine (100 mL) successively. The organic phases were dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. Recrystallization from ethanol furnished product **113a** as a colourless solid (2.01 g, 80%).

**mp.:** 84-85 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.83 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.49 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.37 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.15 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.07 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.89 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.33 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.16 (s, 3 H), 2.38 (s, 3 H), 1.36 (q, $^3J$(H,H) = 7.1 Hz, 2 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.1, 148.8, 144.2, 141.7, 135.7, 132.5, 130.8, 129.5, 127.7, 125.8, 123.9, 118.9, 116.7, 60.7, 35.2, 21.5, 14.4.

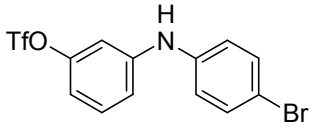
**MS** (70 eV, EI), *m/z* (%): 502 (0.2) [$M^+$], 457 (17), 347 (100), 319 (7), 274 (6), 180 (19), 167 (55), 91 (19).

**IR** (KBr): $\tilde{\nu}$ = 2981 (w), 1711 (vs), 1604 (vs), 1508 (m), 1486 (s), 1349 (s), 1277 (vs), 1176 (s, 1158 (s), 1106 (s), 1006 (m), 834 (m), 812 (m), 768 (m), 706 (w), 656 (w), 587 (m), 545 (m).

**HRMS** for **$C_{23}H_{23}BrN_2O_4S$** (502.0562): found: 502.0548.

| | | |
|---|---|---|
| **$C_{23}H_{23}BrN_2O_4S$**: | required: | C: 54.87; H: 4.61; N: 5.56; |
| | found: | C: 54.58; H: 4.56; N: 5.54. |

## Synthesis of trifluoro-methanesulfonic acid 3-(4-bromo-phenylamino)-phenyl ester (85ae)




Prepared according to **TP 9** from trifluoro-methanesulfonic acid 3-bromo-phenyl ester (387 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110b** (339 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH

(10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 6 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded the amine **85ae** as a colourless oil (277 mg, 70%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.40 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.29 (t, $^3J$(H,H) = 8.0 Hz, 1 H), 7.00-6.95 (m, 3 H), 6.89 (t, $^4J$(H,H) = 2.2 Hz, 1 H), 6.80-6.75 (m, 1 H), 5.82 (s_br, 1 NH).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 150.4, 145.0, 140.4, 132.5, 130.9, 120.8, 119.1 (q, 1J(C,F) = 320 Hz), 116.5, 114.9, 112.9, 109.3.

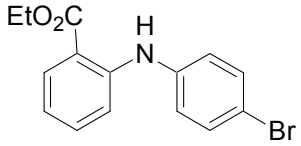
**MS** (70 eV, EI), *m/z* (%): 397 (100) [$M^+$], 234 (9), 183 (67), 155 (32).

**IR** (KBr): $\tilde{\nu}$ = 3418 (m), 1617 (s), 1590 (s), 1489 (vs), 1420 (vs), 1217 (vs), 1139 (vs), 1116 (s), 966 (s), 866 (s), 818 (m), 608 (s).

**HRMS** for **$C_{13}H_9BrF_3NO_3S$** (394,9439): found: 394.9445.

**$C_{13}H_9BrF_3NO_3S$:** required: C: 39.41; H: 2.29; Br: 20.17; N: 3.54;
found: C: 39.73; H: 2.22; Br: 20.28; N: 3.50.

## Synthesis of ethyl 2-(4-bromoanilino)benzoate (85af)




Prepared according to **TP 9** from ethyl 2-iodobenzoate (303 mg, 1.10 mmol), *i*PrMgCl (1.16 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110b** (339 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 2 h. Purification by flash chromatography (pentane/diethyl ether = 49:1) yielded the amine **85af** as a pale yellow oil (255 mg, 80%).

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 9.80 (s_br, 1 NH), 8.05 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 7.12 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.07-6.98 (m, 2 H), 6.70 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.59 (dd, $^3J$(H,H) = 8 .0Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 4.04 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.00 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 168.6, 147.8, 149.3, 134.2, 132.5, 131.9, 123.8, 117.8, 115.8, 114.3, 113.1, 60.7, 14.2.

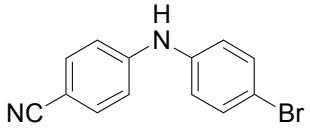
**MS** (70 eV, EI), *m/z* (%): 319 (30) [$M^+$], 273 (5), 194 (100), 166 (22), 139 (6), 83 (3).

**IR** (KBr): $\tilde{\nu}$ = 3311 (w), 2980 (w), 1682 (vs), 1586 (vs), 1518 (vs), 1489 (s), 1454 (vs), 1394 (m), 1368 (m), 1322 (s), 1256 (vs), 1228 (vs), 1163 (s), 1144 (m), 1082 (s), 1007 (m), 838 (m), 802 (m), 749 (s), 699 (m), 598 (w), 496 (m).

**HRMS** for $C_{15}H_{14}BrNO_2$ (319.0208): found: 319.0250.

| | | |
|---|---|---|
| **$C_{15}H_{14}BrNO_2$:** | required: | C: 56.27; H: 4.41; N: 4.37; |
| | found: | C: 56.24; H: 4.07; N: 4.27. |

## Synthesis of 4-(4-bromoanilino)benzonitrile (85ag)




Prepared according to **TP 9** from 4-iodobenzonitrile (252 mg, 1.10 mmol) and azo sulfone **110b** (339 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 15 h. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded amine **85ag** as a colourless solid (199 mg, 73%).

**mp.:** 111-112 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 7.49-7.42 (m, 4 H), 7.04 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.95 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.09 (s_br, 1 NH).

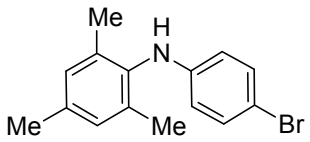
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 147.4, 139.2, 133.8, 132.6, 122.5, 119.6, 116.2, 115.3, 102.2.

**MS** (70 eV, EI), *m/z* (%): 272 (100) [$M^+$], 192 (60), 166 (16), 155 (2), 140 (5), 97 (10), 83 (6), 75 (8), 63 (7).

**IR** (KBr): $\tilde{\nu}$ = 3345 (vs), 2213 (vs), 1609 (s), 1595 (s), 1517 (vs), 11486 (m), 1330 (s), 1172 (s), 1076 (m), 816 (m).

**HRMS** for $C_{13}H_9BrN_2$ (271.9949): found: 271.9972.

## Synthesis of (4-bromo-phenyl)-(2,4,6-trimethyl-phenyl)-amine (85ah)




Prepared according to **TP 9** from mesitylmagnesium bromide (1.5 mL, 1.1 mmol, 0.75 M in THF) and azo sulfone **110b** (339 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and

heating to 75 °C for 1 h. Purification by flash chromatography (pentane/diethyl ether = 49:1) yielded amine **85ah** as a colourless oil (199 mg, 69%).

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 7.13 (m, 2 H), 6.78 (s, 2 H), 6.04 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.21 (s_br, 1 NH), 2.16 (s, 3 H), 1.97 (s, 6 H).

**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 146.6, 136.7, 136.3, 135.7, 132.7, 130.0, 115.2, 113.8, 110.1, 21.3, 18.5.

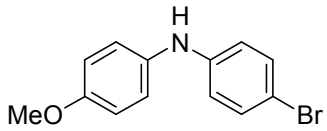
**MS** (70 eV, EI), *m/z* (%): 289 (100) [$M^+$], 274 (19), 208 (25), 194 (29), 180 (18), 91 (8).

**IR** (KBr): $\tilde{\nu}$ = 3399 (w), 2918 (w), 1593 (s), 1489 (vs), 1314 (m), 1287 (m), 1174 (w), 1072 (w), 853 (m), 815 (m), 726 (w), 577 (w), 560 (w).

**HRMS** for **$C_{15}H_{16}BrN$** (289.0466): found: 289.0483.

**$C_{15}H_{16}BrN$:** required: C: 62.08; H: 5.56; N: 4.83;
found: C: 62.46; H: 5.37; N: 4.81.

## Synthesis of *N*-(4-bromophenyl)-4-methoxyaniline (85u)




Prepared according to **TP 8** from 4-methoxyphenylmagnesium bromide (1.2 mL, 1.1 mmol, 0.90 M in THF) and azo sulfone **110b** (339 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 1 h. Purification by flash chromatography (pentane/diethyl ether = 29:1) yielded the amine (**85u**) as a colourless solid (238 mg, 86%).

**mp**.: 87-88 °C.

**$^1$H NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.19 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.96 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.78 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.67 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.38 (s_br, 1 NH), 3.71 (s, 3 H).

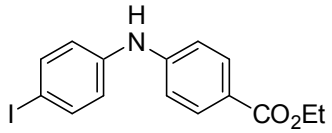
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 156.1, 144.9, 135.4, 132.5, 123.2, 117.4, 115.2, 111.4, 56.0.

**MS** (70 eV, EI), *m/z* (%): 277 (84) [$M^+$], 262 (100), 183 (10), 154 (34), 128 (6).

**HRMS** for **$C_{13}H_{12}BrNO$** (277.0102): found: 277.0114.

Spectral data are in accordance with those reported for compound **85u** in Chapter 11.

## Synthesis of ethyl 4-(4-iodoanilino)benzoate (85g)




Prepared according to **TP 9** from 1,4-diiodobenzene (362 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110c** (332 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 3 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded amine **85g** as a colourless solid (231 mg, 63%).

**mp**.: 157-157.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.87 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.53 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 6.91 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.83 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 6.08 (s_br, 1 NH), 4.28 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.30 (d, $^3J$(H,H) = 7 Hz, 3 H).

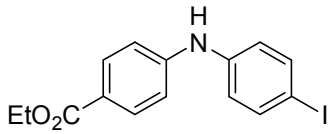
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.3, 146.0, 139.9, 137.3, 130.4, 121.2, 120.7, 114.2, 83.9, 59.5, 13.4.

**MS** (70 eV, EI), *m/z* (%): 367 (100) [$M^+$], 339 (30), 322 (48), 167 (70), 139 (17), 83 (17).

**$C_{14}H_{15}INO_2$**: required: C: 49.07; H: 3.84; N: 3.81;
found: C: 49.16; H: 3.89; N: 3.64.

Spectral data are in accordance with those reported for compound **85g** in chapter 11.

## Synthesis of ethyl 4-(4-iodoanilino)benzoate (85g)




Prepared according to **TP 9** from ethyl 4-iodobenzoate (303 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110f** (386 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 2 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded amine **85g** as a pale yellow solid (261 mg, 71%).

**mp.:** 156-157 °C.

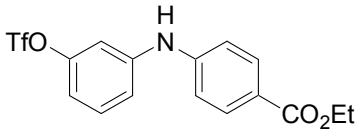
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.93 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.59 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.98 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.92 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.34 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.37 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.4, 146.0, 139.9, 137.3, 130.4, 121.2, 120.7, 114.2, 83.9, 59.6, 13.4.

**MS** (70 eV, EI), *m/z* (%): 367 (100) [$M^+$], 339 (26), 322 (42), 167 (28), 139 (9), 82 (5).

Spectral data are in accordance with those reported for compound **85g** in chapter 11.

## Synthesis of ethyl 4-(3-trifluoromethanesulfonyloxy-phenylamino)-benzoate (85ai)




Prepared according to **TP 9** from trifluoro-methanesulfonic acid 3-iodo-phenyl ester (387 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110c** (332 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 12 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded the amine **85ai** as a colourless solid (296 mg, 76%).

**mp**.: 114.5-115.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.99 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.35 (t, $^3J$(H,H) = 8.4 Hz, 1 H), 7.16-7.13 (m, 1 H) 7.12-7.04 (m, 3 H), 6.92 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 6.23 (s_br, 1 NH), 4.33 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.37 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.2, 150.3, 146.0, 143.4, 131.5, 130.9, 123.3, 119.1 (q, $^1$J(C,F) = 321 Hz), 118.4, 116.1, 114.4, 111.4, 60.7, 14.4.

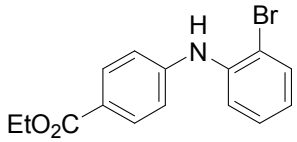
**MS** (70 eV, EI), *m/z* (%): 389 (100) [$M^+$], 361 (12), 344 (36), 228 (8), 183 (17), 155 (21), 129 (5).

**IR** (KBr): $\tilde{\nu}$ = 3342 (vs), 1690 (vs), 1602 (vs), 1534 (s), 1486 (m), 1409 (vs), 1345 (m), 1282 (vs), 1221 (s), 1200 (s), 1176 (s), 1144 (s), 1108 (s), 962 (m), 855 (m), 843 (m), 768 (s), 602 (s).

**HRMS** for **$C_{16}H_{14}F_3NO_5S$** (389.0545): found: 389.0526.

| | | |
|---|---|---|
| **$C_{16}H_{14}F_3NO_5S$**: | required: | C: 49.36; H: 3.62; N: 3.60; |
| | found: | C: 49.54; H: 3.64; N: 3.54. |

## Synthesis of ethyl 4-(2-bromoanilino)benzoate (85o)




Prepared according to **TP 9** from ethyl 4-iodobenzoate (303 mg, 1.10 mmol) *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110d** (339 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 2 h. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded the amine **85o** as a colourless oil (208 mg, 65%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.97 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.58 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 7.40 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 7.27-7.24 (m, 1 H), 7.07 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.87 (dt, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 6.24 (s_br, 1 NH), 4.33 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.38 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 145.4, 138.3, 132.3, 130.4, 127.2, 122.1, 122.0, 117.9, 115.4, 113.5, 87.8, 59.6, 13.5.

**MS** (70 eV, EI), *m/z* (%): 319 (100) [$M^+$], 291 (24), 274 (91), 194 (16), 167 (99), 139 (24), 83 (18).

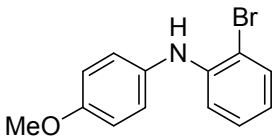
**IR** (KBr): $\tilde{\nu}$ = 3394 (m), 3346 (m), 2980 (m), 1705 (vs), 1608 (vs), 1591 (vs), 1521 (vs), 1462 (m), 1367 (m), 1324 (s), 1276 (vs), 1175 (vs), 1106 (vs), 1023 (s), 844 (m), 768 (s), 748 (s), 698 (w).

**HRMS** for **$C_{15}H_{14}BrNO_2$** (319.0208): found: 319.0186.

| | | |
|---|---|---|
| **$C_{15}H_{14}BrNO_2$**: | required: | C: 56.27; H: 4.41; N: 4.37; |
| | found: | C: 56.01; H: 4.50; N: 4.37. |

Spectral data are in accordance with those reported for compound **85o** in chapter 11.

## Synthesis of ethyl 4-(2-methoxyanilino)benzoate (85aj)




Prepared according to **TP 9** from 4-methoxyphenylmagnesium bromide (1.4 mL, 1.2 mmol, 0.80 M in THF) and azo sulfone **110d** (339 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo*

solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 2 h. Purification by flash chromatography (pentane/diethyl ether = 3:1) yielded amine **85aj** as a colourless oil (185 mg, 67%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.48 (dd, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.4 Hz, 2 H), 7.16-7.07 (m, 1 H), 6.96-6.87 (m, 3 H), 6.65 (dt, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 5.95 (s_br, 1 NH), 3.82 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 156.4, 143.2, 134.1, 132.7, 128.1, 124.7, 119.5, 114.7, 114.0, 110.5, 55.5.

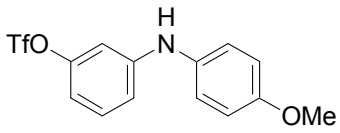
**MS** (70 eV, EI), *m/z* (%): 277 (77) [$M^+$], 262 (100), 197 (3), 182 (17), 167 (4), 154 (36), 128 (7), 77 (3).

**IR** (KBr): $\tilde{\nu}$ = 3392 (m), 2932 (w), 2833 (w), 1595 (s), 1511 (vs), 1454 (s), 1295 (s), 1244 (vs), 1180 (m), 1035 (s), 1020 (s), 817 (m), 743 (s), 552(w).

**HRMS** for **$C_{13}H_{12}BrNO$** (277.0102): found: 277.0074.

| | | |
|---|---|---|
| **$C_{13}H_{12}BrNO$**: | required: | C: 56.14; H: 4.35; N: 5.04; |
| | found: | C: 56.31; H: 4.47; N: 5.02. |

## Synthesis of trifluoro-methanesulfonic acid 3-(4-methoxy-phenylamino)-phenyl ester (85ak)




Prepared according to **TP 9** from trifluoro-methanesulfonic acid 3-iodo-phenyl ester (387 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110e** (290 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 2 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded amine **85ak** as a colourless solid (281 mg, 81%).

**mp**.: 69-70.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.23 (t, $^3J$(H,H) = 8.4 Hz, 1 H), 7.09 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.92 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.82-6.78 (m, 1 H), 6.71 (t, $^4J$(H,H) = 2.2 Hz, 1 H), 6.67-6.63 (m, 1 H), 5.56 (s_br, 1 NH), 3.81 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 156.4, 150.6, 147.6, 133.6, 130.6, 123.9, 119.1 (q, $^1J$(C,F) = 320 Hz), 114.9, 114.4, 110.9, 106.9, 55.5.

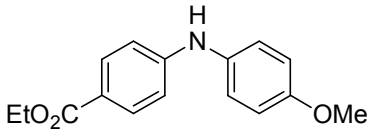
**MS** (70 eV, EI), *m/z* (%): 347 (100) [$M^+$], 332 (10), 214 (12), 186 (24), 155 (6).

**IR** (KBr): $\tilde{\nu}$ = 3386 (s), 1613 (vs), 1514 (vs), 1404 (vs), 1321 (m), 1297 (m), 1248 (vs), 1205 (vs), 1141 (vs), 1112 (vs), 1034 (s), 876 (s), 850 (s), 824 (s), 784 (s), 680 (m), 612 (vs), 511 (m).

**HRMS** for **$C_{14}H_{12}F_3NO_4S$** (347.0439): found: 347.0434.

**$C_{14}H_{12}F_3NO_4S$:** required: C: 48.41; H: 3.48; N: 4.03;
found: C: 48.61; H: 3.71; N: 4.02.

## Synthesis of ethyl 4-(2-methoxyanilino)benzoate (85j)




Prepared according to **TP 8** from ethyl 4-iodobenzoate (303 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110e** (290 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 2 h. Purification by flash chromatography (pentane/diethyl ether = 3:1) yielded amine **85j** as a colourless solid (260 mg, 96%).

**mp**.: 77-78 °C.

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 8.17 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.81 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.70 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.59 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.10 (s_br, 1 NH), 4.22 (q, $^3J$(H,H) = 7.1 Hz, 2H), 3.33 (s, 3 H), 1.07 (d, $^3J$(H,H) = 7.1 Hz, 3 H).

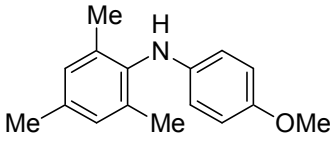
**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 166.3, 156.9, 150.0, 133.9, 131.9, 124.5, 121.2, 115.0, 113.6, 60.2, 55.0, 14.5.

**MS** (70 eV, EI), *m/z* (%): 271 (100) [$M^+$], 256 (59), 228 (63), 183 (6), 167 (7), 154 (18), 128 (5), 113 (2), 77 (2).

**HRMS** for **$C_{16}H_{17}NO_3$** (271.1208): found: 271.1196.

Spectral data match those reported for compound **85j** in chapter 11.

## Synthesis of (4-methoxy-phenyl)-(2,4,6-trimethyl-phenyl)-amine (85al)



Prepared according to **TP 9** from mesitylmagnesium bromide (1.5 mL, 1.1 mmol, 0.75 M in THF) and azo sulfone **85al** (290 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 1 h. Purification by flash chromatography (pentane/diethyl ether = 49:1) yielded amine **85al** as a colourless solid (200 mg, 83%).

**mp**.: 100.5-101.5 °C.

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 6.84 (s, 2 H), 6.75 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.40 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.45 (s_br, 1 NH), 3.35 (s, 3 H), 2.19 (s, 3 H), 2.10 (s, 6 H).

**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 153.7, 141.4, 137.5, 136.0, 135.1, 130.0, 128.7, 115.6, 115.3, 55.6, 21.3, 18.6.

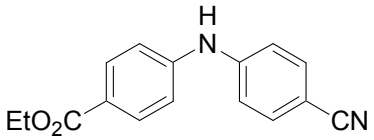
**MS** (70 eV, EI), *m/z* (%): 241 (84) [$M^+$], 226 (100), 208 (7), 196 (3), 182 (4), 167 (3), 133 (5), 91 (8), 77 (5).

**IR** (KBr): $\tilde{\nu}$ = 3352 (s), 1509 (vs), 1462 (s), 1399 (m), 1308 (m), 1289 (s), 1230 (vs), 1174 (s), 1031 (vs), 853 (m), 824 (vs), 640 (s), 630 (s), 501 (m).

**HRMS** for **$C_{16}H_{19}NO$** (241.1467): found: 241.1443.

**$C_{16}H_{19}NO$:** required: C: 76.63; H: 7.94; N: 5.80;
found: C: 76.28; H: 7.73; N: 5.89.

## Synthesis of ethyl 4-(4-cyanoanilino)benzoate (85am)




Prepared according to **TP 9** from ethyl 4-iodobenzoate (303 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110g** (286 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 12 h. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded amine **85am** as a pale yellow solid (172 mg, 71%).

**mp**.: 154.5-155.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.01 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.54 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.16-7.10 (m, 4 H), 6.42 (s_br, 1 NH), 4.32 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.38 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.1, 145.9, 144.7, 133.8, 131.4, 124.4, 119.4, 117.8, 116.9, 103.6, 60.8, 14.3.

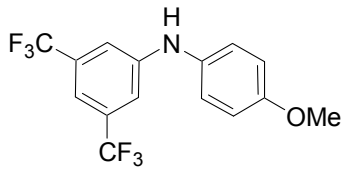
**MS** (70 eV, EI), *m/z* (%): 266 (77) [$M^+$], 238 (29), 221 (100), 192 (37), 166 (7), 139 (4), 110 (4), 83 (3).

**IR** (KBr): $\tilde{\nu}$ = 3332 (m), 2216 (s), 1688 (vs), 1615 (m), 1592 (vs), 1526 (vs), 1498 (m), 1345 (s), 1281 (vs), 1249 (m), 1173 (vs), 1107 (s), 836 (m), 769 (m), 547 (m).

**HRMS** for **$C_{16}H_{14}N_2O_2$** (266.1055): found: 266.1048.

**$C_{16}H_{14}N_2O_2$**: required: C: 72.16; H: 5.30; N: 10.52;
found: C: 72.52; H: 5.47; N: 10.42.

## Synthesis of *N*-(4-methoxyphenyl)-3,5-bis(trifluoromethyl)aniline (85an)




Prepared according to **TP 9** from 4-methoxyphenylmagnesium bromide (1.5 mL, 1.1 mmol, 0.70 M in THF) and azo sulfone **110h** (396 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 15 h. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded amine **85an** as a colourless solid (200 mg, 60%).

**mp.:** 84.3-85.6 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 7.27 (s, 1 H), 6.85 (s, 2 H), 6.73-6.64 (m, 4 H), 4.71 (s_br, 1 NH), 3.31 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 157.4, 147.5, 132.8, 132.8 (q, $^3J$(C,F) = 33 Hz), 124.1 (q, $^2J$(C,F) = 273 Hz), 124.6, 115.2, 113.7 (m), 111.4 (m), 55.0.

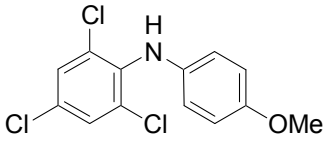
**MS** (70 eV, EI), *m/z* (%): 335 (86) [$M^+$], 320 (100), 303 (3), 290 (4), 272 (8), 252 (3), 223 (17), 164 (14), 153 (7), 107 (10), 77 (25).

**IR** (KBr): $\tilde{\nu}$ = 3359 (s), 1626 (m), 1554 (m), 1511 (s), 1403 (vs), 1288 (vs), 1237 (m), 1171 (m), 1125 (vs), 1025 (w), 869 (m), 821 (m), 701 (m), 683 (w).

**HRMS** for **$C_{15}H_{11}F_6NO$** (335.0745): found: 335.0772.

**$C_{15}H_{11}F_6NO$**: required: C: 53.74; H: 3.31; N: 4.18;
found: C: 53.84; H: 2.97; N: 4.06.

## Synthesis of 2,4,6-trichloro-*N*-(4-methoxyphenyl)aniline (85ao)




Prepared according to **TP 9** from 4-methoxyphenylmagnesium bromide (1.4 mL, 1.1 mmol, 0.80 M in THF) and azo sulfone **110i** (362 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 5 h. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded amine **85ao** as a colourless solid (176 mg, 59%).

**mp.:** 83.1-84.2 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 6.98 (s, 2 H), 7.00 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 6.51 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 5.28 (s_br, 1 NH), 3.31 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 155.7, 137.2, 136.7, 130.1, 128.9, 128.12, 119.7, 114.7, 55.0.

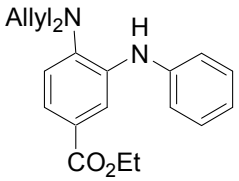
**MS** (70 eV, EI), *m/z* (%): 303 (67) [$M^+$], 300 (67) [$M^+$], 285 (100), 222 (19), 188 (29), 152 (6), 63 (3).

**IR** (KBr): $\tilde{\nu}$ = 3396 (m), 3066 (m), 2833 (m), 1554 (m), 1511 (vs), 1470 (vs), 1445 (s), 1370 (w), 1281 (m), 1240 (vs), 1188 (s), 1106 (m), 1033 (vs), 865 (s), 820 (vs), 766 (s), 519 (m).

**HRMS** for **$C_{13}H_{10}Cl_3NO$** (300.9828): found: 300.9838.

| | | |
|---|---|---|
| **$C_{13}H_{10}Cl_3NO$**: | required: | C: 51.60; H: 3.33; N: 4.63; |
| | found: | C: 52.04; H: 3.07; N: 4.47. |

## Synthesis of ethyl 3-anilino-4-(diallylamino)benzoate (85ap)




Prepared according to **TP 9** from ethyl 4-diallylamino-3-iodo-benzoate (408 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110a** (260 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 12 h.

Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded amine **85ap** as a pale yellow oil (98 mg, 29%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.98 (d, $^4J$(H,H) = 1.8 Hz, 1 H), 7.42 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.33-7.26 (m, 2 H), 7.15-7.10 (m, 2 H), 7.05 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 6.98-6.92 (m, 1 H), 6.47 (s_br, 1 NH), 5.84-5.71 (m, 2 H), 5.22-5.12 (m, 4 H), 4.81 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.64-3.61 (m, 4 H), 1.33 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

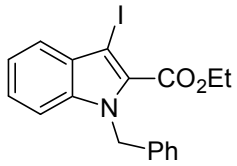
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.7, 142.4, 138.2, 134.3, 131.0, 129.4, 126.0, 121.8, 121.2, 121.2, 118.2, 117.9, 116.0, 60.7, 55.0, 14.3.

**MS** (70 eV, EI), *m/z* (%): 336 (16) [$M^+$], 323 (12), 307 (100), 295 (96), 267 (66), 239 (38), 221 (59), 181 (18), 167 (18), 130 (15), 77 (27).

**IR** (KBr): $\tilde{\nu}$ = 3357 (m), 2980 (m), 1713 (vs), 1596 (vs), 1575 (s), 1520 (vs), 1497 (vs), 1418 (s), 1294 (vs), 1257 (vs), 1237 (vs), 1198 (s), 1114 (s), 1026 (s), 924 (m), 769 (m), 748 (s), 696 (m).

**HRMS** for **$C_{21}H_{24}N_2O_2$** (336.1838): found: 336.1844.

## Synthesis of ethyl 3-iodo-1-benzyl-indole-2-carboxylate (115)[129]




NaH (833 mg, 21.0 mmol) was added to a solution of ethyl 3-iodoindole-2-carboxylate[130] (6.30 g, 20.0 mmol) in 300 mL DMF and the mixture was stirred for 1 h until the evolution of gas had ceased. After addition of benzyl bromide (4.28 g, 25.0 mmol) the reaction was stirred overnight at rt. The mixture was quenched with water and the aqueous phase was extracted with diethyl ether (3x300 mL). The combined organic fractions were washed with saturated $NaHCO_{3(aq)}$ (30 mL), brine (50 ml), dried over $NaSO_4$, filtered and concentrated *in vacuo*. Flash chromatography (pentane/ethyl acetate = 12:1) yielded title compound **115** as a light yellow solid (7.44 g, 86%) which was stored in the dark.

**mp.:** 59-60 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.67 (dt, $^3J$(H,H) = 8.0 Hz, $^4J$(H,H) = 0.9 Hz, 1 H), 7.42-7.37 (m, 2 H), 7.34-7.25 (m, 4 H), 7.11-7.05 (m, 2 H), 5.85 (s, 2 H), 4.44 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.45 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

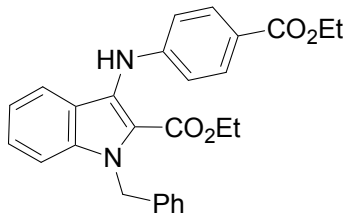
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 161.0, .138.8, 137.8, 130.4, 128.5, 128.3, 127.2, 126.3, 126.1, 124.0, 121.7, 110.9, 67.8, 61.2, 49.0, 14.1.

**MS** (70 eV, EI): *m/z* (%) 405 (50), 232 (9), 204 (19), 150 (4), 128 (6), 91 (100).

**IR** (KBr): $\tilde{\nu}$ = 1702 (vs), 1610 (w), 1493 (s), 1477 (m), 1451 (s), 1397 (m), 1314 (m), 1260 (vs), 1242 (vs), 1201 (s), 1187 (s), 1127 (s), 1013 (m), 773 (w), 746 (s), 734 (s), 695 (m).

**HRMS** for **$C_{18}H_{16}INO_2$** (405.0226): found: 405.0202.

## Synthesis of 1-benzyl-3-(4-ethoxycarbonyl-phenylamino)-1H-indole-2-carboxylic acid ethyl ester (116a)




Prepared according to **TP 9** from ethyl 3-iodo-1-benzyl-indole-2-carboxylate (**115**) (487 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110c** (332 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 1 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded amine **116a** as a pale yellow solid (314 mg, 71%).

**mp**.: 96.5-98 °C.

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 8.15 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.56 (m, 2 H) 7.13-6.91 (m, 8 H), 6.84 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.48 (s, 2 H), 4.19 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.87 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.05 (t, $^3J$(H,H) = 7.1 Hz, 3 H), 0.74 (t, $^3J$(H,H) = 7 Hz, 3.1 H).

**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 166.2, 162.3, 148.7, 139.0, 138.6, 131.6, 128.8, 128.8, 127.3, 126.3, 123.0, 122.7, 120.9, 120.2, 116.9, 115.8, 112.8, 111.2, 60.5, 60.3, 48.4, 14.4, 13.9.

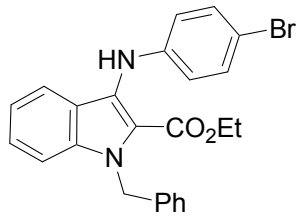
**MS** (70 eV, EI), *m/z* (%): 442 (22) [$M^+$], 351 (33), 279 (13), 277 (39), 261 (15), 233 (78), 205 (41), 178 (11), 103 (12), 91 (100), 65 (28).

**IR** (KBr): $\tilde{\nu}$ = 3414 (m), 1707 (vs), 1664 (s), 1606 (vs), 1586 (s), 1549 (s), 1457 (m), 1371 (s), 1341 (s), 1277 (vs), 1258 (vs), 1173 (s), 1123 (m), 1104 (m), 768 (w), 741 (m), 438 (m).

**HRMS** for **$C_{27}H_{26}N_2O_4$** (442.1893): found: 442.1897.

**$C_{27}H_{26}N_2O_4$**: required: C: 73.28; H: 5.92; N: 6.33;
found: C: 72.97; H: 5.97; N: 6.17.

**Synthesis of 1-benzyl-3-(4-bromo-phenylamino)-1H-indole-2-carboxylic acid ethyl ester (116b)**




Prepared according to **TP 9** from ethyl 3-iodo-1-benzyl-indole-2-carboxylate (**115**) (487 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.95 M in THF) and azo sulfone **110b** (339 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 1 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded amine **116b** as a yellow solid (233 mg, 52%).

**mp**.: 103-104 °C.

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 7.66 (s_br, 1 NH), 7.50 (m, 1 H), 7.16-6.86 (m, 10 H), 6.64 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.46 (s, 2 H), 3.90 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 0.76 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 162.6, 143.6, 139.1, 138.8, 132.2, 130.8, 128.8, 127.3, 126.7, 123.1, 120.3, 119.8, 119.5, 115.6, 113.1, 112.8, 111.1, 60.4, 48.4, 13.9.

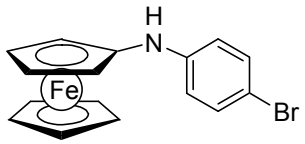
**MS** (70 eV, EI), *m/z* (%): 450 (100) [$M^+$], 359 (60), 313 (20), 285 (41), 206 (12), 91 (23).

**IR** (KBr): $\tilde{\nu}$ = 3412 (m), 1697 (m), 1658 (s), 1585 (s), 1549 (s), 1490 (vs), 1457 (s), 1371 (s), 1338 (vs), 1250 (vs), 1169 (m), 1123 (m), 829 (w), 741 (m), 696 (w).

**HRMS** for **$C_{24}H_{21}BrN_2O_2$** (448.0786): found: 448.0805.

**$C_{24}H_{21}BrN_2O_2$:** required: C: 64.15; H: 4.71; Br: 17.78; N: 6.23;
found: C: 64.10; H: 4.58; Br: 17.72; N: 6.16.

**Synthesis of (4-bromo-phenyl)-ferrocenyl amine (118)**




Prepared from tri-*n*butyltinferrocen (524 mg, 1.10 mmol) and *n*BuLi (0.75 mL, 1.1 mmol, 1.5 M in hexane) following the procedure from Kagan.[106] Subsequent transmetalation with $MgBr_2 \cdot Et_2O$ (1.1 mL, 1.1 mmol, 1 M in toluene/diethyl ether 1:1) afforded the Grignard

species that was brought to reaction according to **TP 9** with and azo sulfone **110b** (339 mg, 1.00 mmol). Reaction time: 2 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 75 °C for 1 h. Purification by flash chromatography (pentane/diethyl ether = 49:1) yielded ferrocenylamine **118** as a yellow solid (205 mg, 58%).

**mp**.: 109-110 °C.

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 7.24 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.50 (d, $^3J$(H,H) = 8.9 Hz, 2 H) 4.24 (s_br, 1 NH), 4.00 (s, 5 H), 3.91 (dd, $^3J$(H,H) = $^4J$(H,H) = 2.5 Hz, 2 H), 3.80 (dd, $^3J$(H,H) = $^4J$(H,H) = 2.5 Hz, 2 H).

**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 145.2, 132.1, 116.6, 110.7, 100.1, 69.2, 64.8, 61.8.

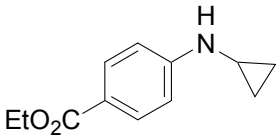
**MS** (70 eV, EI), *m/z* (%): 355 (100) [$M^+$], 233 (22), 220 (11), 186 (12), 154 (94), 128 (25), 102 (9), 76 (7).

**IR** (KBr): $\tilde{\nu}$ = 3421 (m), 1587 (s), 1509 (vs), 1305 (m), 1232 (m), 999 (m), 816 (vs), 502 (w), 488 (m).

**HRMS** for **$C_{16}H_{14}BrFeN$** (354.9659): found: 354.9689.

| | | |
|---|---|---|
| **$C_{16}H_{14}BrFeN$:** | required: | C: 53.97; H: 3.96; Br: 22.44; N: 3.93; |
| | found: | C: 54.11; H: 3.69; Br: 22.32; N: 3.85. |

## Synthesis of ethyl 4-cyclopropylamino-benzoate (120a)




Prepared according to **TP 9** from cyclopropylmagnesium bromide (1.4 mL, 1.1 mmol, 0.80 M in THF) and azo sulfone **110c** (332 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and heating to 75 °C for 2 h. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded amine **120a** as a yellow solid (127 mg, 62%).

**mp**.: 68-69 °C.

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 8.25 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.50 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.23 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.70 (s_br, 1 NH), 1.93-1.87 (m, 1 H), 1.09 (d, $^3J$(H,H) = 7.1 Hz, 3 H), 0.26 (m, 2 H), 0.10 (m, 2 H).

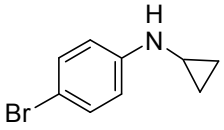
**$^{13}$C-NMR** (75 MHz, $C_6D_6$, 25 °C): δ = 166.7, 152.7, 131.7, 120.1, 112.4, 60.1, 24.7, 14.5, 7.5.

**MS** (70 eV, EI), *m/z* (%): 205 (100) [$M^+$], 176 (48), 160 (85), 132 (88), 117 (19), 105 (9), 65 (8).

**IR** (KBr): $\tilde{\nu}$ = 3355 (s), 2978 (w), 1682 (vs), 1605 (vs), 1522 (s), 1365 (s), 1310 (s), 1286 (vs), 1170 (vs), 1105 (s), 1022 (m), 841 (m), 772 (s), 702 (m).

**HRMS** for **$C_{12}H_{15}NO_2$** (205.1103): found: 205.1086.

## Synthesis of (4-bromo-phenyl)-cyclopropylamine (120b)




Prepared according to **TP 9** from cyclopropylmagnesium bromide (1.4 mL, 1.1 mmol, 0.80 M in THF) and azo sulfone **110b** (339 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and heating to 75 °C for 2 h. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded the amine 1**20b** as a colourless solid (142 mg, 67%).

**mp**.: 25 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.25 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.66 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.15 (s_br, 1 NH), 2.40-2.36 (m, 1 H), 0.72 (m, 2 H), 0.49 (m, 2 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 147.6, 131.8, 114.7, 109.3, 25.2, 7.4.

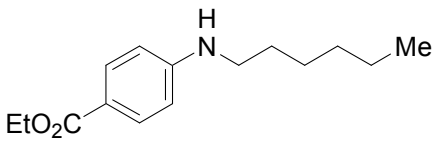
**MS** (70 eV, EI), *m/z* (%): 211 (5) [$M^+$], 184 (30), 155 (13), 132 (100), 117 (20), 105 (17), 91 (15), 76 (28), 65 (21), 56 (22), 50 (28).

**IR** (KBr): $\tilde{\nu}$ = 3390 (m), 2965 (w), 1594 (vs), 1494 (vs), 1450 (m), 1364 (m), 1312 (s), 1262 (m), 1174 (m), 1072 (m), 814 (vs), 500 (m).

**HRMS** for **$C_9H_{10}BrN$** (210.9997): found: 211.0006.

| | | |
|---|---|---|
| **$C_9H_{10}BrN$:** | required: | C: 50.97; H: 4.75; N: 6.60; |
| | found: | C: 51.25; H: 4.92; N: 6.57. |

## Synthesis of ethyl 4-(hexylamino)benzoate (120c)



Prepared according to **TP 9** from *n*hexylzinc iodide (0.75 mL, 1.2 mmol, 1.6 M in THF) and azo sulfone **110c** (332 mg, 1.00 mmol). Reaction time: 3 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 24 h at 50 °C, followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and heating to 75 °C for 15 min. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded amine **120c** as a colourless solid (154 mg, 62%).

**mp.:** 93-94 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.85 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.52 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 4.30 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 4.05 (s_br, 1 NH), 3.14 (t, $^3J$(H,H) = 7.1 Hz, 2 H), 1.61 (quint, $^3J$(H,H) = 7.1 Hz, 2 H), 1.44-1.28 (m, 9 H), 0.89 (t, $^3J$(H,H) = 6.6 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.9, 152.1, 131.5, 118.4, 111.3, 60.1, 43.4, 31.6, 29.3, 26.7, 22.6, 14.4, 14.0.

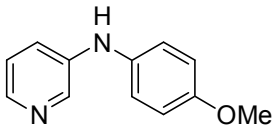
**MS** (70 eV, EI), *m/z* (%): 249 (18) [$M^+$], 204 (11), 178 (100), 150 (21), 105 (4).

**IR** (KBr): $\tilde{\nu}$ = 3374 (m), 2933 (m), 1678 (vs), 1604 (vs), 1577 (m), 1533 (m), 1476 (m), 1423 (m), 1393 (m), 1368 (s), 1343 (s), 1279 (vs), 1265 (vs), 1172 (vs), 1126 (s), 1107 (s), 1089 (m), 1032 (m), 841 (m), 773 (s), 730 (w), 702 (w), 648 (w).

**HRMS** for **$C_{15}H_{23}NO_2$** (249.1729): found: 249.1716.

**$C_{15}H_{23}NO_2$:** required: C: 72.25; H: 9.30; N: 5.62;
found: C: 72.45; H: 9.53; N: 5.60.

## Synthesis of *N*-(4-methoxyphenyl)-3-pyridinamine (125)




Prepared according to **TP 8** from 3-iodopyridine (226 mg, 1.10 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF) and azo sulfone **110e** (290 mg, 1.00 mmol). Reaction time: 1 h. Addition of allyl iodide (510 mg, 3.00 mmol) and NMP (2 mL) stirring for 2 h at rt followed by *in vacuo* solvent removal. Addition of AcOH (10 mL), Zn (650 mg, 10.0 mmol) and TFA (2 mL) and heating to 135 °C for 1 h in a sealed tube in microwave oven. Purification by flash chromatography (pentane/ethyl acetate = 1:2) yielded amine **125** as a colourless solid (136 mg, 68%).

**mp.:** 132.5-133.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.24 (s_br, 1 H), 8.04 (s_br, 1 H), 7.21-7.16 (m, 1 H), 7.10-7.03 (m, 3 H), 7.86 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 5.80 (s_br, 1 NH), 3.78 (s, 3 H).

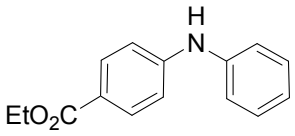
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 155.9, 141.9, 140.4, 138.2, 134.4, 123.8, 122.6, 121.1, 114.8, 55.5.

**MS** (70 eV, EI), *m/z* (%): 200 (78) [$M^+$], 185 (100), 156 (26), 142 (4), 130 (7), 78 (14), 51 (12).

**IR** (KBr): $\tilde{\nu}$ = 3253 (m), 3044 (m), 1606 (m), 1585 (m), 1576 (m), 1512 (vs), 1479 (vs), 1327 (s), 1285 (m), 1252 (vs), 1181 (m), 1033 (s), 819 (s), 782 (m), 699 (s).

**HRMS** for **$C_{12}H_{12}N_2O$** (200.0950): found: 200.0938.

## Synthesis of ethyl 4-anilinobenzoate (85b)




A dry and nitrogen-flushed two-neck-flask, equipped with a magnetic stirrer, a septum and a $H_2$-balloon, was charged with compound **112a** (410 mg, 1.00 mmol), Raney-Ni (1.50 g) and ethanol (15 mL). The flask was evaporated and flushed with $H_2$ under continuous stirring and this procedure was repeated three times. Stirring was continued for 12 h and the reaction mixture was filtered, washed with ethanol and concentrated *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded amine **85b** as a colourless solid (232 mg, 96%).

**mp.:** 112-113 °C.

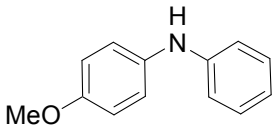
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.93 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.34-7.25 (m, 2 H), 7.19-6.97 (m, 5 H), 6.01 (s_br, 1 NH), 4.35 (q, $^3J$(H,H) = 7.2 Hz, 2 H), 1.38 (t, $^3J$(H,H) = 7.2 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.6, 147.9, 140.9, 131.4, 129.4, 123.1, 121.6, 120.3, 114.8, 60.5, 14.4.

**MS** (70 eV, EI), *m/z* (%): 241 (100) [$M^+$], 213 (41), 196 (94), 167 (52), 139 (5), 115 (3), 98 (6), 83 (8). 65 (2).

Spectral data match those reported for compound **85b** in chapter 11.

## Synthesis of ethyl 4-anilinobenzoate (85z)




A dry and nitrogen-flushed two-neck-flask, equipped with a magnetic stirrer, a septum and a $H_2$-balloon, was charged with compound **112b** (368 mg, 1.00 mmol), Raney-Ni (1.50 g) and

ethanol (15 mL). The flask was evaporated and flushed with $H_2$ under continuous stirring and this procedure was repeated three times. Stirring was continued for 48 h and the reaction mixture was filtered, washed with ethanol and concentrated *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded amine **85z** as colourless solid (171 mg, 85%).

**mp.:** 107.5-108.2 °C.

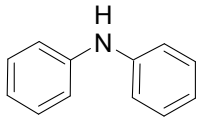
**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 7.26-7.22 (m, 2 H), 7.09 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 6.95-6.85 (m, 5 H), 5.50 (s_br, 1 NH), 3.82 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 155.3, 145.2, 135.8, 129.3, 122.2, 119.7, 115.8, 114.7, 55.6.

**MS** (70 eV, EI), *m/z* (%): 199 (75) [$M^+$], 184 (100), 167 (8), 154 (11), 128 (12), 77 (9).

Spectral data match those reported for compound **85z** in chapter 11.

## Synthesis of diphenylamine (85as)




A dry and nitrogen-flushed two-neck-flask, equipped with a magnetic stirrer, a septum and a $H_2$-balloon, was charged with compound **112c** (337 mg, 1.00 mmol), Raney-Ni (1.50 g) and ethanol (15 mL). The flask was evaporated and flushed with $H_2$ under continuous stirring and this procedure was repeated three times. Stirring was continued for 48 h and the reaction mixture was filtered, washed with ethanol and concentrated *in vacuo*. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded amine **85as** as colourless solid (136 mg, 80%).

**mp.:** 54.2-55.5 °C.

**$^1$H-NMR** (300 MHz, $C_6D_6$, 25 °C): δ = 7.11-7.08 (m, 4 H), 6.85-6.80 (m, 6 H), 4.95 (s_br, 1 NH).

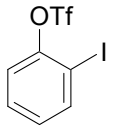
**$^{13}$C-NMR** (75 MHz, , $C_6D_6$, 25 °C): δ = 143.6, 129.5, 121.1, 118.2.

**MS** (70 eV, EI), *m/z* (%): 167 (100) [$M^+$], 139 (74), 123 (5), 109 (84), 93 (18), 81 (14), 65 (28).

Spectral data match those reported in the literature.[131]

# 13. Generation of Polyfunctionalized Arynes and Their Applications to Amination Chemistry

## Synthesis of 2-iodophenyl trifluoromethanesulfonate (137a)




Prepared according to **TP 14** from 2-iodophenol (2.20 g, 10.0 mmol) and trifluorosulfonic acid anhydride (3.38 g, 12.0 mmol). Reaction time: 16 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded compound **137a** as a colourless liquid (3.26 g, 93%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 7.92 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.43 (td, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.33 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 7.11 (td, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 1.3 Hz, 1 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 150.2, 140.8, 130.0, 129.6, 122.0, 118,7 (q, $^1J$(C,F) = 321 Hz), 89.1.

**MS** (70 eV, EI), *m/z* (%): 352 (21) [$M^+$], 313 (25), 236.1 (30), 92.0 (29), 69.0 (23), 64.0 (21) 43.1 (100).

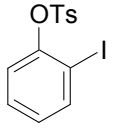
**IR** (KBr): $\tilde{\nu}$ = 3071 (w), 2923 (w), 1463 (s), 1427 (vs), 1248 (vs), 1214 (vs), 1166 (s), 1112 (s), 1138 (vs), 1118 (m), 1042 (m), 1022 (m), 886 (vs), 780 (s), 765 (s), 739 (m), 621 (m), 595 (s).

**HRMS** for **$C_7H_4F_3IO_3S$** (351.8878): found: 351.8885.

**$C_7H_4F_3IO_3S$**: required: C: 23.88; H: 1.15; I: 36.05;
found: C: 24.05; H: 1.22; I: 36.02.

Spectral data matches with that reported in the literature.[132]

## Synthesis of 2-iodophenyl 4-methylbenzenesulfonate (138a)




Prepared according to **TP 14** from 2-iodophenol (5.50 g, 25.0 mmol) and tosyl chloride (5.96 g, 31.0 mmol). Reaction time: 16 h. Purification by recrystallization from ethanol furnished compound **138a** as a colourless solid (8.42 g, 90%).

**mp.:** 85-86 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.79 (m, 3H), 7.33 (m, 4H), 6.97 (m, 1H), 2.46 (s, 3H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 150.0, 145.7, 140.1, 132.9, 129.8, 129.5, 128.8, 128.3, 123.0, 88.8, 21.7.

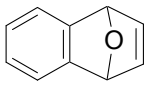
**MS** (70 eV, EI), *m/z* (%): 374 (83) [$M^+$], 155 (100), 91 (54).

**IR** (KBr): $\tilde{\nu}$ = 1462 (s), 1377 (vs), 1199 (s), 1185 (s), 1170 (vs), 1090 (m), 943 (w), 868 (s), 858 (s), 812 (m), 766 (vs), 734 (s), 708 (s), 665 (s), 561 (vs), 549 (s).

**HRMS** for **$C_{13}H_{11}IO_3S$** (373.9474): found: 373.9507.

**$C_{13}H_{11}IO_3S$:** required: C: 41.73; H: 2.96; S: 8.57;
found: C: 41.38; H: 2.96; S: 8.31.

## Synthesis of 1,4-dihydro-1,4-epoxynaphthalene (141a)




Prepared according to **TP 15** from 2-iodophenyl trifluoromethanesulfonate (**137a**) (352 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 1.10 M in THF) and furan (304 mg, 5.00 mmol). Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded compound **141a** as a colourless solid (60 mg, 42%).

**mp**.: 52-53 °C.

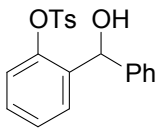
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.17 (dd, $^3J$(H,H) = 4.9 Hz, $^3J$(H,H) = 3.1 Hz, 2 H), 6.95 (m, 2 H), 6.89 (dd, $^3J$(H,H) = 4.9 Hz $^3J$(H,H) = 3.1 Hz, 2 H), 5.63 (s, 2 H)

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.0, 143.0, 125.0, 120.3, 82.3.

**MS** (70 eV, EI), *m/z* (%): 144 (19) [$M^+$], 128 (15), 115 (100), 89 (9), 63 (4).

Spectral data match those reported in the literature.[133]

## Synthesis of 2-[hydroxy(phenyl)methyl]phenyl 4-methylbenzenesulfonate (143a)




Prepared according to **TP 15** from 2-iodophenyl 4-methylbenzenesulfonate (**138a**) (748 mg, 2.00 mmol), *i*PrMgCl (1.6 mL, 2.2 mmol, 1.4 M in THF) and benzaldehyde (318 mg,

3.00 mmol) at −78 °C. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the title compound **143a** as a colourless solid (660 mg, 93%).

**mp**.: 116-117 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.78 (dt, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 1.8 Hz, 2 H), 7.28 (m, 11 H), 6.94 (dd, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 1.8 Hz, 1 H), 6.12 (s, 1 H), 2.47 (s, 3 H).

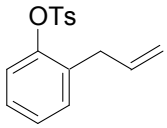
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 146.8, 145.8, 142.2, 137.6, 132.5, 129.9, 129.2, 128.7, 128.5, 128.3, 127.6, 127.3, 126.3, 122.0, 69.3, 21.7.

**MS** (70 eV, EI), *m/z* (%): 353 (22) $[M-H]^+$, 199.1 (100), 181.1 (53), 121.0 (26), 91.1 (41).

**IR** (KBr): $\tilde{\nu}$ = 3628 (s), 1454 (m), 1357 (vs), 1195 (s), 1178 (s), 1152 (s), 1089 (s), 885 (vs), 875 (s), 834 (s), 818 (s), 783 (s), 764 (s), 723 (s), 700 (s), 662 (s).

**$C_{20}H_{18}O_4S$:** required: C: 67.78; H: 5.12;
found: C: 67.69; H: 5.01.

## Synthesis of 2-allylphenyl 4-methylbenzenesulfonate (143b)




Prepared according to **TP 15** from 2-iodophenyl 4-methylbenzenesulfonate (**138a**) (748 mg, 2.00 mmol), *i*PrMgCl (1.6 mL, 2.2 mmol, 1.4 M in THF), CuCN·2LiCl (2.2 mL, 2.2 mmol, 1.0 M in THF) and allyl bromide (0.20 mL, 2.4 mmol) at −20 °C. Purification by flash chromatography (pentane/diethyl ether = 49:1) yielded the title compound **143b** as a colourless oil (460 mg, 79%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.76 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.33 (d, $^3J$(H,H) = 8.8 Hz, 2 H), 7.16 (m, 3 H), 7.03 (m, 1 H), 5.77 (m, 1 H), 5.01 (m, 2 H), 3.23 (dt; $^3J$(H,H) = 6.6 Hz, $^4J$(H,H) = 1.3 Hz, 2 H), 2.46 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 147.9, 145.3, 135.5, 133.4, 133.2, 130.6, 129.8, 128.4, 127.3, 127.0, 122.2, 116.4, 33.9.

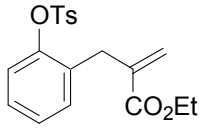
**MS** (70 eV, EI), *m/z* (%): 288 (2) $[M^+]$, 155 (17), 133 (100), 105 (29), 91 (75 ), 65 (13).

**IR** (KBr): $\tilde{\nu}$ = 3078 (m), 1640 (s), 1598 (s), 1486 (vs), 1452 (vs), 1373 (vs), 1192(vs), 1158 (vs), 1116 (s), 1092 (vs), 919 (s), 873 (vs), 815 (vs), 774 (vs), 736 (vs), 711 (vs), 684 (s), 663 (vs), 567 (vs).

**HRMS** for **$C_{16}H_{16}O_3S$** (288.0820): found: 288.0799.

**$C_{16}H_{16}O_3S$:** required: C: 66.64; H: 5.59; S: 11.12;
found: C: 66.27; H: 5.53; S: 11.06.

## Synthesis of ethyl 2-(2-{[(4-methylphenyl)sulfonyl]oxy}benzyl)acrylate (143c)




Prepared according to **TP 15** from 2-iodophenyl 4-methylbenzenesulfonate (**138a**) (748 mg, 2.00 mmol), *i*PrMgCl (1.6 mL, 2.2 mmol, 1.4 M in THF), CuCN·2LiCl (2.2 mL, 2.2 mmol, 1.0 M in THF) and ethyl (2-bromomethyl) acrylate (460 mg, 2.20 mmol) at −20 °C. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the title compound **143c** as a colourless solid (640 mg, 89%).

**mp**.: 46-47 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.75 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.32 (d, $^3J$(H,H) = 8.0 Hz, 2 H), 7.17 (m, 3 H), 7.09 (m, 1 H), 6.18 (s, 1 H), 5.30 (m, 1 H), 4.15 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.48 (s, 2 H), 2.48 (s, 3 H), 1.24 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.6, 148.2, 145.4, 138.4, 133.1, 132.1, 131.2, 129.8, 128.4, 127.7, 127.0, 126.7, 122.2, 60.7, 32.0, 21.7, 14.1.

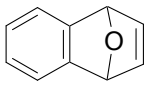
**MS** (70 eV, EI), *m/z* (%): 360 (1) $[M]^+$, 315 (2), 205 (20), 189 (11), 159 (100), 131 (16), 91 (19).

**IR** (KBr): $\tilde{\nu}$ = 2983 (w), 1716 (vs), 1488 (s), 1452 (s), 1373 (vs), 1193 (vs), 1180 (vs), 1158 (vs), 1085(vs), 883 (s), 815 (vs), 775 (vs), 713 (s), 661 (m), 562 (vs)

**HRMS** for **$C_{19}H_{20}O_5S$** (360.1031): found: 360.1029.

**$C_{19}H_{20}O_5S$:** required: C: 63.32; H: 5.57;
found: C: 63.43; H: 5.54.

## Synthesis of 1,4-dihydro-1,4-epoxynaphthalene (141a)




Prepared according to **TP 15** from 2-iodophenyl 4-methylbenzenesulfonate (**138a**) (748 mg, 2.00 mmol), *i*PrMgCl (1.6 mL, 2.2 mmol, 1.4 M in THF) and furan (608 mg, 10.0 mmol). Reaction time: 4 h. Purification by flash chromatography (pentane/diethyl ether = 19:1) yielded compound 141a as a colourless solid (60 mg, 87%).

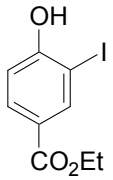
**mp**.: 52-53 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.17 (dd, $^3J$(H,H) = 4.9 Hz, $^3J$(H,H) = 3.1 Hz, 2 H), 6.95 (m, 2 H), 6.89 (dd, $^3J$(H,H) = 4.9 Hz $^3J$(H,H) = 3.1 Hz, 2 H), 5.63 (s, 2 H)

**MS** (70 eV, EI), *m/z* (%): 144 (20) $[M^+]$, 128 (15), 115 (100), 89 (9), 63 (4).

Spectral data match those reported in the literature and with compound **141a**.

## Synthesis of ethyl 3-iodo-4-hydroxybenzoate (145a)




Prepared according to **TP 2** from ethyl 4-hydroxybenzoate (4.99 g, 30.0 mmol), iodine (7.36 g, 29.0 mmol) and $Ag_2SO_4$ (9.04 g, 29.0 mmol) in EtOH (250 mL). Purification by flash chromatography ($CH_2Cl_2$) yielded compound **145a** as a colourless solid (6.66 g, 76%).

**mp**.: 112-114 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.37 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.94 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.00 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 5.92 (s, 1 H), 4.35 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.38 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.0, 158.7, 140.2, 132.9, 131.0, 124.8, 114.6, 85.1, 61.1, 14.3.

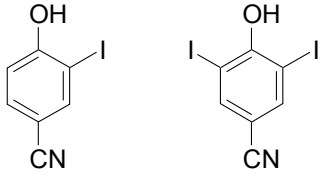
**MS** (70 eV, EI), *m/z* (%): 292 (37) [$M^+$], 264 (33), 247 (100), 92.0 (24), 43.0 (30).

**IR** (KBr): $\tilde{\nu}$ = 3344 (vs), 1686 (vs), 1597 (vs), 1574 (vs), 1498 (s), 1391 (m), 1369 (vs), 1352 (s), 1286 (vs), 1262 (vs), 1175 (s), 1148 (m), 1124 (s), 828 (m), 767 (vs), 670 (s), 632 (s).

**HRMS** for **$C_9H_9IO_3$** (291.9596): found: 291.9578.

**$C_9H_9IO_3$:** required: C: 37.01; H: 3.11; I: 43.45;
found: C: 36.98; H: 3.21; I: 43.45.

## Synthesis of 4-hydroxy-3-iodo-benzonitrile (145b) and 4-hydroxy-3,5-diiodo-benzonitrile (146a)




Prepared according to **TP 2** from 4-hydroxybenzonitrile (3.57 g, 30.0 mmol), iodine (7.36 g, 29.0 mmol) and $Ag_2SO_4$ (9.04 g, 29.0 mmol) in EtOH (250 mL). Purification by flash

chromatography ($CH_2Cl_2$) yielded compound **145b** as a colourless solid (4.78 g, 65%) and diiodinated product **146a** (2.20 g, 20%).

**mp**.: 145-146 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 10.56 (s_br, 1 OH), 7.82 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.32 (dd, $^3J$(H,H) = 8.8 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 6.85 (d, $^3J$(H,H) = 8.8 Hz, 1 H),

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 160.6, 142.4, 133.2, 117.7, 115.0, 103.5, 84.0.

**MS** (70 eV, EI), *m/z* (%): 245 (100) [$M^+$], 118 (13), 90 (18), 63 (13).

**IR** (KBr): $\tilde{\nu}$ = 2226 (vs), 1592 (s), 1564 (m), 1498 (m), 1397 (s), 1349 (m), 1295 (s), 1208 (m), 1039 (m), 894 (m), 821 (s), 732 (m), 581 (m).

**HRMS** for **$C_7H_4INO$** (244.9338): found: 244.9326.

Spectral data match those reported in the literature[134]

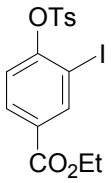
**mp**.: 208-209.5 °C.

**$^1$H-NMR** (300 MHz, DMSO-$d_6$, 25 °C): δ = 8.20 (s, 2 H).

**$^{13}$C-NMR** (75 MHz, DMSO-$d_6$, 25 °C): δ = 160.4, 143.0, 116.6, 106.4, 86.7.

Spectral data match those of the commercially available substrate.

## Synthesis of ethyl 3-iodo-4-{[(4-methylphenyl)sulfonyl]oxy}benzoate (138b)




Prepared according to **TP 14** from ethyl 3-iodo-4-hydroxybenzoate (**145a**) (5.84 g, 20.0 mmol) and 4-methyl-benzenesulfonyl chloride (TsCl) (4.57 g, 24.0 mmol). Reaction time: 16 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) furnished compound **138b** as a colourless very viscous oil, which crystallized after 1 week (8.47 g, 95%).

**mp**.: 71.5-73 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.39 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.99 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.78 (d, $^4J$(H,H) = 8.4 Hz, 2 H), 7.38 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.31 (d, $^4J$(H,H) = 8.4 Hz, 2 H), 4.34 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 2.44 (s, 3 H), 1.38 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

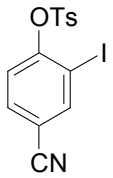
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.2, 153.2, 146.0, 141.3, 132.5, 130.3, 129.9, 128.8, 122.4, 89.8, 61.6, 21.8, 14.2.

**MS** (70 eV, EI), *m/z* (%): 446 (31) [$M^+$], 401 (6), 291 (4), 247 (11), 155 (100), 91 (81), 65 (10).

**IR** (KBr): $\tilde{\nu}$ = 1721 (vs), 1592 (m), 1472 (m), 1368 (vs), 1293 (vs), 1277 (vs), 1254 (vs), 1179 (vs), 1123 (s), 1088 (s), 1040 (s), 875 (s), 857 (s), 767 (s), 752 (s), 680 (s), 582 (s).

**HRMS** for **$C_{16}H_{15}IO_5S$** (445.9685): found: 445.9687.

## Synthesis of 4-cyano-2-iodophenyl 4-methylbenzenesulfonate (138c)




Prepared according to **TP 14** from 4-hydroxy-3-iodo-benzonitrile (**145b**) (3.92 g, 16.0 mmol) and 4-methyl-benzenesulfonyl chloride (3.65 g, 19.0 mmol). Reaction time: 16 h. Purification by recrystallization from ethanol furnished compound **138c** as a colourless solid (6.00 g, 94%).

**mp**.: 150-151.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.01 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.80 (d, $^4J$(H,H) = 8.4 Hz, 2 H), 7.63 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.46 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.35 (d, $^4J$(H,H) = 8.4 Hz, 2 H), 2.46 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 153.3, 146.4, 143.4, 133.3, 132.2, 130.0, 128.7, 123.2, 116.2, 112.2, 90.7, 21.8.

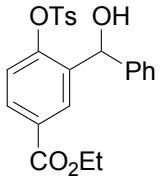
**MS** (70 eV, EI), *m/z* (%): 399 (11) [$M^+$], 245 (6), 206 (3), 155 (100), 91 (92 ( 65 (17).

**IR** (KBr): $\tilde{\nu}$ = 2228 (s), 1587 (s), 1476 (vs), 1353 (vs), 1216 (vs), 1188 (s), 1154 (vs), 1088 (vs), 1039 (s), 867 (vs), 816 (vs), 804 (vs), 690 (s), 670 (vs), 577 (vs).

**HRMS** for **$C_{14}H_{10}INO_3S$** (398.9426): found: 398.9413.

| | | |
|---|---|---|
| **$C_{14}H_{10}INO_3S$:** | required: | C: 42.12; H: 2.52; N: 3.51; |
| | found: | C: 42.01; H: 2.63; N: 3.54. |

## Synthesis of ethyl 3-[hydroxy(phenyl)methyl]-4-{[(4-methylphenyl)sulfonyl]oxy} benzoate (143d)



Prepared according to **TP 15** from ethyl 3-iodo-4-{[(4-methylphenyl)sulfonyl]oxy}benzoate (**138c**) (399 mg, 1.00 mmol), *i*PrMgCl (1.1 mL, 1.1 mmol, 0.9 M in THF) and benzaldehyde (212 mg, 2.00 mmol) at −78 °C. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the title compound **143d** as a colourless oil (409 mg, 96%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.25 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.88 (dd, $^3J$(H,H) = 8.8 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.71 (d, $^4J$(H,H) = 8.4 Hz, 2 H), 7.34-7.24 (m, 7 H), 7.10 (d, $^4J$(H,H) = 8.8 Hz, 1 H), 6.06 (d, $^3J$(H,H) = 3.5 Hz, 1 H), 4.32 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 3.05 (d, $^3J$(H,H) = 3.5 Hz, 1 OH), 2.45 (s, 3 H), 1.35 (t, $^3J$(H,H) = 7.1 Hz, 3 H).

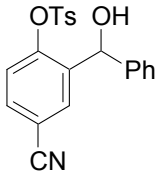
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.4, 149.8, 145.9, 141.9, 137.4, 132.1, 130.0, 129.90, 129.86, 129.3, 128.3, 127.5, 126.8, 126.4, 121.3, 69.5, 61.2, 21.6, 14.1.

**MS** (70 eV, EI), *m/z* (%): 426 (2) [$M^+$], 425 (10), 409 (8), 381 (4), 271 (100), 253 (39), 225 (37), 193 (19), 155 (18), 105 (16), 91 (50), 77 (11).

**IR** (KBr): $\tilde{\nu}$ = 3479 (m), 2982 (w), 1715 (vs), 1597 (s), 1484 (s), 1371 (vs), 1292 (vs), 1247 (vs), 1178 (vs), 1112 (s), 1089 (vs), 1021 (s), 917 (w), 858 (s), 776 (s), 720 (s), 701 (s), 669 (m), 565 (s).

**HRMS** for **$C_{23}H_{22}O_6S$** (426.1137): found: 426.1172.

## Synthesis of 4-cyano-2-[hydroxy(phenyl)methyl]phenyl 4-methylbenzenesulfonate (143e)




Prepared according to **TP 15** from 4-cyano-2-iodophenyl 4-methylbenzenesulfonate (**138c**) (446 mg, 1.00 mmol), *i*PrMgCl (1.1 mL, 1.1 mmol, 0.9 M in THF) and benzaldehyde (212 mg, 2.00 mmol) at −78 °C. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the title compound **143e** as a colourless oil (360 mg, 95%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.86 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.72 (d, $^4J$(H,H) = 8.4 Hz, 2 H), 7.50 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.38-7.23 (m, 7 H), 7.17 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 6.02 (d, $^3J$(H,H) = 3.5 Hz, 1 H), 2.91 (d, $^3J$(H,H) = 3.5 Hz, 1 OH), 2.49 (s, 3 H).

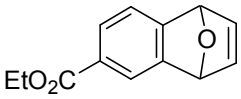
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.5, 146.3, 141.1, 138.9, 132.8, 132.4, 131.9, 130.1, 128.5, 128.3, 128.0, 126.4, 122.4, 117.8, 111.1, 69.3, 21.7.

**MS** (70 eV, EI), *m/z* (%): 378 (2) [M−H]$^+$, 362 (2), 224 (100), 206 (76), 177 (5), 155 (24), 146 (24), 91 (75), 77 (12), 65 (11).

**IR** (KBr): $\tilde{\nu}$ = 3459 (m), 2233 (s), 1598 (s), 1482 (vs), 1382 (vs), 1225 (s), 1172 (vs), 1090 (vs), 1039 (s), 851 (vs), 729 (s), 700 (s), 572 (s).

**HRMS** for **$C_{21}H_{17}NO_4S$** (379.0878): found: 379.0908.

## Synthesis of 3,6-dihydro-1-ethoxycarbonyl-3,6-epoxynaphthalene (140b)




Prepared according to **TP 15** from ethyl 3-iodo-4-{[(4-methylphenyl)sulfonyl]oxy}benzoate (**138b**) (446 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF) and furan (304 mg, 5.00 mmol). Reaction time: 18 h at rt. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded compound **140b** as a colourless oil (158 mg, 73%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.87-7.85 (m, 1 H), 7.75 (dd, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 7.27 (d, $^3J$(H,H) = 7.5 Hz, 1 H), 7.03-6.97 (m, 2 H), 5.74-5.72 (m, 2 H), 4.31 (q, $^3J$(H,H) = 7.1 Hz, 2 H), 1.35 (t, $^3J$(H,H) = 7.1 Hz, 2 H).

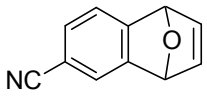
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.3, 154.3, 149.4, 143.3, 142.3, 127.9, 127.5, 120.6, 119.8, 82.09, 82.07, 60.8, 14.3.

**MS** (70 eV, EI), *m/z* (%): 216 (7) [$M^+$], 203 (17), 190 (23), 171 (34), 162 (19), 143 (40), 129 (31), 115 (100), 89 (12), 63 (7).

**IR** (KBr): $\tilde{\nu}$ = 2982 (w), 1714 (vs), 1367 (m), 1288 (vs), 1255 (vs), 1169 (s), 1102 (s), 1075 (s), 994 (m), 873 (m), 847 (s), 768 (s), 698 (m), 640 (m).

**HRMS** for **$C_{13}H_{12}O_3$** (216.0786): found 216.0789.

## Synthesis of 1-cyano-3,6-dihydro-3,6-epoxynaphthalene (140c)




Prepared according to **TP 15** from 4-cyano-2-iodophenyl 4-methylbenzenesulfonate (**138c**) (399 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF) and furan (304 mg, 5.00 mmol). Reaction time: 24 h at rt. Purification by flash chromatography (pentane/diethyl ether = 1:1) yielded **140c** as a colourless solid (130 mg, 77%).

**mp**.: 97-98 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 7.45 (s, 1 H), 7.35-7.33 (m, 2 H), 7.05-7.01 (m, 2 H), 5.76-5.72 (m, 2 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 154.6, 150.5, 143.1, 142.5, 130.9, 122.8, 120.6, 119.1, 108.8, 82.1, 81.9.

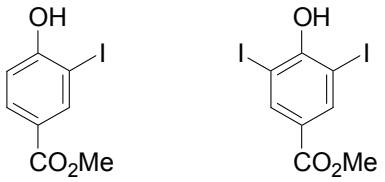
**MS** (70 eV, EI), *m/z* (%): 169 (20) [$M^+$], 141 (100), 114 (47), 88 (10), 75 (7), 63 (16).

**IR** (KBr): $\tilde{\nu}$ = 2225 (vs), 1455 (m), 1418 (m), 1277 (s), 1200 (w), 1072 (w), 992 (s), 863 (vs), 852 (s), 842 (vs), 746 (m), 705 (s), 645 (m), 614 (s), 577 (w).

**HRMS** for **$C_{11}H_7NO$** (169.0528): found 169.0515.

**$C_{11}H_7NO$**: required: C: 78.09; H: 4.17; N: 8.28;
found: C: 77.89; H: 4.07; N: 8.32.

## Synthesis of methyl 3-iodo-4-hydroxybenzoate (145c) and methyl 3,5-diiodo-4-hydroxybenzoate (146b)




Prepared according to **TP 2** from methyl 4-hydroxybenzoate (3.04 g, 20.0 mmol), iodine (4.83 g, 19.0 mmol) and $Ag_2SO_4$ (5.91 g, 19.0 mmol) in EtOH (150 mL). Purification by flash chromatography ($CH_2Cl_2$) yielded compound **145c** and compound **146b** as colourless solids (3.11 g, 56%) and (1.62 g, 20%).

**mp**.: 158-159 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 10.07 (s, 1 OH), 8.25 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.72 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 6.82 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 3.74 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 1665.4, 160.6, 140.7, 131.0, 122.7, 114.3, 83.4, 51.7.

**MS** (70 eV, EI), *m/z* (%): 277 (60) [$M^+$], 247 (100), 218 (11), 190 (2), 120 (5), 92 (13), 63 (7).

**IR** (KBr): $\tilde{\nu}$ = 3332 (vs), 1691 (vs), 1596 (s), 1572 (s), 1438 (m), 1411 (s), 1288 (vs), 1273 (vs), 1126 (m), 968 (w), 833 (w), 766 (s), 670 (w), 631 (w).

**HRMS** for **$C_8H_7IO_3$** (277.9440): found: 277.9467.

**mp**.: 170.6-171.4 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.34 (s, 2 H), 6.13 (s, 1 OH), 3.88 (s, 3 H).

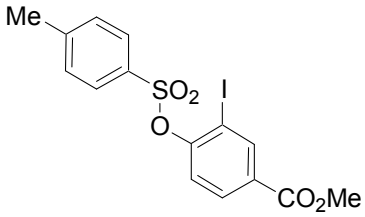
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 163.9, 157.2, 140.8, 126.0, 81.6, 52.4.

**MS** (70 eV, EI), *m/z* (%): 404 (100) [$M^+$], 373 (78 ), 344 (6), 277 (4), 245 (4), 217 (10), 119 (11), 91 (13), 62 (14).

**IR** (KBr): $\tilde{\nu}$ = 3377 (s), 1710 (vs), 1580 (m), 1542 (m), 1433 (s), 1300 (vs), 1260 (vs), 1227 (vs), 1133 (s), 1096 (s), 968 (w), 761 (m), 705 (m).

**HRMS** for **$C_8H_6I_2O_3$** (403.8406): found: 403.8387.

## Synthesis of methyl 3-iodo-4-{[(4-methylphenyl)sulfonyl]oxy}benzoate (138d)




Prepared according to **TP 14** from methyl 4-hydroxy-3-iodobenzoate (**145c**) (3.05 g, 11.0 mmol) and 4-methylbenzenesulfonyl chloride (2.54 g, 13.0 mmol). Reaction time: 12 h. Recrystallization from ethanol yielded **138d** as a colourless solid (4.51 g, 95%).

**mp**.: 83.5-84 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.39 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.98 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.77 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.38 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.31 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 3.88 (s, 3 H), 2.43 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.6, 153.2, 146.1, 141.3, 132.4, 130.8, 129.9, 128.8, 122.4, 89.8, 52.5, 21.8.

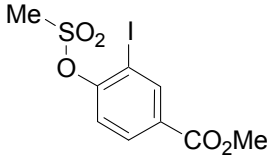
**MS** (70 eV, EI), *m/z* (%): 432 (36) [$M^+$], 401 (4), 245 (4), 181 (4), 155 (90), 119 (12), 91 (100), 65 (17).

**IR** (KBr): $\tilde{\nu}$ = 1719 (vs), 1594 (m), 1438 (m), 1373 (vs), 1291 (vs), 1176 (vs), 1119 (m), 1091 (m), 1034 (m), 867 (s), 830 (m), 770 (s), 746 (s), 677 (s), 576 (s), 550 (m).

**HRMS** for **$C_{15}H_{13}IO_5S$** (431.9528): found: 431.9527.

**$C_{15}H_{13}IO_5S$**: required: C: 41.68; H: 3.03; S: 7.42;
found: C: 42.00; H: 3.06; S: 7.53.

## Synthesis of methyl 3-iodo-4-[(methylsulfonyl)oxy]benzoate (147a)



Prepared according to **TP 14** from methyl 4-hydroxy-3-iodobenzoate (**145c**) (1.39 g, 5.00 mmol) and methanesulfonyl chloride (687 mg, 6.00 mmol). Reaction time: 12 h. Purification by flash chromatography ($CH_2Cl_2$) yielded compound **147a** as a colourless solid (1.61 g, 90%).

**mp**.: 81.5-82.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.49 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.01 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.46 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 3.89 (s, 3 H), 3.30 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.4, 152.5, 141.3, 131.1, 130.2, 122.5, 89.2, 52.5, 39.6.

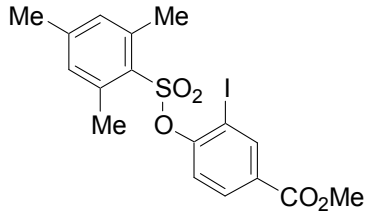
**MS** (70 eV, EI), *m/z* (%): 356 (100) [$M^+$], 324 (14), 278 (86), 2467), 51), 221 (21), 150 (53), 119 (67), 107 (16), 79 (13), 63 (48).

**IR** (KBr): $\tilde{\nu}$ = 1715 (vs), 1587 (m), 1475 (s), 1438 (s), 1350 (vs), 1330 (s), 1277 (vs), 1205 (s), 1171 (vs), 1115 (vs), 1038 (s), 961 (s), 864 (vs), 834 (vs), 783 (vs), 768 (vs), 730 (s), 659 (m), 557 (s).

**HRMS** for **$C_9H_9IO_5S$** (355.9215): found: 355.9245.

**$C_9H_9IO_5S$**: required: C: 30.35; H: 2.55; I: 35.63; S: 9.00;
found: C: 30.63; H: 2.57; I: 35.60; S: 8.86.

## Synthesis of methyl 3-iodo-4-[(mesitylsulfonyl)oxy]benzoate (148a)




Prepared according to **TP 14** from methyl 4-hydroxy-3-iodobenzoate (**145**) (723 mg, 2.60 mmol) and mesitylsulfonyl chloride (6.75 mg, 3.10 mmol). Reaction time: 12 h. Purification by flash chromatography (Pentane/$CH_2Cl_2$ = 2:1) yielded compound **148a** as a colourless solid (960 mg, 81%).

**mp**.: 105.5-106.7 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.47 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.92 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.05 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.01 (s, 2 H), 3.89 (s, 3 H), 2.61 (s, 6 H), 2.34 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.7, 153.6, 144.4, 141.5, 140.5, 132.0, 131.6, 130.8, 129.7, 122.0, 90.2, 52.5, 23.1, 21.2.

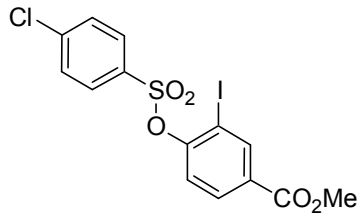
**MS** (70 eV, EI), *m/z* (%): 460 (15) [$M^+$], 246 (14), 183 (41), 119 (100), 91 (22), 77 (16).

**IR** (KBr): $\tilde{\nu}$ = 1722 (vs), 1604 (m), 1588 (m), 1475 (m), 1432 (m), 1372 (vs), 1292 (vs), 1282 (vs), 1247 (s), 1210 (s), 1176 (vs), 1038 (m), 862 (m), 844 (m), 771 (s), 732 (vs), 668 (vs), 583 (m).

**HRMS** for **$C_{17}H_{17}IO_5S$** (459.9841): found: 459.9834.

**$C_{17}H_{17}IO_5S$**: required: C: 44.36; H: 3.72; S: 6.97;
found: C: 44.51; H: 3.73; S: 7.26.

## Synthesis of methyl 4-{[(4-chlorophenyl)sulfonyl]oxy}-3-iodobenzoate (149a)




Prepared according to **TP 14** from methyl 4-hydroxy-3-iodobenzoate (**145c**) (3.05 g, 11.0 mmol) and 4-chlorobenzenesulfonyl chloride (2.79 g, 13.0 mmol). Reaction time: 12 h. Recrystallization from ethanol yielded compound **149a** as a colourless solid (4.92 g, 99%).

**mp**.: 79.5-80.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.40 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.00 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.86 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.50 (d, $^3J$(H,H) = 8.4 Hz, 2H), 7.42 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 3.84 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.5, 152.9, 141.7, 141.4, 133.9, 130.9, 130.2, 129.7, 122.5, 112.5, 89.6, 52.5.

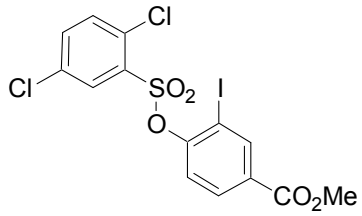
**MS** (70 eV, EI), *m/z* (%): 451 (72) [$M^+$], 420 (7), 276 (15), 245 (19), 175 (100), 150 (13), 119 (18), 111 (46), 63 (11).

**IR** (KBr): $\tilde{\nu}$ = 3093 (m), 1726 (vs), 1588 (m), 1568 (w), 1474 (m), 1436 (m), 1390 (vs), 1282 (vs), 1248 (s), 1209 (s), 1180 (vs), 1114 (m), 1093 (s), 1036 (s), 910 (w), 884 (m), 869 (s), 829 (s), 734 (s), 660 (s), 608 (m), 577 (s), 482 (m).

**HRMS** for **$C_{14}H_{10}ClIO_5S$** (451.8982): found 451.8965.

**$C_{14}H_{10}ClIO_5S$**: required: C: 37.15; H: 2.23; S: 7.08;
found: C: 36.95; H: 2.26; S: 7.32.

## Synthesis of methyl 4-{[(2,5-dichlorophenyl)sulfonyl]oxy}-3-iodobenzoate (150a)




Prepared according to **TP 14** from methyl 4-hydroxy-3-iodobenzoate (**145c**) (834 mg, 3.00 mmol) and 2,5-dichlorobenzenesulfonyl chloride (882 mg, 3.60 mmol). Reaction time: 12 h. Purification by flash chromatography (pentane/$CH_2Cl_2$ = 2:1) yielded compound **150a** as a colourless solid (1.40 g, 96%).

**mp**.: 116.2-117.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.47 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.03-7.97 (m, 2 H), 7.61-7.53 (m, 2 H), 7.24 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 3.90 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.5, 153.2, 141.6, 135.8, 135.4, 133.5, 133.4, 132.0, 131.6, 131.0, 130.3, 122.5, 89.2, 52.6.

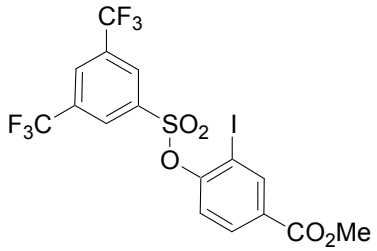
**MS** (70 eV, EI), *m/z* (%): 485 (80) [$M^+$], 277 (100), 245 (23), 208 (58), 150 (44), 119 (43), 109 (19), 63 (21).

**IR** (KBr): $\tilde{\nu}$ = 3089 (m), 2955 (m), 1715 (vs), 1590 (m), 1455 (s), 1394 (vs), 1295 (vs), 1256 (s), 1207 (vs), 1175 (vs), 1115 (s), 1093 (s), 848 (vs), 837 (vs), 768 (s), 743 (s), 598 (s), 582 (s).

**HRMS** for **$C_{14}H_9Cl_2IO_5S$** (485.8592): found 485.8613.

**$C_{14}H_9Cl_2IO_5S$**: required: C: 34.52; H: 1.86; S: 6.58;
found: C: 34.77; H: 1.84; S: 6.66.

## Synthesis of methyl 4-({[3,5-bis(trifluoromethyl)phenyl]sulfonyl}oxy)-3-iodobenzoate (151a)




Prepared according to **TP 14** from methyl 4-hydroxy-3-iodobenzoate (**145c**) (834 mg, 3.00 mmol) and 3,5-bis(trifluoromethyl)-benzenesulfonyl chloride (1.12 g, 3.60 mmol). Reaction time: 12 h. Purification by flash chromatography (pentane/$CH_2Cl_2$ = 3:1) yielded compound **151a** as a colourless solid (1.62 g, 98%).

**mp**.: 55.6-56.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.44 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.39 (s_br, 2 H), 8.20 (s_br, 1 H), 8.08 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.51 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 3.92 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.4, 152.5, 141.7, 138.3, 133.3 (q, $^2J$(C,F) = 35 Hz), 131.3, 129.2 (m), 128.3 (m), 122.9, 122.3 (q, $^1J$(C,F) = 271 Hz), 113.7, 88.9, 52.7.

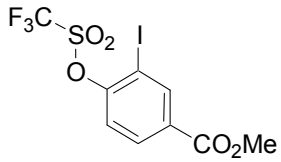
**MS** (70 eV, EI), *m/z* (%): 554 (100) [$M^+$], 534 (12), 522 (13), 276 (69), 245 (7), 213 (14), 150 (17), 119 (8).

**IR** (KBr): $\tilde{\nu}$ = 3090 (m), 2963 (m), 1721 (vs), 1589 (m), 1440 (s), 1406 (vs), 1360 (s), 1289 (vs), 1269 (vs), 1254 (vs), 1179 (vs), 1151 (vs), 1111 (s), 870 (s), 770 (s), 740 (s), 682 (s), 660 (s), 592 (vs).

**HRMS** for **$C_{16}H_9F_6IO_5S$** (553.9120): found 553.9123.

**$C_{16}H_9F_6IO_5S$**: required: C: 34.68; H: 1.64;
found: C: 34.71; H: 1.66.

## Synthesis of methyl 3-iodo-4-[(trifluoromethylsulfonyl)oxy]benzoate (137b)




Prepared according to **TP 14** from methyl 4-hydroxy-3-iodobenzoate (**145c**) (1.39 g, 5.00 mmol) and trifluoromethylsulfonic acid anhydride (1.69 g, 6.00 mmol) at −20 °C. Reaction time: 12 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded compound **137b** as a colourless oil (1.75 g, 85%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.56 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.08 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.38 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 3.93 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.2, 153.1, 142.1, 131.4, 131.3, 121.8, 118.7 (q, $^1J$(C,F) = 320 Hz), 88.8, 52.8.

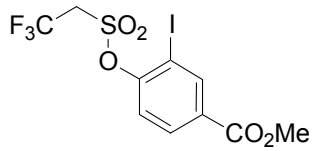
**MS** (70 eV, EI), *m/z* (%): 410 (92) [$M^+$], 314 (25), 277 (100), 245 (11), 221 (11), 150 (57), 119 (48), 94 (19), 77 (11), 63 (43).

**IR** (KBr): $\tilde{\nu}$ = 1732 (vs), 1589 (w), 1473 (w), 1430 (vs), 1292 (s), 1245 (vs), 1173 (vs), 1137 (vs), 1114 (s), 1034 (m), 887 (vs), 845 (m, 767 (s), 748 (s), 610 (vs).

**HRMS** for **$C_9H_6F_3IO_5S$** (409.8933): found: 409.8938.

**$C_9H_6F_3IO_5S$**: required: C: 26.36; H: 1.47;
found: C: 26.57; H: 1.52.

## Synthesis of methyl 3-iodo-4-{[(2,2,2-trifluoroethyl)sulfonyl]oxy}benzoate (152a)




Prepared according to **TP 14** from methyl 4-hydroxy-3-iodobenzoate (**145c**) (834 mg, 3.00 mmol) and 2,2,2-trifluoroethanesulfonyl chloride (655 mg, 3.60 mmol) at −20 °C. Reaction time: 12 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded compound **152a** as a colourless solid (1.66 g, 83%).

**mp.:** 86.5-87.3 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.53 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.06 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.46 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 4.27 (q, $^3J$(H,F) = 8.4 Hz, 2 H), 3.93 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.4, 152.1, 141.7, 131.3, 130.8, 122.6, 120.7 (q, $^1J$(C,F) = 279 Hz), 88.8, 55.1 (q, $^2J$(C,F) = 34 Hz), 52.7.

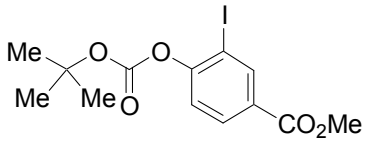
**MS** (70 eV, EI), *m/z* (%): 424 (100) [$M^+$], 392 (16), 276 (81), 247 (15), 220 (10), 150 (28), 119 (21), 63 (8) .

**IR** (KBr): $\tilde{\nu}$ = 3019 (w), 2962 (w), 1725 (vs), 1438 (w), 1370 (vs), 1335 (s), 1278 (vs), 1255 (m), 1146 (s), 1105 (s), 883 (vs), 768 (m).

**HRMS** for **$C_{10}H_8F_3IO_5S$** (423.9089): found: 423.9078.

| | | |
|---|---|---|
| **$C_{10}H_8F_3IO_5S$**: | required: | C: 28.32; H: 1.90; |
| | found: | C: 28.34; H: 1.91. |

## Synthesis of methyl 4-[(*t*butoxycarbonyl)oxy]-3-iodobenzoate (153a)




A dry and argon-flushed 25 mL Schlenk-flask, equipped with a magnetic stirring bar and a septum, was charged with methyl 4-hydroxy-3-iodobenzoate (**145c**) (556 mg, 2.00 mmol) and DMAP (30 mg, 0.20 mmol) and THF (10 mL) was added. The mixture was cooled to 0 °C and subsequently di(*t*butyl) dicarbonate (655 mg, 3.60 mmol) dissolved in THF (3 mL) was added dropwise. On completion of the addition the reaction mixture was allowed to warm to rt and was stirred overnight. The reaction mixture was poured into water (20 mL) and the aqueous phase was extracted with diethyl ether (2 x 30 mL). The organic fractions were washed with brine (30 mL), dried over $Na_2SO_4$, filtered and concentrated *in vacuo*.

Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded compound **153a** as a colourless oil (710 mg, 94%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.49 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.02 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.22 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 3.90 (s, 3 H), 1.56 (s, 9 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 164.9, 154.8, 150.2, 140.9, 131.0, 129.4, 122.6, 90.2, 84.7, 52.4, 27.7.

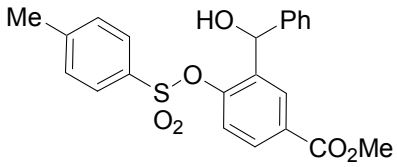
**MS** (70 eV, EI), *m/z* (%): 278 (53) $[M\text{-Boc}]^+$, 247 (29), 217 (2), 119 (4), 57 (100).

**IR** (KBr): $\tilde{\nu}$ = 2982 (m), 2952 (w), 1763 (vs), 1727 (vs), 1435 (m), 1371 (s), 1278 (vs), 1241 (vs), 1148 (vs), 1112 (vs), 1048 (m), 1039 (m), 847 (m), 772 (m), 743 (m), 672 (m).

**HRMS** for **$C_{13}H_{15}IO_5$** (377.9964): not detectable

**$C_{13}H_{15}IO_5$**: required: C: 41.29; H: 4.00;
found: C: 41.33; H: 4.00.

## Synthesis of methyl 3-[hydroxy(phenyl)methyl]-4-{[(4-methylphenyl)sulfonyl]oxy}benzoate (143f)




Prepared according to **TP 15** from methyl 3-iodo-4-[(methylsulfonyl)oxy]benzoate (**138d**) (432 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF) and benzaldehyde (212 mg, 2.00 mmol) at −78 °C. Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 3:2) yielded the title compound **143f** as a colourless solid (372 mg, 90%).

**mp.:** 112-113 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.11 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.78 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.61 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.24-7.12 (m, 7 H), 6.99 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 5.96 (s, 1 H), 3.76 (s, 3 H), 2.36 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.9, 149.9, 146.0, 141.8, 137.5, 132.2, 130.2, 130.0, 129.9, 129.1, 128.4, 128.3, 127.6, 126.4, 121.5, 69.5, 52.3, 21.7.

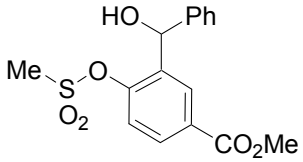
**MS** (70 eV, EI), *m/z* (%): 412 (0.1) $[M^+]$, 381 (5), 257 (100), 239 (42), 225 (6), 179 (23), 155 (5), 91 (17).

**IR** (KBr): $\tilde{\nu}$ = 3481 (vs), 1707 (vs), 1596 (m), 1439 (m), 1386 (vs), 1319 (vs), 1180 (vs), 1119 (s), 1090 (s), 859 (s), 845 (s), 776 (s), 717 (vs), 700 (s), 660 (m), 551 (vs).

**HRMS** for **$C_{22}H_{20}O_6S$** (412.0981): found 412.0965.

| | | |
|---|---|---|
| **$C_{22}H_{20}O_6S$**: | required: | C: 64.06; H: 4.89; S: 7.77; |
| | found: | C: 63.91; H: 4.92; S: 7.53. |

## Synthesis of methyl 3-[hydroxy(phenyl)methyl]-4-[(methylsulfonyl)oxy]benzoate (154a)




Prepared according to TP from methyl 3-iodo-4-[(methylsulfonyl)oxy]benzoate (**147a**) (178 mg, 0.500 mmol), *i*PrMgCl (0.60 mL, 0.55 mmol, 0.90 M in THF) and benzaldehyde (106 mg, 1.00 mmol) at −78 °C. Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 1:1) yielded the title compound **154a** as a colourless solid (118 mg, 70%).

**mp.:** 151.5-152.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.11 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.78 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.61 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.38-7.28 (m, 5 H), 6.15 (s, 1 H), 3.90 (s, 3 H), 2.93 (s, 3 H), 2.64 (s_br, 1 OH).

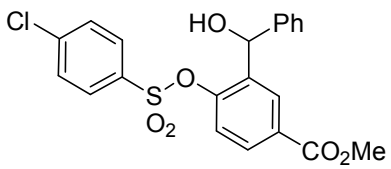
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.9, 149.5, 141.9, 136.8, 130.6, 130.4, 129.3, 128.7, 128.1, 126.7, 121.5, 70.5, 52.4, 38.0.

**MS** (70 eV, EI), *m/z* (%): 336 (6), 305 (9), 257 (100), 239 (17), 225 (6), 209 (6), 179 (42), 152 (11), 141 (5), 105 (20), 77 (14).

**IR** (KBr): $\tilde{\nu}$ = 3512 (s), 1703 (vs), 1593 (m), 1441 (m), 1374 (vs), 1304 (vs), 1258 (vs), 1193 (s), 1159 (vs), 1042 (s), 966 (vs), 916 (m), 852 (vs), 788 (vs), 773 (vs), 708 (vs), 527 (s).

**HRMS** for **$C_{16}H_{16}O_6S$** (336.0668): found: 336.0676.

## Synthesis of methyl 4-{[(4-chlorophenyl)sulfonyl]oxy}-3-[hydroxy(phenyl)methyl]benzoate (155a)




Prepared according to **TP 15** from methyl 4-{[(4-chlorophenyl)sulfonyl]oxy}-3-iodobenzoate (**149a**) (452 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF)

and benzaldehyde (212 mg, 2.00 mmol) at −78 °C. Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 1:1) yielded the title compound **155a** as a colourless solid (410 mg, 95%).

**mp.:** 140.5-141.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.26 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.92 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.77 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.51 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.34-7.28 (m, 5 H), 7.12 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 5.98 (s, 1 H), 3.90 (s, 3 OH).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 166.2, 150.2, 142.2, 142.0, 137.7, 134.1, 130.8, 130.7, 130.2, 129.8, 128.9, 128.2, 126.9, 121.8, 112.9, 70.3, 52.7.

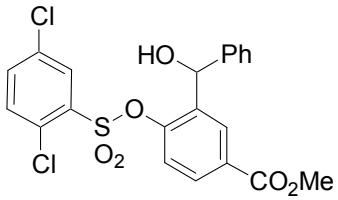
**MS** (70 eV, EI), *m/z* (%): 432 (1) [$M^+$], 401 (3), 257 (100), 239 (27), 209 (3), 179 (25), 159 (4), 111 (7), 77 (5), 51 (3).

**IR** (KBr): $\tilde{\nu}$ = 3470 (s), 1708 (vs), 1606 (m), 1587 (m), 1458 (m), 1439 (s), 1398 (m), 1378 (vs), 1290 (vs), 1258 (s), 1195 (s), 1186 (vs), 1171 (s), 1086 (s), 1043 (m), 856 (vs), 839 (s), 781 (vs), 764 (s), 702 (s), 616 (s).

**HRMS** for **$C_{21}H_{17}ClO_6S$** (432.0431): found 432.0418.

| | | |
|---|---|---|
| **$C_{21}H_{17}ClO_6S$**: | required: | C: 58.27; H: 3.96; S: 7.41; |
| | found: | C: 58.62; H: 4.24; S: 7.60. |

## Synthesis of methyl 4-{[(2,5-dichlorophenyl)sulfonyl]oxy}-3-[hydroxy(phenyl)methyl]benzoate (156a)




Prepared according to **TP 15** from methyl 4-{[(2,5-dichlorophenyl)sulfonyl]oxy}-3-iodobenzoate (**150a**) (486 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF) and benzaldehyde (212 mg, 2.00 mmol) at −78 °C. Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded the title compound **156a** as a colourless solid (404 mg, 87%).

**mp.:** 124.5-125.2 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.28 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.96 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.93 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.60-7.57 (m, 2 H), 7.33-7.26 (m, 5 H), 7.12 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 6.25 (s, 1 H), 3.89 (s, 3 H). 2.75 (s_br, 1 OH).

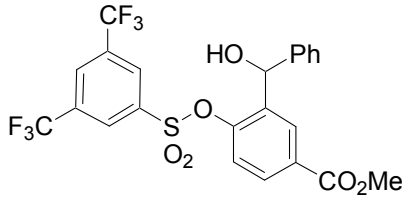
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.7, 149.5, 141.7, 137.4, 135.4, 135.2, 133.5, 133.4, 131.6, 131.5, 130.6, 130.3, 129.6, 128.5, 127.8, 126.4, 121.4, 69.6, 52.3.

**MS** (70 eV, EI), *m/z* (%): 466 (5) [$M^+$], 435 (28), 257 (100), 239 (71), 225 (7), 197 (7), 179 (31), 148 (13), 105 (21), 77 (17).

**IR** (KBr): $\tilde{\nu}$ = 3450 (m), 1714 (vs), 1610 (m), 1454 (s), 1439 (s), 1387 (vs), 1293 (vs), 1270 (s), 1248 (s), 1196 (s), 1163 (s), 1103 (s), 1042 (s), 907 (m), 860 (vs), 842 (s), 771 (s), 745 (s), 591 (s).

**HRMS** for **$C_{21}H_{16}Cl_2O_6S$** (466.0045): found: 466.0086.

## Synthesis of methyl 4-({[3,5-bis(trifluoromethyl)phenyl]sulfonyl}oxy)-3-[hydroxy(phenyl)methyl]benzoate (157a)




Prepared according to **TP 15** from methyl 4-({[3,5-bis(trifluoromethyl)phenyl]sulfonyl}oxy)-3-iodobenzoate (**151a**) (277 mg, 0.500 mmol), *i*PrMgCl (0.60 mL, 0.55 mmol, 0.90 M in THF) and benzaldehyde (106 mg, 2.00 mmol) at −78 °C. Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the title compound **157a** as a colourless solid (208 mg, 78%).

**mp.:** 111-112 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.86 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 8.33 (s_br, 2 H), 8.21 (s_br, 1 H), 7.99 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.30-7.19 (m, 6 H), 6.05 (s, 1 H), 3.92 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.7, 149.4, 141.5, 138.3, 136.9, 133.4 (q, $^2J$(C,F) = 35 Hz), 131.0, 130.9, 129.0 (m), 128.5, 128.2 (m), 126.9, 122.2 (q, $^1J$(C,F) = 273 Hz), 121.7, 112.9, 70.8, 52.9.

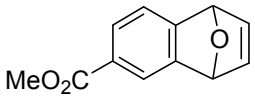
**MS** (70 eV, EI), *m/z* (%): 534 (3) [$M^+$], 515 (6), 503 (9), 257 (100), 239 (11), 213 (22), 179 (28), 152 (5), 105 (7).

**IR** (KBr): $\tilde{\nu}$ = 3472 (m), 1709 (vs), 1608 (m), 1445 (m), 1372 (vs), 1363 (vs), 1280 (vs), 1198 (vs), 1179 (vs), 1149 (vs), 1109 (vs), 910 (s), 862 (vs), 769 (m), 697 (m), 627 (m), 591 (m).

**HRMS** for **$C_{23}H_{16}F_6O_6S$** (534.0572): found: 534.0573.

| | | |
|---|---|---|
| **$C_{23}H_{16}F_6O_6S$**: | required: | C: 51.69; H: 3.02; |
| | found: | C: 51.95; H: 3.06. |

## Synthesis of 3,6-dihydro-1-methoxycarbonyl-3,6-epoxynaphthalenene (140d)




Prepared according to **TP 15** from methyl 4-{[(4-chlorophenyl)sulfonyl]oxy}-3-iodobenzoate (**149a**) (452 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF) and furan (304 mg, 5.00 mmol). Reaction time: 3 h. Purification by flash chromatography (pentane/diethyl ether = 2:1) yielded compound **140d** as a colourless solid (188 mg, 93%).

**mp**.: 99.5-101 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.85-7.83 (m, 1 H), 7.75 (dd, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 1.4 Hz, 1 H), 7.29-7.27 (m, 1 H), 7.05-6.98 (m, 2 H), 5.74-5.72 (m, 2 H), 3.80 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 167.9, 154.8, 149.5, 143.3, 141.4, 128.1, 127.3, 120.7, 119.9, 82.6, 82.5, 52.0.

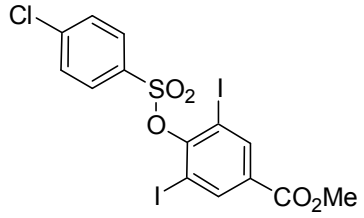
**MS** (70 eV, EI), *m/z* (%): 202 (11) [$M^+$], 176 (33), 174 (40), 171 (28), 146 (27), 143 (36), 129 (20), 115 (100), 89 (9), 75 (3), 63 (7).

**IR** (KBr): $\tilde{\nu}$ = 3014 (m), 1727 (vs), 1569 (m), 1453 (m), 1429 (m), 1275 (vs), 1244 (s), 1216 (m), 1191 (m), 1132 (s), 1072 (m), 994 (m), 976 (m), 901 (m), 876 (m), 854 (s), 829 (s), 791 (m), 769 (s), 725 (s), 675 (m), 645 (m).

**HRMS** for **$C_{12}H_{10}O_3$** (202.0630): found 202.0629.

**$C_{12}H_{10}O_3$**: required: C: 71.28; H: 4.98;
found: C: 71.23; H: 4.98.

## Synthesis of methyl 4-{[(4-chlorophenyl)sulfonyl]oxy}-3,5-diiodobenzoate (149b)




Prepared according to **TP 14** from methyl 4-hydroxy-3,5-diiodobenzoate (**146b**) (1.62 g, 4.00 mmol), 4-chlorobenzenesulfonyl chloride (1.16 g, 4.80 mmol). Reaction time: 12 h. Recrystallization from ethanol yielded **149b** as a colourless solid (2.21 g, 95%).

**mp**.: 140-141 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.39 (s, 2 H), 7.90 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.52 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 3.85 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 163.3, 154.7, 141.9, 141.7, 136.4, 131.1, 130.5, 129.9, 89.2, 52.9.

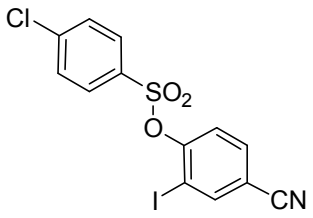
**MS** (70 eV, EI), *m/z* (%): 578 (43) [$M^+$], 402 (27), 372 (20), 276 (21), 245 (29), 175 (100), 158 (12), 111 (33), 63 (9).

**IR** (KBr): $\tilde{\nu}$ = 3435 (m), 1716 (vs), 1584 (m), 1543 (m), 1478 (m), 1441 (m), 1397 (s), 1371 (vs), 1279 (vs), 1208 (vs), 1184 (vs), 1174 (vs), 1126 (m), 1095 (s), 1047 (m), 965 (w), 873 (s), 873 (s), 764 (s), 743 (s), 718 (s), 645 (m), 616 (s), 557 (m), 478 (m).

**HRMS** for **$C_{14}H_9ClI_2O_5S$** (577.7949): found 577.7953.

**$C_{14}H_9ClI_2O_5S$**: required: C: 29.06; H: 1.57;
found: C: 29.29; H: 1.60.

## Synthesis of 4-cyano-2-iodophenyl 4-chlorobenzenesulfonate (149c)




Prepared according to **TP 14** from 4-cyano-2-iodophenol (**145b**) (1.22 g, 5.00 mmol), 4-chlorobenzenesulfonyl chloride (1.27 g, 6.00 mmol). Reaction time: 12 h. Recrystallization from ethanol yielded **149c** as a colourless solid (1.60 g, 77%).

**mp**.: 149-150 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.05 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.86 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.67 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.53 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.49 (d, $^3J$(H,H) = 8.4 Hz, 1 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 153.4, 144.0, 142.5, 134.2, 133.9, 130.6, 130.3, 123.8, 116.5, 113.1, 90.9.

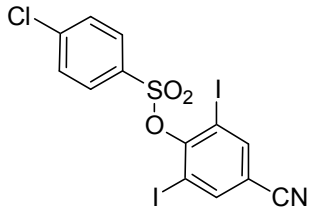
**MS** (70 eV, EI), *m/z* (%): 418 (13) [$M^+$], 175 (100), 111 (79), 89 (6), 75 (28), 62 (11).

**IR** (KBr): $\tilde{\nu}$ = 3066 (m), 2229 (vs), 1587 (s), 1570 (s), 1477 (vs), 1399 (m), 1361 (vs), 1283 (m), 1214 (vs), 1181 (s), 1174 (s), 1155 (s), 1087 (vs), 1016 (m), 918 (m), 875 (vs), 833 (s), 825 (vs), 809 (vs), 759 (s), 704 (m), 665 (m), 640 (vs), 588 (m), 542 (s), 490 (m).

**HRMS** for **$C_{13}H_7ClINO_3S$** (418.8880): found 418.8871.

**$C_{13}H_7ClINO_3S$**: required: C: 37.21; H: 1.68; N: 3.34;
found: C: 37.24; H: 1.68; N: 3.34.

## Synthesis of 4-cyano-2,6-diiodophenyl 4-chlorobenzenesulfonate (149d)




Prepared according to **TP 14** from 2,6-diiodo-4-cyanophenol (**146a**) (3.69 g, 10.0 mmol), 4-chlorobenzenesulfonyl chloride (2.53 g, 12.0 mmol). Reaction time: 12 h. Recrystallization from ethanol yielded **149d** as a colourless solid (4.40 g, 81%).

**mp**.: 167-167.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.12 (s, 2 H), 7.91 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.53 (d, $^3J$(H,H) = 8.9 Hz, 2 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 155.1, 143.8, 142.0, 136.2, 130.4, 129.9, 114.6, 113.9, 91.1.

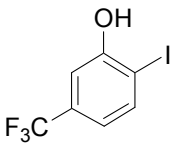
**MS** (70 eV, EI), *m/z* (%): 544 (10) [$M^+$], 371 (15), 242 (9), 175 (100), 111 (46), 88 (18), 75 (13), 62 (7).

**IR** (KBr): $\tilde{\nu}$ = 3063 (m), 2235 (s), 1586 (w), 1530 (w), 1420 (s), 1378 (vs), 1217 (s), 1183 (s), 1095 (s), 1053 (w), 882 (m), 819 (vs), 758 (s), 743 (w), 658 (m), 627 (vs), 596 (m), 551 (m).

**HRMS** for **$C_{13}H_6ClI_2NO_3S$** (544.7846): found 544.7834.

**$C_{13}H_6ClI_2NO_3S$**: required: C: 28.62; H: 1.11; N: 2.57;
found: C: 28.75; H: 1.13; N: 2.57.

## Synthesis of 2-iodo-5-(trifluormethyl)phenol (145d)




Prepared according to **TP 14** from 3-(trifluormethyl)phenol (1.62 g, 10.0 mmol), iodine (2.29 g, 9.00 mmol) and $Ag_2SO_4$ (3.09 g, 9.00 mmol). Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded compound **145d** as a colourless solid (2.47 g, 86%).

**mp**.: 35-36 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.79-7.76 (m, 1 H), 7.23-7.21 (m, 1 H), 6.95-6.91 (m, 1 H), 5.56 (s, 1 OH).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 155.6, 139.3, 132.8 (q, $^2J$(C,F) = 33 Hz), 123.4 (q, $^1J$(C,F) = 273 Hz), 118.84 (m), 111.9 (m), 89.8.

**MS** (70 eV, EI), *m/z* (%): 288 (100) [$M^+$], 269 (9), 161 (24), 133 (13), 113 (21), 83 (8), 71 (5), 63 (16).

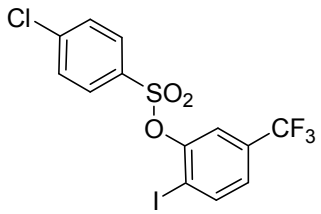
**IR** (KBr): $\tilde{\nu}$ = 3368 (m), 1601 (m), 1416 (vs), 1328 (vs), 1232 (vs), 1181 (vs), 1127 (vs), 1074 (vs), 1019 (s), 909 (m), 861 (m), 814 (m), 747 (m), 709 (w).

**HRMS** for **$C_7H_4F_3IO$** (287.9259): found 287.9284.

**$C_7H_4F_3IO$**: required: C: 29.19; H: 1.40;
found: C: 29.20; H: 1.49.

Spectral data match those reported in the literature.[135]

## Synthesis of 2-iodo-5-(trifluoromethyl)phenyl 4-chlorobenzenesulfonate (149e)




Prepared according to **TP 14** from 2-iodo-5-(trifluormethyl)phenol (**145d**) (1.44 g, 5.00 mmol), 4-chlorobenzenesulfonyl chloride (1.27 g, 6.00 mmol). Reaction time: 12 h. Recrystallization from ethanol yielded **149e** as a colourless solid (2.10 g, 91%).

**mp**.: 64.5-65.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.92 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 7.88 (d, $^3J$(H,H) = 8.4 Hz, 2 H), 7.58-7.52 (m, 3 H), 7.25 (m, 1 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 150.0, 141.9, 140.9, 133.8, 133.1 (q, $^2J$(C,F) = 33 Hz), 130.2, 129.8, 127.2 (q, $^1J$(C,F) = 273 Hz), 126.4 (q, $^4J$(C,F) = 4 Hz), 120.6 (q, $^4J$(C,F) = 4 Hz), 94.8.

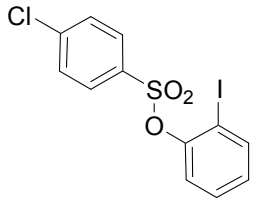
**MS** (70 eV, EI), *m/z* (%): 461 (17) [$M^+$], 297 (9), 175 (100), 160 (11), 132 (14), 111 (70), 75 (19), 63 (12).

**IR** (KBr): $\tilde{\nu}$ = 3098 (m), 1924 (w), 1605 (m), 1582 (w), 1477 (m), 1391 (vs), 1325 (vs), 1259 (m), 1199 (vs), 1174 (vs), 1123 (vs), 1024 (m), 916 (vs), 906 (s), 830 (m), 823 (m), 779 (vs), 757 (s), 714 (s), 656 (m), 619 (s), 555 (m), 485 (w), 475 (m).

**HRMS** for **$C_{13}H_7ClF_3IO_3S$** (461.8805): found: 461.8800.

**$C_{13}H_7ClF_3IO_3S$**: required: C: 33.75; H: 1.53; I: 27.43;
found: C: 33.78; H: 1.64; I: 27.27.

## Synthesis of 2-iodo-5-(trifluoromethyl)phenyl 4-chlorobenzenesulfonate (149f)




Prepared according to **TP 14** from 2-iodophenol (2.20 g, 10.0 mmol), 4-chlorobenzenesulfonyl chloride (2.54 g, 12.00 mmol). Reaction time: 12 h. Recrystallization from ethanol yielded **149f** as a colourless solid (3.66 g, 93%).

**mp**.: 89-90 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.85 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.78-7.74 (m, 1 H), 7.51 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.37-7.33 (m, 2 H), 7.03-6.95 (m, 1 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 149.8, 141.4, 140.2, 134.3, 130.3, 129.5, 128.6, 123.1, 112.6, 90.0.

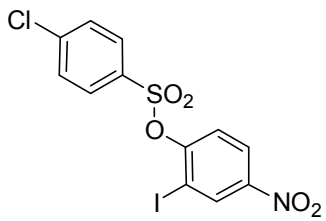
**MS** (70 eV, EI), *m/z* (%): 394 (62) [$M^+$], 298 (4), 218 (20), 190 (17), 175 (100), 139 (4), 111 (66), 92 (42), 75 (27), 64 (32).

**IR** (KBr): $\tilde{\nu}$ = 1584 (m), 1572 (m), 1462 (s), 1380 (vs), 1283 (m), 1199 (vs), 1174 (vs), 1085 (s), 866 (vs), 854 (vs), 774 (vs), 727 (vs), 619 (vs), 606 (vs), 557 (vs), 483 (m).

**HRMS** for **$C_{12}H_8ClIO_3S$** (393.8927): found: 393.8937.

| | | |
|---|---|---|
| **$C_{12}H_8ClIO_3S$**: | required: | C: 36.52; H: 2.04; |
| | found: | C: 36.89; H: 2.08; |

## Synthesis of 4-nitro-2-iodophenyl 4-chlorobenzenesulfonate (149g)




Prepared according to **TP 14** from 4-nitro-2-iodophenol (**69**) (2.65 g, 10.0 mmol), 4-chlorobenzenesulfonyl chloride (2.54 g, 12.0 mmol). Reaction time: 12 h. Recrystallization from ethanol yielded compound **149g** as a pale yellow solid (3.99 g, 91%).

**mp**.: 149-150 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.05 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.86 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.67 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.53 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.49 (d, $^3J$(H,H) = 8.4 Hz, 1 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 153.4, 144.0, 142.5, 134.2, 133.9, 130.6, 130.3, 123.8, 116.5, 113.1, 90.9.

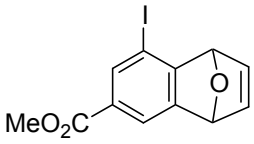
**MS** (70 eV, EI), *m/z* (%): 439 (24) [$M^+$], 175 (100), 159 (4), 139 (6), 111 (79), 91 (2), 75 (22), 63 (19).

**IR** (KBr): $\tilde{\nu}$ = 3096 (m), 1584 (m), 1572 (m), 1523 (vs), 1476 (s), 1460 (s), 1398 (s), 1361 (vs), 1347 (vs), 1292 (m), 1250 (m),1209 (vs), 1183 (s), 1173 (s), 1113 (m), 1087 (s), 1035 (m), 902 (m), 884 (vs), 845 (vs), 828 (s), 766 (vs), 754 (s), 737 (s), 710 (s), 652 (s), 615 (s), 548 (m), 483 (m).

**HRMS** for **$C_{12}H_7ClINO_5S$** (438.8778): found: 438.8774.

**$C_{12}H_7ClINO_5S$**: required: C: 32.79; H: 1.60; S: 7.29; N: 3.19;
found: C: 32.64; H: 1.43; S: 7.10; N: 3.14.

## Synthesis of 3,6-dihydro-1-methoxycarbonyl-7-iodo-3,6-epoxynaphthalene (141e)




Prepared according to **TP 15** from methyl 4-{[(4-chlorophenyl)sulfonyl]oxy}-3,5-diiodobenzoate (**149b**) (578 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF) and furan (304 mg, 5.00 mmol). Reaction time: 5 h. Purification by flash chromatography (pentane/diethyl ether = 3:1) yielded title compound **141e** as a colourless solid (231 mg, 71%).

**mp**.: 121.0-122.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.02 (d, $^4J$(H,H) = 1.4 Hz, 1 H), 7.77 (m, 1 H), 7.08-7.06 (m, 2 H), 5.87 (m, 1 H), 5.65 (m, 1 H), 3.87 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 165.5, 159.8, 151.3, 143.8, 141.9, 136.5, 129.3, 120.1, 86.0, 85.5, 82.4, 52.4.

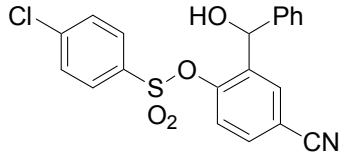
**MS** (70 eV, EI), *m/z* (%): 327 (15) [$M^+$], 301 (29), 270 (17), 240 (35), 173 (100), 142 (25), 129 (17), 114 (40), 102 (5),87 (11), 74 (7), 63 (13).

**IR** (KBr): $\tilde{\nu}$ = 3010 (m), 1724 (vs), 1571 (m), 1454 (m), 1431 (m), 1375 (m), 1274 (vs), 1234 (m), 1218 (m), 1193 (m), 1175 (m), 1163 (m), 1131 (s), 1073 (m), 993 (m), 976 (m), 898 (m), 872 (m), 855 (s), 794 (m), 766 (s), 715 (s), 672 (m), 645 (m).

**HRMS** for **$C_{12}H_9IO_3$** (327.9596): found: 327.9605.

**$C_{12}H_9IO_3$** : required.: C: 43.93; H: 2.76;
found: C: 43.70; H: 2.94.

## Synthesis of 4-cyano-2-[hydroxy(phenyl)methyl]phenyl 4-chlorobenzenesulfonate (155b)




Prepared according to **TP 15** from 4-cyano-2-iodophenyl 4-chlorobenzenesulfonate (**149c**) (210 mg, 0.500 mmol), *i*PrMgCl (0.60 mL, 0.55 mmol, 0.90 M in THF) and benzaldehyde (106 mg, 1.00 mmol) at −78 °C. Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the title compound **155b** as a colourless oil (187 mg, 93%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.96 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.75 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.57-7.51 (m, 3 H), 7.39-7.30 (m, 5 H), 7.24 (d, $^3J$(H,H) = 8.4 Hz, 1 H), 6.02 (s, 1 H), 4.65 (s_br, 1 OH).

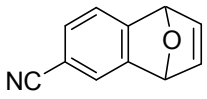
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 149.2, 141.7, 141.1, 138.5, 132.7, 132.4, 129.8, 129.5, 128.6, 128.0, 126.8, 126.5, 121.9, 111.2, 69.4.

**MS** (70 eV, EI), *m/z* (%): 399 (0.1) [$M^+$], 382 (2), 280 (3), 251 (2), 224 (100), 206 (47), 175 (10), 146 (27), 111 (18), 77 (11).

**IR** (KBr): $\tilde{\nu}$ = 3436 (m), 2234 (s), 1584 (m), 1480 (vs), 1397 (vs), 1384 (vs), 1224 (m), 1198 (vs), 1173 (vs), 1091 (vs), 853 (vs), 763 (s), 700 (s), 620 (m).

**HRMS** for **$C_{20}H_{14}ClNO_4S$** (399.0332): found: 399.0304.

## Synthesis of 7-cyano-1,4-dihydro-1,4-epoxynaphthalene (141c)




Prepared according to **TP 15** from 4-cyano-2-iodophenyl 4-chlorobenzenesulfonate (**149c**) (419 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF) and furan (304 mg, 5.00 mmol). Reaction time: 5 h. Purification by flash chromatography (pentane/diethyl ether = 1:1) yielded title compound **141c** as a colourless solid (132 mg, 78%).

**mp**.: 97.0-98.5°C.

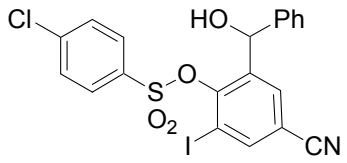
**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 7.45 (s, 1 H), 7.36-7.33 (m, 2 H), 7.06-7.00 (m, 2 H), 5.76-5.71 (m, 2 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 154.5, 150.5, 143.0, 142.5, 130.9, 122.7, 120.6, 119.1, 108.8, 82.3, 82.0.

**MS** (70 eV, EI), *m/z* (%): 169 (16) [$M^+$], 141 (100), 114 (48), 88 (11), 74 (5), 63 (12).

Spectral data match those of compound **141c.**

## Synthesis of 4-cyano-2-[hydroxy(phenyl)methyl]-6-iodophenyl 4-chlorobenzenesulfonate (155c)




Prepared according to **TP 15** from 4-cyano-2,6-diiodophenyl 4-chlorobenzenesulfonate (273 mg, 0.500 mmol), *i*PrMgCl (0.60 mL, 0.55 mmol, 0.90 M in THF) and benzaldehyde (106 mg, 2.00 mmol) at −78 °C. Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 3:1) yielded the title compound **155c** as a colourless solid (158 mg, 62%).

**mp.:** 124.9-127 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.98 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.95 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.80 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.60 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.38-7.28 (m, 5 H), 6.40 (s, 1 H).

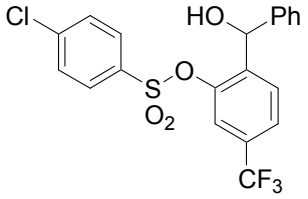
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 150.7, 142.7, 141.6, 135.0, 132.2, 130.7, 129.2, 129.0, 128.6, 128.0, 127.8, 126.0, 116.6, 113.9, 89.1, 71.3.

**MS** (70 eV, EI), *m/z* (%): 524 (5) [M−H]$^+$, 507 (11), 350 (100), 332 (78), 271 (27), 175 (19), 111 (33), 77 (18).

**IR** (KBr): $\tilde{\nu}$ = 3457 (m), 2237 (s), 1585 (m), 1433 (s), 1376 (vs), 1196 (s), 1090 (vs), 848 (vs), 798 (vs), 757 (s), 703 (vs), 637 (s), 591 (m).

**HRMS** for **$C_{20}H_{13}ClINO_4S$** (524.9299): found: 523.9231 [M−H]$^+$.

## Synthesis of 2-[hydroxy(phenyl)methyl]phenyl 4-chlorobenzenesulfonate (155d)



Prepared according to **TP 15** from 2-iodo-5-(trifluoromethyl)phenyl 4-chlorobenzenesulfonate (**149e**) (232 mg, 0.500 mmol), *i*PrMgCl (0.60 mL, 0.55 mmol, 0.90 M in THF) and benzaldehyde (106 mg, 1.00 mmol) at −78 °C. Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 3:1) yielded the title compound as a colourless oil (200 mg, 91%).

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 7.65 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.58 (br_d, $^3J$(H,H) = 8.2 Hz, 1 H), 7.44-7.32 (m, 3 H), 7.22-7.14 (m, 5 H), 7.10 (s_br, 1 H), 6.00 (s, 1 H), 2.70 (br_s, 1 OH).

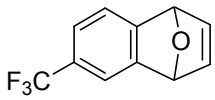
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 146.4, 141.9, 141.5, 141.3, 133.4, 131.2 (q, $^3J$(C,F) = 33 Hz), 129.9, 129.8, 129.7, 128.6, 128.0, 126.5, 125,7 (q, $^2J$(C,F) = 273 Hz), 124,4 (q, $^4J$(C,F) = 4 Hz), 118.9 (q, $^4J$(C,F) = 4 Hz), 69.7.

**MS** (70 eV, EI), *m/z* (%):442 (0.1) [$M^+$], 423 (11), 407 (14), 363 (363 (25), 323 (20), 267 (100), 249 (34), 189 (25), 175 (7), 111 (14), 105 (8), 77 (8).

**IR** (KBr): $\tilde{\nu}$ = 3543 (m), 3414 (m), 1586 (m), 1478 (m), 1415 (s), 13854 (s), 1326 (vs), 1192 (vs), 1174 (vs), 1131 (vs), 1088 (vs), 922 (s), 831 (s), 816 (s), 787 (vs), 758 (m), 723 (m), 700 (m), 621 (m), 557 (m).

**HRMS** for **$C_{20}H_{14}ClF_3O_4S$** (442.0253): found: 442.0292.

## Synthesis of 1,4-dihydro-7-trifluoromethyl-1,4-epoxynaphthalene (141f)




Prepared according to **TP 15** from 2-iodo-5-(trifluoromethyl)phenyl 4-chlorobenzenesulfonate (**149e**) (463 mg, 1.00 mmol), *i*PrMgCl (1.6 mL, 1.1 mmol, 0.70 M in THF) and furan (304 mg, 5.00 mmol). Reaction time: 3 h. Purification by flash chromatography (pentane/diethyl ether = 9:1) yielded title compound **141f** as a colourless oil (159 mg, 75%).

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C): δ = 7.45 (s, 1 H), 7.32-7.27 (m, 2 H), 7.06-7.02 (m, 2 H), 5.75-5.72 (m, 2 H).

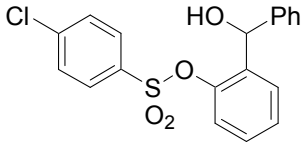
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C): δ = 153.3, 150.3, 143.1, 142.7, 127.6 (q, $^2J$(C,F) = 30 Hz), 123.2 (q, $^1J$(C,F) = 272 Hz), 122.9 (q, $^3J$(C,F) = 4 Hz), 119.9, 116.9 (q, $^3J$(C,F) = 4 Hz), 82.1, 77.3.

**MS** (70 eV, EI), *m/z* (%): 212 (10) [$M^+$], 199 (38), 184 (100), 164 (22), 151 (13), 13 (23), 115 (72), 107 (4), 88 (5), 75 (4), 63 (6).

**IR** (KBr): $\tilde{\nu}$ = 1427 (w), 1355 (m), 1321 (vs), 1275 (s), 1164 (s), 1121 (vs), 1049 (s), 994 (m), 871 (m), 851 (s), 837 (s), 750 (w), 698 (m), 636 /m), 543 (w).

**HRMS** for **$C_{11}H_7F_3O$** (212.0449): found 212.0461.

## Synthesis of 2-[hydroxy(phenyl)methyl]phenyl 4-chlorobenzenesulfonate (155e)




Prepared according to **TP 15** from 2-iodophenyl 4-chlorobenzenesulfonate (**149f**) (394 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF) and benzaldehyde (212 mg, 2.00 mmol) at −78 °C. Reaction time: 1 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded the title compound **155e** as a colourless oil (355 mg, 95%).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.81 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.53 (d, $^3J$(H,H) = 8.9 Hz, 2 H), 7.45 (dd, $^3J$(H,H) = 7.5 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.40-7.23 (m, 7 H), 7.00-6.97 (m, 1 H), 6.13 (d, $^2J$(H,H) = 3.3 Hz, 1 H), 2.66 (d, $^2J$(H,H) = 3.3 Hz, 1 OH).

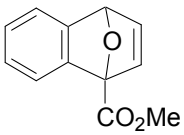
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 146.7, 142.1, 137.3, 133.9, 129.8, 129.7, 129.3, 128.8, 128.4, 127.8, 127.5, 127.0, 126.4, 121.6, 69.5.

**MS** (70 eV, EI), *m/z* (%): 374 (29) [$M^+$], 357 (34), 295 (68), 269 (19), 255 (14), 199 (100), 181 (37), 121 (28), 105 (16), 7 (16).

**IR** (KBr): $\tilde{\nu}$ = 3542 (w), 1584 (w), 1478 (m), 1452 (m), 1377 (vs), 1190 (vs), 1155 (s), 1087 (vs), 1014 (m), 883 (s), 835 (s), 779 (vs), 764 (vs), 699 (m), 623 (m), 554 (s).

**HRMS** for **$C_{19}H_{15}ClO_4S$** (374.0380): found: 374.0377.

## Synthesis of methyl 1,4-epoxynaphthalene-1(4H)-carboxylate (141g)




Prepared according to **TP 15** from 2-iodophenyl 4-chlorobenzenesulfonate (**149f**) (394 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF) and methyl-2-furoate (630 mg, 5.00 mmol). Reaction time: 6 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded compound **141g** as a pale yellow solid (101 mg, 50%).

**mp.:** 81-83 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.53-7.49 (m, 1 H), 7.44-7.40 (m, 1 H), 7.24-7.21 (m, 2 H), 7.18-7.15 (m, 2 H), 5.96 (d, $^3J$(H,H) = 1.8 Hz, 1 H), 4.14 (s, 3 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 168.2, 147.7, 147.2, 143.6, 142.5, 125.7, 125.1, 120.6, 119.9, 90.4, 82.5, 52.9.

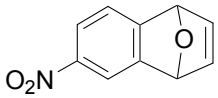
**MS** (70 eV, EI), *m/z* (%): 202 (6) [$M^+$], 189 (19), 176 (34), 145 (22), 142 (24), 131 (18), 115 (100), 102 (8), 89 (21), 77 (12), 63 (15).

**IR** (KBr): $\tilde{\nu}$ = 1763 (vs), 1742 (vs), 1444 (s), 1355 (s), 1328 (s), 1277 (m), 1201 (s), 1170 (s), 1105 (s), 1050 (m) 1034 (m), 863 (m), 763 (s), 725 (m), 694 (m), 639 (s).

**HRMS** for **$C_{12}H_{10}O_3$** (202.0630): found: 202.0617.

Spectral data match those of the literature.[136]

## Synthesis of 1,4-dihydro-7-nitro-1,4-epoxynaphthalene (141h)




Prepared according to **TP 15** from 2-iodo-4-nitrophenyl 4-chlorobenzenesulfonate (439 mg, 1.00 mmol), PhMgCl (0.65 mL, 1.1 mmol, 1.6 M in THF) and furan (304 mg, 5.00 mmol). Reaction time: 12 h. Purification by flash chromatography (pentane/diethyl ether = 4:1) yielded title compound **141h** as a pale yellow solid (147 mg, 78%).

**mp**.: 104.0-105.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 8.03 (d, $^4J$(H,H) = 2.2 Hz, 1 H), 7.95 (dd, $^3J$(H,H) = 8.4 Hz, $^4J$(H,H) = 2.2 Hz, 1 H), 7.35 (d, $^4J$(H,H) = 8.4 Hz, 1 H), 7.10-7.02 (m, 2 H), 5.80-5.78 (m, 2 H).

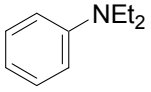
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 156.8, 151.7, 146.2, 143.8, 143.5, 142.7, 122.7, 120.5, 115.6, 82.4.

**MS** (70 eV, EI), *m/z* (%): 189 (7) [$M^+$], 163 (18), 144 (16), 115 (100), 89 (18), 77 (4),64 (11), 51 (3).

**IR** (KBr): $\tilde{\nu}$ = 3434 (w), 1602 (m), 1543 (m), 1518 (vs), 1445 (m), 1380 (w), 1363 (m), 1340 (vs), 1317 (s), 1301 (m), 1277 (s), 1198 (m), 1172 (m), 1140 (s), 1056 (s), 988 (s), 869 (s), 849 (vs), 749 (s), 753 (s), 734 (m), 700 (vs), 673 (m), 642 (s), 568 (m), 543 (m).

**HRMS** for **$C_{10}H_7NO_3$** (189.0426): found: 189.0430.

## Synthesis of *N,N*-diethylaniline (156)




Prepared according to **TP 15** from 2-iodophenyl 4-chlorobenzenesulfonate (**149f**) (394 mg, 1.00 mmol), *i*PrMgCl (1.2 mL, 1.1 mmol, 0.90 M in THF), and a solution of magnesium

diethylamide, prepared from diethylamine (219 mg, 3.00 mmol) and MeMgCl (1.1 mL, 3.1 mmol, 2.8 M in THF) in THF (3 mL). Reaction time: 2 h. Purification by flash chromatography (pentane/diethyl ether = 29:1) yielded title compound **156** as a pale yellow oil (101 mg, 68%).

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C): δ = 7.34-7.21 (m, 2 H), 6.71-6.67 (m, 3 H), 3.38 (q, $^{3}J$(H,H) = 7.0 Hz, 4 H), 1.18 (t, $^{3}J$(H,H) = 7.0 Hz, 6 H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C): δ = 148.2, 129.7, 115.9, 112.3, 44.7, 13.0.

**MS** (70 eV, EI), *m/z* (%): 149 (39) [$M^+$], 134 (100), 120 (43), 91 (3), 77 (12).

Spectral data match those of the literature.[137]

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# Lebenslauf

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5.) I. Sapountzis, P. Knochel "A New General Preparation of Polyfunctional Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Nitroarenes" *J. Am. Chem. Soc.* **2002**, *124*, 9390-9391.

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**Übersichtsartikel und Bücher:**

1.) P. Knochel, W. Dohle, N. Gommermann, F. F. Kneisel, F. Kopp, T. Korn, I. Sapountzis and V. A. Vu "Highly Functionalized Magnesium Organometallics Prepared via a Halogen-Metal Exchange" *Angew. Chem.* **2003**, *115*, 4438-4456; *Angew. Chem. Int. Ed.* **2003**, *42*, 4302-4320.

2.) P. Knochel, I. Sapountzis, N. Gommermann "Carbon-Carbon Bond Forming Reactions Mediated by Organomagnesium Reagents" in A. de Meijere, F. Diederich (Eds.) *Metal-Catalyzed Cross-Coupling Reactions*, Wiley-VCH, Weinheim, **2004**, im Druck.

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I. Sapountzis, P. Knochel "Compatibility of Nitro-Group with Grignard Reagents **-** Extending the Scope of the Iodine-Magnesium Exchange Reaction" (Poster P15) **ICOMC 20**, 07. - 12. July 2002 in Korfu, Griechenland.

I. Sapountzis, P. Knochel " New Applications of Functionalized Grignard-Reagents in the Preparation of Diarylamines "(Poster 20), **Schering Chemistry Workshop** , 20. - 23. August 2003 in Berlin, Deutschland.

**Vorträge:**

I. Sapountzis, P. Knochel "Compatibility of Nitro-Group with Grignard Reagents – Extending the Scope of the Iodine-Magnesium Exchange Reaction" Vortrag und Posterpräsentation (Poster A-29), **ORCHEM 2002**, 12. - 14. September 2002 in Bad Nauheim, Deutschland.

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**Sprachkenntnisse:**

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|---|---|
| Deutsch | Muttersprache |
| Griechisch | Muttersprache |
| Englisch | fließend in Wort und Schrift |
| Französisch | ausbaufähig |

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