Dissertation zur Erlangung des Doktorgrades
der Fakultät für Chemie und Pharmazie
der Ludwig-Maximilians-Universität München

Preparation of Functionalized Organomagnesium Reagents by *ortho*-Magnesiation, Sulfoxide-, Iodine- and Bromine-Magnesium Exchange Reactions.

Christian Bernhard Rauhut

aus

München

2008

Erklärung
Diese Dissertation wurde im Sinne von § 13 Abs. 3 der Promotionsordnung vom 29. Januar 1998 von Professor Dr. Paul Knochel betreut.

Ehrenwörtliche Versicherung
Diese Dissertation wurde selbstständig, ohne unerlaubte Hilfe erarbeitet.

München, am 06.12.2007

Christian Bernhard Rauhut

Dissertation eingereicht am 30.10.2008

1. Gutachter: Prof. Dr. Paul Knochel

2. Gutachter: Prof. Dr. Manfred Heuschmann

Mündliche Prüfung am 10.12.2008

This work was carried out from November 2005 to October 2008 under the guidance of Prof. Knochel at the Fakultät für Chemie und Pharmazie der Ludwig-Maximilians-Universität, Munich.

I would like to thank Prof. Dr. Paul Knochel, for giving me the opportunity of doing my Ph.D.in his group, for his support and for his guidance in the course of my scientific research.

I am also very grateful to Prof. Dr. Manfred Heuschmann for agreeing to be my "Zweitgutachter", as well as Prof. Dr. I. P. Lorenz, Prof. Dr. H. Langhals, Prof. Dr. H. Zipse and Prof. Dr. H. R. Pfaendler for the interest shown in this manuscript by accepting to be referees.

I thank Georg Manolikakes, Albrecht Metzger, Fabian Piller, Christoph Rohbogner and Stefan Wunderlich for the careful correction of this manuscript.

I thank all past and present co-workers I have met in the Knochel's group for their kindness and their help. Special thanks to Dr. Murthy Cheemala, Dr. Srinivas Dubbaka and his wife Thresen, Dr. Ching-Yuan Liu and his wife Chaofang for some special lectures in asian cooking and culture.

I would like to thank Laurin Melzig for fruitful collaboration in the sulfoxide chemistry, and my lab F2.004 for not complaining too much about my sulfur chemistry and for all the fun we had.

I would also like to thank Beatrix Cammelade,Vladimir Malakov, Simon Matthe, and Yulia Tsvik for their help in organizing everyday life in the lab and in the office, as well as the analytical team of the LMU for their invaluable help.

Special thanks to the БЦТИАД-crew, who helped me a lot keeping my fine motoric skills on a high level, and all the people who joined our out-door and sportive activities.

Very special thanks to my family and to Kathrin for their love and endless support.

Parts of this Ph. D. thesis have been published:

1) Christian B. Rauhut, Viet Anh-Vu, Frasier F. Fleming, Paul Knochel, „Preparation of Functionalized Alkylmagnesium Derivatives Using an I/Mg-Exchange", *Org. Lett.* **2008**, *10*, 1187.
2) Christian B. Rauhut, Laurin Melzig, Paul Knochel, „*Meta*- and *Para*-Difunctionalization of Arenes via a Sulfoxide-Magnesium Exchange Reaction", *Org. Lett.* **2008**, *10*, 3891.
3) Laurin Melzig, Christian B. Rauhut, Paul Knochel, „*Meta*-and *Para*-Difunctionalization of Arenes via a *Ortho*-Magnesiation and a Subsequent Sulfoxide-Magnesium Exchange", *Synthesis* ***2009****, manuscript in press*.
4) Christian B. Rauhut, Christian Cervino, Arkady Krasovskiy, Paul Knochel, „Stereoselective Preparation of Cyclopropylmagnesium Reagents via Br/Mg-exchange using *i*PrMgCl·LiCl in the Presence of Dioxane", *Synlett* ***2009***, 67.
5) Christian B. Rauhut, Laurin Melzig, Paul Knochel, „Functionalization of Furan and Thiophene via *ortho*-Magnesiation and Subsequent Sulfoxide-Magnesium Exchange Reaction", *manuscript in preparation*.

to Kathrin, my love.

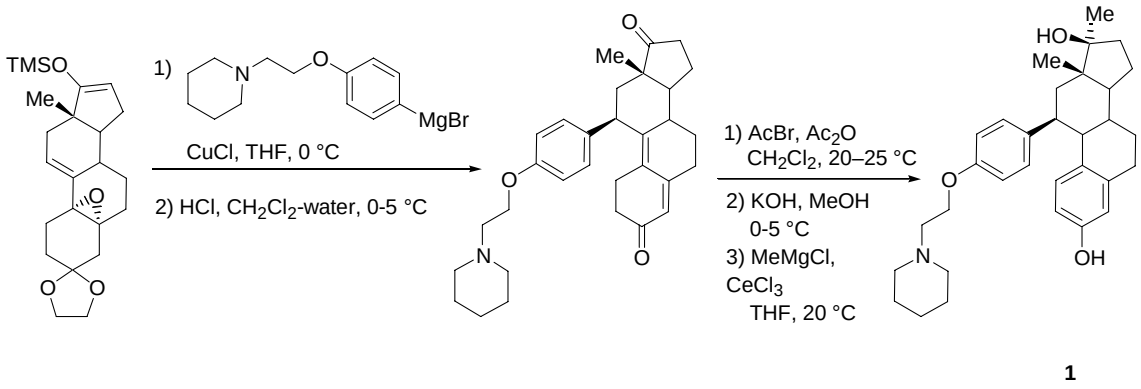
Abbreveations:

Ac	acetyl
aq.	aqueous
Ar	aryl
CH_2Cl_2	dichloromethane
dba	trans,trans-dibenzyledenacetone
DMF	N,N-dimethylforamid
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)pyrimidone
DMSO	dimethyl sulfoxide
Eq.	equation
equiv	equivalent
EI	electron-impact
Et	ethyl
FG	functional group
GC	gas chromatography
h	hour
HRMS	high resolution mass spectrospcopy
*i*Pr	*iso*-propyl
IR	infra-red
J	coupling constant (NMR)
LDA	lithium diisopropylamide
M	molarity
m	*meta*
m	multiplett (NMR)
Me	methyl
min	minute
mp.	melting point
MS	mass spectroscopy
NMP	N-methyl-2-2pyrrolidine
NMR	nuclear magnetic resonance
o	*ortho*
p	*para*
Ph	phenyl

SET	single electron transfer
S-Phos	2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl
*t*Bu	*tert*-butyl
tfp	tri-(2-furyl)phosphine
THF	tetrahydrofuran
TLC	thin layer chromatography
TMEDA	N,N,N',N'-tetrametyhlethylendiamine
tmp	2,2,6,6-tetramethylpiperidyl
TP	typical procedure

1. Introduction

Carbon-carbon bond formation is of central interest in preparative organic chemistry, since it allows the formation of complex structures. Organometallic chemistry contributes a major part to this objective by providing a range of reactive and selective reagents. From highly reactive organolithium derivatives, across magnesium reagents to zinc or boron compounds, a variety of organometallic intermediates have found numerous applications in synthetic chemistry.[1] Many of these approaches were established in modern process chemistry.[2] Examples are the preparation of Tamoxifen,[3] with the addition of phenylmagnesium bromide to an intermediate keton, or the preparation of 17α-methyl-11β-arylestradiol (**1**) for osteoporosis treatment (Scheme 1).[4]



Scheme 1: Stereoselective preparation of 17α-methyl-11β-arylestradiol (**1**).

[1] a) Hartung, C. G.; Snieckus V. in *Modern Arene Chemistry*, Astruc D., Ed., Wiley-VCH, Weinheim, **2002**, 330; b) Schlosser, M. *Organometallics in Synthesis: A Manual*, Schlosser, M., Ed., Wiley, Chichester, **2002**, 1; c) Knochel, P. *Handbook of Functionalized Organometallics*, Knochel, P., Ed.,Wiley-VCH, Weinheim, **2005**; d) Boudier, A.; Bromm L. O.; Lotz, M.; Knochel P. *Angew. Chem., Int. Ed.* **2000**, *39*, 4414.

[2] Wu, G. G.; Huang, M. in *Organometallics in Process Chemistry,* Larsen, R. D. Ed., Springer, Berlin, **2004**, 1.

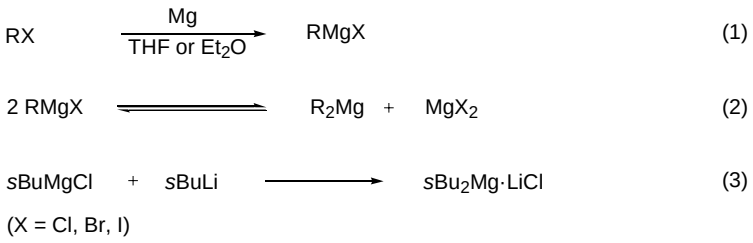
[3] a) Harper, M. J. K.; Walpole, A. L. *Nature* **1966**, *212*, 87; b) Bedford, G. R.; Richardson, D. N. *Nature* **1966**, *212*, 733; c) Robertson, D. W.; Katzenellenbogen, J. A. *J. Org. Chem.* **1982**, *47*, 2387; d) McCague, R. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1011.

[4] Larkin, J. P.; Wehrey, C.; Boffelli, P.; Lagraulet, H.; Lemaitre, G.; Nedelec, A.; Prat, D. *Org. Process Res. Dev*. **2002**, *6*, 20.

1.1. Preparation of organomagesium reagents

1.1.1. Direct oxidative insertion of magnesium in organic halides

Since the first preparation of organomagnesium reagents by *Victor Grignard* in 1901,[5] a range of improvements was achieved. Still, the most convenient method for the preparation of organomagnesium reagents is the oxidative insertion of Mg into carbon-halogen bonds (Scheme 2, Eq. 1). Although the detailed mechanism of the insertion is not clear, a radical pathway is generally accepted.[6] The induction period for the insertion depends on the amount of moisture present, and the surface of the magnesium turnings which is in general passivated, i.e. coated with magnesium oxides and $Mg(OH)_2$. These coatings can be removed by addition of Grignard reagent, 1,2-dibromoethane, or diisobutylaluminium hydride which is used in process chemistry.[7] The discovery of the *Schlenk* equilibrium revealed the behaviour of organomagnesium reagents in etheral solutions (Eq. 2).[8] Depending on temperature, solvent and additives (e.g. 1,4-dioxane or [15]-crown-5)[9] the equilibrium can be shifted from the mono alkylmagnesium species to the dialkyl magnesium species. *Knochel* demonstrated that the more reactive dispecies can be generated from the corresponding magnesium and lithium compounds avoiding the *Schlenk* equilibrium (Eq. 3).

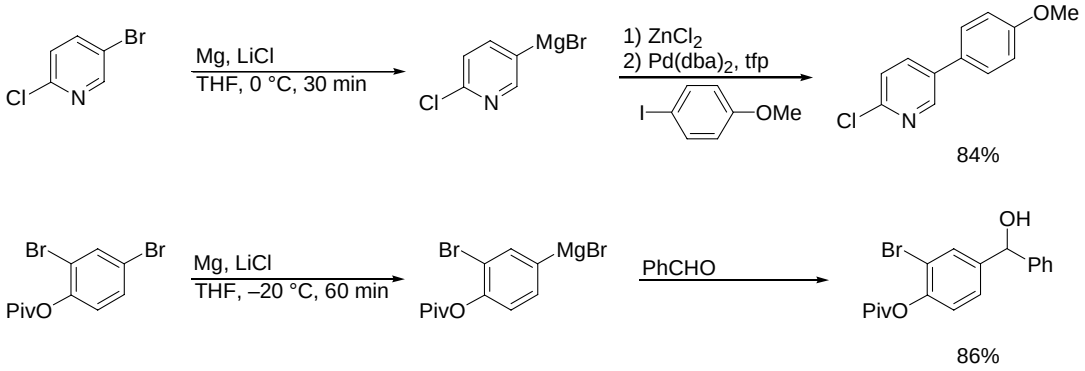


Scheme 2: Formation of the dialkyl magnesiumspecies by the *Schlenk* equilibrium and the alternative formation by transmetalation.

The use of activated *Rieke* magnesium, prepared by the reaction of lithium naphthalenide with magnesium chloride, opened new perspectives in organometallic

[5] Grignard, V. *Ann. Chim.* **1901**, *24*, 433.
[6] a) Walborsky, H. M. *Acc. Chem. Res.* **1990**, *23*, 286; b) Garst, J. F. *Acc. Chem. Res.* **1991**, *24*, 95; c) Rogers, H. R.; Hill, C. L.; Fujiwara, Y.; Rogers, R. J.; Mitchell, H. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1980**, *102*, 217; d) Garst, J. F. in *Grignard Reagents*, Richey, Jr., H. G., Ed, Wiley, Chicester, **2000**, 185; e) Kharash, M. S.; Reinmuth, O. in *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, New York, **1954**; f) Hamdouchi, C.; Walborsky, H. M. in *Handbook of Grignard-Reagents*, Silverman, G. S.; Rakita, P. E., Eds, Marcel Dekker, New York, **1995**, 145; g) Oshima, K. in *Main Group Metals in Organic Synthesis*, Yamamoto, H.; Oshima, K, Eds, Wiley-VCH, Weinheim, **2004**.
[7] Tilstam, U.; Weinmann, H. *Org. Process Res. Dev.* **2002**, *6*, 906.
[8] Schlenk, W.; Schlenk, Jr., W. *Chem. Ber.* **1929**, *62*, 920.
[9] Krasovskiy, A.; Straub, B. F.; Knochel, P. *Angew. Chem. Int. Ed.* **2006**, *45*, 159.

chemistry.[10] With this highly reactive magnesium it was possible to perform a magnesium insertion into carbon-halogen bonds of compounds bearing other sensitive functionalities. But, using the pyrophoric magnesium on large scale involved questionable safety hazards. In contrast, *Knochel* reported recently that the utilization of LiCl in combination with magnesium turnings or powder and low reaction temperatures allowed to the preparation of various functionalized aryl and heteroaryl magnesium derivatives (Scheme 3).[11]



Scheme 3: Oxidative direct insertion of Mg into carbon-halogen bonds under mild conditions.

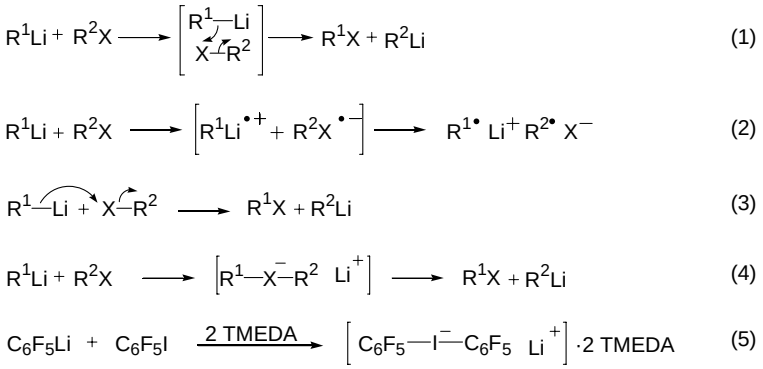
1.1.2. Halogen-magnesium exchange reactions

The main drawbacks of the direct insertion of magnesium in carbon-halogen bonds are still the incompatibility of some reduceable electrophilic functional groups and the exothermic reaction itself which is not easy to control during industrial processes.[12] One alternative for the preparation of functionalized organomagnesium reagents is the halogen-magnesium exchange reaction, first demonstrated by *Prévost*.[13] He was able to prepare cinnamylmagnesium bromide from cinnamyl bromide and EtMgBr in 14% yield. The driving force of the halgon/magnesium-exchange reaction is the stability of the resulting Grignard reagent ($sp > sp^2(vinyl) > sp^2(aryl) > sp^3(prim) > sp^3(sec)$).[14] For the halogen-metal exchange reaction three general mechanistic models are present in

[10] a) Rieke, R. D. *Science* **1989**, *246*, 1260; b) Rieke, R. D.; Hanson, M. V. *Tetrahedron* **1997**, *53*, 1925; c) Lee, J.; Velarde-Ortiz, R.; Guijarro, A.; Wurst, J. R.; Rieke, R. D. *J. Org. Chem.* **2000**, *65*, 5428.
[11] Piller, F. M.; Appukkuttan, P.; Gavryushin, A; Helm, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2008**, *47*, 6802.
[12] Bush, F. R.; De Antonis, D. M. in *Grignard Reagents: New Developements*, Richey H. G. Jr, Ed, Wiley, New York, **2000**, 165.
[13] Prévost, C. *Bull. Soc. Chim. Fr.* **1931**, *49*, 1372.
[14] Hauk, D.; Lang, S.; Murso, A. *Org. Process Res. Dev*. **2006**, *10*, 733.

literature.[15] The four center transition state, a radical mechanism and a nucleophilic attack on the halogen atom leading to an ate-complex.

The four center transition state model describes the exchange reaction as a concerted, if not entirely synchronous, bond-breaking and bond-making mechanism (Scheme 4, Eq 1).[16]



Scheme 4: Four centre transition state, radical and ate-complex theory are the three models for the halogen-metal exchange.

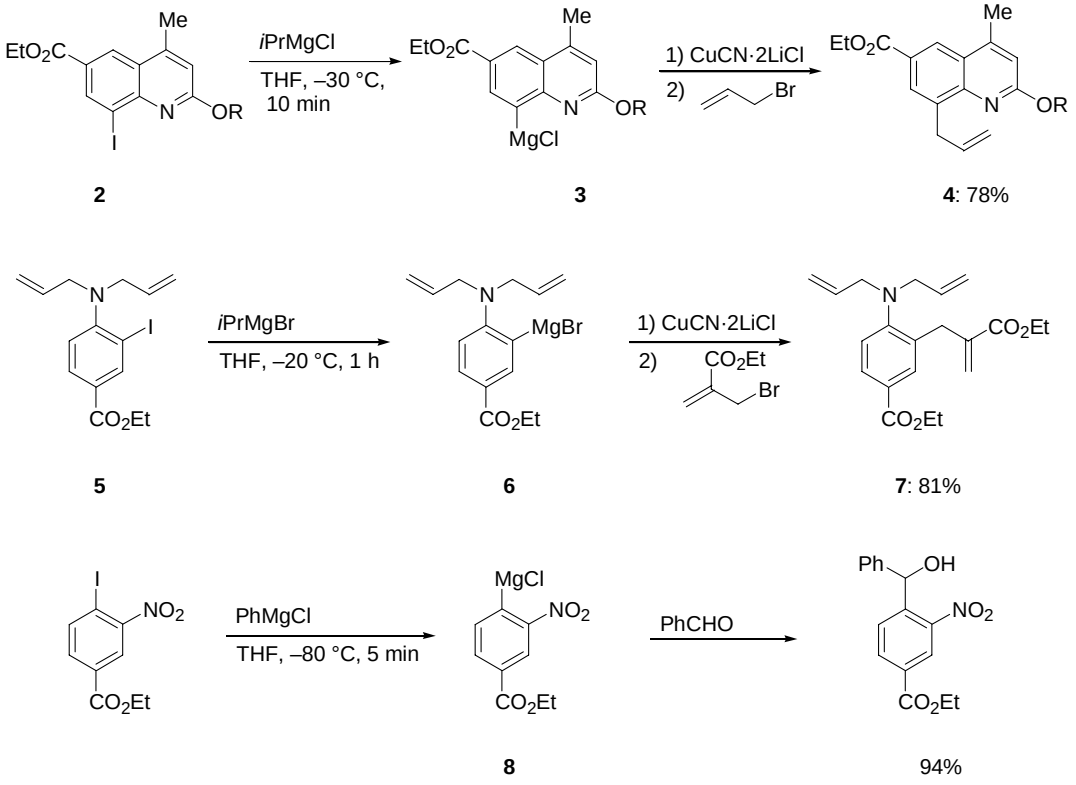
In the radical theory, the first step is a SET leading to a caged ion radical pair (Eq. 2). Then, the lithium cation and the halogen anion can be extruded and the radicals can undergo recombination, disproportionation or diffusion processes giving different products. During the reaction of *n*BuLi with *n*BuBr in cumene, *Bryce-Smith* observed a huge amount of dimerized solvent which can be explained by radical reaction with solvent molecules and their recombination.[17]

The most favoured explanation developed from the "X-philic" reaction (Eq. 3)[18] to the ate-complex theory (Eq. 4). This model is supported by the isolation and X-ray characterization of an at room temperature stable ate-complex (Eq. 5).[19] Recently, quantum chemical calculations were published, strengthening the ate-complex theory in the case of a halogen-magnesium exchange reaction.

Tamborski reported the influence of the halogen atom on the exchange rate for aromatic systems (I>Br>Cl>>F), and the rate-enhancing effect of electron withdrawing fluoride substituents.[20]

[15] Bailey, F. M.; Patricia, J. J. *J. Organomet. Chem.* **1988**, *352*, 1 and references therein.
[16] Wakefield, B. J. in *The Chemistry of Organolithium Compounds*, Pergamon Press, New York, **1974**.
[17] Bryce-Smith, D. *J. Chem. Soc.* **1956**, 1603.
[18] Zefirov, N. S.; Makhon`khov, D. I. *Chem. Rev.* **1982**, *82*, 615.
[19] Farnham, W. B.; Calabrese, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 2449.
[20] Tamborski, C.; Moore, G. J. *J. Organomet. Chem.* **1971**, *26*, 153.

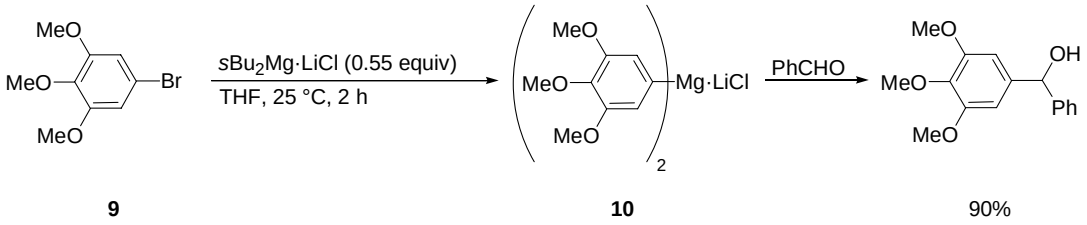
The practical value of the halogen-magnesium exchange was demonstrated by the preparation of various functionalized aryl and heteroaryl magnesium derivatives.[21] Thus, the functionalized iodoquinoline **2** was rapidly converted to the corresponding organometallic compound **3**, furnishing after the reaction with allyl bromide the quinoline derivative **4** in 78% yield (Scheme 5). The aniline derivative **5** was converted in 1 h to the Grignard reagent **6**, and then reacted with ethyl 2-bromo-methacrylate giving the ester **7** in 81% yield.[22] Even nitro groups are compatible with an I/Mg-exchange reaction leading to arylmagnesium chlorides of type **8**, even though it is necessary to use PhMgCl instead of the more nucleophilic *i*PrMgCl.[23]



Scheme 5: Smooth I/Mg-exchange reactions using aromatic iodides.

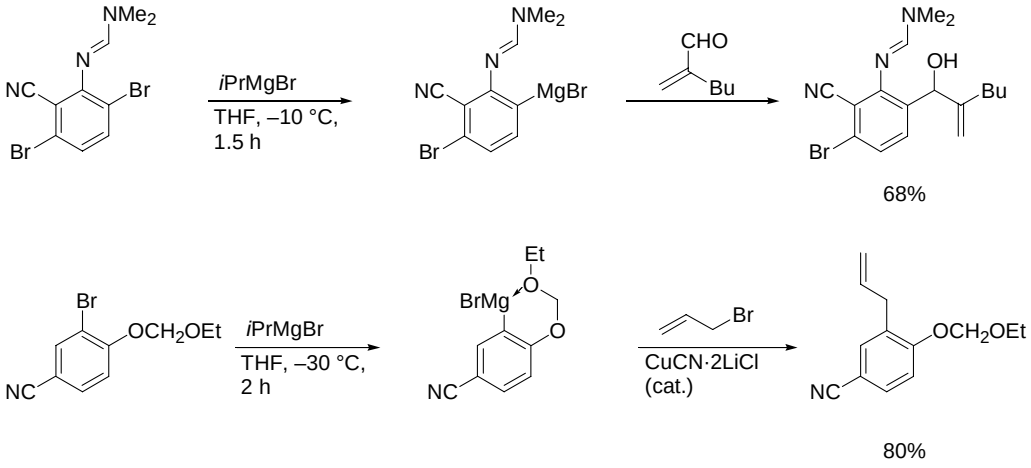
Knochel also reported efficient reagents for the Br/Mg-exchange reaction, even for the conversion of electron rich substrates, like **9**, which allow a convenient preparation of functionalized arylmagnesium reagents of type **10** starting from the cheaper aryl bromides (Scheme 6).

[21] For a review see: Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F. F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V.-A. *Angew. Chem. Int. Ed.* **2003**, *42*, 4302.
[22] a) Staubnitz, A.; Dohle, W.; Knochel, P. *Synthesis* **2003**, 223; b) Jensen, A. E.; Dohle, W.; Sapountzis, I.; Lindsay, D. M.; Vu, V.-A.; Knochel, P. *Synthesis*, **2002**, 63.
[23] Sapountzis, I.; Knochel, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 1610.



Scheme 6: Br/Mg-exchange performed with an electron rich aryl bromide.

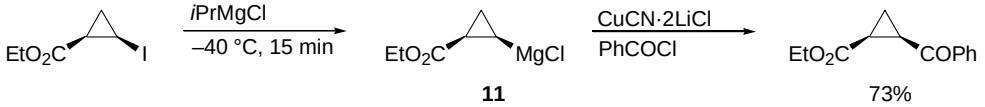
The exchange rate is increased when coordinating functionalities are present in *ortho* position. These groups are able to form a complex with the exchange reagent and allow therefore a smooth magnesiation at low temperatures (Scheme 7).[24]



Scheme 7: Br/Mg-exchange reactions supported by chelating functionalities.

The halogen-magnesium exchange on sp^3-hybridized carbon is more challenging, since the gain of energy is muss less important (both reagents have the same hybridization). In strained systems, like cyclopropyl bromides, the carbon-carbon bond has an increased *p*-character compared to the carbon-halogen bond, reducing the strain. Following this assumption, the *s*-character of the carbon-halogen bond is increased compared to non-strained aliphatic systems. With an increased *s*-character a negative charge in an exocyclic orbital is better stabilized, due to favored distribution around the core. Recently, *Knochel* and *Marek* reported a stereoselective I/Mg-exchange reaction leading to functionalized cyclopropane derivatives of type **11** (Scheme 8).[25]

[24] a) Varchi, G.; Jensen, A. E.; Dohle, W.; Ricci, A.; Cahiez, G.; Knochel, P. *Synlett* **2001**, 477; b) Abarbi, M.; Dehmel, F.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 7449.
[25] Vu, V.-A.; Marek, I.; Polborn, K.; Knochel, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 351.

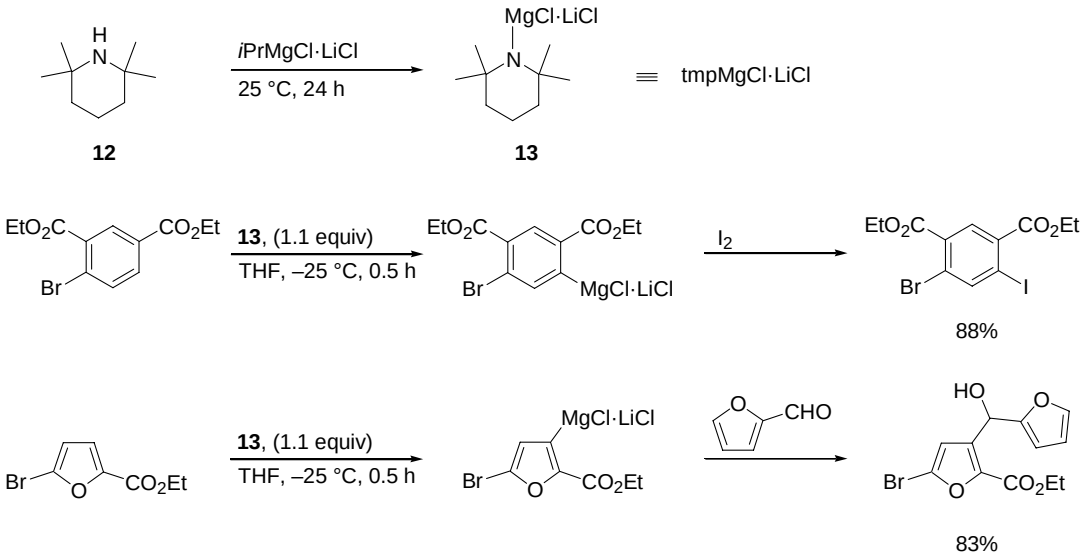


Scheme 8: An I/Mg-exchange reaction for converting a cyclopropyl iodide to the corresponding magnesium derivative **11**.

1.1.3 *ortho*-Magnesiation with magnesium amides

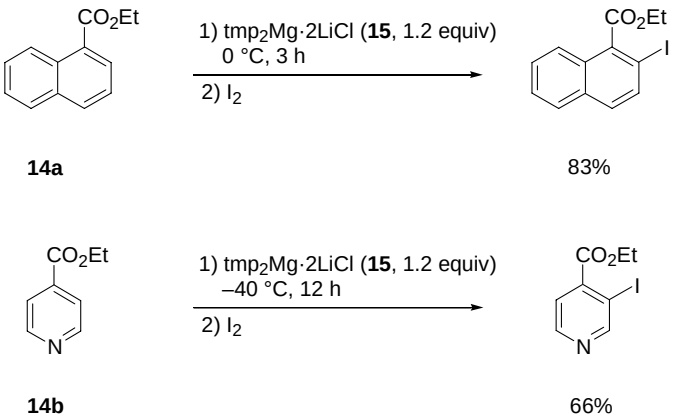
A third important approach for the generation of magnesium derivatives is the deprotonation using magnesium bases. Reacting secondary amines with Grignard reagents furnishes the corresponding magnesium amides which are less nucleophilic than the origin organomagnesium compound (Scheme 9). The preparation of magnesiated species with magnesium amides was already described by *Hauser* for the self condensation of various esters.[26] The use of sterically hindered amines, like 2,2,6,6-tetramethylpiperidine (**12** = tmp), for the preparation of these bases prevents unwanted nucleophilc side reactions.[27] Recently, *Knochel* reported the use of tmpMgCl·LiCl (**13**)[28] which displays a better solubility than tmpMgCl and a higher reactivity for the magnesiation of functionalized aromatic and heteroaromatic compounds (Scheme 9). The main advantages of tmpMgCl·LiCl compared to tmpLi or LDA[29] are the long term stability of this reagent at 25 °C, the better compatibility with sensitive functional groups and the greater stability of the metalated products.

[26] Hauser, C. R.; Walker, H. G. Jr. *J. Am. Chem. Soc.* **1947**, *69*, 295.
[27] a) Zhang, M.-X.; Eaton, P. E. *Angew. Chem. Int. Ed.* **2002**, *41*, 2169; b) Kondo, Y.; Akihiro, Y.; Sakamoto, T. *J. Chem. Soc. Perkin Trans.1* **1996**, 2331; c) Eaton, P. E.; Lee, C. H.; Xiong, Y. *J. Am. Chem. Soc.* **1989**, *111*, 8016; d) Eaton, P. E.; Zhang, M.-X.; Komiya, N.; Yang, C.-G., Steele, I.; Gilardi, R. *Synlett* **2003**, *9*, 1275; e) Eaton, P. E.; Martin, R. M. *J. Org. Chem.* **1988**, *53*, 2728; f) Shilai, M.; Kondo, Y.; Sakamoto, T. *J. Chem. Soc. Perkin Trans. 1* **2001**, 442.
[28] Krasovskiy, A.; Krasovskaya, V.; Knochel, P. *Angew. Chem. Int. Ed.* **2006**, *45*, 2958.
[29] a) Schlosser, M. *Angew. Chem. Int. Ed.* **2005**, *44*, 376; b) Turck, A.; Plé, N.; Mongin, F.; Quéguiner, G. *Tetrahedron* **2001**, *57*, 4489; c) Schlosser, M. *Eur. J. Org. Chem.* **2001**, *21*, 3975; d) Hodgson, D. M.; Bray, C. D.; Kindon, N. D. *Org. Lett.* **2005**, *7*, 2305; e) Plaquevent, J.-C.; Perrad, T.; Cahard, D. *Chem. Eur. J.* **2002**, *8*, 3300; f) Chang, C.-C.; Ameerunisha, M. S. *Coord. Chem. Rev.* **1999**, *189*, 199; g) Whisler, M. C.; MacNeil, S.; Snieckus, V.; Beak, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 2206; h) Quéguiner, G.; Marsais, F.; Snieckus, V.; Epsztajn, J. *Adv. Heteocycl. Chem.* **1991**, *52*, 187.



Scheme 9: Preparation of tmpMgCl·LiCl (**13**) and its utilization for deprotonation.

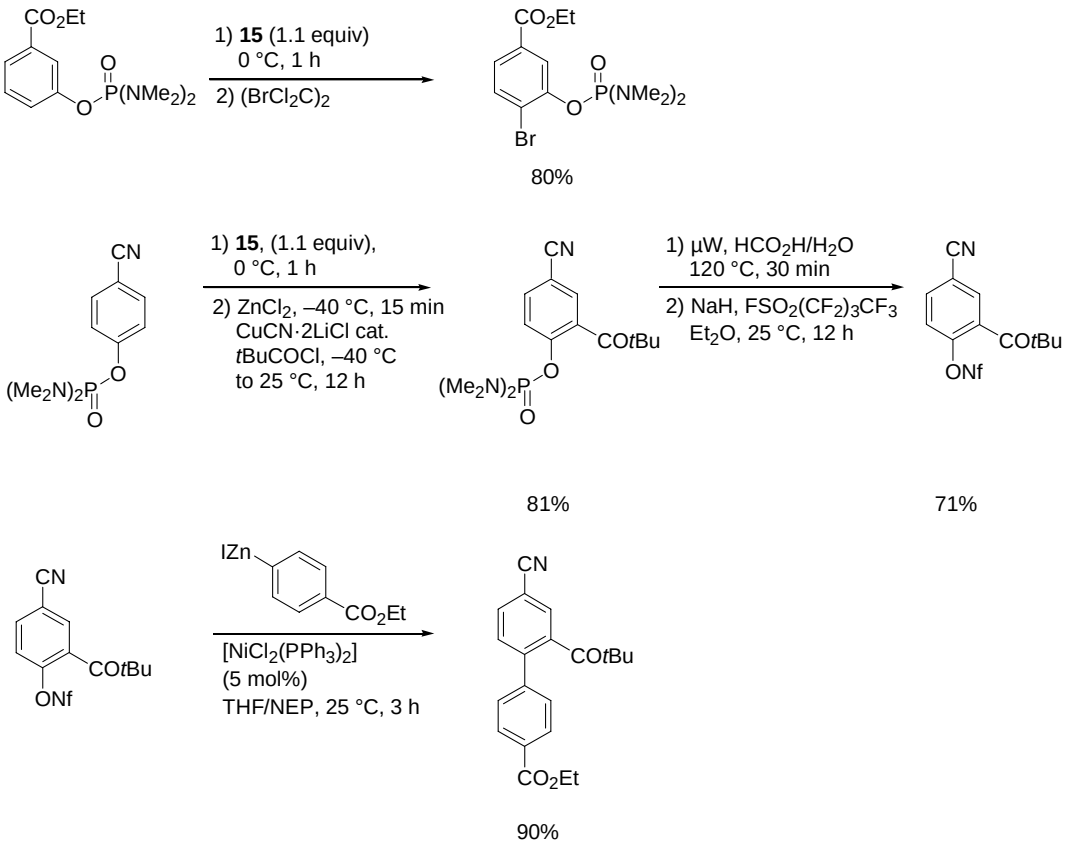
Recent reports showed, that less electron poor aromatics like **14a**–**b** can be metalated with $tmp_2Mg·2LiCl$ (**15**), prepared from tmpLi and $MgCl_2$ (Scheme 10).[30]



Scheme 10: Magnesiation of aromatic substrates with $tmp_2Mg·2LiCl$ (**15**).

[30] Clososki, G. C.; Rohbogner, C.; Knochel, P. *Angew. Chem. Int. Ed.* **2007**, *46*, 7681.

The use of the strong directing tetramethylphosphorodiamidate group, allowed to metalate a range of aromatic alcohols.[31] The strong directing ability of this donor group facilitated the preparation of *para*,*meta*-difunctionalized aromatics (Scheme 11).



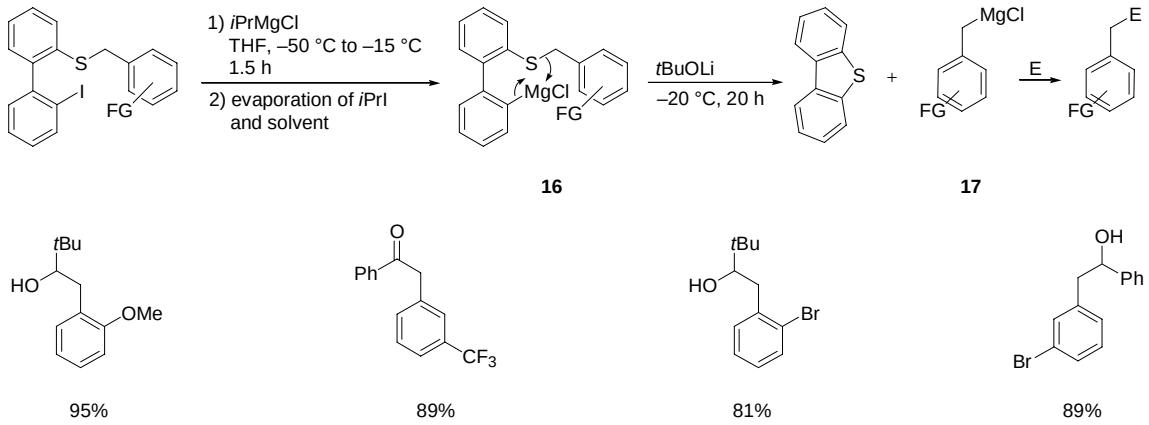
Scheme 11: Use of the strong directing tetramethylphosphorodiamidate group for *ortho*-magensiation.

1.1.4. Sulfur-magnesium exchange reaction

The preparation of benzylic Grignard reagents was the target of intensive studies, because of their high reactivity and synthetic applicability.[32] *Knochel* reported the first S/Mg-exchange reaction allowing a preparation of functionalized benzylic magnesium reagents.[33] The first step was an I/Mg-exchange reaction using *i*PrMgCl leading to a magnesiated species **16** which underwent a cyclylization after the addition of *t*BuOLi,

[31] Rohbogner, C.; Clososki, G. C.; Knochel, P. *Angew. Chem. Int. Ed.* **2008**, *47*, 1503.
[32] a) van den Ancker, T. R.; Raston, C. L. *Organometallics* **1995**, *14*, 584; b) Alonso, T.; Harvey, S.; Junk, P. C.; Raston, C. L.; Skelton, B.; White, A. H. *Organometallics* **1987**, *6*, 2110; c) Appler, H.; Gross, L. W.; Mayer, B.; Neumann, W. P. *J. Organomet. Chem.* **1985**, *291*, 9; d) Scholz, J.; Thiele, K.-H.; *J. Organomet. Chem.* **1986**, *314*,7; e) Rieke, R. D. *Acc. Chem. Res.* **1977**, *10*, 301; f) Harvey, S.; Raston, C. L. *J. Chem. Soc. Chem. Commun.* **1988**, 652; g) Engelhardt, L. M.; Harvey, S.; Raston, C. L.; White, A. H. *J. Organomet. Chem.* **1988**, *341*, 39; h) Nicoletti, T. M.; Raston, C. L.; Sargent, M. V. *J. Chem. Soc. Chem. Commun.* **1990**, 133; i) de Boer, H. J. R.; Akkerman, O. S.; Bickelhaupt, F. *J. Organomet. Chem.* **1987**, *321*, 291; j) van den Ancker, T. R.; Harvey, S.; Raston, C. L. *J. Organomet. Chem.* **1995**, *502*, 35; k) Harvey, S.; Junk, P. C.; Raston, C. L.; Salem, G. *J. Org. Chem.* **1988**, *53*, 3134.
[33] Stoll, A. H.; Krasovskiy, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2006**, *45*, 606.

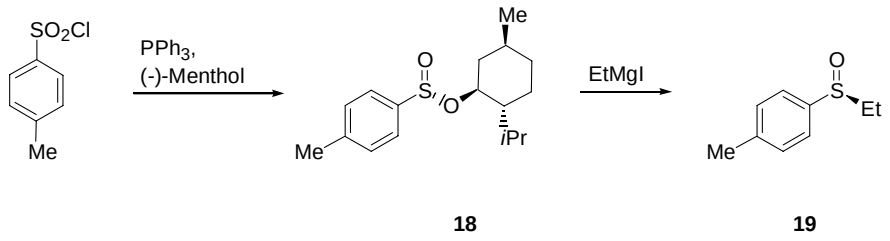
furnishing the benzylic magnesium reagent **17** (Scheme 12). The driving force of the S/Mg-exchange is the formation of the cyclic dibenzothiophene. Evaporation of the solvent and *i*PrI was necessary, due to the high reactivity of the resulting benzylic magnesium reagent **17** which underwent side reactions with the iodide.



Scheme 12: S/Mg-exchange reaction leading to functionlized benzylmagnesium reagents.

1.1.5. Sulfoxide-magnesium exchange reaction

With the preparation of diastereomerically pure sulfinate esters of menthol, reported by *Andersen*[34] in 1962, a new chapter of chiral auxilliaries was opened.[35] The reaction of organometallic reagents with diastereomerically pure sulfinates facilitated the preparation of the corresponding sulfoxides with inversion of the stereo centre at the sulfur atom (Scheme 13).

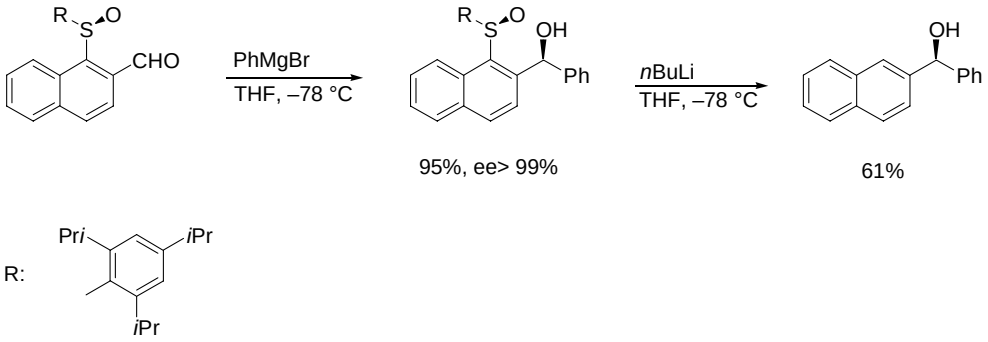


Scheme 13: Preparation of the Andersen-sulfinate **18** and consecutive reaction with ethylmagnesium bromide to the sulfoxide **19**.

[34] a) Andersen, K. K. *Tetrahedron Lett.* **1962**, *3*, 93; b) Andersen, K. K.; Gaffield, W.; Papanikolau, N. E.; Foley, J. W.;Perkins, R. I. *J. Am. Chem. Soc.* **1964**, 86*,* 5637.

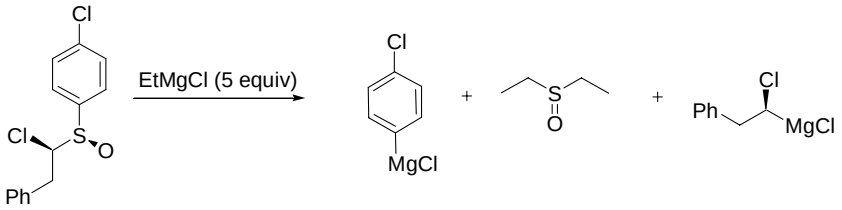
[35] a) Han, Z.; Krishnamurty, D.; Grover, P.; Fang, Q. K.; Su, X.; Wilkinson, H. S.; Lu, Z.-H.; Magira, D. Senanayake, C. *Tetrahedron* **2005**, *61*, 6386; For a review see: Senanayake, C. H. ; Krishnamurthy, D.; Lu, Z.-H.; Han, Z.; Gallou, I. *Aldrichim. Acta* **2005**, *38*, 93.

Kagan reported the utilization of a sulfoxide moiety for the preparation of chiral ferrocene derivatives.[36] Further development of this method facilitated the synthesis of new planar chiral P-N-ligands for palladium-catalyzed allylic substitution reactions.[37]
The sulfoxide moiety was also used for inducing stereochemistry during an addition of organomagnesium reagents to aldehydes in *ortho*-position to the sulfoxide (Scheme 14), and a consecutive sulfoxide-metal exchange reaction.[38]



Scheme 14: Utilization of a sulfoxide moiety for inducing chirality.

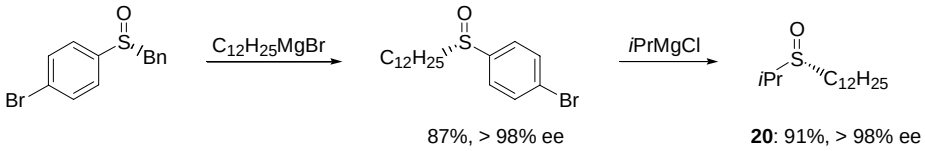
Both approaches availed themselves on highly reactive lithium derivatives which have a low compatibility towards functional groups.
In contrast, *Hoffmann* and *Satoh* reported the generation of magnesium carbenoids by a sulfoxide/magnesium exchange performed on α-chloro-sulfoxides (Scheme 15).[39]



Scheme 15: Sulfoxide-magnesium exchange using 5 equiv of EtMgCl led to chiral carbenoids and a range of reactive byproducts.

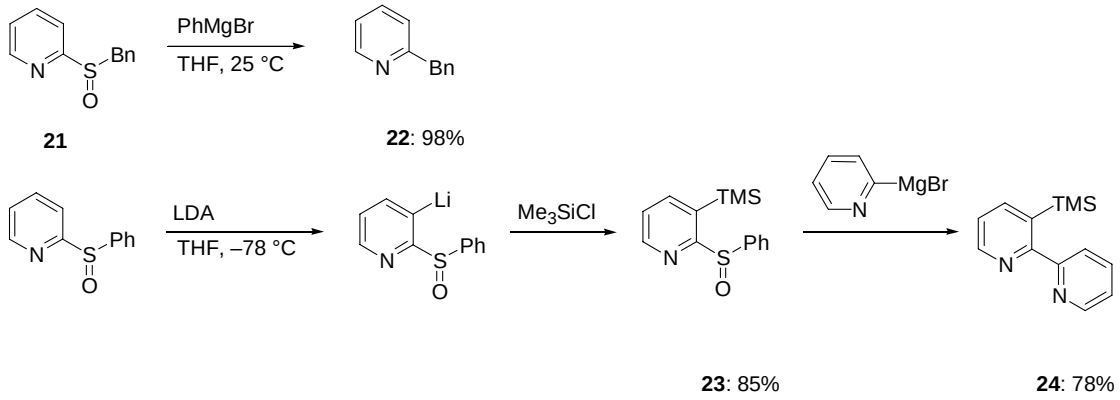
[36] a) Guillaneux, D.; Kagan, H. B. *J. Org. Chem.* **1995**, *60*, 2502; b) Kagan, H. B.; Luukas T. O. in *Transition Metals for Organic Synthesis* Beller, M.; Bolm, C., Eds., Wiley-VCH, Weinheim, **2004**, 479.
[37] Kloetzing, R. J.; Knochel, P. *Tetrahedron: Asymm.* **2006**, *17*, 116.
[38] a) Nakamura, S.; Yasuda, H.; Watanabe, Y.; Toru, T. *Tetrahedron Lett.* **2000**, *41*, 4157; b) Nakamura, S.; Yasuda, H.; Watanabe, Y.; Toru, T. *J. Org. Chem.* **2000**, *65*, 8640; c) Nakamura, S.; Oda, M.; Yasuda, H.; Toru, T. *Tetrahedron* **2001**, *57*, 8469; d) Almorín, A.; Carreno, M. C.; Somoza, Á.; Urbano, A. *Tetrahedron Lett.* **2003**, *44*, 5597; e) Ruano, J. L.; Ruano, A. M.; Tato, F.; Cardenas, D. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005**, *180*, 1443; f) Sugimoto, H.; Nakamura, S.; Shibata, Y.; Shibata, N.; Toru, T. *Tetrahedron Lett.* **2006**, *47*, 1337.
[39] a) Hölzer, B.; Hoffmann, R. W. *Chem. Commun.* **2003**, 732; b) Hoffmann, R. W.; Hölzer, B.; Knopff, O.; Harms, K. *Angew. Chem. Int. Ed.* **2000**, *39*, 3072 c) Satoh, T.; Miura, M.; Sakai, K.; Yokoyama, Y. *Tetrahedron* **2006**, *62*, 4253; d) Sugiyama, S.; Shimizu, H.; Satoh, T. *Tetrahedron Lett.* **2006**, *47*, 8771; e) Satoh, T.; Akita, K. *Chem. Pharm. Bull.* **2003**, *51*, 181; f) Satoh, T.; Taguchi, D.; Suzuki, C.; Fujisawa, S. *Tetrahedron* **2001**, *57*, 493; g) Satoh, T. *Chem. Soc. Rev.* **2007**, *36*, 1561.

Lockard, Capozzi and others demonstrated the enantioselective preparation of dialkylsulfoxides of type **20** starting from chiral sulfoxides (Scheme 16).[40]



Scheme 16: Preparation of chiral dialkylsulfoxides.

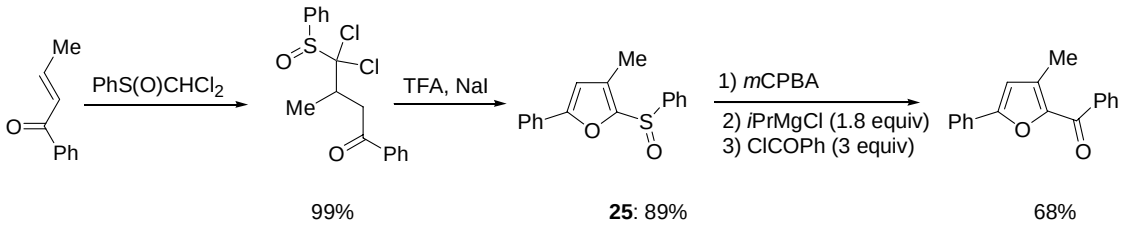
Oae, *Furukawa* and others described a sulfoxide-metal exchange with heteroaryl sulfoxides leading to ligand exchange reactions or ligand coupling reactions (Scheme 17).[41] The pyridine derivative **21** gave with different organometallic species (e.g. MeMgBr, *n*BuLi, or PhMgBr) the benzylic-substituted pyridine **22**.[41a] On the other hand the reaction of substituted 2-(phenylsulfinyl)pyridines, like **23**, with various pyridylmagnesium bromides furnished products of type **24**, according to the so-called ligand exchange reaction.[41c]



Scheme 17: Ligand coupling led to **22**, and ligand exchange gave the bipyridyl **24**.

[40] a) Lockard, J. P.; Schroeck, C. W.; Johnson, C. R. *Synthesis* **1973**, 485; b) Capozzi, M. A. M.; Cardellicchio, C.; Naso, F.; Rosito, V. *J. Org. Chem.* **2002**, *67*, 7289.
[41] a) Oae, S.; Kawai, T.; Furukawa, N. *Tetrahedron Lett.* **1984**, *25*, 69; b) Kawai, T.; Furukawa, N. *Tetrahedron Lett.* **1984**, *25*, 2549; c) Furukawa, N.; Shibutani, T.; Fujihara, H. *Tetrahedron Lett.* **1989**, *30*, 7091; d) Shibutani, T.; Fujihara, H.; Furukawa, N. *Tetrahedron Lett.* **1991**, *32*, 2943.

Recently, *Satoh* reported the utilization of a sulfinyl group for the synthesis of functionalized furans.[42] Major drawback was the low compatibility of functional groups, only H and Me substituents were reported in position three and four of furan **25**.

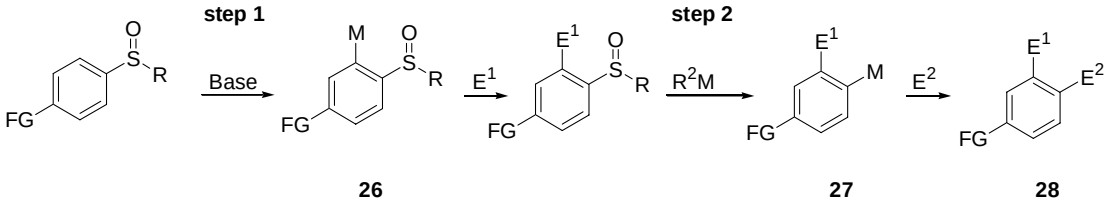


Scheme 18: Utilization of a 1,1-dichlorosulfoxide for the synthesis of furans.

[42] Miyagawa, T.; Satoh, T. *Tetrahedron Lett.* **2007**, *48*, 4849.

1.2. Objectives

In this work, we planned to establish a new route to 1,2,4-trisubstituted aromatic compounds. The reagents used in the synthetic sequence should be compatible with a broad range of functionalities. A sulfoxide moiety will be used, serving two purposes: first it should act as a metalating directing group, leading to *ortho*-metalated sulfoxides of type **26** which can be reacted with electrophiles and second the sulfoxide group should be the source of a new carbon-metal bond generated by a sulfoxide-metal exchange reaction (Scheme 19). This metal species **27** can be reacted with a second electrophile to generate the desired trisubstituted arenes of type **28**.



FG: functional group
M: metal

Scheme 19: General approach to 1,2,4 trisubstituted arenes of type **28**.

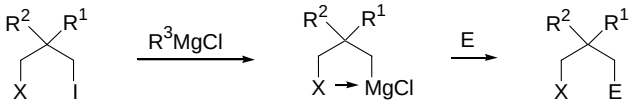
The details of this work are:

- Optimization of the ligand R, leading to a chemoselctive metalation (step 1, Scheme 19) and regioselective cleavage of the sulfur-carbon bond leading to **27**.
- Determining the scope of compatible functionalities.
- Optimization of R^2M for smooth cleavage (step 2) and good compatibility with FG and E^1.
- Further applications of this two-step procedure to heteroaromatic systems.

A second project will be the examination of an I/Mg-exchange reaction on sp^3-hybridzed carbon with unstrained systems. *Vu* demonstrated that it is possible to perform an I/Mg-exchange on Csp^3 in the presence of a carboxylic ester in γ-position to the carbon-iodine bond.[43] It will be studied if a complexation, as shown for the Br/Mg-exchange on aromatic systems, might increase the rate of exchange. For this purpose aliphatic primary iodides of type **29** will be examined. A second task will be the

[43] a) Vu, V.-A. PhD-Thesis Ludwig-Maximilians-Universität, Munich, **2003**; b) Rauhut, C. B.; Vu, V.-A.; Fleming, F. F.; Knochel, P. *Org. Lett.* **2008**, *10*, 1187.

examination of the possible substitution pattern of the iodide (Scheme 20, R^1, R^2), and the influence of the exchange reagents nature.

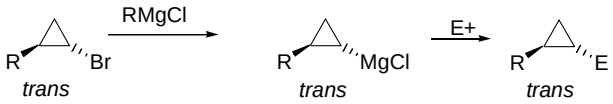


29

X: Heteroatom for chelation

Scheme 20: I/Mg-exchange performed on Csp^3 with a chelating heteroatom in γ-position to the carbon-iodine bond.

A third topic will be extension of the stereoselective Br/Mg-exchange on cyclopropyl bromides which was initially explored by *Cervino* (Scheme 21).[44] Additional experiments for cross-coupling reactions will be performed.



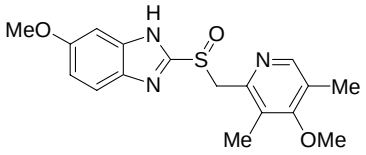
Scheme 21: Stereoselective Br/Mg-exchange and consecutive reaction with electrophiles.

[44] a) Cervino, C. *Diploma thesis*, Ludwig-Maximilians-Universität, Munich **2005**; b) Rauhut, C. B.; Cervino, C.; Krasovskiy, A.; Knochel, P. *Synlett* **2009**, 67.

2. Results and discussion

2.1. Sulfoxide-magnesium exchange on aromatic systems

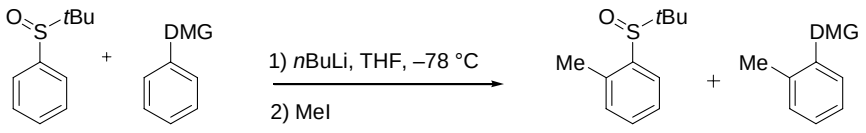
The sulfoxide group offers the organic chemist a range of interesting properties. Using its stereochemistry for racemic resolution,[36-37] or for inducing stereo chemistry, is well described. Some sulfoxides and sulfoxide derivatives are of commercial interest, since they show biologic activity and are used as drugs like Omeprazole (**30**, Figure 1).[45]



30

Figure 1: Omeprazole **30**, a proton pump ihibitor.

The excellent metalating directing abilities of the sulfoxide moiety were described by *Snieckus*,[46] when he demonstrated that the influence of the sulfoxide function is much stronger than ethers, amidates and amides (Scheme 22).



31 **32** **33** **34**

DMG	Methylated product Yield, % **33**	**34**	Starting Materials Yield, % **31**	**32**
$CON(iPr)_2$	78	<1	9	95
$OCON(iPr)_2$	85	<1	4	86
OMOM	86	<1	3	85
SO_2tBu	41	44	45	36

Scheme 22: Intermolecular metalation competition between a sulfoxide and various directing groups.

In this case the *t*Bu-sulfoxide moiety was employed which showed a special stability against organometallic reagents, and thereby allowed the utilization of *n*BuLi for deprotonation. This extraordinary stability is, from the point of view of a preparative chemist, also its disadvantage, as the functionality is then tied to the molecule. To

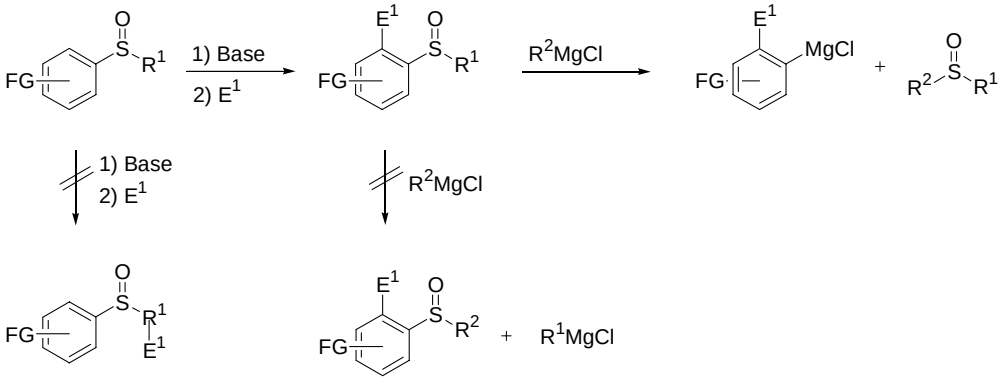
[45] a) Shaojun, S.; Klotz, U. *Eur. J. Clin. Pharmacol.* **2008**, *64*, 935; for a review on proton pump inhibitors see: Katz, P. O.; Koch, F. K.; Ballard, E. D.; Bagin, R. G.; Gautille, T. C.; Checani, G. C.; Hogan, D. L.; Pratha, V. S. V. *Aliment Pharmacol Ther* **2007**, *25*, 197.
[46] Quesnelle, C.; Iihama, T.; Aubert, T.; Terrier, H.; Snieckus, V. *Tetrahedron Lett.* **1992**, *33*, 2625.

increase the synthetic value of the sulfoxide function, it should be possible to remove it, and give rise to a reactive intermediate. This approach is also well described for some special cases (e.g. heterocyclic sulfoxides or ferrocenes),[36-37,40] but mainly lithium reagents were used for the sulfoxide-metal exchange. More reactive *α*-chloro-sulfoxides were transformed with organomagnesium reagents to the corresponding carbenoids. Unfortunately the sulfoxide-magnesium exchange reagents were used in great excess (up to 5 equiv). The consecutive reactions required the addition of stoichometric amounts of electrophile which led to product/by-product ratios up to 1:5. The challenges during purification and the waste of resources needed an improvement of the sulfoxide-magnesium exchange.

A synthetic strategy including the metalation of a sulfoxide and after functionalization, a sulfoxide-metal exchange brings up four main requirements:

- a general structure allowing a chemoselective metalation (Scheme 23)
- a general structure leading to a chemoselective sulfoxide-magnesium exchange
- a mild exchange reagent which is compatible with functional groups
- a convenient access to various sulfoxides.

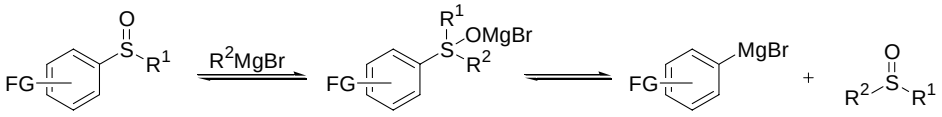
As the *t*Bu-sulfoxide moiety is inert towards organometallic reagents, and other aliphatic groups bearing *α*-acidic protons,[40a,47] an aromatic electron rich system for R^1 should fulfill the demand for a selective metalation.



Scheme 23: Theorical pathway of the optimized sulfoxide-functionalization and exchange.

[47] a) Yamakazi, T.; Ishikawa, N. *Chem. Lett.* **1985**, 889; b) Pyne, S. G.; Dikic, B. *J. Chem. Soc. Chem. Commun.* **1989**, 826.

Furukawa proposed a mechanism for the ligand-exchange,[41a] which supports the use of an electron rich arene (R^1: electron rich arene) in the sulfoxide moiety, regarding the selective cleavage of a sulfoxide-carbon bond (Scheme 24). In this equilibrium the favoured expelled organomagnesium reagent should be the most stable one (i.e. the electron poorest).



Scheme 24: Proposed mechanism for the sulfoxide-magnesium exchange.

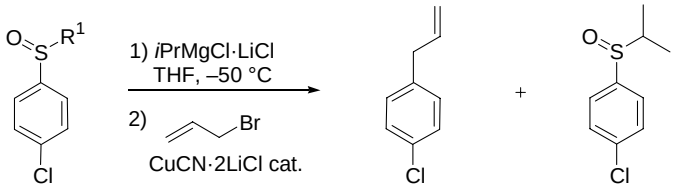
Following this assumption a range of diaryl sulfoxides were prepared. Many synthetic routes are described for preparing chiral and racemic sulfoxides.[34-35,48] A convenient access is the oxidation of the corresponding thioether with cheap and commercial available oxidants like *m*CPBA or H_2O_2.[49] *Jendralla* showed that the reaction of organometallic compounds with thiocyanates leads to the corresponding sulfides in good yields.[50] Thus, 4-(dimethylamino)phenyl thiocyanate (**35**)[51] was prepared on large scale (500 mmol) and reacted with 4-chlorophenylmagnesium bromide (**36**, –20 °C to 25 °C). After aqueous workup the crude mixture was oxidized with *m*CPBA (1.1 equiv, 1 M in CH_2Cl_2), giving **37a** in 64% yield (Table 1, entry 1). Reaction of 4-methoxylbenzene sulfinyl chloride[52] (**38**) with **36** (–20 °C to 25 °C) led to 4-chlorophenyl 4-methoxyphenyl sulfoxide **37b** in 85% yield (entry 2). The sulfoxide **37c** was obtained by performing a Br/Li-exchange with (4-bromophenoxy)(triisopropyl)silane[53] and a consecutive reaction with *S*-(4-chlorophenyl) benzenesulfonothioate[54] (**39**) leading to the thioether **40**.

The crude sulfide was oxidized with mCPBA (1 h, –20 °C), giving the sulfoxide **37c** in 66% yield (entry 3). In analogous manner **37d** was obtained in 76% yield (entry 4) from (4-bromo-2,6-diisopropylphenyl)dimethylamine,[55] *n*BuLi and **39**. Similarly the sulfide

[48] Manchena, O. G.; Bolm, C. *Org. Lett.* **2006**, *11*, 2349.
[49] a) Ternay, A. L. Jr.; Chasar, D. W.; Sax, M. *J. Org. Chem.* **1967**, *32*, 2465; b) Amos, R. A. *J. Org. Chem.* **1985**, *50*, 1311; c) Nelsen, S. F.; Luo, Y.; Lockard, J. V.; Zink, J. I. *J. Org. Chem.* **2006**, *71*, 4286; d) Sathicq, A. G.; Romanelli, G. P.; Palermo, V.; Vázquez, P. G.; Thomas, H. J. *Tetrahedron Lett.* **2008**, *49*, 1441; e) Hinsberg, O. *Chem. Ber.* **1910**, *43*, 289.
[50] Jendralla, H.; Chen, L. *Synthesis* **1990**, 827.
[51] Brewster, R. Q.; Schroeder, W. *Org. Synth.* **1943**, *19, 79*.
[52] Peyronneau, M.; Roques, N.; Mazieres, S.; Le Roux, C. *Synlett* **2003**, 631.
[53] Wipf, P.; Methot, J.-L. *Org. Lett.* **2000**, *26*, 4213.
[54] Kolesnikov, V. T.; Vid, L. V.; Kuz'menko, L. O. *Zhurnal Organicheskoi Khimii* **1982**, *10*, 2163, or in analogous manner to: Fujiki, K.; Tanifuji, N., Sasaki, Y.; Yokoyama, T. *Synthesis* **2002**, 343.
[55] Yamano, M.; Goto, M.; Kawaguchi, S.; Yamada, M.; Kawakami, J.-I. *PCT Int. Appl.* **2007**, 96.

41 was obtained from 5-bromo-1,2,3-trimethoxybenzene and **39** in 89% yield and oxidized with *m*CPBA (–20 °C, 1.1 equiv in CH_2Cl_2) to the sulfoxide **37e** in 73% yield (entry 5). The dibutylamino substituted sulfoxide **37f** was prepared from dibutyl(4-iodophenyl)amine and **39** in 27% yield (entry 6), using the above described sequence.

For the comparison of the sulfoxide moieties, THF (25 ml) was mixed with tetradecane (0.25 g). Six *Schlenk*-flasks were charged with 1.0 mmol of a sulfoxide (**37a-f**, Scheme 25 and Table 1) and 2.0 mL of the tetradecane/THF mixture. *i*PrMgCl·LiCl (1.1 mmol, 1.46 M in THF) was added at –50 °C and after full conversion the ratio **42**/$C_{14}H_{30}$ was checked by GC by reacting aliquots with allyl bromide and CuCN·2LiCl (cat., Scheme 25 and Table 1). The best results were obtained with *p*$MeOC_6H_4$ and *p*$NMe_2C_6H_4$ as ligands.



37 **42**

Scheme 25: Benchmark experiment for chemoselectivity of the sulfoxide magnesium exchange reaction.

Table 1: Evaluation of the ligands for the sulfoxide-magnesium exchange reaction.

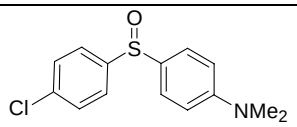
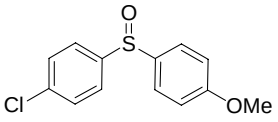
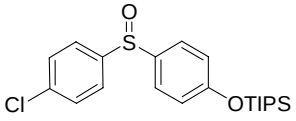
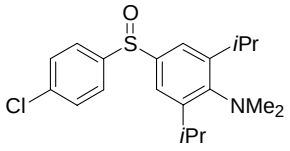
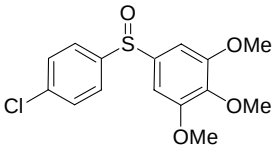
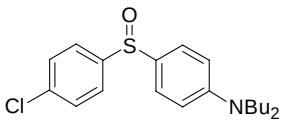
Entry	Sulfoxide	Ratio **42**/$C_{14}H_{30}$
1	 **37a**	3.65
2	 **37b**	3.49
3	 **37c**	3.44

Table 1 continued:

Entry	Sulfoxide	Ratio **42**/$C_{14}H_{30}$
4	 **37d**	3.19
5	 **37e**	3.03
6	 **37f**	2.04

The next task was the determination of the appropriate sulfoxide-magnesium exchange reagent. We noticed on an early stage that arylmagnesium derivatives do not react with sulfoxides at low temperature which is advantageous during the deprotonation step. So we focussed on aliphatic reagents and examined in a benchmark reaction, comparable to the ligand test, five Grignard reagents. **37a** was dissolved in a THF/tetradecane mixture and the magnesium reagents (**43a–43e**) were added at –50 °C. The reaction progress was checked with aliquots reacted with allyl bromide (Table 2). With *i*PrMgCl·LiCl (**43a**) 74% conversion was achieved after 10 min. The other reagents displayed a lower reactivity (23-52% conversion, entry 2-5).

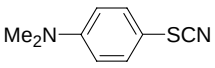
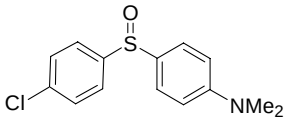
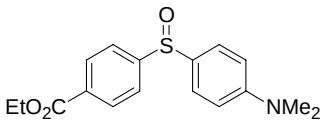
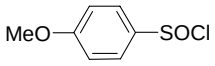
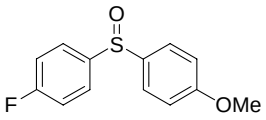
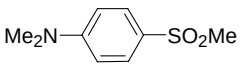
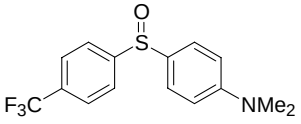
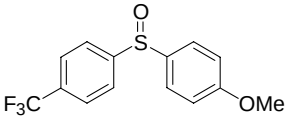
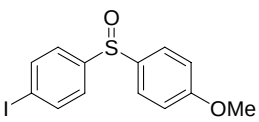
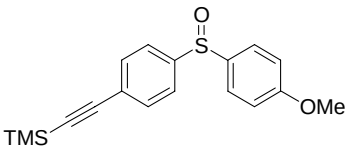
Table 2: Comparison of the magnesium reagents **43a-43e** by the reaction with the sulfoxide **37a**.

Entry	Grignard reagent	Conversion/%[a]
1	*i*PrMgCl·LiCl (**43a**)	74
2	*i*PrMgBr·LiBr(**43b**)	50
3	$ClMg(CH_2)_5MgCl·2LiCl$(**43c**)	47
4	*c*HexMgCl(**43d**)	23
5	*c*PrMgBr·LiCl(**43e**)	52

[a] Determined by GC-Analysis with $C_{14}H_{30}$ as internal standard.

With these elementary observations in hand, we prepared a range of functionalized sulfoxides (Table 3, entries 1-6). Thus, ethyl 4-iodobenzoate was treated with *i*PrMgCl·LiCl at –20 °C for 10 min, generating the corresponding aromatic magnesium reagent. Then 4-(dimethylamino)phenyl thiocyanate (**35**) was added, and the resulting crude sulfide was oxidized with *m*CPBA leading to the sulfoxide **37g** in 59% yield overall (entry 2). 4-Fluoro-phenylmagnesium bromide (**44**) was reacted with 4-methoxylbenzene sulfinyl chloride (**38**) (–20 °C) furnishing the fluorinated sulfoxide **37h** in 69% yield (entry 3).

Table 3: Preparation of functionalized sulfoxides (**37a**, **37g**–**k**).

Entry	Electrophile	Product	Yield(%)[a]
1			64
	35	**37a**	
2			59
	35	**37g**	
3			69
	38	**37h**	
4			82
	45	**37i**	
5			82
	38	**37j**	
6			98[b]
	46	**37k**	

[a] Isolated yield of analytically pure product. [b] Using an alkynyl zinc reagent, $Pd(dba)_2$ and tfp.

1-Bromo-(4-trifluoromethyl)benzene was treated with *i*PrMgCl·LiCl for 14 h, leading to the analogous magnesium reagent which was reacted with methyl 4-dimethylaminosulfinate (**45**) or **38** respectively, furnishing the sulfoxides **37i**–**j** in 82% yield (entries 4–5). Reaction of 1,4-diiodobenzene with *i*PrMgCl·LiCl and the sulfinyl chloride **38** gave 4-iodophenyl 4-methoxyphenyl sulfoxide (**46)** in 73% yield. This sulfoxide was transformed in a Negishi cross-coupling reaction[56] with trimethylsilylethynyl zinc chloride, prepared from ethynyl(trimethyl)silane, *i*PrMgCl·LiCl and zinc chloride (1.0 M in THF), to the desired alkyne-substituted sulfoxide **37k** in 98% yield (entry 6).

Having these sulfoxides in hands, we developed a convenient protocol for their functionalization. It turned out that tmpMgCl·LiCl (**13**, 1.1 equiv) reacts regioselectively at –30 °C with these starting materials, furnishing the monometalated species within 20 min. Further reactions with various electrophiles led to a range of difunctionalized sulfoxides (Table 4). Thus, the smooth metalation of **37a**, provided after reaction with 1,2-dibromo-tetrachloroethane the sulfoxide **47a** in 88% yield (Table 4, entry 1). When zinc chloride (1.0 M in THF) was added after deprotonation, followed by an aryl iodide and a catalyst system (like $Pd(PPh_3)_4$, or $Pd(dba)_2$ and tris-*o*-furylphosphine) the aromatic products **47b**–**d** were obtained in 69-82% yield (entries 2-4). Deprotonation of **37a** with subsequent reaction with TosCN furnished the nitrile **47e** in 73% yield (entry 4). Negishi cross-coupling with 4-iodobenzonitrile led to the sulfoxide **47f** in 92% yield (entry 6). The fluorinated sulfoxide **37h** was metalated according to the same procedure, and reaction with *S*-(4-fluorophenyl) benzenesulfonothioate gave the sulfoxide **47g** in 81% yield (entry 7). The trifluoromethyl-substituted substrate **37i** was deprotonated with the conditions described above, and converted with a Negishi cross-coupling with 1-chloro-4-iodobenzene to the derivative **47h** in 91% yield (entry 8). To demonstrate that this procedure can be performed on large scale, the sulfoxide **47i** was prepared on a 40 mmol scale with 75% yield (entry 9).[57] The functionalization of **37j** with an alkynyl derivative led, after *in situ* reaction with iodine, in a cross-coupling reaction to the sulfoxide **47j** (79% yield, entry 10). An alkynyl group was used as primary functionality (**37k**) and combined with

[56] a) Negishi, E.; Valente, L. F.; Kobayashi, M. *J. Am. Chem. Soc.* **1980**, *102*, 3298; b) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340; c) Zeng, X.; Quian, M.; Hu, Q.; Negishi, E. *Angew. Chem. Int. Ed.* **2004**, *43*, 2259.

[57] Melzig, L.; Rauhut, C. B.; Knochel, P. *Synthesis*, **2009**, in press.

one electron poor arene, one electron rich aromatic ring and with a second alkynyl function in 67-73% yield (**47k**–**m**, entries 11-13).

Table 4: Functionalization with tmpMgCl·LiCl (**13**).

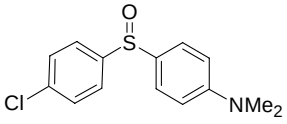
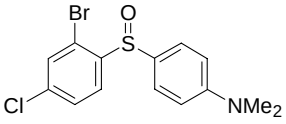
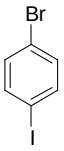
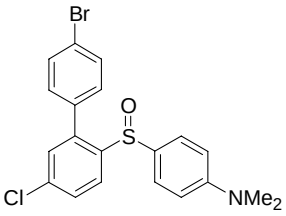
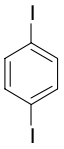
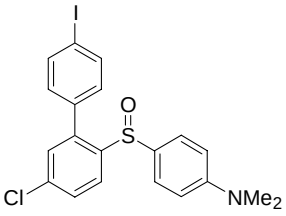
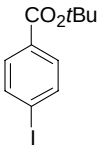
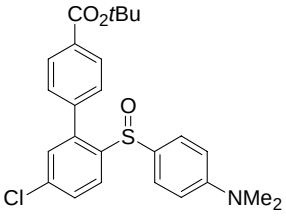
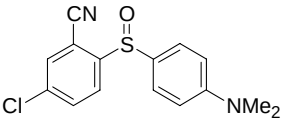
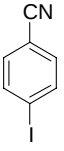
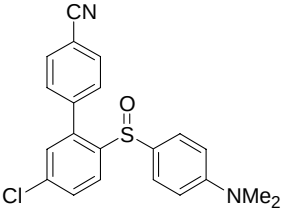
Entry	Sulfoxide	Electrophile	Difunctionalized Sulfoxide	Yield (%)[a]
1	 **37a**	$Cl_2BrCCBrCl_2$	 **47a**	88
2	**37a**		 **47b**	82[b]
3	**37a**		 **47c**	69[b]
4	**37a**		 **47d**	79[b]
5	**37a**	TosCN	 **47e**	73
6	**37a**		 **47f**	92[b]

Table 4 continued:

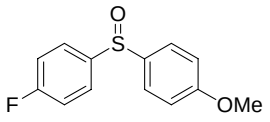
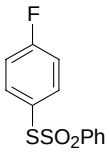
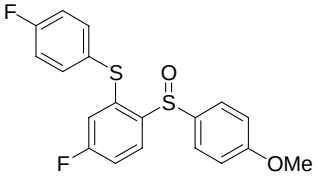
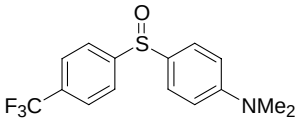
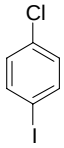
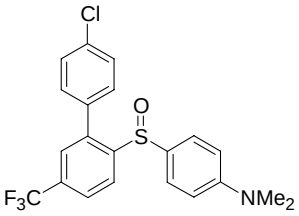
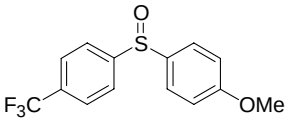
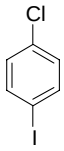
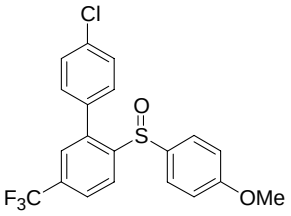
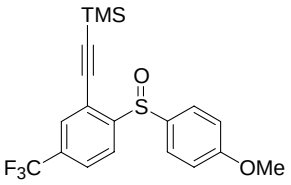
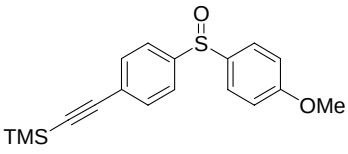
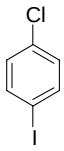
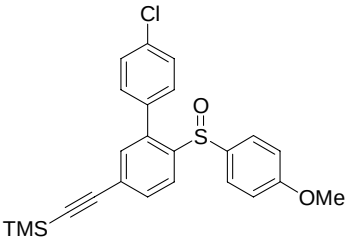
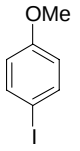
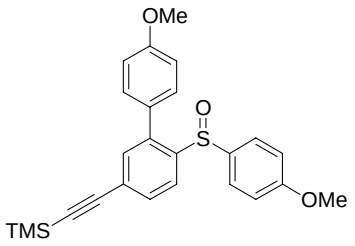
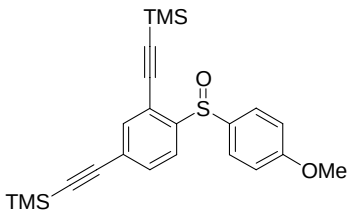
Entry	Sulfoxide	Electrophile	Difunctionalized Sulfoxide	Yield (%)[a]
7	 **37h**		 **47g**	81
8	 **37i**		 **47h**	91 [b]
9	 **37j**		 **47i**	75 [b]
10	**37j**	i) I_2 ii) TMS—≡—ZnCl	 **47j**	79[d]
11	 **37k**		 **47k**	73 [b]

Table 4 continued:

Entry	Sulfoxide	Electrophile	Difunctionalized Sulfoxide	Yield (%)[a]
12	**37k**		 **47l**	67[b]
13	**37k**	i) I_2 ii) TMS—≡—ZnCl	 **47m**	72[d]

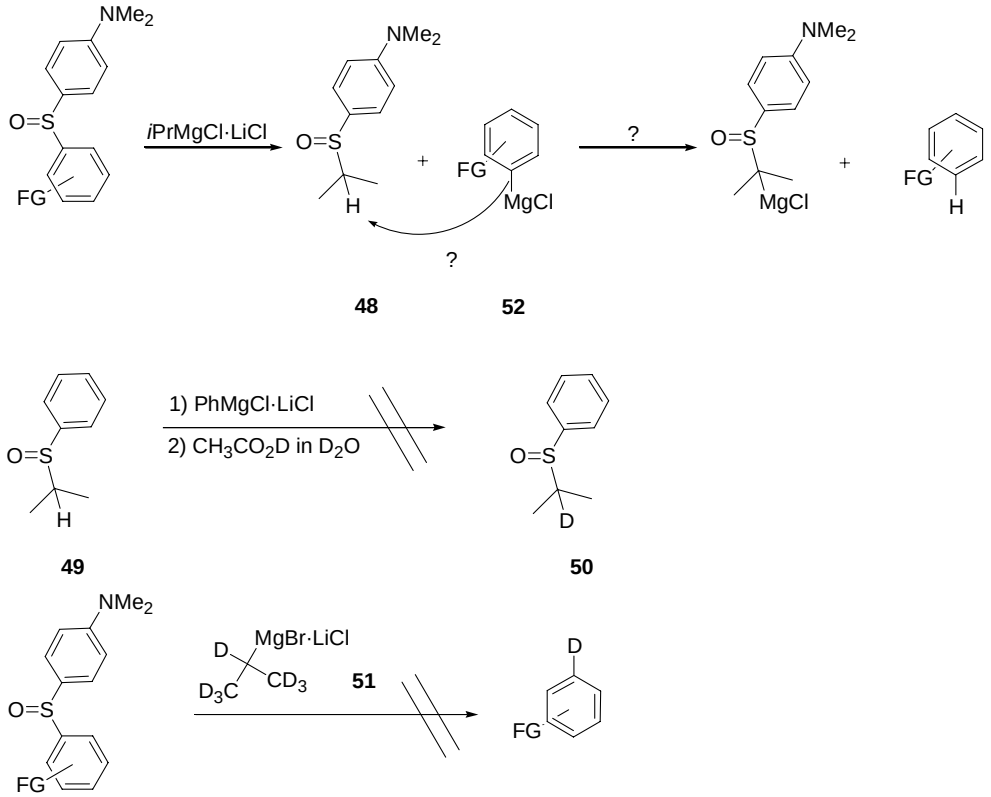
[a] Isolated yield of analytically pure product. [b] Using 1.1 equiv of zinc chloride (1.0 M in THF) and a palladium catalyst like $Pd(PPh_3)_4$ or $Pd(dba)_2$ and tfp. [d] Using a palladium catalyst like $Pd(PPh_3)_4$ or $Pd(dba)_2$ and tfp.

With these functionalized sulfoxides in hands, the stability of the functional groups and the reactivity of the sulfoxides towards *i*PrMgCl·LiCl was examined. In preliminary experiments we observed a slightly higher reactivity of the sulfoxide moiety in an intermolecular competition reaction between diphenylsulfoxide and iodobenzene (65:35) with *i*PrMgCl·LiCl. But even the reaction of **47a** with *i*PrMgCl·LiCl was not chemoselective and led to a mixture of Br/Mg- and sulfoxide-magnesium exchange. This increased reactivity of the bromide resulted possibly in the strong electron withdrawing character of the sulfoxide moiety. The same effect was observed in the case of the sulfoxide-magnesium exchange of the ethyl 4-benzoate-substituted sulfoxide **37b** (Table 3, entry 2).

Although the sulfoxide **37g** was prepared from ethyl 4-iodobenzoate via a I/Mg-exchange with *i*PrMgCl·LiCl at –20 °C, in that case the sulfoxide-magnesium exchange (at –50 °C) led to a mixture of desired product and a large amount of decomposed product. By attaching the bromide on a second arene (**47b**, Table 5, entry 2) the inductive effect of the sulfoxide was decreased and the sulfoxide-magnesium exchange was the dominant reaction in the presence of *i*PrMgCl·LiCl. The reaction of the

sulfoxide **47c**, which is the iodinated analogue of the bromide **47b**, with *i*PrMgCl·LiCl resulted only in an I/Mg-exchange.

Thus, the sulfoxides of type **47** were reacted with *i*PrMgCl·LiCl (up to 7 h, –50 °C) and the reaction progress was determined by GC, by reacting aliquots with iodine or water. The iodolysis revealed the iodinated product and a significant amount of protonated species (up to 35%, depending on sulfoxide substrate). The first possible source for the proton was the acidic proton generated with the sulfoxide-magnesium exchange (Scheme 26, compound **48**).



Scheme 26: Excluding deprotonation of the formed sulfoxide **48** as H^+-source.

To verify this, the model compound **49** was stirred with PhMgCl·LiCl at –50 °C. Aliquots of the reaction were quenched with a solution of freshly distilled Ac_2O in D_2O, the solvent was removed and the residue was analyzed by ^{1}H-NMR, but no deuterium incorporation (**50**) could be observed. The temperature was increased stepwise to 0 °C, but no deprotonation of sulfoxide **49** could be observed. A second assumption pointed on an intramolecular reaction during the exchange process. To exclude this pathway the heptadeuterated magnesium reagent **51** was prepared and reacted with several functionalized sulfoxides. Aliquots of these reactions were checked by GC-MS, but the isotope pattern did not confirm the intramolecular pathway. A third assumption was that

the generated magnesium reagent **52** acts as a ligand and forms a stable complex which does not react with the offered electrophiles and is then hydrolysed during workup. To rule out this possibility we prepared solutions of 4-methoxyphenyl magnesium bromide and 4-carbethoxyphenylmagnesium chloride and injected them before the addition of *i*PrMgCl·LiCl in standard sulfoxide magnesium exchange reactions. But still the ratio of protonated species to iodinated species were constant. Moisture infiltrating through grindings or tubing was obviated by repeating a sulfoxide-magnesium exchange with five fold amount of substrate which should have reduced the relative amount of protonated species. Monitoring the protonated species during the 5 h reaction time revealed a constant ratio (iodinated product : protonated species) which also militates against penetrating moisture.

In summary we assume that the side reaction occurs during the exchange process, and it was observed that the relative amount of protonated species was decreased by using 2-methyl-THF as solvent. This and the utilization of 0.8 equiv of electrophile led to a convenient and efficient process.

Thus, the sulfoxide **47b** was stirred with *i*PrMgCl·LiCl (5 h, –50 °C, in THF) and reacted with TosCN yielding the nitrile **53a** in 59% (Table 5, entry 1). Cross-coupling reactions with aryl iodides led to the expected products **53b**–**c** in 50-56% yield (entry 2-3), but due to the presence of a bromidesubstituent this substrate is prone to undergo unwanted cross-coupling reactions. Reaction with benzaldehyde led to the desired alcohol **53d** in 60% yield (entry 4). Performing the reaction in 2-methyl-THF and quenching with 3,4-dichlorobenzaldehyde led to the chlorinated alcohol **53e** in 63% yield (entry 5).

Subjecting the carboxylic ester-substituted sulfoxide **47d** to a sulfoxide-magnesium exchange reaction (–50 °C, 7 h) furnished, with ethyl 2-bromoacrylate,[58] the product **53f** in 60% yield (entry 6). Cross-coupling with 4-iodobenzonitrile or reaction with 3,4-dichlorobenzaldehyde gave the desired products **53g**–**h** in 50-54% yield (entries7–8). The long reaction time for the sulfoxide-magnesium exchange seems to be the reason for the low yields. With different substitution pattern, and a resulting fast sulfoxide-magnesium exchange, the product was obtained in 78% yield.[59] Using the nitrile **47e** the sulfoxide-magnesium exchange was performed in 5 min and yielded, after a cross-coupling with 4-iodoanisole, the biphenyl **53i** in 84% yield (entry 9). The 2-(4-

[58] a) Villiéas, J.; Rambaud, M. *Synthesis*, **1982**, *11*, 924; b) Villiéras, J.; Rambaud, M. *Org. Synth.*, **1988**, *66*, 220.
[59] Rauhut, C. B.; Melzig, L.; Knochel, P. *Org. Lett.* **2008**, *10*, 3891.

cyanobenzene)-substituted sulfoxide **47f** showed, possible due to the increased sterical hindrance, a longer reaction time (–50 °C, 2 h) and led after cross-coupling reaction or addition to 3,4-dichlorobenzaldehyde to the expected ptoducts **53j**–**k** in 60–63% yield (entries 10–11). The sulfide **47g** gave after 1 h at –50 °C with a prestirred mixture of *N,N,N',N'*-tetramethyldiaminomethane and trifluoroacetic anhydride,[60] the expected amine **53l** in 66% yield (entry 12). This sulfide and related structures were described recently, due to their biological activity, acting as serotonin reuptake inhibitors.[61] The sulfoxides bearing a trifluoromethyl moiety **47h**–**i** underwent a smooth sulfoxide-magnesium exchange (–50 °C, 3 h) and led with benzaldehyde, DMF or in a Negishi cross-coupling reaction to the expected products **53m**–**o** in 68–83% yield (entries 13–15). The aldehyde **53o** was prepared on large scale (25 mmol) to demonstrate the possibility of upscaling this procedure. With the sterically less hindered alkyne-substituent, the sulfoxide **47j** showed an excellent exchange rate (–50 °C, 5 min) and gave the biphenyl **53p** in 87% yield (entry 16). Sulfoxide **47k** performed the exchange reaction in 3 h and gave after cross-coupling reaction or reaction with DMF the terphenyl **53q** and the corresponding aldehyde **53r** in 68% yield (entries 17-18). The bisalkynylated sulfoxide **47m** reacted with *i*PrMgCl·LiCl within 5 min giving, with 3,4-dichlorobenzaldehyde, the expected alcohol **53s** in 72% yield (entry 19).

[60] a) Millot, N.; Piazza, C.; Avolio, S.; Knochel, P. *Synthesis* **2000**, 941; b) Gommermann, N.; Koradin, C.; Knochel, P. *Synthesis* **2002**, 2143.
[61] Polivka, Z.; Dobrovsk, K.; Silhankova, A.; Sindelar, K.; Mickova, R.; Valenta, V.; Krejci, I. *PCT Int. Appl.* WO 9717325, **1997**.

Table 5: Sulfoxide-magnesium exchange leading to a broad range of 1,2,4-trifunctionalized arenes.

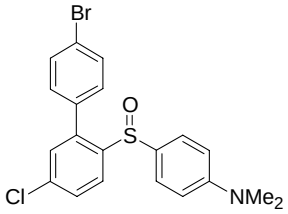
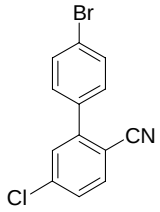
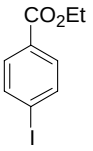
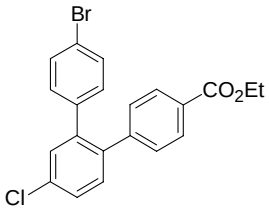
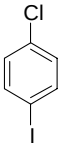
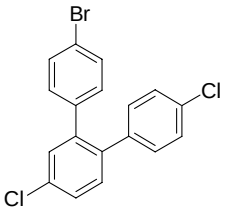
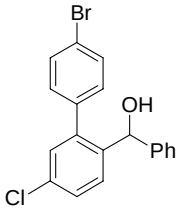
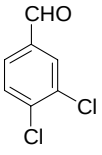
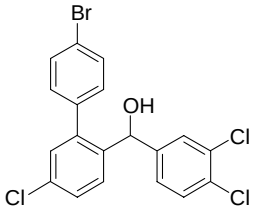
Entry	Sulfoxide	Electrophile	Product	Yield (%)[a]
1	 **47b**	TosCN	 **53a**	59
2			 **53b**	50[b]
3			 **53c**	56[b]
4		PhCHO	 **53d**	60
5			 **53e**	63

Table 5 continued:

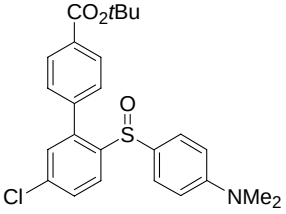
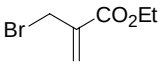
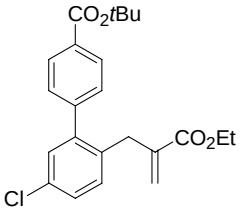
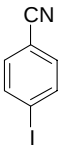
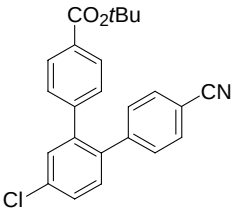
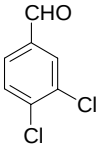
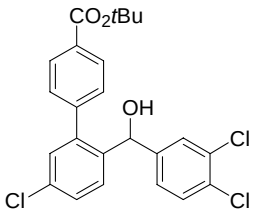
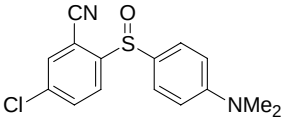
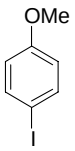
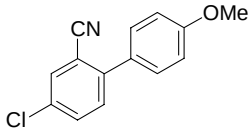
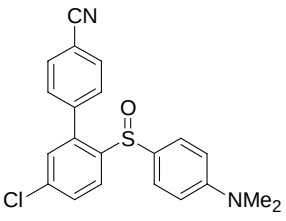
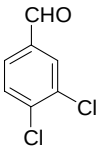
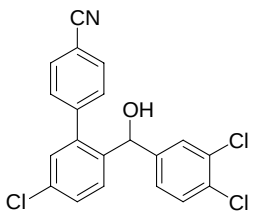
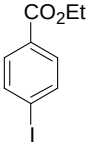
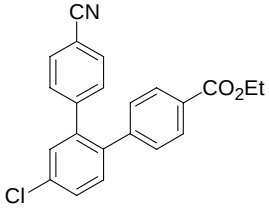
Entry	Sulfoxide	Electrophile	Product	Yield (%)[a]
6	 **47d**		 **53f**	60[c]
7			 **53g**	54[b]
8			 **53h**	50
9	 **47e**		 **53i**	84[b]
10	 **47f**		 **53j**	63
11			 **53k**	60[b]

Table 5 continued:

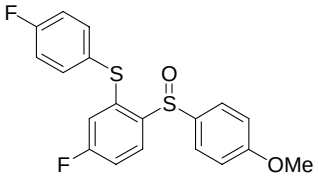
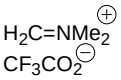
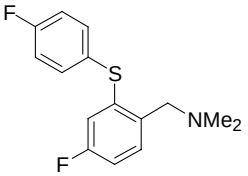
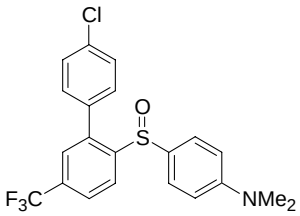
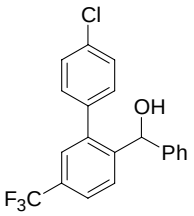
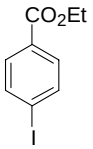
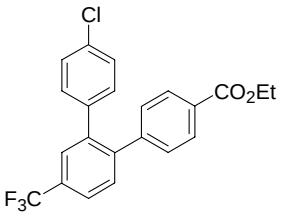
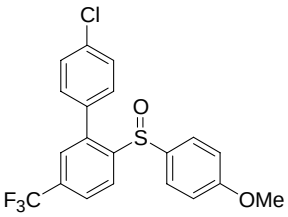
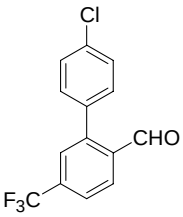
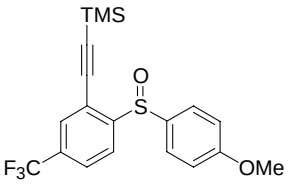
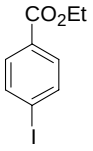
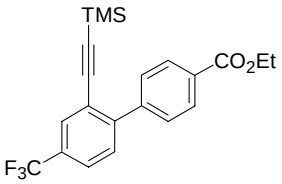
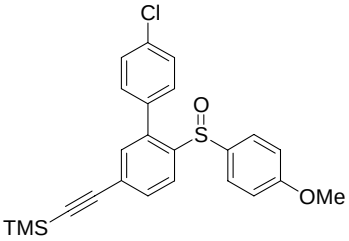
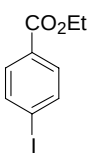
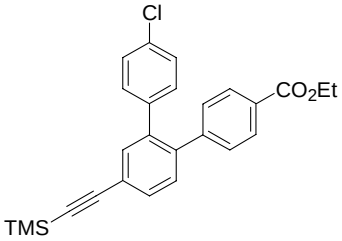
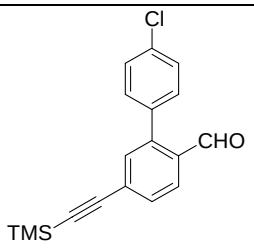
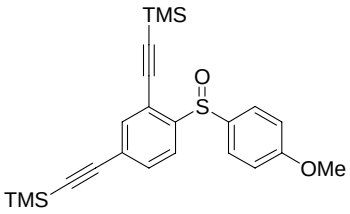
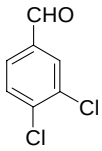
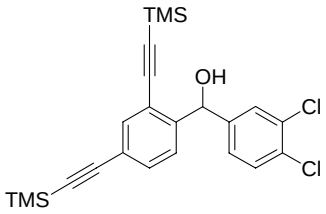
Entry	Sulfoxide	Electrophile	Product	Yield (%)[a]
12	 **47g**		 **53l**	66
13	 **47h**	PhCHO	 **53m**	68
14	**47h**		 **53n**	79[b]
15	 **47i**	DMF	 **53o**	83
16	 **47j**		 **53p**	87[b]
17	 **47k**		 **53q**	68[b]

Table 5 continued:

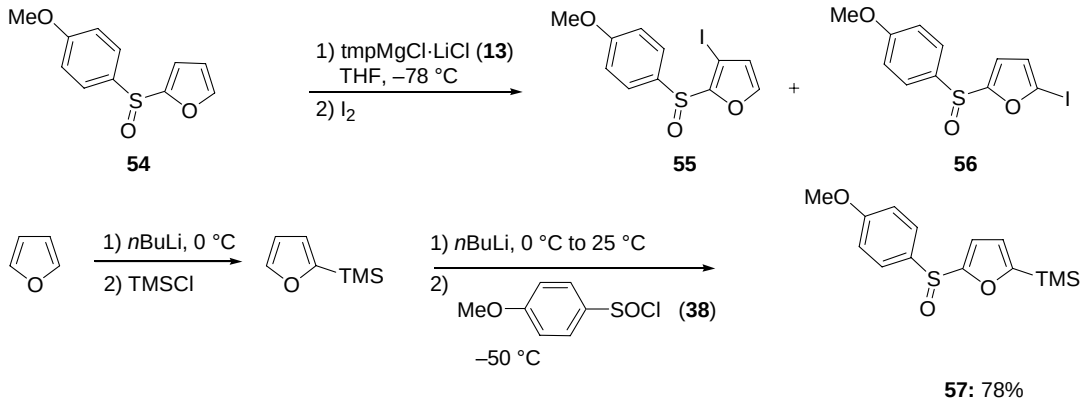
Entry	Sulfoxide	Electrophile	Product	Yield (%)[a]
18		DMF		68
	47k		**53r**	
19				72
	47m		**53s**	

[a] Isolated yield of analytically pure product. [b] Using 1.1 equiv of zinc chloride (1.0 M in THF) and a palladium catalyst like $Pd(PPh_3)_4$ or $Pd(dba)_2$ and tfp. [c] using CuCN·2LiCl (5 mol %, 1 M in THF).[62]

[62] Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.

2.2. Full functionalization of the furan ring

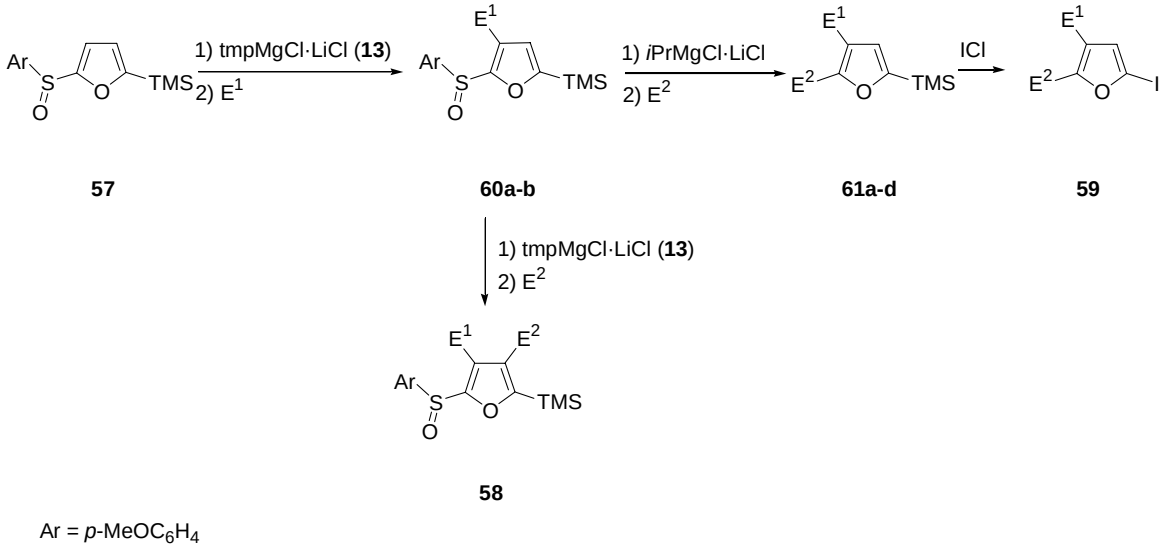
The development of previous described two-step difunctionalization of aromatic substrates, allowed us to search for further applications. A full functionalization of furan seemed to offer a good possibility to demonstrate the scope of this procedure.[63] Preliminary experiments showed that 2-[(4-methoxyphenyl)sulfinyl]furan (**54**) suits our requirements, but as the 5-position is very acidic, even at –78 °C a mixture of **55** and **56** was obtained after deprotonation with tmpMgCl·LiCl and consecutive reaction with iodine (Scheme 27). Using trimethylsilyl chloride to block this position led to the starting sulfoxide **57**.



Scheme 27: Preparation of the elementary furyl sulfoxide **57**.

The utilization of the silyl group should allow the generation of a 2-iodofuran with ICl after the difunctionalization-procedure. The generated furan could be used for further extensions with *i*PrMgCl·LiCl or cross-coupling reactions. One additional option of this approach was a second deprotonation of the furan in position 4, but it turned out that in that case the reaction is too slow and **58** was only obtained in 45% yield (Scheme 28).

[63] For reviews and selected publications for furan see: a) Lipshutz, B. H. *Chem. Rev.* **1986**, *86*, 795; b) Hou, X. L.; Cheung, H. Y.; Hon, T. Y.; Kwan, P. L.; Lo, T. H.; Tong, S. Y.; Wong, H. N. C. *Tetrahedron* **1998**, *54*, 1955; c) Padwa, A. Zhang, H. *J. Org. Chem.* **2007**, *72*, 2570.



57 **60a-b** **61a-d** **59**

58

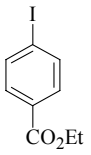
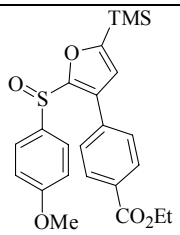
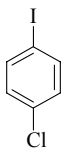
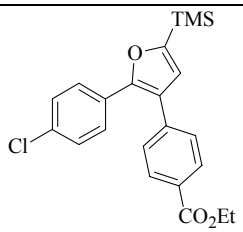
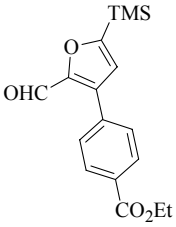
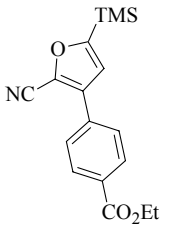
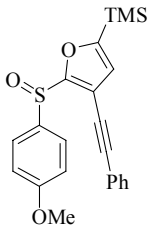
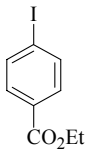
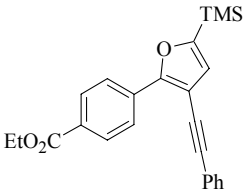
Scheme 28: General approach for the furan functionalization.

The more convenient route was to perform the sulfoxide-magnesium exchange first, followed by transformation of the trimethylsilyl group to iodine.[64] This furan **59** can be functionalized with the well described iodine I/Mg-exchange.[21] Thus, the sulfoxide **57** was treated with tmpMgCl·LiCl, achieving full deprotonation at –40 °C within 20 min. The metalated species was reacted in a cross-coupling reaction with ethyl 4-iodobenzoate, furnishing the sulfoxide **60a** in 77% yield (Table 6, entry 1). Using the previous described protocol for introducing alkynes, the sulfoxide **60b** was obtained in 69% yield (entry 4).

With these furans in hands, the sulfoxide-magnesium exchange was examined. Thus, the sulfoxide **60a** was reacted with *i*PrMgCl·LiCl (–40 °C, 20 min), transmetalated with zinc chloride (1.0 M in THF) and transformed with ethyl 4-iodobenzoate and a palladium catalyst to the corresponding furan **61a** in 68% yield (Table 6, entry 1). Reaction with DMF gave the aldehyde **61b** in 76% yield (entry 2). The nitrile **61c** was generated in 63% yield (entry 3) by the reaction of the magnesiated species with TosCN. Substrate **60b** performed the sulfoxide-magnesium exchange at –78 °C in 15 min, and the consecutive cross-coupling led to the expected furan **61d** in 68% yield (entry 4).

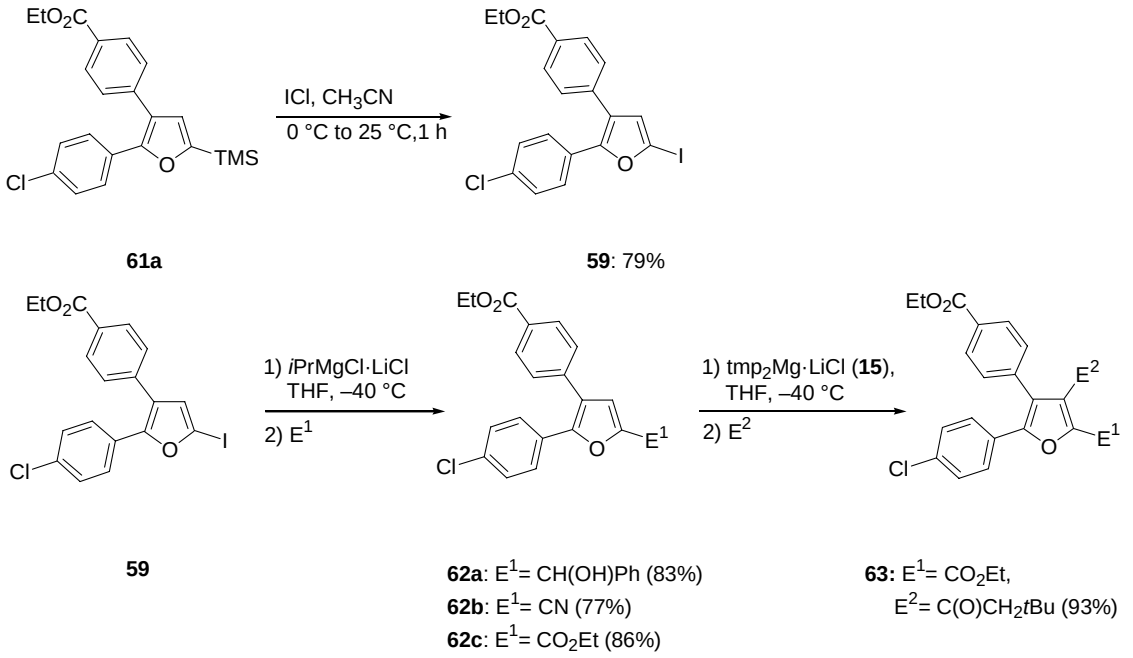
[64] a) Nakayama, K.; Harigaya, Y.; Okamoto, H.; Tanaka, A. *J. Heterocycl. Chem.* **1991**, *28*, 853; b) Koyanagi, J.; Yamamoto, K.; Nakayama, K.; Tanaka, A. *J. Heterocycl. Chem.* **1997**, 34, 407; c) Campo, M. A.; Larock, R. C. *J. Am. Chem. Soc.* **2002**, *124*, 14326.

Table 6: Deprotonation and sulfoxide-magnesium exchange of functionalized furans.

Entry	Electrophile E^1	Sulfoxide, Yield (%)[a]	Electrophile E^2	Furan	Yield (%)[a]
1		 **60a:** 77		 **61a**	68[b]
2		**60a**	DMF	 **61b**	76
3		**60a**	TosCN	 **61c**	63
4	i) I_2 ii) Ph—≡—ZnCl	 **60b:** 69[c]		 **61d**	68[b]

[a] Isolated yield of analytically pure product. [b] Using 1.1 equiv of zinc chloride (1.0 M in THF) and a palladium catalyst like $Pd(PPh_3)_4$ or $Pd(dba)_2$ and tfp. [c] Using $Pd(dba)_2$ and tfp.

For further substitution the trimethylsilyl group was converted to iodine by reaction with ICl, furnishing **59** in 79% yield (Scheme 29).



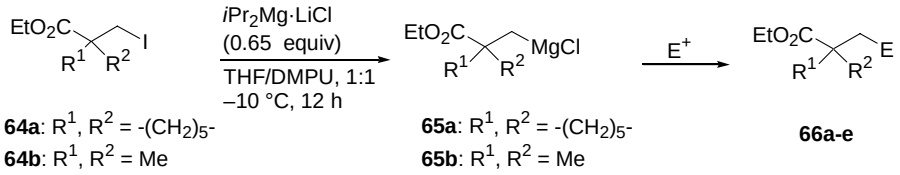
Scheme 29: Pathway to polyfunctionalized furans.

The I/Mg-exchange was performed with *i*PrMgCl·LiCl (–40 °C, 20 min) and the resulting organomagnesium compound was reacted with benzaldehyde, TosCN or ethyl cyanoformate leading to the expected products **62a**–**c** in 77–86% yield (Scheme 29). The metalation of **62c** with tmp_2Mg·LiCl (**15**, –40 °C, 25 min) and consecutive copper mediated acylation using 3,3-dimethylbutanoyl chloride led to the furan **63** in 93% yield (Scheme 29).

2.3. I/Mg-exchange on Csp3-centers

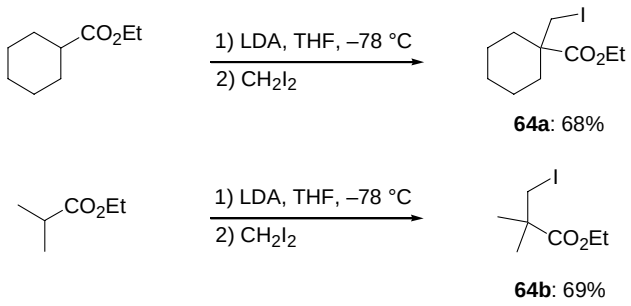
Recently, I/Mg- and Br/Mg-exchange reactions on Csp^2-centers have allowed the synthesis of a range of polyfunctional aryl and hetereoaryl magnesium compounds.[21,65] Nevertheless, the extension of this procedure to Csp^3-centers failed in most cases due to the slow I/Mg-exchange rate of alkyl iodides. In case of strained systems, e. g. cyclopropyl halides, compareable results were obtained. Simultaneous to our investigations, an alkoxide-directed I/Mg-exchange was reported, but the use of 2.1 equiv of *n*BuLi excluded most functional groups.[66] A second disadvantage of this approach was the excess of *n*BuLi which afforded in most cases a stoichometric amount of electrophile, leading to huge amounts of byproducts.

In preliminary experiments *Vu* could demonstrate that electron poor alkyl iodides can be subjected to an I/Mg-exchange reaction.[43a] Optimization of the reaction conditions led to the utilization of *i*Pr_2Mg·LiCl, and a DMPU/THF 1:1 mixture (Scheme 30).



Scheme 30: I/Mg-exchange on β-iodoesters **64a**–**b**.

Thus, the alkyl iodide **64a** was prepared by deprotonation of ethyl cyclohexyl carboxylate with LDA and consecutive reaction with CH_2I_2, giving the iodoester **64a** in 68% yield (Scheme 31). Enolization of ethyl 2-methylpropanoate with LDA gave after reaction with CH_2I_2 the alkyl iodide **64b** in 69% yield.



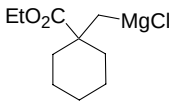
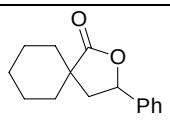
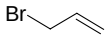
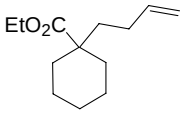
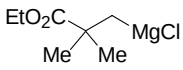
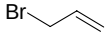
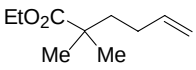
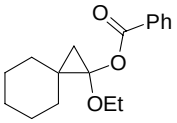
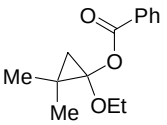
Scheme 31: Preparation of the carboxylic esters **64a**–**b**.

[65] a) Krasovskiy A.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 3396; b) Liu, C.; Ren, H.; Knochel, P. *Org. Lett.* **2006**, *8*, 614; c) Inoue, A.; Kitagawa, K.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **2001**, *66*, 4333.

[66] Fleming, F. F.; Subrahmanyan, G. ; Vu, V. A. ; Mycka R. J. ; Knochel P. *Org. Lett.* **2007**, *9*, 4507.

An I/Mg-exchange was then performed in a 1:1 THF/DMPU mixture, leading after 14 h at –10 °C to the corresponding homoenolates **65a**–**b** which were then reacted with various electrophiles. The reaction of **65a** with benzaldehyde gave the expected alcohol which furnished after spontaneous lactonization the spirolactone **66a** in 68% yield (Table 7, entry 1). A copper(I)-catalyzed (5 mol %) reaction of **65a**–**b** with allyl bromide led to the expected alkenes **66b**–**c** in 68-78% yield (entry 2-3). Interestingly, the copper(I)-mediated (1.1 equiv) reaction with benzoyl chloride did not furnish the expected ketones, but the cycopropylderivates **66d**–**e** were obtained in 71–75% yield (entries 4-5).

Table 7: Reaction of the homo enolates **65a**–**b** with various eletrophiles.

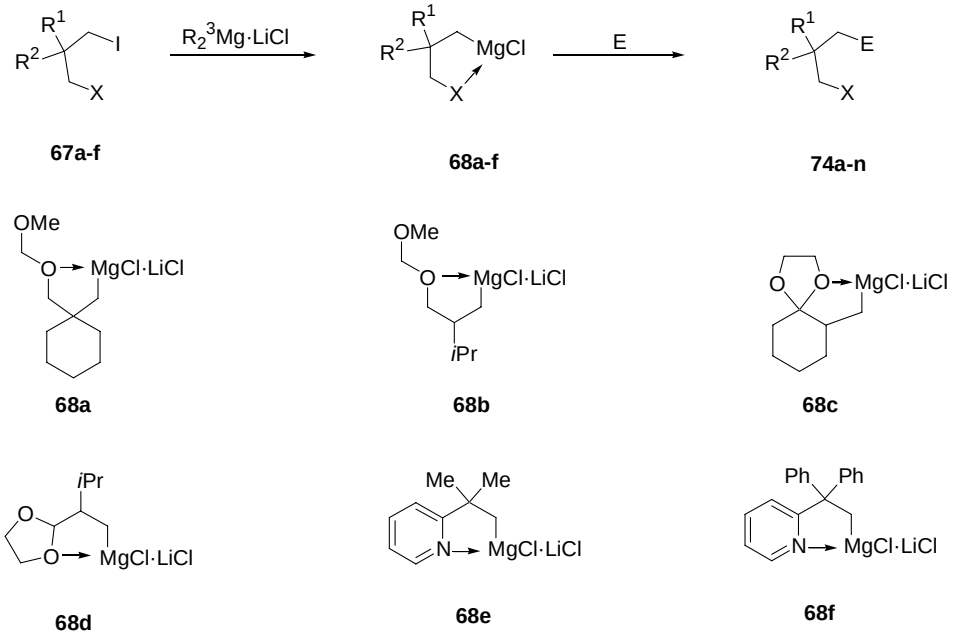
Entry	Mg-Reagent	Electrophile	Product	Yield(%)[a]
1		PhCHO		68
	65a		**66a**	
2				78[b]
	65a		**66b**	
3				68[b]
	65b		**66c**	
4		PhCOCl		71[c]
	65a		**66d**	
5		PhCOCl		75[c]
	65b		**66e**	

[a] Isolated yield of analytically pure product; [b] using CuCN·2LiCl (5 mol %, 1 M in THF); [c] Using 1.1 equiv of CuCN·2LiCl (1.0 M in THF).

These structures could be explained by an equilibrium of the homo enolates **65a**–**b** with an intramolecular attack leading to a cyclopropyl semi-acetal anion. Depending on the

electrophile one nucleophilic center (carbon or oxygen) performs the reaction. Similar reactivities were observed by *Ruehlmann*[67] and others.

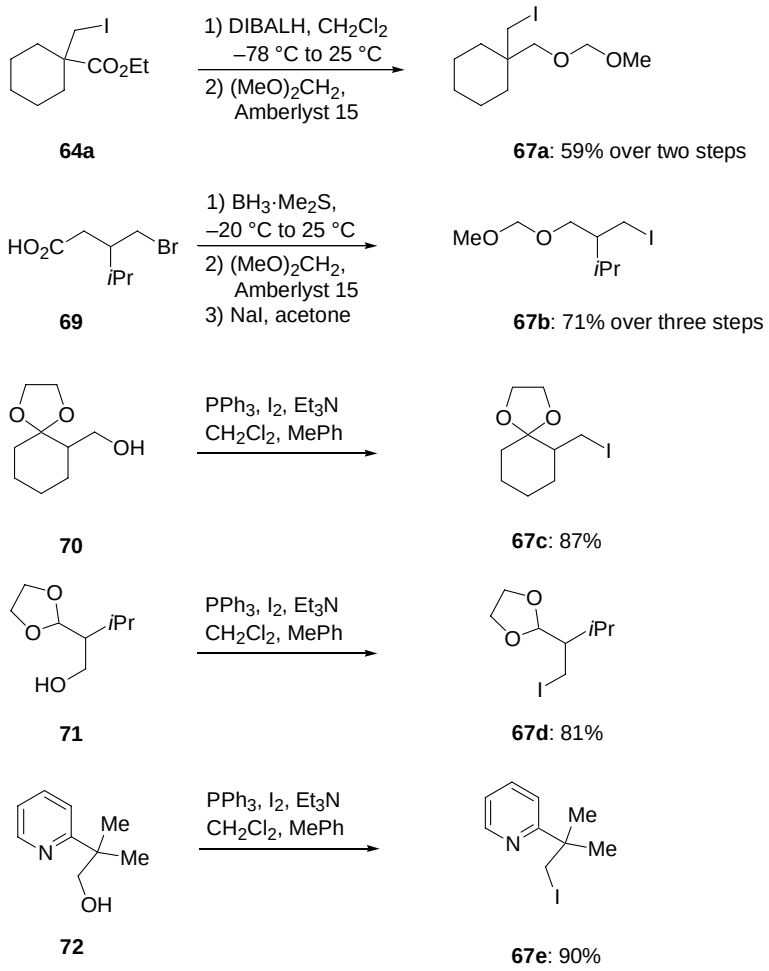
A further extension of the I/Mg-exchange was the examination of chelating substrates. Heteroatoms (oxygen and nitrogen) were placed in *γ*-position to the carbon-iodine bond (**67a**–**f**) which should form an intramolecular complex after the I/Mg-exchange reaction (Scheme 32, **68a**–**f**).



Scheme 32: Conversion of the iodides **67a**–**f** to their corresponding stabilized Grignard reagents **68a**–**f**.

Thus, ethyl 1-(iodomethyl)cyclohexanecarboxylate (**64a**) was reduced with DIBAL-H (CH_2Cl_2, –78 °C to 25 °C) and the resulting alcohol was reacted with dimethoxymethane and Amberlyst 15® furnishing the iodide **67a** in 59% yield over both steps (Scheme 33). 2-(Bromomethyl)-3-methylbutanoic acid **69** was treated with borane dimethyl sulfide (–20 °C to 25 °C, 14 h), leading to the corresponding alcohol (81% yield) which was reacted with dimethoxymethane and Amberlyst 15® giving corresponding MOM-protected bromide in 90% yield. A reaction with NaI in acetone[68] furnished the expected iodide **67b** in 98% yield (71% over three steps; Scheme 33). 1,4-Dioxaspiro[4.5]dec-6-ylmethanol[69] **70** was reacted with PPh_3 and iodine,[70] generating

[67] a) Ruehlmann K. *Synthesis* **1971**, 236; b) Nakamura E.; Kuwajima, I. *J. Am. Chem. Soc.* **1983**, *105*, 651; c) Nakamura E.; Shimada, J.-I.; Kuwajima, I. *Organometallics*, **1985**, *4*, 641; d) Reissig, H.-U.; Holzinger, H.; Glomsda, G. *Tetrahedron*, **1989**, *45*, 3139.
[68] Finkelstein, H. *Chem. Ber.* **1910**, *43*, 1528.
[69] a) Nicolaou, K. C.; Dai,W. M. *J. Am. Chem. Soc.***1992**, *114*, 3908; b) Plieninger, H.; Zeltner, M. *Chem. Ber.* **1987**, *108*, 3286.
[70] Appel, R. *Angew. Chem*, **1975**, *87*, 863.



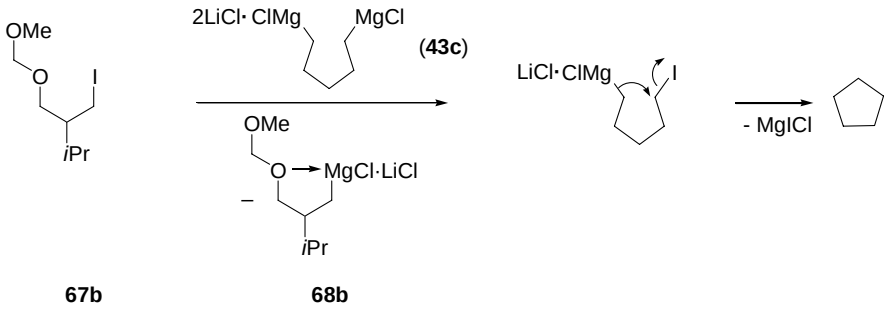
Scheme 33: Preparation of the starting iodides.

the spiro-acetal **67c** in 87% yield. 2-[1-(Bromomethyl)-2-methylpropyl]-1,3-dioxolane[71] **71** was converted in the same fashion to the iodide **67d** in 81% yield. For the preparation of the pyridine derivative **67e**, 2-methyl-2-pyridin-2-ylpropan-1-ol[72] (**72**) was treated with iodine and PPh_3, giving the iodide **67e** in 90% yield. The diphenyl-substituted pyridine derivative **67f** was prepared according to literature procedures.[73]

With these starting materials in hands the I/Mg-exchange and the influence of the chelating group was examined. Performing the I/Mg-exchange reaction with *i*PrMgCl·LiCl leads to a slow and incomplete reaction, but using *i*Pr_2Mg·LiCl (**73**) (0.75 equiv) for the I/Mg-exchange allows the formation of the magnesium reagent **67a** within 5 h at 25 °C. Quenching with CO_2 afforded the carboxylic acid **74a** with 63% yield (Table 9, entry 1). Although the exchange reagent **73** was also used to prepare other alkylmagnesium species such as **67b**, **67c**, **67e** and **67f** (Scheme 32), often an

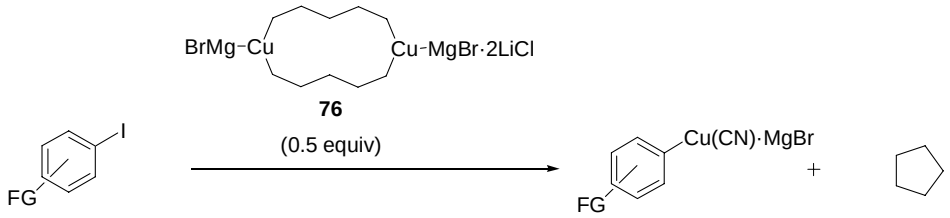
[71] Rrehs, G.; Urban, E. *Tetrahedron*, **1996**, *52*,1221.
[72] a) Rocca, P. *Tetrahedron*, **1998**, *54*, 8771; b) Brocard, J. *Annales de Chimie*, **1972**, *7*, 387; c) Eisch, J. J.; Csaba, K.A.; Chobe, P.; Boleslawski, M. P. *J. Org. Chem.* **1987**, 52, 4427.
[73] Eisch, J. J.; Kovacs, C. A.; Chobe, P.; Boleslawski, M. P. *J. Org. Chem.* **1987**, *52*, 4427.

excess of iPr$_2$Mg·LiCl (up to 1.1 equiv, corresponding to 2.2 isopropyl units) was required to achieve full conversion. This excess led to side reactions with the added electrophiles. We solved this problem by using a dimagnesium species such as **75** (Scheme 34).[74]



Scheme 34: Cyclisation during an I/Mg-exchange reaction.

Recently, a similar approach was reported for an I/Cu-exchange reaction, by using pentane-1,5-dimagnesium bromide and CuCN·2LiCl to generate the exchange reagent **76** (Scheme 35).[75] As the detection of cyclopentane in the crude reaction mixture was difficult, the cuprate of 3-phenyl-substituted 1,5-*bis*(bromomagnesio)pentane was prepared and used for the I/Cu-exchange. Then, it was possible to detect cyclopentylbenzene as main byproduct (94%).



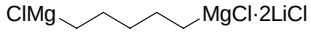
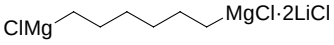
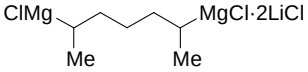
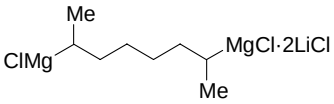
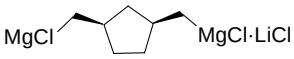
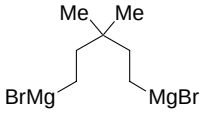
FG= *p*-CO_2Et, *m*-CO_2Et, *m*-CN, *p*-CO_2tBu, *m*-COC_6H_4*m*-OMe, *m*-F, *p*-Br

Scheme 35: An I/Cu-exchange reaction reported by *Yang* using the bis-cuprate **76**.

For the improvement of the I/Mg-exchange on Csp^3-centers a range of 1,5– and 1,6–dimagnesium reagents (Table 8, **77a**–**f**) was prepared, and compared by their reaction with the alkyl iodide **67b** at –10 °C in THF. The conversion of **67b** was determined by GC, by reacting aliquots with a sat. aq. NH_4Cl-solution. The dimagnesium reagents **43a** and **77a** displayed comparable results i.e. >80% conversion after 1 h (Table 8, entries 1–2). The other magnesium derivatives **77b**–**e** showed a lower reactivity (22-54% conversion after 1 h, entries 3-6).

[74] For a review see: Bickelhaupt, F. *Angew. Chem. Int. Ed.* **1987**, *26*, 990.
[75] Yang, X.; Knochel, P. *Synlett* **2004**, 82.

Table 8: Comparison of dimagnesium reagents **43c** and **77a**–**e** by their reaction with the iodide **67b**.

Entry	Mg-Reagent	Conv.[a] after 0.5h	Conv.[a] after 1h	Conv.[a] after 2h	Conv.[a] after 3h
1	 **43c**	61	84	95	-
2	 **77a**	72	89	96	-
3	 **77b**	38	42	69	76
4	 **77c**	14	22	29	37
5	 **77d**	39	54	73	84
6	 **77e**	29	39	48	-

[a] Conversion was determined by reacting aliquots of the reaction mixture with a sat. aq. NH_4Cl-solution and GC-analysis.

Remarkably, in the case of **77d,** the formation of norbornane during the I/Mg-exchange was observed on GC which supports the cyclisation assumed in Scheme 34. To proof this assumption 3-phenyl-substituted 1,5-*bis*(bromomagnesium)pentane was prepared and its conversion to cyclopentylbenzene during an I/Mg-exchange was confirmed by GC and GC-MS.

In order to make a decision between the utilization of **43c** or **77a**, the isolated yields of the reaction of **43c** and **77a** with **67b** and a consecutive copper(I)-catalyzed reaction with allyl bromide were compared (71% for **43c**, and 70% for **77a**, see also Table 9, entry 3). The Mg-insertion for the preparation of **43c** was slightly cleaner. Iodolysis revealed that 92% of the reactive reagent was the desired di-magnesiumcompound, 5% reduced species, i.e. hexanemagnesium chloride, and 3% eliminated product, i.e. pent-4-

enemagnesium chloride. In comparison, the reagent **77a** was obtained only in 88% purity.

Thus, the reaction of the alkyl iodide **67b** with $ClMg(CH_2)_5MgCl{\cdot}2LiCl$ (**77a**, 1.1 equiv, 25 °C, 2 h) provided the Grignard reagent **68b** which reacted smoothly with CO_2 or allyl bromide, leading to the MOM-derivatives **74b**–**c** in 71-73% yield (Table 9, entry 2-3). The treatment of the alkyl iodide **67c** with the exchange reagent **43c** at –15 °C led to the Grignard reagent **68c** after 3 h. Quenching with 3-bromo-2-methylprop-1-ene, benzaldehyde or propionyl chloride gave the desired products with 63–72% yield (entries 4–6).

Table 9: I/Mg-Exchange reaction and subsequent reaction with an electrophile.

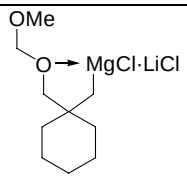
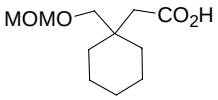
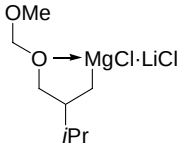
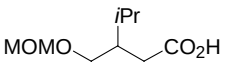
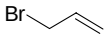
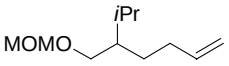
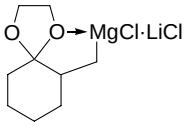
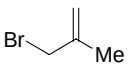
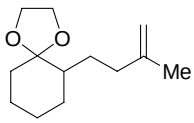
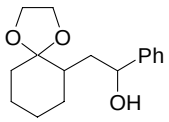
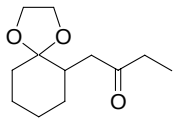
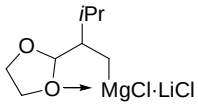
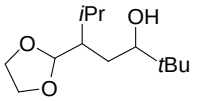
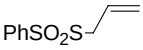
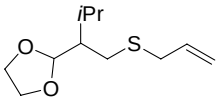
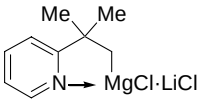
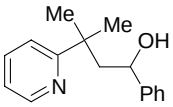
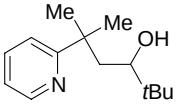
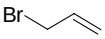
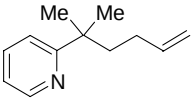
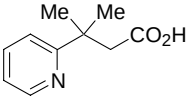
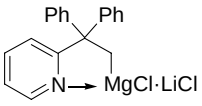
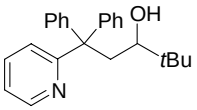
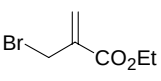
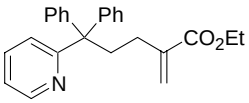
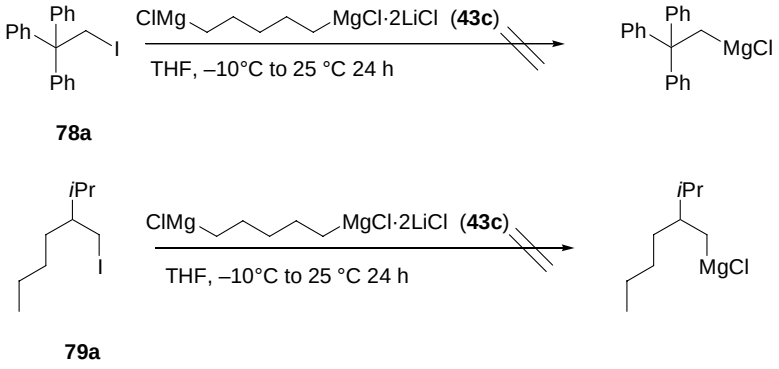
Entry	Mg-Reagent	Electrophile	Product	Yield (%)[a]
1	 **68a**	CO_2	 **74a**	63[b]
2	 **68b**	CO_2	 **74b**	73[b]
3	**68b**		 **74c**	71[c]
4	 **68c**		 **74d**	72[c]
5	**68c**	PhCHO	 **74e**	72[c]

Table 9 continued:

Entry	Mg-Reagent	Electrophile	Product	Yield (%)[a]
6		EtCOCl		63[c,d]
	68c		**74f**	
7		*t*BuCHO		72[c]
	68d		**74g**	
8				58[c]
	68d		**74h**	
9		PhCHO		56[b]
	68e		**74i**	
10		*t*BuCHO		61[b]
	68e		**74j**	
11				64[b]
	68e		**74k**	
12		CO_2		75[b]
	68e		**74l**	
13		*t*BuCHO		59[b]
	68f		**74m**	
14				59[b]
	68f		**74n**	

[a] Isolated yield of analytically pure product; [b] Using iPr$_2$Mg·LiCl (0.65–1.1 equiv) as exchange reagent. [c] Using ClMg(CH$_2$)$_5$MgCl·2LiCl (1.1 equiv) as exchange reagent. [d] After transmetalation using CuCN·2LiCl (1.0 equiv).

The reaction of the β-iodoacetal **67d** with the 1,5-dimagnesium species **43c** gave within 3 h at –20 °C the corresponding magnesium reagent **68d**. Quenching with *t*BuCHO or *S*-allyl benzenesulfonothiate[76] furnished the expected products **74g-h** (entries 7–8) with 58–72% yield. Nitrogen containing heterocycles such as pyridine were also compatible with our reaction conditions. Thus, the reaction of the pyridine derivative **67e** using *i*Pr_2Mg·LiCl (**73**) led after 1.5 h at 25 °C to the Grignard reagent **68e** which was trapped with benzaldehyde, *t*BuCHO, allyl bromide or CO_2 in 56–75% yield (entries 9–12)[77]. For the pyridine derivative **67f** a similar exchange could be performed with *i*Pr_2Mg·LiCl (25 °C, 2.5 h). Reacting **68f** with pivalaldehyde or ethyl 2-(bromomethyl)acrylate led to the expected products **74m–n** (entries 13–14) in 59% yield. To proof the role of the chelatisation, we examined the I/Mg-exchange reaction with two similar alkyl iodides without a heteroatom in *γ*-position to the carbon iodine bond (Scheme 36). Neither the triphenyl-substituted iodide **78a**,[78] nor the oxygen free analogue of **78b** underwent a I/M-exchange.

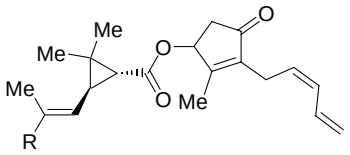


Scheme 36: Attempted I/Mg-exchange reactions without a heteroatom in *γ*-position to the carbon iodine bond.

[76] Kozikowski, A. P.; Anes, A.; Wetter, H. *J. Organomet. Chem.* **1978**, *3*, 164.
[77] Pasquinet, E.; Rocca, P.; Godard, A.; Marsais, F.; Quéguiner, G. *J. Chem. Soc*., *Perkin Trans. 1*, **1998**, 3807.
[78] Patrick, T. B.; Zhang, L.; Li, Q. *J. Fluorine Chem.* **2000**, *102*, 11.

2.4. Br/Mg-Exchange on cyclopropylbromides

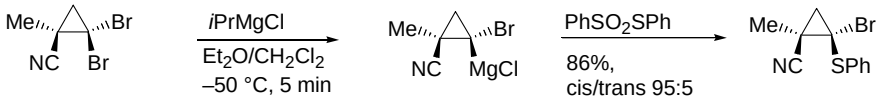
The first reported cyclopropane synthesis was performed in Munich by *Perkin.*[79] Diethyl malonate was treated with sodium ethylate and dibromoethane. Later, many interesting cyclopropanes were discovered in natural proucts, e.g. thujene or chrysanthemic acid.[80] The structural elucidation of pyrethrin I (**79a**; Figure 2) and pyrethrin II (**79b**) by *Staudinger* facilitated the synthesis of these strong neurotoxins which are now still used as insecticides.[81]



79a: R = Me: pyrethrin I
79b: R = CO_2Me: pyrethrin II

Figure 2: Structure of pyrethrin I and II.

Therefore, the functionalization of cyclopropanes is of general interest. *De Lang*[82] published already a stereoselective Br/Li-exchange, and after transmetalation to zinc, some consecutive cross-coupling reactions. Recently, a stereoselective I/Mg-exchange on cyclopropyl derivatives, and one example for a stereoselective Br/Mg-exchange (Scheme 37) was published.[83]



80 **81** **82**

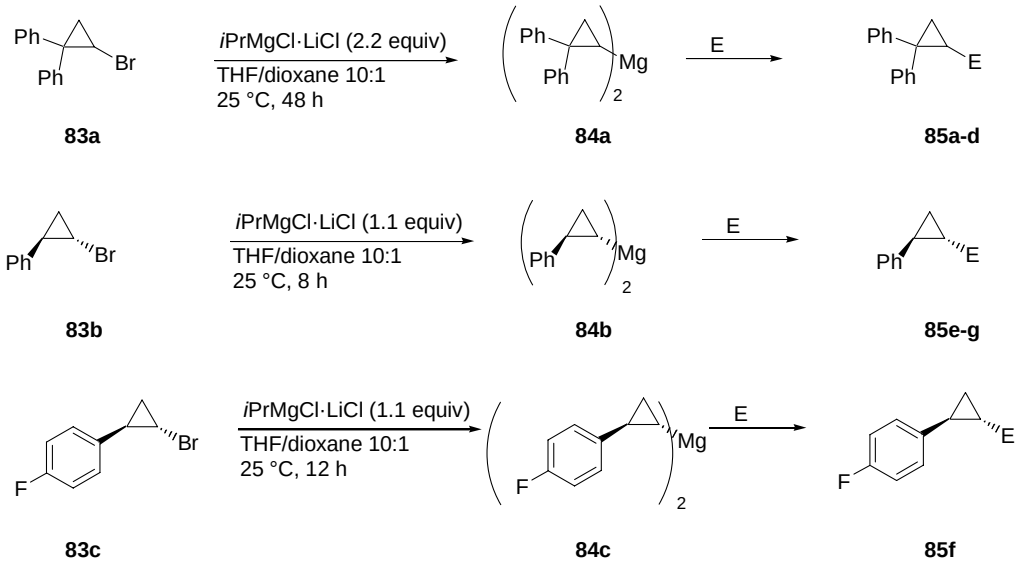
Scheme 37: Stereoselective Br/Mg-exchange and subsequent reaction with an electrophile.

Due to the coordinating effect of the nitrile group the treatment of the cyclopropyl dibromide **80** with *i*PrMgCl gave only the magnesiated cyclopropyl derivative **81** (Scheme 37). Consecutive reactions with various electrophiles led to the expected functionalized cyclopropanes of type **82**.

---

[79] Perkin, W. H. *Chem. Ber.* **1884**, *17*, 54.
[80] For reviews see: a) de Meijere, A.; Wessjohann, L. *Synlett*, **1990**, 20; b) de Meijere, A.; Hopf, H. *Chem. Rev.* **2006**, *106*, 4785; c) Brackmann, F.; de Meijere, A. *Chem. Rev.* **2007**, *107*, 4493.
[81] a) Staudinger, H.; Ruzicka, L. *Helv. Chim. Acta* **1924**, *7*, 177; b) Staudinger, H.; Ruzicka, L. *Helv.. Chim. Acta* **1924**, *7*, 201.
[82] De Lang, R. J.; Brandsma, L. *Synth. Commun.* **1998**, *28*, 225.
[83] Kopp, F.; Sklute, G.; Polborn, K.; Marek, I.; Knochel, P. *Org. Lett.* **2005**, *7*, 3789.

Extension of the Br/Mg-exchange to cyclopropyl derivatives without a chelating or a electron withdrawing group turned out to be much slower (Scheme 38).[44b]



Scheme 38: Br/Mg-exchange with *i*PrMgCl·LiCl in a THF/dioxane-mixture (10:1).

The reactivity of *i*PrMgCl·LiCl in THF was too low and did not lead to full conversion, however the utilization of a THF/dioxane-mixture (10:1) gave, due to the shifted *Schlenk*-equilibrium, shorter reaction times. Under these conditions the cyclopropyl bromide **83a**[84] was subjected to a Br/Mg-exchange within 48 h at 25 °C giving the magnesiated intermediate **84a**. Addition to 3,4-dichlorobenzaldehyde (–30 °C to 25 °C, 2.2 equiv) gave the expected alcohol **85a** in 64% yield (Table 10, entry 1). Reaction of the Grignard reagent **84a** with $PhSO_2SMe$ (–30 °C to 25 °C, 2.2 equiv) furnished the thio ether **85b** in 73% yield (entry 2). Transmetalation with zinc chloride (1.0 M in THF) and a consecutive Negishi cross-coupling reaction using $Pd(dba)_2$ (4 mol%), tris-*o*-furylphosphine (8 mol%) and ethyl 4-iodobenzoate (2.2 equiv) furnished the ester **85c** in 62% yield (entry 3). A similar cross-coupling with 4-bromo-chlorobenzene (2.3 equiv), $Pd(OAc)_2$ (1 mol%) and S-Phos[85] (1.5 mol%) gave the cyclopropane **85d** in 67% yield (entry 4). The *E*-cyclopropyl bromide **83b** was converted to the magnesiated species **84b** in 8 h at 25 °C (1.1 equiv). Transmetalation with zinc chloride (1.0 M in THF) and a cross-coupling reaction with 1-iodo-2-(trifluormethyl)benzene (1.2 equiv), $Pd(dba)_2$ (2 mol%), tris-*o*-furylphosphine (4 mol%) gave the cyclopropane **85e** in 46% yield (entry 5). The cross-coupling reaction with 4-bromobenzonitrile (1.2 equiv) or

[84] Sydnes, L. K.; Bakstad, E. *Acta Chem. Scand.* **1996**, *50*, 446.
[85] a) Altman, R. A.; Buchwald, S. L. *Nature Protocols* **2007**, *2*, 3115; b) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2004**, *43*, 1871.

ethyl 4-bromobenzoate (1.2 equiv) catalyzed by $Pd(OAc)_2$ (1 mol%) and *S*-Phos (1.5 mol%) furnished the cyclopropylderivatives **85f**–**g** in 51-58% yield (entries 6-7).

Table 10: Br/Mg-exchange on cyclopropyl derivatives **83a**–**c** and subsequent reactions with electrophiles.

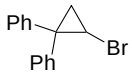
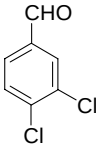
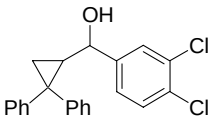
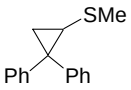
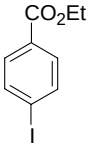
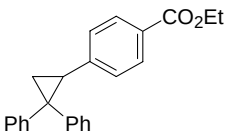
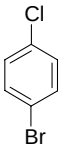
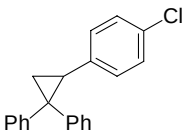
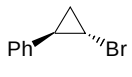
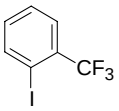
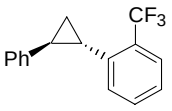
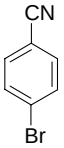
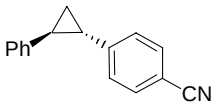
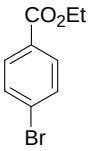
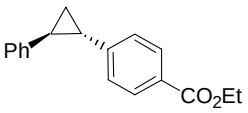
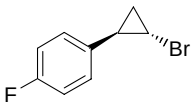
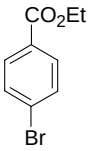
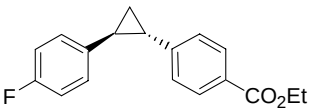
Entry	Cyclopropyl bromide	Electrophile	Product	Yield/%[a]
1	 **83a**		 **85a**	64
2		$PhSO_2SMe$	 **85b**	73
3	**83a**		 **85c**	62[c]
4	**83a**		 **85d**	67[b]
5	 **83b**		 **85e**	46[c]

Table 10 continued:

Entry	Cyclopropyl bromide	Electrophile	Product	Yield/%[a]
6	**83b**		 **85f**	58[b]
7	**83b**		 **85g**	51[b]
8	 **83c**		 **85h**	54[b]

[a] Isolated yields; [b] Using 1.1 equiv of zinc chloride (1.0 M in THF), *S*-Phos (1.5 mol%) and $Pd(OAc)_2$ (1 mol%); [c] Using 1.1 equiv of zinc chloride (1.0 M in THF), [c]$Pd(dba)_2$ (2 mol%) and tfp (4 mol%).

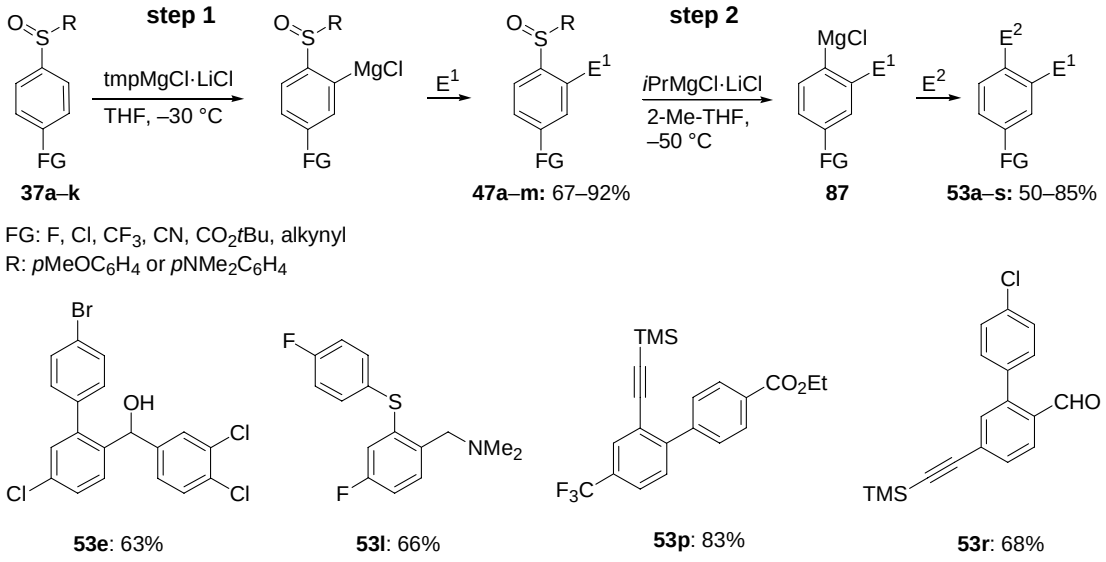
The 4-fluorobenzene-substituted cyclopropyl bromide[86] **83c** was treated with *i*PrMgCl·LiCl in 10:1 THF/dioxane for 12 h at 25 °C, furnishing the corresponding organomagnesium reagent which gave after transmetalation with zinc chloride (1.0 M in THF) and cross-coupling reaction, with ethyl 4-bromobenzoate (1.2 equiv), $Pd(OAc)_2$ (1 mol%) and S-Phos (1.5 mol%), the ester **85h** in 54% yield.

[86] **83b** was prepared from the corresponding dibromide **86** according to: Dehmlow, E. V.; Lissel, M.; Heider, J. *Tetrahedron* **1977**, *33*, 363.

3. Summary and outlook

3.1 Sulfoxide-magnesium exchange on aromatic systems

In summary, we have developed a convenient two-step synthesis for the preparation of 1,2,4-trisubstituted arenes, using a sulfoxide moiety for the two crucial steps: first we employed the excellent directing abilities of the sulfoxide group for an *ortho*-metalation with tmpMgCl·LiCl which has proven to have a good tolerance towards many functional groups and second, we performed a sulfoxide-magnesium exchange reaction, generating a new reactive organometallic intermediate which was trapped with a range of electrophiles.



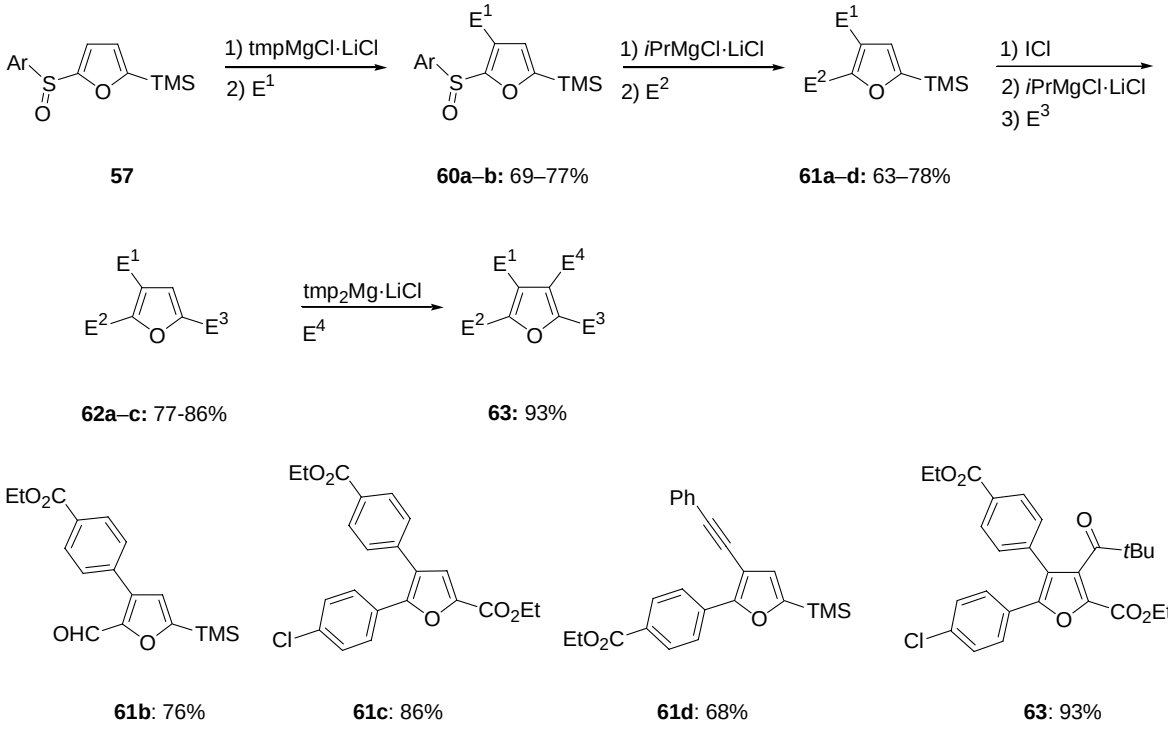
Scheme 39: Two-step synthesis of 1,2,4-trifunctionalized arenes.

The chemoselective metalation (Scheme 39, step 1) was achieved due to an electron rich ligand (pMeOC$_6$H$_4$ or pNMe$_2$C$_6$H$_4$) on the sulfoxide function. The selective cleavage of a sulfur-carbon bond led to the functionalized Grignard reagents of type **87**, and not to RMgX, and gave therefore access to smooth reactions with various electrophiles leading to trisubstituted arenes of type **53**.

Extensions of this work could be the application of the two-step synthesis for the preparation of a 1,2,3-trisubstituted aromatics, by starting from *meta*-substituted sulfoxides. Furthermore the sulfoxide group could be used as a protecting group for an organometallic function which can be cleaved after other planned steps furnishing again the metal species.

3.2. Full functionalization of the furan ring

The application of the developed two-step sequence for the functionalization of furan, was accomplished on a few selected examples, demonstrating the power of this sequence for providing a substrate with range of functionalities.



57 **60a–b:** 69–77% **61a–d:** 63–78%

62a–c: 77-86% **63:** 93%

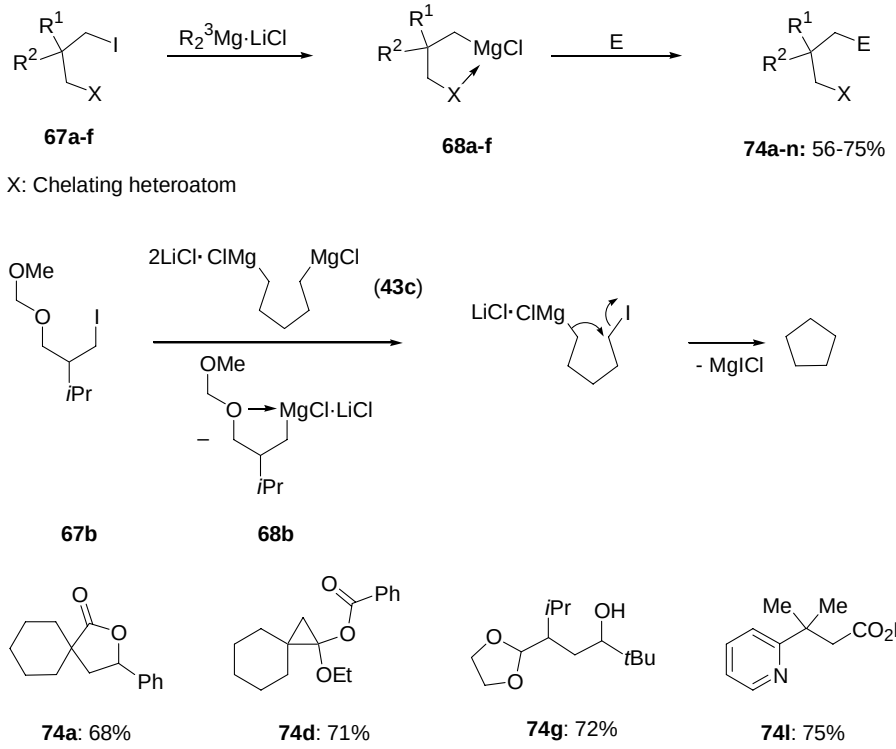
61b: 76% **61c**: 86% **61d**: 68% **63**: 93%

Scheme 40: Functionalization of furan with the developed two-step synthesis and consecutive reactions.

Future work could be the application of the sulfoxide route to other heteroaromatics, like thiophene, benzofuran or pyrrole.

3.3. I/Mg-exchange on Csp^3-centers

The examination of the I/Mg-exchange reaction on Csp^3-centers revealed that this reaction proceeds under the influence of chelating functionalities, providing additional stability. A new reagent for the I/Mg-exchange reaction was developed which facilitated the reduction of reagent excess, and led therefore to decreasing amounts of byproducts.

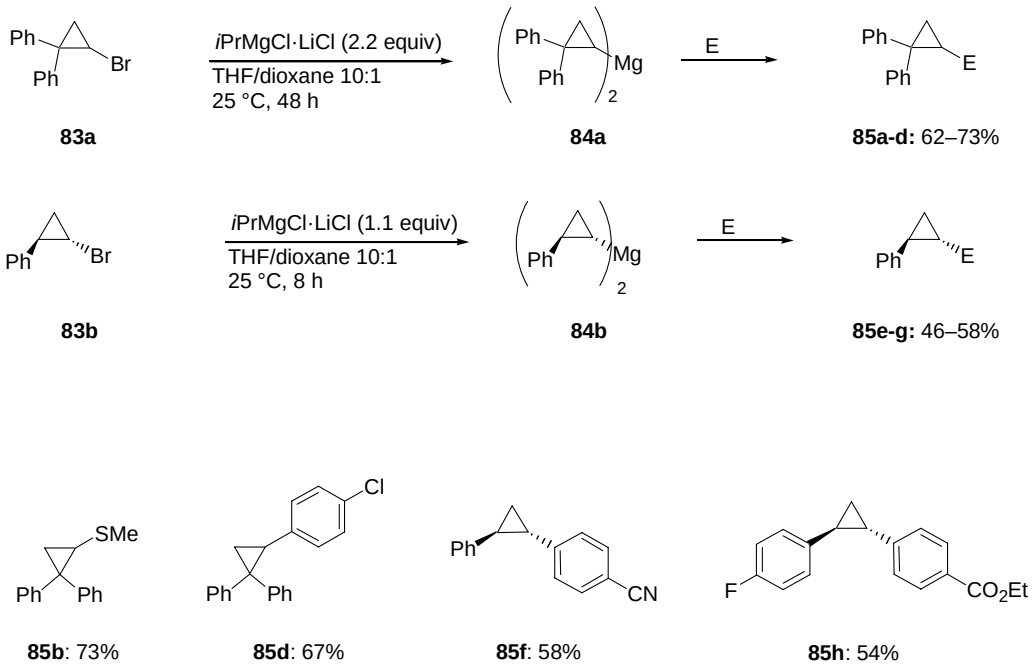


Scheme 41: Chelation of the formed Grignard reagents **68a**–**f**, and demonstration of the new Mg/I-exchange reagent **77a**.

Future works could be the preparation of chiral Csp^3-organomagnesium reagents. The chelatization and the new cyclizing I/Mg-exchange reagent could give an impulse for new experiments.

3.4. Br/Mg-Exchange on cyclopropyl bromides

The Br/Mg-exchange reaction was performed with commercially available *i*PrMgCl·LiCl in a THF/dioxane mixture, leading to a shifted *Schlenk*-equilibrium,[8-9] and therefore to an increased reactivity of the Grignard reagent. The formed organometallic species were quenched with various eletrophiles, including Negishi cross-coupling reactions with aryl bromides.



Scheme 42: Br/Mg-exchange with retention of configuration, and consecutive reaction with electrophiles.

4. Experimental section

4.1. General considerations

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

4.1.1. Solvents

Diethyl ether was was predried over calcium hydride and dried with the solvent purification system SPS-400-2 from INNOVATIVE TECHNOLOGIES INC (Al_2O_3, 1-3 mm, ICN, Eschwege, Germany).
DMF was heated to reflux for 14 h over CaH_2 and distilled from CaH_2.
Ethanol was treated with magnesium turnings (10 g/L), heated to reflux and distilled.
DMPU was heated to reflux for 14 h over CaH_2 and distilled from CaH_2.
Methanol was treated with magnesium turnings (10 g/L), heated to reflux and distilled.
2-Methyl-THF was distilled from sodium benzophenone ketyl under nitrogen and stored under argon.
NMP was heated to reflux for 14 h over CaH_2 and distilled from CaH_2.
THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen.

4.1.2. Chromatography

Thin layer chromatography (TLC) was performed using aluminium plates coated with SiO_2 (Merck 60, F-254). The spots were visiualized by UV light or by staining of the TLC plate with the solution below followed by heating if necessary:

-Phosphormolybdic acid (5.0 g), $Ce(SO_4)_2$ (2.0 g), conc. H_2SO_4 (12.0 mL) in water (230 mL)

- Iodine absorbed on silica gel

-$KMnO_4$ (0.3g), K_2CO_3 (20 g), KOH (0.3 g), in water (300 mL).

Flash column chromatography was performed using SiO_2 60 (0.04-0.063 mm, 230-400 mesh) from Merck.

4.1.3. Analytical Data

NMR-spectra were recorded on *Bruker* ARX 200, AC 300 WH 400 or AMX 600 instruments. Chemical shifts are reported as δ-values in ppm relative to the solvent peak.
For the characterization of the observed signal multiplicities the following abbreviations were used: s (singlet), d (doublet), t (triplet), dd (doublet of doublet), q (quartet) m (multiplet).
For the characterization of the observed C-signal the following abbreviations were used: CH_3 (primary), CH_2 (secondary), CH (tertiary), and no description for quarternary carbon.

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 281 IR spectrometer. Samples were measured either as film between potassium bromide plates (film), as potassium bromide tablets (KBr) or neat (ATR, Smiths Detection DuraSampl IR II Diamond ATR).
The absorption bands were reported in wavenumbers (cm^{-1}). For the characterization the following abbreviations were used: br (broad), vs (very strong), s (strong), m (medium), w (weak).

Gas chromatography was performed with machines of type *Hewlett-Packard* 6890 or 5890 series II, using a column of type HP 5 (*Hewlett-Packard*, 5% phenylmethylpolysiloxane; length: 15 m, diameter: 0.25 mm; film thickness 0.25 µm) The detection was accomplished by using a flame ionization detector. Alkanes like decane or tetradecane were used as internal standards.

Mass Spectra were recorded on Finnigan MAT 95Q or Finnigan MAT 90 instrument for electron impact ionization (EI). High resolution mass spectra (HRMS) was recorded on the same instrument.

4.1.4. Reagents

CuCN·2LiCl solution was prepared by drying CuCN (8.96 g, 100 mmol) and LiCl (8.48 g, 200 mmol) in a *Schlenk*-flask under vacuum for 5 h at 140 °C. After cooling to 25 °C dry THF (100 mL) was added and the mixture was stirred for 24 h.

$ZnCl_2$ solution was prepared by melting and drying $ZnCl_2$ (27.3 g, 200 mmol) with a Bunsen burner in vacuum for 15 min. After cooling to 25 °C THF (200 mL) and a stirring bar was added and the mixture was stirred until all solids were dissolved.

tmpMgCl·LiCl solution was prepared by adding 2,2,6,6-tetramethylpiperidine (19.8 g, 126 mmol) to freshly titrated[87] *i*PrMgCl·LiCl (100 mL, 120 mmol, 1.20 M in THF) and continuously stirring of the resulting mixture for 24 h at 25 °C.

$tmp_2MgCl·2LiCl$ was prepared according to literature: In a dry argon-flushed Schlenk tube, 2,2,6,6-tetramethylpiperidine (tmpH; 5.07 mL, 30 mmol) was dissolved in THF (30 mL). This solution was cooled to –40°C, and *n*BuLi (12.5 mL, 30 mmol, 2.4 M in hexane) was added dropwise. After the addition was complete, the reaction mixture was warmed to 0 °C and stirred at this temperature for 30 min. Freshly titrated tmpMgCl·LiCl (30 mL, 30 mmol, 1.0 M in THF) was then added dropwise to the tmpLi solution, and the reaction mixture was stirred at 0 °C for 30 min, warmed to 25 °C, and stirred for 1 h. The solvents were then removed *in vacuo* without heating, affording a yellowish solid. Freshly distilled THF was slowly added with vigorous stirring, until the salts had completely dissolved. The fresh $TMP_2Mg·2LiCl$ solution was titrated prior to use at 0 °C with benzoic acid using 4-(phenylazo) diphenylamine as indicator. A concentration of 0.6 M in THF was obtained.

***i*PrMgCl·LiCl** was used as a 1.2 M solution in THF purchased by Chemetall.

***n*BuLi** was used as a 1.5 M solution in hexane purchased by Chemetall.

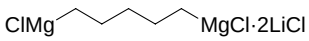
***t*BuLi** was used as a 1.5 M solution in hexane purchased by Chemetall.

MeLi was used as a 1.7 M solution in diethyl ether purchased by Chemetall.

[87] a) Lin, H. S.; Paquette, L. *Synth. Commun.* **1994**, *24*, 2503; b) Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 890.

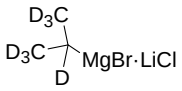
4.1.5. Non-commercial available Grignard-reagents

1,5-Bis(chloromagnesio)pentane (**43c**)



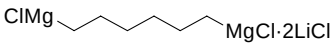
A dry and argon-flushed two necked *Schlenk*-flask, equipped with a stirring bar, a septum and a reflux condenser was charged with LiCl (7.21 g, 170.0 mmol). The salt was dried in high vacuum for 15 min at 400 °C. After cooling to 25 °C magnesium turnings (5.47 g, 225.0 mmol) and THF (45 mL) were added. 1,6-Dichloropentane (10.6 g, 9.8 mL, 75.0 mmol in 30 mL THF) was added dropwise, and the reaction mixture was heated at reflux for 2 h. The solids were allowed to sediment, then the THF-solution was collected (75 mL) and the concentration of magnesium reagent was determined by titration (c = 0.615 M, yield: 62%).

2-Bromomagnesio propane(d_7) (**51**)



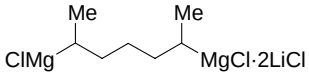
A dry and argon-flushed two necked *Schlenk*-flask, equipped with a stirring bar, a septum and a reflux condenser was charged with LiCl (1.80 g, 42.4 mmol). The salt was dried in high vacuum for 15 min at 400 °C. After cooling to 25 °C magnesium turnings (1.12 g, 46.0 mmol) and THF (35 mL) were added and a water bath (25 °C) was placed under the flask. Isopropyl bromide(d_7) (5.0 g, 38.5 mmol) was added dropwise, and the reaction mixture was stirred for 4 h. The solids were allowed to sediment over night, then the THF-solution was collected (31 mL) and the concentration of magnesium reagent was determined by titration (c = 1.06 M, yield: 85%).

1,6-Bis(chloromagnesio)hexane (**77a**)



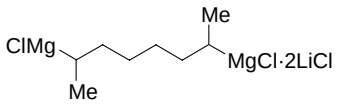
A dry and argon-flushed two necked *Schlenk*-flask, equipped with a stirring bar, a septum and a reflux condenser was charged with LiCl (9.33 g, 220.0 mmol). The salt was dried in high vacuum for 15 min at 400 °C. After cooling to 25 °C magnesium turnings (7.29 g, 300.0 mmol) and THF (70 mL) were added. 1,6-Dichlorohexane (15.5 g, 14.8 mL, 100.0 mmol in 30 mL THF) was added dropwise, and the reaction mixture was heated at reflux for 2 h. The solids were allowed to sediment, then the THF-solution was collected (105 mL) and the concentration of magnesium reagent was determined by titration (c = 0.737 M, yield: 77%).

2,6-Bis(chloromagnesio)heptane (**77b**)



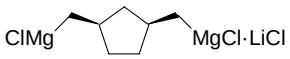
A dry and argon-flushed two necked *Schlenk*-flask, equipped with a stirring bar, a septum and a reflux condenser was charged with LiCl (2.76 g, 65.0 mmol). The salt was dried in high vacuum for 15 min at 400 °C. After cooling to 25 °C magnesium turnings (2.19 g, 90.0 mmol) and THF (20 mL) were added. The magnesium turnings were activated with 1,2-dibromoethane (90 µL, 1.0 mmol). 2,6-Dichloroheptane (5.07 g, 30.0 mmol in 10 mL THF) was added dropwise, and the reaction mixture was heated to reflux for 4 h. The solids were allowed to sediment over night, then the THF-solution was collected (32 mL) and the concentration of magnesium reagent was determined by titration (c = 0.55 M, yield: 59%).

2,7-Bis(chloromagnesio)octane (**77c**)



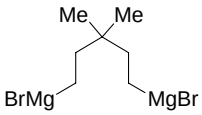
A dry and argon-flushed two necked *Schlenk*-flask, equipped with a stirring bar, a septum and a reflux condenser was charged with LiCl (2.76 g, 65.0 mmol). The salt was dried in high vacuum for 15 min at 400 °C. After cooling to 25 °C magnesium turnings (2.26 g, 93.0 mmol) and THF (20 mL) were added. The magnesium turnings were activated with 1,2-dibromoethane (90 µL, 1.0 mmol). 2,7-Dichloroctane (5.66 g, 30.9 mmol in 10 mL THF) was added dropwise, and the reaction mixture was heated to reflux for 4 h. The solids were allowed to sediment over night, then the THF-solution was collected (27 mL) and the concentration of magnesium reagent was determined by titration (c = 0.97 M, yield: 84%).

1,3-Bis(chloromagnesiomethyl)cyclopentane (**77d**)



A dry and argon-flushed two necked *Schlenk*-flask, equipped with a stirring bar, a septum and a reflux condenser was charged with LiCl (1.91 g, 45.0 mmol). The salt was dried in high vacuum for 15 min at 400 °C. After cooling to 25 °C magnesium turnings (2.99 g, 123.0 mmol) and THF (27 mL) were added. The magnesium turnings were activated with 1,2-dibromoethane (90 µL, 1.0 mmol). 1,3-bis-(chloromethyl)-cyclopentane (6.86 g, 41.0 mmol in 14 mL THF) was added dropwise, and the reaction mixture was stirred at 25 °C for 24 h. The solids were allowed to sediment, then the THF-solution was collected (48 mL) and the concentration of *bis*magnesium reagent was determined by titration (c = 0.60 M, yield: 70%).

1,5-Bis(bromomagnesio)-3,3-dimethyl-pentane (**77e**)



A dry and argon-flushed two necked *Schlenk*-flask, equipped with a stirring bar, a septum and a reflux condenser was charged with LiCl (3.82 g, 90.0 mmol). The salt was dried in high vacuum for 15 min at 400 °C. After cooling to 25 °C magnesium turnings (4.25 g, 175.0 mmol) and THF (40 mL) were added. 1,5-Dibromo-3,3-dimethylpentane (20.6 g, 79.5 mmol in 20 mL THF) was added dropwise, and the reaction mixture was heated at reflux for 2 h. The solids were allowed to sediment, then the THF-solution was collected (66 mL) and the concentration of *bis*magnesium reagent was determined by titration (c = 0.46 M, yield: 38%).

4.2. Typical procedures

Typical Procedure for preparation of sulfoxides of type **37** with the *p*$NMe_2C_6H_4$-ligand (TP1):

In a dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, 4-(dimethylamino)phenyl thiocyanate (**35**, 10.0 mmol, 1.78 g) was dissolved in THF (10 mL) and cooled to –20 °C. A solution of a functionalized magnesium reagent (11.0 mmol, approx 1 M) was added and the reaction mixture was allowed to warm to 25 °C. The reaction mixture was quenched with sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. The crude sulfide was dissolved in CH_2Cl_2 (40 mL) and cooled to –20 °C. *m*CPBA (2.70 g, 11.0 mmol, 70% in water) dissolved in CH_2Cl_2 (10 mL) was added slowly. After stirring for 1 h at –20 °C the reaction mixture was quenched with a sat. aq. $Na_2S_2O_3$-solution (20 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification yielded the products of type **37**.

Typical procedure for preparation of sulfoxides of type **37** with the *p*$MeOC_6H_4$-ligand (TP2):

A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution (approx. 0.5 M, 10.0 mmol in THF) of the appropriate magnesium reagent and cooled to –20 °C. 4-Methoxybenzene sulfinyl chloride (**44**; 2.48 g, 13.0 mmol) was added slowly and the reaction mixture was allowed to warm to 25 °C. The reaction mixture was quenched with sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification yielded the products **37**.

Typical procedure for preparation of sulfoxides of type **37** using the sulfinate **45** (TP3):

A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution (approx. 0.5 M, 15.0 mmol in THF) of the appropriate magnesium reagent and cooled to –50 °C. Methyl 4-(dimethylamino)benzenesulfinate (**45**; 3.29 g, 16.5 mmol) was added slowly and the reaction mixture was allowed to warm to 25 °C and stirred for additional 30 min. The reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification yielded the products of type **37**.

Typical procedure for deprotonation of sulfoxides and Negishi type cross-coupling reactions (TP4):

A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a sulfoxide of type **37** (1.0 mmol) dissolved in THF (2 mL). The reaction mixture was cooled to –30 °C and tmpMgCl·LiCl (0.92 mL, 1.1 mmol, 1.20 M in THF) was added dropwise. After 20 min of stirring at –30 °C zinc chloride (1.0 mL, 1.0 mmol, 1.0 M in THF) was added, and the reaction mixture was allowed to warm to 25 °C. A palladium catalyst and an electrophile were added and the reaction mixture was stirred at 25 °C to 50 °C, depending on the subtrate. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographical purification yielded the products of type **47**.

Typical procedure for the sulfoxide-magnesium exchange leading to arenes of type **53** (TP5):

A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of sulfoxide of type **47** (1.0 mmol) in 2-methyl-THF (2 mL).

The reaction mixture was cooled to –50 °C and *i*PrMgCl·LiCl (0.92 mL, 1.1 mmol, 1.20 M in THF) was added dropwise. After stirring at –50 °C until GC analysis showed full conversion of the sulfoxide the desired electrophile (0.8 mmol) was added and the reaction mixture was stirred at the given temperature until GC analysis showed full conversion of the electrophile. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (20 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographical purification yielded the products of type **53**.

Typical procedure for the sulfoxide-magnesium exchange leading to furans of type **61** (TP6):

A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of a furan of type **60** (1.0 mmol) in 2-methyl-THF (2.0 mL). The reaction mixture was cooled to –50 °C and *i*PrMgCl·LiCl (0.92 mL, 1.1 mmol, 1.20 M in THF) was added dropwise. After stirring at –50 °C until GC analysis showed full conversion of the sulfoxide the desired electrophile (0.80 mmol) was added and the reaction mixture was stirred at the given temperature until GC analysis showed full conversion of the electrophile. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (20 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographical purification yielded the products of type **61**.

Typical procedure for the iodine-magnesium exchange leading to furans of type **62** (TP7):

A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of furan of type **61** (1.0 mmol) in THF (2 mL). The reaction mixture was cooled to –40 °C and *i*PrMgCl·LiCl (0.92 mL, 1.1 mmol, 1.20 M in THF) was added dropwise. After stirring at –40 °C for 20 min GC analysis showed full conversion of the furane, the desired electrophile (1.1 mmol) was added and the reaction mixture was stirred at the given temperature until GC analysis showed full conversion

of the electrophile. The reaction mixture was quenched with sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (30 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification yielded the products of type **62**.

Typical procedure for the bromine-magnesium exchange leading to cyclopropanes of type **83a**–**d** (TP8):

A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar was charged with *i*PrMgCl·LiCl (4.40 mmol, 4.40 ml, 1 M in THF) and dioxane (0.2 mL). 2-Bromo-1,1-diphenylcyclopropane (546 mg, 2.00 mmol) was added and the reaction mixture was stirred at 25 °C for 2 d, until GC analysis showed full conversion of the bromide. The desired electrophile was added and the reaction mixture was stirred at the given temperature until GC analysis showed full conversion of the electrophile. The reaction mixture was quenched with sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (30 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification yielded the products of type **83a**–**d**.

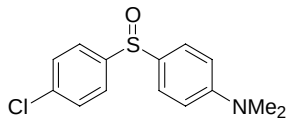
Typical procedure for the bromine-magnesium exchange leading to cyclopropanes of type **83e**–**f** (TP9):

A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar was charged with *i*PrMgCl·LiCl (2.20 ml, 2.20 mmol, 1 M in THF) and dioxane (0.2 mL). E-(2-bromocyclopropyl)benzene (394 mg , 2.00 mmol) was added and the reaction mixture was stirred at 25 °C for 8 h, until GC analysis showed full conversion of the bromide. The desired electrophile was added and the reaction mixture was stirred at the given temperature until GC analysis showed full conversion of the electrophile. The reaction mixture was quenched with sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (30 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification yielded the products of type **83e**–**g**.

4.3. Preparation of functionalized organomagnesium reagents

4.3.1. Preparation of diarylsulfoxides

[4-(4-Chloro-benzenesulfinyl)phenyl]dimethylamine (**37a**)



According to **TP1** the sulfoxide **37a** was prepared from 4-chloro-phenyl magnesium bromide (110 mmol, 0.88 M in THF) and dimethyl-(4-thiocyanato-phenyl)-amine (17.8 g, 100 mmol) and purified by flash chromatography (pentane / ethyl acetate = 1:1, silica gel), furnishing **37a** as a colourless solid (17.9 g, 64% yield).

mp (°C): 128-129.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.99 (s, 6 H), 6.65–6.70 (m, 2 H), 7.38–7.46 (m, 4 H), 7.49–7.54 (m, 2 H).

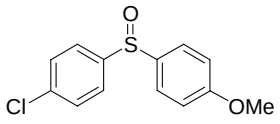
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 40.1 (CH_3), 112.0 (CH), 126.0 (CH), 127.7 (CH), 129.2 (CH), 130.3, 136.3, 144.8, 152.5.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2892 (w), 1596 (s), 1570 (w), 1554 (w), 1509 (m), 1471 (m), 1446 (m), 1388 (w), 1363 (m), 1233 (m), 1192 (m), 1091 (s), 1083 (s), 1060 (m), 1045 (vs), 1010 (s), 826 (s), 815 (m), 807 (s), 799 (m), 738 (s), 711 (w), 607 (w).

MS (EI, 70 eV): *m/z* (%) = 279 (19), 263 (34), 233 (25), 232 (23), 231 (80), 230 (30), 168 (100), 152 (25), 136 (30), 44 (19).

HRMS (EI): calcd. for $C_{14}H_{14}{}^{35}ClNO^{32}S$: 279.0485, found: 279.0479.

4-Chlorophenyl 4-methoxyphenyl sulfoxide (**37b**)



According to **TP2** the sulfoxide **37b** was prepared from 4-chloro-phenyl magnesium bromide (114 mL, 100 mmol, 0.88 M in THF) and 4-methoxybenzene sulfinyl chloride

(24.7 g, 130 mmol) and purified by recrystalization (pentane) furnishing **37b** as a colourless solid (22.6 g, 85% yield).

mp (°C): 67-68.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 3.81 (s, 3 H), 6.92–6.97 (m, 2 H), 7.39–7.43 (m, 2 H), 7.51–7.56 (m, 4 H).

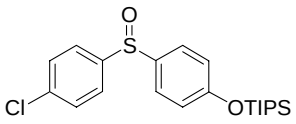
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 55.6 (CH_3), 115.0 (CH), 126.0 (CH), 127.3 (CH), 129.5 (CH), 136.2, 137.0, 144.3, 162.3.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2970 (w), 2944 (w), 2839 (w), 1739 (m), 1591 (m), 1577 (m), 1493 (s), 1473 (s), 1441 (w), 1388 (w), 1304 (m), 1246 (vs), 1168 (s), 1085 (vs), 1032 (vs), 1008 (vs), 828 (vs), 793 (s), 736 (vs), 714 (s).

MS (EI, 70 eV): *m/z* (%) = 266 (15), 250 (10), 220 (29), 219 (12), 218 (91), 203 (16), 155 (69), 139 (47), 123 (100), 95 (10).

HRMS (EI): calcd. for $C_{13}H_{11}{}^{35}ClO_2{}^{32}S$: 266.0168, found: 266.0172.

{4-[(4-Chlorophenyl)sulfinyl]phenoxy}(triisopropyl)silane (**37c**)



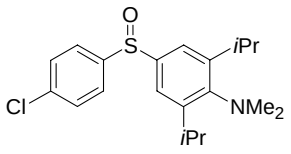
A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar was charged with a solution (4-bromophenoxy)(triisopropyl)silane (7.20 g, 21.9 mmol) in THF (12 mL). The solution was cooled to –78 °C and *n*BuLi (11.1 mL, 26.2 mmol, 2.35 M in hexane) was added dropwise, and stirred for additional 1.5 h at –78 °C. Then *S*-(4-chlorophenyl) benzenesulfonothioate (6.86 g, 24.1 mmol) was added and reaction mixture was allowed to warm to 25 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether 5:1, silica gel) yielded {4-[(4-chlorophenyl)thio]phenoxy}(triisopropyl)-silane as a colourless solid (6.60 g, 80% yield).

The sulfide (4.08 g, 10.4 mmol) was dissolved in CH_2Cl_2 (60 mL) and cooled to –20 °C. *m*CPBA (3.08 g, 12.5 mmol, 70% in water) dissolved in CH_2Cl_2 (25 mL) was added slowly. After stirring for 1 h at –20 °C the reaction mixture was quenched with a sat. aq.

$Na_2S_2O_3$-solution (20 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 6:1, silica gel) yielded **37c** as a colourless oil (3.22 g, 82% yield, 66% over two steps).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.06 (d, J = 6.84 Hz, 18 H), 1.17–1.29 (m, 3 H), 6.91–6.94 (m, 2 H), 7.40–7.54 (m, 6 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 12.6 (CH), 17.8 (CH_3), 120.9 (CH), 126.0 (CH), 127.3 (CH), 129.4 (CH), 136.6, 136.9, 144.4, 159.2.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2945 (s), 2867 (s), 1587 (s), 1491(s), 1390 (w), 1268 (s), 1164 (w), 1091 (m), 1046 (s), 1011 (m), 904 (s), 882 (m), 836 (m), 738 (s), 684 (m), 589 (w), 555 (m).
MS (EI, 70 eV): *m/z* (%) = 408 (15), 392 (14), 368 (11), 367 (46), 366 (27), 365 (100), 360 (10), 339 (15), 337 (30), 323 (11), 311 (23), 310 (12), 309 (47), 295 (22), 293 (12), 235 (11), 206 (11), 163 (18), 159 (23), 150 (22), 147 (10) 136 (12), 135 (17), 121 (14), 59 (11).
HRMS (EI): calcd. for $C_{21}H_{29}{}^{35}ClO_2{}^{32}S^{28}Si$: 408.1346, found: 408.1366.

{4-[(4-Chlorophenyl)sulfinyl]-2,6-diisopropylphenyl}dimethylamine (**37d**)

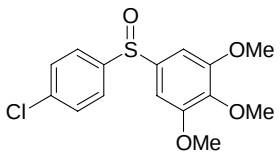


A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar was charged with a solution (4-bromo-2,6-diisopropylphenyl)dimethylamine (11.4 g, 40.0 mmol) in THF (80 mL). The solution was cooled to –78 °C and *n*BuLi (17.9 mL, 42.0 mmol, 2.35 M in hexane) was added dropwise, and stirred for additional 1 h at –78 °C. Then *S*-(4-chlorophenyl) benzenesulfonothioate (12.5 g, 44.0 mmol) was added and reaction mixture was allowed to warm to 25 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was

removed under reduced pressure. {4-[(4-Chlorophenyl)thio]-2,6-diisopropylphenyl}-dimethylamine was obtained as a colourless solid (14.6 g, 92% purity, 98% yield).
The crude sulfide was dissolved in CH_2Cl_2 (180 mL) and cooled to –20 °C. *m*CPBA (10.9 g, 44.0 mmol, 70% in water) dissolved in CH_2Cl_2 (50 mL) was added slowly. After stirring for 1 h at –20 °C the reaction mixture was quenched with a sat. aq. $Na_2S_2O_3$-solution (50 mL) and extracted three times with diethyl ether (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 10:1, silica gel) yielded **37d** as a colourless solid (11.1 g, 76% over two steps).

mp (°C): 139–140.
^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.15 (d, J = 6.84 Hz, 6 H), 1.16 (d, J = 6.84 Hz, 6 H), 2.80 (s, 6 H), 3.30 (sep, J = 6.84 Hz, 2 H), 7.30 (s, 2 H), 7.40–7.44 (m, 2 H), 7.54–7.59 (m, 2 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 24.1 (CH_3), 28.6 (CH), 43.9 (CH_3), 120.6 (CH), 126.1 (CH), 129.4 (CH), 136.8, 141.8, 144.4, 151.1.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3083 (w), 2961 (s), 2926 (m), 2867 (m), 2784 (m), 1572 (w), 1475 (m), 1458 (m), 1444 (m), 1387 (w), 1232 (w), 1148 (w), 1089 (m), 1076 (m), 1048 (vs), 1008 (m), 940 (w), 814 (m), 738 (m), 604 (m), 546 (w).
MS (EI, 70 eV): *m/z* (%) = 363 (73) , 348 (14), 317 (12), 315 (32), 300 (20), 253 (14), 252 (100), 222 (14), 220 (28), 159 (11).
HRMS (EI): calcd. for $C_{20}H_{26}{}^{35}ClNO^{32}S$: 363.1424, found: 363.1416.

4-Chlorophenyl 3,4,5-trimethoxyphenyl sulfoxide (**37e**)



The sulfide **40** (10.7 g, 34.5 mmol) was dissolved in CH_2Cl_2 (150 mL) and cooled to –20 °C. *m*CPBA (9.34 g, 38.0 mmol, 70% in water) dissolved in CH_2Cl_2 (50 mL) was added slowly. After stirring for 1 h at –20 °C the reaction mixture was quenched with a sat. aq. $Na_2S_2O_3$-solution (50 mL) and extracted three times with ethyl acetate (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the

solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 2:1, silica gel) yielded **37e** as a colourless solid (8.23 g, 73% yield).

mp (°C): 129–130.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 3.83 (s, 3 H), 3.85 (s, 6 H), 6.84 (s, 2 H), 7.41–7.46 (m, 2 H), 7.54–7.59 (m, 2 H).

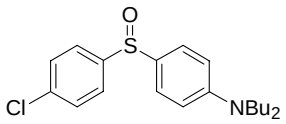
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 56.4 (CH_3), 60.9 (CH_3), 101.6 (CH), 126.1 (CH), 129.6 (CH), 137.3, 139.7, 140.4, 144.2, 154.1.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2944 (w), 1584 (m), 1496 (m), 1467 (m), 1429 (w), 1404 (s), 1306 (m), 1225 (s), 1176 (w), 1123 (s), 1192 (s), 1068 (m), 1047 (m), 1008 (m), 990 (m), 824 (m), 736 (m), 699 (w), 612 (m).

MS (EI, 70 eV): *m/z* (%) = 326 (71) , 295 (12), 280 (19), 278 (49), 265 (18), 263 (50), 216 (12), 215 (100), 199 (18), 183 (96), 182 (11), 168 (28), 143 (11).

HRMS (EI): calcd. for $C_{15}H_{15}{}^{35}ClO_4{}^{32}S$: 326.0380, found: 326.0395.

Dibutyl{4-[(4-chlorophenyl)sulfinyl]phenyl}amine (**37f**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a reflux condenser was charged with Mg (1.74 g, 71.7 mmol) in THF (20 mL). A solution of dibutyl(4-iodophenyl)amine (19.8 g, 59.8 mmol) in THF (35 mL) was added dropwise, and heated for additional 12 h at reflux. Then the reaction mixture was cooled to –40 °C and *S*-(4-chlorophenyl) benzenesulfonothioate (17.0 g, 59.8 mmol) was added and reaction mixture was allowed to warm to 25 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Dibutyl{4-[(4-chlorophenyl)thio]phenyl}amine was obtained as a crude product (10.8 g, 70% purity by GC analysis, 36 % yield)

The crude sulfide (10.8 g, 21.6 mmol) was dissolved in CH_2Cl_2 (60 mL) and cooled to –20 °C. *m*CPBA (7.00 g, 28.4 mmol, 70% in water) dissolved in CH_2Cl_2 (40 mL) was added slowly. After stirring for 1 h at –20 °C the reaction mixture was quenched with a sat. aq. $Na_2S_2O_3$-solution (20 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 1:1, silica gel) yielded **37f** as a colourless oil (6.02 g, 76% yield, 27% over two steps).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 0.92 (t, J = 7.39 Hz, 6 H), 1.28–1.35 (m, 4 H), 1.49–1.55 (m, 4 H), 3.23–3.25 (m, 4 H), 6.58 (d, J = 9.04 Hz, 2 H), 7.35–7.41 (m, 4 H), 7.51–7.53 (m, 2 H).

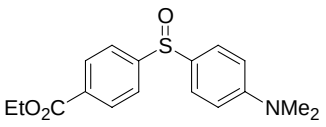
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 13.9 (CH_3), 20.2 (CH_2), 29.1 (CH_2), 50.7 (CH_2), 111.4 (CH), 125.9 (CH), 128.1 (CH), 128.9, 129.0 (CH), 136.1, 144.7, 150.6.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2955 (s), 2929 (s), 2871 (m), 1586 (s), 1494 (vs), 1463 (m), 1396 (w), 1366 (m), 1285 (m), 1219 (m), 1185 (m), 925 (w), 799 (s).

MS (EI, 70 eV): *m/z* (%) = 363 (43) , 347 (21), 322 (40), 321 (18), 320 (100), 315 (11), 306 (17), 304 (34), 280 (16), 278 (39), 272 (32), 264 (14), 262 (22), 252 (24), 248 (13), 184 (10), 167 (11), 161 (15), 119 (17), 105 (18), 104 (10), 41 (17).

HRMS (EI): calcd. for $C_{20}H_{26}{}^{35}ClNO^{32}S$: 363.1424, found: 363.1416.

Ethyl 4-{[4-(dimethylamino)phenyl]sulfinyl}benzoate (**37g**)



According to **TP1** the sulfoxide **37g** was prepared from 4-carbethoxyphenyl magnesium chloride (13.0 mL, 10 mmol, 0.77 M in THF) and dimethyl-(4-thiocyanato-phenyl)amine (1.96 g, 11 mmol) and purified by flash chromatography (pentane / ethyl acetate = 2:3, silica gel), furnishing **37g** as a yellow oil (1.86 g, 59% yield).

mp (°C): 86–88.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.39 (t, J =7.15 Hz, 3 H), 2.99 (s, 6 H), 4.38 (q, J = 7.15 Hz, 2 H), 6.56–6.70 (m, 2 H), 7.43–7.45 (m, 2 H), 7.64–7.68 (m, 2 H), 8.09–8.13 (m, 2 H).

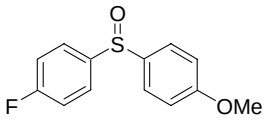
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.2 (CH_3), 40.0 (CH_3), 61.2 (CH_2), 111.9 (CH), 124.3 (CH), 127.9 (CH), 129.8, 130.0 (CH), 131.9, 151.1, 152.5, 165.7.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2160 (m), 2030 (m), 2022 (m), 2012 (m), 1974 (m), 1716 (w), 1600 (m), 1594 (m), 1512 (m), 1444 (m), 1366 (s), 1316 (m), 1274 (w), 1230 (m), 1196 (m), 1172 (m), 1122 (s), 1104 (s), 1090 (s), 1070 (s), 1036 (w), 1016 (s), 860 (m), 852 (m), 810 (s), 764 (s), 718 (m), 708 (m), 686 (s).

MS (EI, 70 eV): *m/z* (%) = 317 (26), 301 (21), 270 (17), 269 (100), 241 (12), 168 (98), 136 (15).

HRMS (EI): calcd. for $C_{17}H_{19}O_3N^{32}S$: 317.1086, found: 317.1083.

4-Fluorophenyl 4-methoxyphenyl sulfoxide (**37h**)



According to **TP2** the sulfoxide **37h** was prepared from 4-fluoro-phenyl magnesium bromide (111 mL, 100 mmol, 0.90 M in THF) and 4-methoxybenzene sulfinyl chloride (24.7 g, 130 mmol) and purified by recrystalization (pentane) furnishing **37h** as a colourless solid (22.8 g, 91% yield).

mp (°C): 83–85.

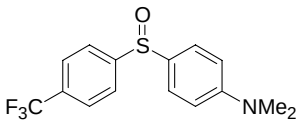
^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 3.79 (s, 3 H), 6.92–6.95 (m, 2 H), 7.09–7.15 (m, 2 H), 7.51–7.60 (m, 4 H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 55.4 (CH_3), 114.8 (CH), 116.4 (d, J = 22.7 Hz, CH), 126.9 (d, J = 8.9 Hz, CH), 127.0 (CH), 136.5, 141.4 (d, J = 3.0 Hz), 162.1, 164.0 (d, J = 251.2 Hz, CF).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3052 (w), 2836 (w), 1592 (s), 1577 (s), 1496 (s), 1436 (m), 1410 (m), 1311 (m), 1303 (m), 1254 (s), 1215 (s), 1154 (m), 1089 (s), 1076 (s), 1035 (s), 855 (s), 828 (vs), 810 (s), 798 (s).

MS (EI, 70 eV): *m/z* (%) = 251 (8), 250 (49), 233 (8), 203 (13), 202 (100), 187 (17), 154 (43), 139 (23), 123 (60), 101 (8).
HRMS (EI): calcd. for $C_{13}H_{11}FO_2{}^{32}S$: 250.0464, found: 250.0470.

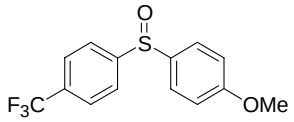
Dimethyl(4-{[4-(trifluoromethyl)phenyl]sulfinyl}phenyl)amine (**37i**)



According to **TP3** the sulfoxide **37i** was prepared from 4-(trifluoromethyl)benzene magnesium bromide (25.0 mL, 15 mmol, 0.60 M in THF) and methyl 4-(dimethylamino)benzenesulfinate (**45**, 3.29 g, 16.5 mmol) and purified by flash chromatography (pentane / ethyl acetate = 2:1, silica gel), furnishing **37i** as a colourless solid (3.82 g, 82% yield).

mp (°C): 120–122.
^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.98 (s, 6 H), 6.85–6.70 (m, 2 H), 7.42–7.47 (m, 2 H), 7.65–7.72 (m, 4 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 40.1 (CH_3), 112.0 (CH), 123.6 (q, J = 271.0 Hz, CF_3), 124.8 (CH), 125.9 (q, J = 3.9 Hz, CH), 127.9 (CH), 129.8, 132.0 (q, J = 32.7 Hz), 150.7, 152.6.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2906 (w), 2808 (w), 1600 (s), 1511 (m), 1399 (m), 1369 (m), 1316 (s), 1164 (s), 1140 (s), 1102 (m), 1090 (s), 1075 (m), 1055 (s), 1048 (vs), 1012 (m), 965 (w), 944 (w), 836 (m), 811 (m), 803 (m), 695 (m), 608 (w), 595 (w).
MS (EI, 70 eV): *m/z* (%) = 313 (20), 265 (50), 264 (13), 168 (100), 136 (15), 119 (5).
HRMS (EI): calcd. for $C_{15}H_{14}ONF_3{}^{32}S$: 313.0748, found: 313.0744.

4-Methoxyphenyl 4-(trifluoromethyl)phenyl sulfoxide (**37j**)



According to **TP2** the sulfoxide **37j** was prepared from 4-trifluoromethyl-phenylmagnesium bromide (60.0 mL, 30.0 mmol, 0.5 M in THF) and 4-methoxybenzene sulfinyl chloride (7.43 g, 39.0 mmol) and purified by flash chromatography (pentane / ethyl acetate = 2:1, silica gel), furnishing **37j** as a colourless solid (7.43 g, 82% yield).

mp (°C): 92–94.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 3.78 (s, 3 H), 6.93–6.95 (m, 2 H), 7.54–7.57 (m, 2 H), 7.67–7.71 (m, 4 H).

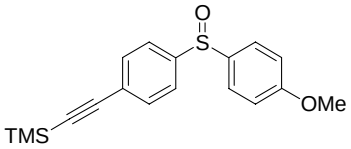
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 55.4 (CH_3), 115.0 (CH), 123.4 (q, J = 274.3 Hz, CF_3), 124.7 (CH), 126.1 (q, J = 3.8 Hz, CH), 127.3 (CH), 132.4 (q, J = 32.6 Hz), 135.9, 150.2, 162.4.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2839 (w), 1592 (s), 1575 (m), 1491 (s), 1398 (m), 1319 (s), 1305 (s), 1245 (vs), 1183 (s), 1172 (s), 1167 (s), 1141 (s), 1128 (vs), 1106 (s), 1101 (s), 1088 (vs), 1073 (s), 1057 (vs), 1043 (vs), 1022 (s), 1012 (vs), 1004 (s), 956 (m), 845 (m), 834 (s), 823 (vs), 794 (s), 732 (m), 696 (s), 597 (m).

MS (EI, 70 eV): *m/z* (%) = 300 (24), 284 (11), 253 (16), 252 (100), 237 (12), 155 (95), 139 (29), 123 (59), 92 (10).

HRMS (EI): calcd. for $C_{14}H_{11}O_2F_3{}^{32}S$: 300.0432, found: 300.0427.

({4-[(4-Methoxyphenyl)sulfinyl]phenyl}ethynyl)(trimethyl)silane (**37k**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with ethinyl(trimethyl)silane (1.96 g, 20.0 mmol) and *i*PrMgCl·LiCl (15.2 mL,

19.0 mmol, 1.25 M in THF) was added at 25 °C. After cessation of gas evolution the reaction mixture was heated to 60 °C for 5 min. After cooling to 25 °C a zinc chloride solution (20.0 mL, 20.0 mmol, 1.0 M in THF) was slowly added. The resulting mixture was stirred for 30 min at 25 °C, then 4-iodophenyl 4'-methoxyphenyl sulfoxide (**46**, 5.37 g, 15.0 mmol), $Pd(dba)_2$ (0.173 g, 0.30 mmol) and tris-*o*-furylphosphine (0.139 g, 0.60 mmol) were added and the reaction mixture was stirred 14 h at 25 °C. The reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvents were removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 2:1, silica gel) yielded **37k** a colourless solid (4.85 g, 98% yield).

mp (°C): 122–124.

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 0.21 (9 H), 3.78 (3 H), 6.90–6.93 (m, 2 H), 7.49–7.52 (m, 6 H).

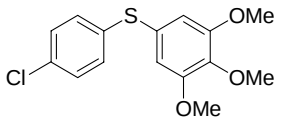
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = –0.3 (CH_3), 55.4 (CH_3), 96.7, 103.6, 114.8 (CH), 124.3 (CH), 125.6, 127.3 (CH), 132.5 (CH), 136.4, 145.7, 162.2.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2958 (w), 2155 (m), 1591 (s), 1576 (m), 1491 (s), 1481 (m), 1407 (m), 1304 (m), 1245 (vs), 1187 (m), 1171 (m), 1086 (s), 1058 (m), 1046 (s), 1023 (m), 1010 (m), 845 (m), 835 (s), 829 (s), 816 (s), 795 (m), 759 (m), 697 (m), 552 (m).

MS (EI, 70 eV): *m/z* (%) = 328 (12), 313 (17), 312 (18), 297 (26), 281 (20), 280 (100), 266 (17), 265 (84), 158 (23), 155 (16), 143 (12), 139 (50), 123 (25).

HRMS (EI): calcd. for $C_{18}H_{20}O_2{}^{32}S^{28}Si$: 328.0953, found: 328.0945.

5-[(4-Chlorophenyl)thio]-1,2,3-trimethoxybenzene (**40**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar was charged with a solution of 5-bromo-1,2,3-trimethoxybenzene (9.51 g, 38.5 mmol) in THF (70 mL). The solution was cooled to –78 °C and *n*BuLi (18.0 mL, 42.4 mmol, 2.35 M in hexane) was

added dropwise, and stirred for additional 1.5 h at –78 °C. Then, *S*-(4-chlorophenyl) benzenesulfonothioate (12.3 g, 43.0 mmol) was added and reaction mixture was allowed to warm to 25 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 5:1, silica gel) yielded a colourless solid (10.8 g, 89% yield).

mp (°C): 55–56.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 3.79 (s, 6 H), 3.84 (s, 3 H), 6.63 (s, 2 H), 7.16–7.26 (m, 4 H).

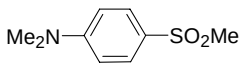
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 56.2 (CH_3), 60.9 (CH_3), 109.7 (CH), 128.6, 129.2 (CH), 130.6 (CH), 132.4, 135.6, 138.2, 153.7.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2933 (w), 2834 (w), 1575 (s), 1499 (m), 1471 (m), 1433 (m), 1402 (s), 1304 (m), 1228 (s), 1122 (vs), 1088 (s), 992 (m), 876 (w), 811 (m), 771 (w), 740 (w), 620 (w).

MS (EI, 70 eV): *m/z* (%) = 313 (4), 312 (20), 310 (62), 297 (23), 296 (11), 295 (100), 267 (21), 143 (15), 124 (20), 44 (11), 43 (53).

HRMS (EI): calcd. for $C_{15}H_{15}{}^{35}ClO_3{}^{32}S$: 310.0430, found: 310.0417.

Methyl 4-(dimethylamino)benzenesulfinate (**45**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar was charged with a solution of 4-(dimethylamino)benzenesulfonyl chloride[88] (18.0 g, 81.9 mmol) in CH_2Cl_2 (80 mL). Triethylamine (81.0 g, 110 mL, 800 mmol) and triphenylphosphine (21.5 g, 82.0 mmol) were added and the reaction mixture was cooled to 0 °C. Then, methanol (3.3 mL, 82 mmol) in CH_2Cl_2 (50 mL) was added slowly and the reaction mixture was allowed to warm to 25 °C and stirred for 14 h. The solvent was removed

[88] Binisti, C.; Assogba, L.; Touboul, E; Mounier, M.; Huet, J.; Ombetta, J.-E.; Dong, C. Z.; Redeuilh, C.; Heymans, F.; Godfroid, J.-J. *Eur. J. Med. Chem.* **2001**, *36*, 809.

under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 1:1, silica gel) yielded a colourless solid (11.67 g, 72% yield).

mp (°C): 45–47.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 3.01 (s, 6 H), 3.40 (s, 3 H), 6.68–6.75 (m, 2 H), 7.47–7.54 (m, 2 H).

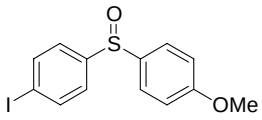
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 40.1 (CH_3), 48.6 (CH_3), 111.4 (CH), 126.7 (CH), 129.4, 152.8.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2939 (w), 2904 (w), 2823 (w), 1590 (vs), 1513 (s), 1444 (m), 1368 (s), 1227 (m), 1202 (m), 1105 (vs), 1082 (s), 1069 (s), 955 (s), 825 (m), 812 (s), 655 (s), 631 (m), 616 (m), 566 (m)

MS (EI, 70 eV): *m/z* (%) = 199 (21), 169 (11), 168 (100), 152 (11), 136 (25), 120 (9), 77 (8).

HRMS (EI): calcd. for $C_9H_{13}O_2N^{32}S$: 199.0667, found: 199.0653.

4-Iodophenyl 4'methoxyphenyl sulfoxide (**46**)



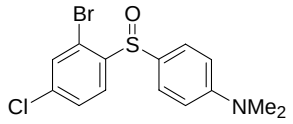
A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with 1,4-diiodobenzene (9.93 g, 30.0 mmol) in THF (30 mL) and cooled to 0 °C. *i*PrMgCl·LiCl (25.2 mL, 31.5 mmol, 1.25 M in THF) was added slowly and the reaction mixture was stirred for additional 10 min and then cooled to –50 °C. 4-Methoxybenzene sulfinyl chloride (5.53 g, 29.0 mmol) was added dropwise and after addition the reaction mixture was allowed to warm to 25 °C. After 30 min at 25 °C the reaction mixture was quenched with sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL) and dried ($MgSO_4$). After filtration the solvents were removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 2:1, silica gel) yielded a colourless solid (7.62 g, 73% yield).

mp (°C): 116–117.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 3.77 (s, 3 H), 6.89–6.94 (m, 2 H), 7.25–7.32 (m, 2 H), 7.49–7.54 (m, 2 H), 7.72–7.77 (m, 2 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 55.4 (CH_3), 97.1, 114.9 (CH), 126.0 (CH), 127.1 (CH), 136.2, 138.1 (CH), 145.8, 162.1.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3003 (w), 2840 (w), 1592 (s), 1574 (s), 1561 (m), 1491 (vs), 1464 (m), 1444 (m), 1407 (m), 1387 (vw), 1377 (m), 1304 (m), 1248 (vs), 1184 (m), 1168 (m), 1083 (s), 1038 (s), 1020 (m), 1000 (s), 827 (m), 808 (s), 795 (m), 713 (m).
MS (EI, 70 eV): *m/z* (%) = 358 (15), 342 (9), 311 (14), 310 (100), 295 (15), 155 (37), 139 (33), 123 (36), 76 (11).
HRMS (EI): calcd. for $C_{13}H_{11}O_2{}^{127}I^{32}S$: 357.9524, found: 357.9509.

4.3.2. Functionalization of diarylsulfoxides

{4-[(2-bromo-4-chlorophenyl)sulfinyl]phenyl}dimethylamine (**47a**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with the sulfoxide **37a** (0.839 g, 3.0 mmol) dissolved in THF (6 mL). The reaction mixture was cooled to –30 °C and tmpMgCl·LiCl (2.9 mL, 3.3 mmol, 1.14 M in THF) was added dropwise. After 20 min of stirring at –30 °C, 1,2-dibromo-1,1,2,2-tetrachlorethane (1.17 g, 3.60 mmol) was added and the reaction mixture was allowed to warm to 25 °C. The reaction mixture was quenched with a sat. aq. NH_4Cl-solution (100 mL) and extracted three times with ethyl acetate (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvents were removed under reduced pressure. Flash chromatographical purification (diethyl ether, silica gel) yielded a colourless solid (948 mg, 88% yield).

mp (°C): 134–135.
^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.96 (s, 6 H), 6.59–6.64 (m, 2 H), 7.45–7.50 (m, 3 H), 7.52 (dd, J = 8.38 Hz, J = 1.98 Hz, 1 H), 8.05 (d, J = 8.38 Hz, 1 H).

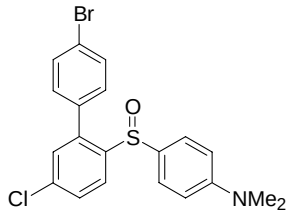
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 40.0 (CH_3), 111.6 (CH), 120.2, 127.1 (CH), 128.3, 128.4, 128.7 (CH), 132.6 (CH), 137.0 (CH), 143.9, 152.4.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 1716 (m), 1590 (s), 1564 (m), 1552 (m), 1512 (m), 1440 (m), 1362 (s), 1226 (m), 1200 (m), 1194 (m), 1080 (s), 1048 (s), 1034 (w), 1016 (w), 994 (s), 944 (m), 916 (m), 874 (m), 834 (m), 812 (s), 798 (s), 780 (w), 762 (s), 708 (m), 696 (m), 668 (m), 660 (m), 632 (m), 610 (s).

MS (EI, 70 eV): *m/z* (%) = 359 (12), 357 (13), 344 (22), 341 (15), 311 (20), 309 (15), 168 (10), 167 (100), 152 (14), 136 (19).

HRMS (EI): calcd. for $C_{14}H_{13}ON^{79}Br^{35}Cl^{32}S$: 356.9590, found: 356.9585.

{4-[(4'-bromo-5-chlorobiphenyl-2-yl)sulfinyl]phenyl}dimethylamine (**47b**)



According to **TP4** the sulfoxide **47b** was prepared starting from sulfoxide **37a** (1.40 g, 5.0 mmol), using $Pd(PPh_3)_4$ (0.11 g, 0.10 mmol) and 1-bromo-4-iodobenzene (1.58 g, 5.6 mmol) for the cross-coupling. The reaction mixture was stirred for 2 h at 50 °C. Flash chromatographical purification (pentane / ethyl acetate = 2:1, silica gel) yielded **47b** as a colourless solid (1.79 g, 82% yield).

mp (°C): 147–149.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.92 (s, 6 H), 6.42–6.52 (m, 2 H), 6.87–6.89 (m, 2 H), 6.94–6.97 (m, 2 H), 7.15 (d, J = 2.20 Hz, 1 H), 7.43–7.45 (m, 2 H), 7.56 (dd, J = 8.44 Hz, J = 2.20 Hz, 1 H), 8.17 (d, J = 8.44 Hz, 1 H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 40.0 (CH_3), 111.4 (CH), 122.6 (CH), 125.6 (CH), 127.8 (CH), 128.5, 129.0, 129.9 (CH), 130.8 (CH), 131.4 (CH), 135.9, 136.2, 140.5, 142.8, 152.0.

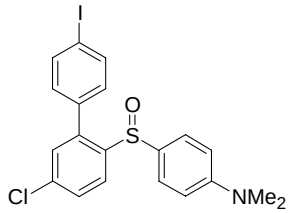
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3053 (m), 2905 (m), 2813 (m), 1590 (vs), 1568 (m), 1552 (m), 1509 (s), 1489 (m), 1446 (m), 1363 (s), 1299 (m), 1191 (m), 1083 (s), 1071 (m),

1064 (m), 1057 (m), 1037 (s), 1021 (s), 1008 (s), 945 (m), 887 (w), 835 (m), 802 (s), 717 (m), 554 (w).

MS (EI, 70 eV): *m/z* (%) = 435 (12), 432 (9), 387 (7), 169 (8), 168 (100), 136 (20).

HRMS (EI): calcd. for $C_{20}H_{17}ON^{79}Br^{35}Cl^{32}S$: 432.9903, found: 432.9895.

{4-[(4'-iodo-5-chlorobiphenyl-2-yl)sulfinyl]phenyl}dimethylamine (**47c**)



According to **TP4** the sulfoxide **47c** was prepared starting from sulfoxide **37a** (1.40 g, 5.0 mmol), using $Pd(PPh_3)_4$ (0.11 g, 0.10 mmol) and 1,4-diiodobenzene (3.30 g, 10.0 mmol) for the cross-coupling. The reaction mixture was stirred for 1.5 h at 50 °C Flash chromatographical purification (pentane / ethyl acetate = 1:1, silica gel) yielded **47c** as a colourless solid (1.66 g, 69% yield).

mp (°C): 141–141.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.90 (s, 6 H), 6.42 (d, J = 9.06 Hz, 2 H), 6.80 (d, J = 8.11 Hz, 2 H), 6.87 (d, J = 9.06 Hz, 2 H), 7.13 (d, J = 2.38 Hz, 1 H), 7.54 (dd, J = 8.58 Hz, J = 2.38 Hz, 1 H), 7.62 (d, J = 8.11 Hz, 2 H), 8.15 (d, J = 8.58 Hz, 1 H).

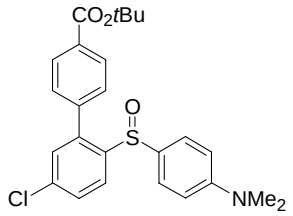
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 40.0 (CH_3), 94.2, 111.4 (CH), 125.6 (CH), 127.8 (CH), 128.4 (CH), 128.8, 129.8 (CH), 130.9 (CH), 136.2, 136.4, 137.3 (CH), 140.5, 142.7, 152.0.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 1716 (m), 1590 (s), 1510 (m), 1446 (m), 1362 (s), 1278 (m), 1224 (m), 1190 (m), 1082 (s), 1066 (m), 1052 (m), 1036 (s), 1020 (s), 1004 (s), 944 (m), 886 (m), 838 (s), 824 (s), 802 (w), 760 (m), 750 (m), 742 (m), 732 (m), 714 (m), 702 (s), 690 (m), 608 (s).

MS (EI, 70 eV): *m/z* (%) = 481 (25), 467 (35), 465 (22), 464 (83), 432 (15), 169 (12), 168 (100), 152 (30), 151 (22), 136 (31).

HRMS (EI): calcd. for: $C_{20}H_{18}ON^{35}Cl^{127}I^{32}S$ [M+H]: 481.9842, found: 481.9841.

*t*Butyl 5'-chloro-2'-{[4-(dimethylamino)phenyl]sulfinyl}biphenyl-4-carboxylate (**47d**)



According to **TP4** the sulfoxide **47d** was prepared starting from sulfoxide **37a** (2.80 g, 10.0 mmol), using $Pd(dba)_2$ (0.12 g, 0.20 mmol), tris-*o*-furylphosphine (93 mg, 0.40 mmol) and *tert*-butyl 4-iodobenzoate (3.65 g, 12.0 mmol) for the cross-coupling. The reaction mixture was stirred for 15 min at 50 °C. Flash chromatographical purification (pentane / ethyl acetate = 1:1, silica gel) yielded **47d** as a colourless solid (3.61 g, 79% yield).

mp (°C): 137–139.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.62 (s, 9 H), 2.92 (s, 6 H), 6.40–6.45 (m, 2 H), 6.85–6.90 (m, 2 H), 7.14–7.18 (m, 3 H), 7.57 (dd, J = 8.38 Hz, J = 2.21 Hz, 1 H), 7.91–7.95 (m, 2 H), 8.18 (d, J = 8.60 Hz, 1 H).

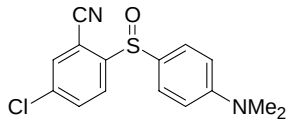
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 28.2 (CH_3), 40.1 (CH_3), 81.4, 111.6 (CH), 125.6 (CH), 127.8 (CH), 128.7 (CH), 129.2 (CH), 129.3, 129.4 (CH), 130.0 (CH), 131.8, 136.3, 140.9, 141.1, 142.9, 152.1, 165.3.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2360 (w), 2342 (w), 1712 (vs), 1592 (vs), 1554 (m), 1516 (s), 1474 (w), 1446 (m), 1366 (vs), 1310 (m), 1294 (vs), 1282 (s), 1254 (m), 1236 (m), 1218 (m), 1190 (m), 1170 (s), 1120 (s), 1092 (s), 1086 (s), 1066 (s), 1040 (vs), 1024 (s), 1012 (s), 948 (m), 922 (w), 880 (m), 862 (m), 850 (m), 824 (m), 814 (m), 802 (vs), 774 (s), 730 (w), 710 (m), 668 (w), 636 (w), 610 (m).

MS (EI, 70 eV): *m/z* (%) = 457 (22), 456 (17), 455 (67), 384 (20), 383 (42), 382 (27), 351 (28), 170 (19), 169 (40), 168 (100), 152 (31), 136 (83), 119 (15).

HRMS (EI): calcd. for $C_{25}H_{26}O_3N^{35}Cl^{32}S$: 455.1322, found: 455.1319.

5-Chloro-2-{[4-(dimethylamino)phenyl]sulfinyl}benzonitrile (**47e**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with the sulfoxide **37a** (2.80 g, 10.0 mmol) dissolved in THF (20 mL). The reaction mixture was cooled to –30 °C and tmpMgCl·LiCl (9.17 mL, 11.0 mmol, 1.20 M in THF) was added dropwise. After 20 min of stirring at –30 °C, TosCN (2.36 g, 12.0 mmol) was added and the reaction mixture was stirred for 2 h at 25 °C. The reaction mixture was then quenched with a sat. aq. NH_4Cl-solution (100 mL) and extracted three times with ethyl acetate (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvents were removed under reduced pressure. Flash chromatographical purification (diethyl ether, silica gel) yielded an orange solid (2.23 g, 73% yield).

mp (°C): 179–180.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.99 (s, 6 H), 6.66 (d, J = 9.06 Hz, 2 H), 7.52 (d, J = 9.06 Hz, 2 H), 7.59 (d, J = 1.97 Hz, 1 H), 7.77 (dd, J = 8.51, 1.97 Hz, 1 H), 8.19 (d, J = 8.51 Hz, 1 H).

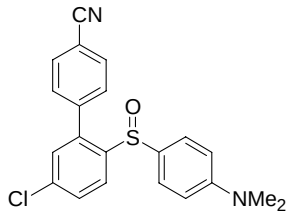
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 40.0 (CH_3), 110.5, 111.9 (CH), 114.0, 125.7 (CH), 128.1, 128.5 (CH), 133.2 (CH), 133.8 (CH), 136.5, 148.9, 152.8.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3075 (m), 1592 (vs), 1551 (m), 1518 (s), 1454 (m), 1441 (m), 1430 (m), 1376 (s), 1233 (m), 1196 (m), 1180 (m), 1082 (s), 1052 (s), 1034 (s), 996 (m), 832 (m), 811 (m), 796 (m).

MS (EI, 70 eV): *m/z* (%) = 304 (15), 288 (6), 258 (6), 256 (19), 255 (6), 169 (11), 168 (100), 152 (6), 136 (15), 42 (19).

HRMS (EI): calcd. for $C_{15}H_{13}{}^{35}ClN_2O^{32}S$: 304.0437, found: 304.0433.

5'-Chloro-2'-{[4-(dimethylamino)phenyl]sulfinyl}biphenyl-4-carbonitrile (**47f**)



According to **TP4** the sulfoxide **47f** was prepared starting from sulfoxide **37a** (2.80 g, 10.0 mmol), using $Pd(PPh_3)_4$ (0.22 g, 0.20 mmol) and 4-iodo benzonitrile (2.75 g, 12.0 mmol) for the cross-coupling. The reaction mixture was stirred for 2 h at 50 °C. Flash chromatographical purification (pentane / ethyl acetate = 1:1, silica gel) yielded a colourless solid (3.50 g, 92% yield).

mp (°C): 161–163.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.90 (s, 6 H), 6.37 (d, J = 8.82 Hz, 2 H), 6.78 (d, J = 8.82 Hz, 2 H), 7.07–7.08 (m, 1 H), 7.16-7.17 (m, 1 H), 7.35-7.38 (m, 1 H), 7.44–7.49 (m, 1 H), 7.57–7.62 (m, 2 H), 8.21 (d, J = 8.38 Hz, 1 H).

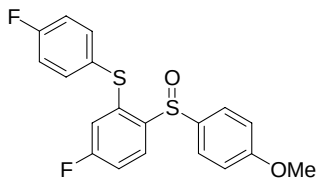
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 40.2 (CH_3), 111.7 (CH), 125.2 (CH), 126.0 (CH), 126.1, 128.4 (CH), 128.7, 129.0, 129.1 (CH), 130.3 (CH), 132.7 (CH), 136.6, 138.1, 140.3, 143.2, 152.5.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2228 (w), 1588 (vs), 1508 (s), 1444 (m), 1364 (s), 1304 (w), 1228 (m), 1192 (m), 1084 (s), 1036 (vs), 944 (m), 844 (s), 828 (s), 800 (s), 756 (m), 608 (m), 588 (m), 568 (m).

MS (EI, 70 eV): *m/z* (%) = 382 (29), 380 (77), 332 (28), 177 (27), 170 (23), 169 (51), 168 (56), 152 (26), 136 (100), 119 (20).

HRMS (EI): calcd. for $C_{21}H_{17}{}^{35}ClN_2O^{32}S$: 380.0750, found: 380.0753.

4-Fluoro-2-[(4-fluorophenyl)thio]phenyl 4-methoxyphenyl sulfoxide (**47g**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with the sulfoxide **37h** (1.75 g, 7.0 mmol,) dissolved in THF (14 mL). The reaction mixture was cooled to –30 °C and tmpMgCl·LiCl (6.9 mL, 7.7 mmol, 1.11 M in THF) was added dropwise. After 20 min of stirring at –30 °C, *S*-(4-fluorophenyl) benzenesulfonothioate (2.25 g, 8.4 mmol) was added and the reaction mixture was stirred for 2 h at 25 °C. The reaction mixture was then quenched with a sat. aq. NH_4Cl-solution (100 mL) and extracted three times with ethyl acetate (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvents were removed under reduced pressure. Flash chromatographical purification (diethyl ether, silica gel) yielded a colourless liquid (2.14 g, 81% yield).

mp (°C): 131–133.

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 3.79 (s, 3 H), 6.68 (dd, J = 8.82 Hz, J = 2.62 Hz, 1 H), 6.89–6.92 (m, 2 H), 6.98–7.02 (m, 2 H), 7.10–7.14 (m, 1 H), 7.20–7.22 (m, 2 H), 7.60–7.63 (m, 2 H), 8.08 (dd, J = 9.06 Hz, J = 5.72 Hz, 1 H).

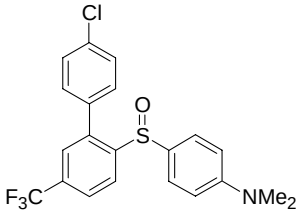
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 55.4 (CH_3), 114.7 (CH), 115.2 (d, J = 21.9 Hz, CH), 116.9 (d, J = 22.0 Hz, CH), 117.7 (d, J = 24.4 Hz, CH), 126.9 (d, J = 9.4 Hz, CH), 127.4 (d, J = 3.5 Hz), 128.4 (CH), 134.8 (d, J = 8.5 Hz, CH), 135.7, 137.3 (d, J = 8.2 Hz), 140.5 (d, J = 2.9 Hz), 162.1, 163.0 (d, J = 250.0 Hz, CF), 164.2 (d, J = 253.4 Hz, CF).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3080 (w), 2966 (w), 2940 (w), 2228 (m), 2216 (m), 2190 (m), 2184 (m), 2174 (m), 2160 (m), 2098 (m), 2032 (m), 2022 (m), 1976 (m), 1908 (w), 1750 (w), 1718 (m), 1588 (s), 1578 (m), 1564 (m), 1490 (s), 1458 (s), 1442 (s), 1398 (w), 1382 (m), 1368 (w), 1304 (m), 1278 (m), 1248 (s), 1222 (s), 1202 (s), 1182 (m), 1170 (m), 1158 (m), 1128 (w), 1088 (m), 1078 (m), 1050 (s), 1030 (s), 1020 (s), 892 (s), 862 (s), 834 (s), 824 (vs).

MS (EI, 70 eV): *m/z* (%) = 377 (22), 376 (77), 361 (18), 360 (68), 328 (20), 265 (97), 252 (66), 231 (38), 219 (100), 217 (28), 188 (35), 155 (63), 139 (25), 123 (98), 43 (30), 42 (64).

HRMS (EI): calcd. for $C_{19}H_{14}O_2F_2{}^{32}S$: 376.0403, found: 376.0394.

(4-{[4'-Chloro-5-(trifluoromethyl)biphenyl-2-yl]sulfinyl}phenyl)dimethylamine (**47h**)



According to **TP4** the sulfoxide **47h** was prepared starting from sulfoxide **37i** (1.88 g, 6.0 mmol), using $Pd(dba)_2$ (69 mg, 0.12 mmol), tris-*o*-furylphosphine (56 mg, 0.23 mmol) and 1-iodo-4-chlorobenzene (1.57 g, 6.6 mmol) for the cross-coupling. The reaction mixture was stirred for 1.5 h at 50 °C. Flash chromatographical purification (pentane / ethyl acetate = 2:1, silica gel) yielded a colourless solid (2.32 g, 91% yield).

mp (°C): 150–152.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.91 (s, 6 H), 6.41–6.45 (m, 2 H), 6.84–6.87 (m, 2 H), 7.01–7.03 (m, 2 H), 7.29–7.31 (m, 2 H), 7.39 (d, J = 1.43 Hz, 1 H), 7.85 (dd, J = 8.34 Hz, J = 1.91 Hz, 1 H), 8.40 (d, J = 8.11 Hz, 1 H).

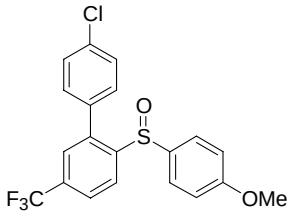
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 40.0 (CH_3), 111.5 (CH), 123.5 (q, J = 273.1 Hz, CF_3), 124.5 (CH), 125.2 (q, J = 3.8 Hz, CH), 126.9 (q, J = 3.7 Hz, CH), 128.1 (CH), 128.4, 128.6 (CH), 130.5 (CH), 132.2 (q, J = 32.9 Hz), 134.6, 135.4, 139.6, 148.7, 152.2.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2817 (w), 1595 (vs), 1515 (m), 1412 (m), 1366 (m), 1326 (s), 1294 (m), 1256 (s), 1234 (m), 1170 (s), 1137 (vs), 1087 (s), 1052 (s), 1041 (s), 1023 (s), 1014 (s), 948 (m), 841 (m), 825 (m), 803 (s), 743 (m), 720 (m), 697 (m), 660 (m), 657 (m).

MS (EI, 70 eV): *m/z* (%) = 426 (6), 423 (17), 170 (5), 169 (9), 168 (100), 136 (14).

HRMS (EI): calcd. for $C_{21}H_{17}O^{35}ClF_3{}^{32}S$: 423.0671, found: 423.0667.

4'-Chloro-5-(trifluoromethyl)biphenyl-2-yl 4-methoxyphenyl sulfoxide (**47i**)



According to **TP4** the sulfoxide **47i** was prepared starting from sulfoxide **37j** (10.5 g, 35.0 mmol), using $Pd(dba)_2$ (201 mg, 0.35 mmol), tris-*o*-furylphosphine (162 mg, 0.70 mmol) and 1-iodo-4-chlorobenzene (10.0 g, 42.0 mmol) for the cross-coupling. The reaction mixture was stirred for 7 h at 50 °C. Flash chromatographical purification (pentane / diethyl ether = 1:1, silica gel) yielded a colourless solid (10.8 g, 75% yield).

mp (°C): 113–115.

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 3.74 (s, 3 H), 6.71 (d, J = 8.58 Hz, 2 H), 6.95 (d, J = 8.58 Hz, 2 H), 7.05 (d, J =8.58 Hz, 2 H), 7.34 (d, J = 8.58 Hz, 2 H), 7.41 (s, 1 H), 7.86–7.87 (m, 1 H), 8.37 (d, J = 8.11 Hz, 1 H).

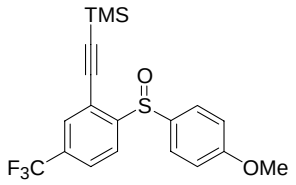
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 55.4 (CH_3), 114.5 (CH), 123.5 (q, J = 272.9 Hz, CF_3), 124.6 (CH), 125.4 (q, J = 3.9 Hz, CH), 127.1 (q, J = 3.7 Hz, CH), 128.1 (CH), 128.8 (CH), 130.6 (CH), 132.6 (q, J = 32.9 Hz), 134.7, 135.0, 135.2, 139.7, 148.2, 162.1.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 1594 (m), 1578(w), 1495 (m), 1468 (w), 1443 (w), 1412 (m), 1393 (w), 1327 (s), 1307 (m), 1292 (m), 1272 (w), 1253 (s), 1240 (m), 1174 (s), 1135 (vs), 1104 (w), 1089 (s), 1075 (s), 1044 (s), 1023 (s), 1012 (s), 966 (w), 949 (w), 910 (m), 839 (s), 827 (s), 822 (s), 815 (s), 795 (m), 822 (s), 815 (s), 794 (m), 743 (m), 697 (m), 661 (m), 656 (m).

MS (EI, 70 eV): *m/z* (%) = 412 (9), 410 (23), 394 (7), 362 (9), 251 (6), 157 (5), 156 (8), 155 (100), 139 (20), 124 (30), 123 (28).

HRMS (EI): calcd. for $C_{20}H_{14}O_2{}^{35}ClF_3{}^{32}S$: 410.0355, found: 410.0355.

[2-(4-Methoxybenzenesulfinyl)-5-trifluoromethylphenylethynyl]trimethyl-silane (**47j**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with the sulfoxide **37j** (2.19 g, 7.00 mmol) dissolved in THF (14 mL). The reaction mixture was cooled to –30 °C and tmpMgCl·LiCl (6.4 mL, 7.70 mmol, 1.20 M in THF) was added dropwise. After 20 min of stirring at –30 °C iodine (2.13 g, 8.40 mmol) was added and the reaction mixture was allowed to warm to 25 °C. In second dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar trimethylethynylsilane (1.38 g, 14.0 mmol) was mixed slowly with *i*PrMgCl·LiCl (8.80 mL, 10.5 mmol, 1.20 M). After cessation of gas evolution the reaction mixture was heated to 60 °C for 5 min. After cooling to 25 °C a zinc chloride solution (11.0 mL, 11.0 mmol, 1.0 M in THF) was added slowly. The resulting zinc reagent was transferred to the previously prepared crude iodide. $Pd(dba)_2$ (81 mg, 0.14 mmol), tris-*o*-furylphosphine (65 mg, 0.28 mmol) were added and the reaction mixture was stirred at 50 °C for 4 h. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvents were removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 4:1, silica gel) yielded a yellow oil (2.19 g, 79% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 0.28 (s, 9 H), 3.80 (s, 3 H), 6.91–6.93 (m, 2 H), 7.62–7.65 (m, 2 H), 7.68 (d, J = 1.28 Hz, 1 H), 7.68 (dd, J = 8.53 Hz, J = 1.38 Hz, 1 H), 8.23 (d, J = 8.07 Hz, 1 H).

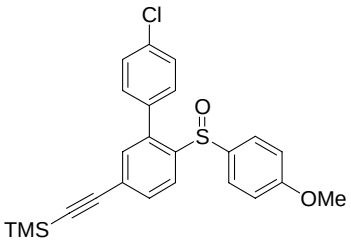
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = –0.5 (CH_3), 55.5 (CH_3), 98.7, 105.8, 114.6 (CH), 121.0, 123.1 (q, J = 272.9 Hz, CF_3), 124.0 (CH), 125.9 (q, J = 3.4 Hz, CH), 128.2 (CH), 130.2 (q, J = 3.8 Hz, 1 H), 132.5 (q, J = 33.1 Hz), 135.4, 151.4, 162.3.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2960 (w), 2161 (w), 1593 (m), 1577 (m), 1495 (s), 1464 (w), 1402 (m), 1326 (vs), 1303 (m), 1250 (s), 1168 (s), 1128 (vs), 1087 (s), 1054 (s), 1038 (s), 900 (s), 840 (s), 826 (s), 796 (m), 759 (m), 754 (m), 692 (m), 655 (m), 645 (m).

MS (EI, 70 eV): *m/z* (%) = 397 (5), 396 (21), 382 (15), 381 (57), 380 (12), 304 (29), 295 (11), 289 (21), 276 (10), 155 (14), 139 (13), 73 (100).

HRMS (EI): calcd. for $C_{19}H_{19}O_2F_3{}^{32}S^{28}Si$: 396.0827, found: 396.0832.

[4'-Chloro-6-(4-methoxybenzenesulfinyl)biphenyl-3-ylethynyl]trimethylsilane (**47k**)



According to **TP4** the sulfoxide **47k** was prepared starting from sulfoxide **37k** (1.97 g, 6.00 mmol), using $Pd(dba)_2$ (69 mg, 0.12 mmol), tris-*o*-furylphosphine (56 mg, 0.24 mmol) and 4-iodo-chlorobenzene (1.57 g, 6.60 mmol) for the cross-coupling. The reaction mixture was stirred for 3 h at 50 °C. Flash chromatographical purification (pentane / ethyl acetate = 3:1, silica gel) gave a slightly yellow solid (1.91 g, 73% yield).

mp (°C): 147–149.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.22 (s, 9 H), 3.74 (s, 3 H), 6.67–6.72 (m, 2 H), 6.93–6.95 (m, 2 H), 7.01–7.05 (m, 2 H), 7.26–7.32 (m, 3 H), 7.67 (dd, J = 8.02 Hz, J = 1.70 Hz, 1 H), 8.14 (d, J = 8.26 Hz, 1 H).

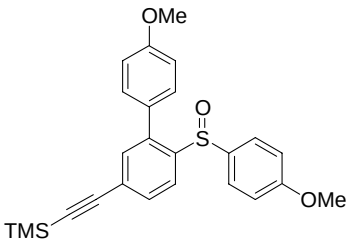
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = –0.3 (CH_3), 55.4 (CH_3), 97.2, 103.4, 114.3 (CH), 124.0 (CH), 125.6, 128.0 (CH), 128.6 (CH), 130.6 (CH), 131.9 (CH), 133.5 (CH), 134.4, 135.4, 135.7, 139.1, 143.9, 161.9.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2958 (w), 2838 (m), 2157 (m), 1589 (s), 1494 (s), 1470 (m), 1461 (m), 1443 (m), 1300 (m), 1252 (s), 1246 (s), 1184 (m), 1175 (m), 1094 (m), 1083 (s), 1064 (m), 1047 (s), 1021 (m), 1013 (m), 886 (m), 845 (vs), 841 (vs), 837 (vs), 829 (vs), 813 (s), 795 (m), 762 (s), 748 (m), 733 (m).

MS (EI, 70 eV): *m/z* (%) = 440 (33), 438 (83), 390 (75), 375 (48), 299 (35), 155 (76), 139 (57), 73 (100).

HRMS (EI): calcd. for $C_{24}H_{23}O_2{}^{35}Cl^{32}S^{28}Si$: 438.0877, found: 438.0866.

({4'-Methoxy-6-[(4-methoxyphenyl)sulfinyl]biphenyl-3-yl}ethynyl)(trimethyl)silane (**47l**)



According to **TP4** the sulfoxide **47l** was prepared starting from sulfoxide **37k** (1.97 g, 6.00 mmol), using $Pd(dba)_2$ (69 mg, 0.12 mmol) tris-*o*-furylphosphine (56 mg, 0.24 mmol) and 4-iodo-4-methoxybenzene (1.54 g, 6.60 mmol) for the cross-coupling. The reaction mixture was stirred for 2 h at 50 °C. Flash chromatographical purification (pentane / ethyl acetate = 2:1, silica gel) yielded a slightly yellow solid (1.74 g, 67% yield).

mp (°C): 59–61.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.22 (s, 9 H), 3.73 (s, 3 H), 3.84 (s, 3 H), 6.67–6.69 (m, 2 H), 6.85–6.87 (m, 2 H), 6.93–6.96 (m, 2 H), 7.03–7.05 (m, 2 H), 7.28 (d, J = 1.67 Hz, 1 H), 7.64 (dd, J = 8.23 Hz, J = 1.55 Hz, 1 H), 8.12 (d, J = 8.11 Hz, 1 H).

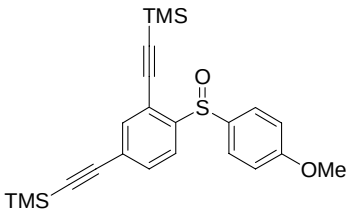
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = –0.2 (CH_3), 55.4 (2 CH_3), 96.7, 103.8, 113.8 (CH), 114.2 (CH), 123.7 (CH), 125.4, 127.7 (CH), 129.7, 130.6 (CH), 131.3 (CH), 133.7 (CH), 135.8, 140.2, 144.1, 159.6, 161.7.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2158 (s), 2030 (s), 1974 (s), 1716 (s), 1608 (m), 1592 (m), 1512 (s), 1494 (s), 1460 (s), 1366 (m), 1246 (vs), 1176 (s), 1044 (s), 1024 (s), 888 (m), 826 (s), 796 (m), 758 (m), 700 (w), 616 (w).

MS (EI, 70 eV): *m/z* (%) = 435 (19), 434 (41), 419 (28), 418 (57), 403 (32), 387 (23), 386 (65), 371 (30), 310 (19), 296 (16), 295 (54), 249 (20), 185 (11), 155 (25), 73 (100).

HRMS (EI): calcd. for $C_{25}H_{26}O_3{}^{32}S^{28}Si$: 434.1372, found: 434.1370.

[{4-[(4-methoxyphenyl)sulfinyl]-1,3-phenylene}bis(ethyne-2,1-diyl)]bis(trimethylsilane) (**47m**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with the sulfoxide **37k** (657 mg, 2.00 mmol) dissolved in THF (4 mL). The reaction mixture was cooled to –30 °C and tmpMgCl·LiCl (2.33 mL, 2.80 mmol, 1.20 M in THF) was added dropwise. After 20 min of stirring at –30 °C iodine (711 mg, 2.80 mmol) was added and the reaction mixture was allowed to warm to 25 °C. In second dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar trimethylethynylsilane (393 mg, 4.0 mmol) was added slowly to *i*PrMgCl·LiCl (2.50 mL, 3.0 mmol, 1.20 M in THF). After cessation of gas evolution the reaction mixture was heated to 60 °C for 5 min. After cooling to 25 °C a zinc chloride solution (3.0 mL, 3.0 mmol, 1.0 M in THF) was added slowly. The resulting zinc reagent was transferred to the previously prepared crude iodide. $Pd(dba)_2$ (23 mg, 0.04 mmol), tris-*o*-furylphosphine (19 mg, 0.08 mmol) were added and the reaction mixture was stirred at 50 °C for 4 h. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvents were removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 9:2, silica gel) yielded **47m** as a yellow oil (0.61 g, 72% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 0.22 (s, 9 H), 0.25 (s, 9 H), 3.80 (s, 3 H), 6.89–6.90 (m, 2 H), 7.53 (s, 1 H), 7.59–7.61 (m, 3 H), 8.00 (d, J = 8.35 Hz, 1 H).

^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = –0.4 (CH_3), –0.3 (CH_3), 55.5 (CH_3), 97.3, 99.3, 102.9, 104.2, 114.5 (CH), 120.3, 123.4 (CH), 125.5, 128.2 (CH), 132.6 (CH), 136.1, 136.4 (CH), 147.1, 162.1.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2958 (m), 2900 (w), 2837 (w), 2151 (m), 1738 (w), 1592 (m), 1578 (m), 1495 (m), 1460 (m), 1409 (w), 1378 (w), 1302 (m), 1248 (s), 1171 (m),

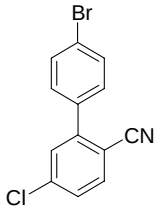
1084 (m), 1059 (m), 1036 (m), 950 (m), 836 (vs), 825 (vs), 796 (m), 757 (s), 724 (m), 700 (m), 674 (w), 648 (m), 620 (m).

MS (EI, 70 eV): *m/z* (%) = 425 (17), 424 (51), 411 (11), 410 (33), 409 (100), 408 (13), 381 (7), 336 (8), 323 (9), 287 (9), 273 (6).

HRMS (EI): calcd. for $C_{23}H_{28}O_2{}^{32}S^{28}Si_2$: 424.1349, found: 424.1336.

4.3.3. Sulfoxide-Magnesium Exchange

4'-Bromo-5-chlorobiphenyl-2-carbonitrile (**53a**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of the sulfoxide **47b** (435 mg, 1.00 mmol) in THF (2 mL). The reaction mixture was cooled to –50 °C and *i*PrMgCl·LiCl (0.88 mL, 1.1 mmol, 1.25 M in THF) was added dropwise. After stirring at –50 °C for 5 h TosCN (145 mg, 0.8 mmol) was added and the reaction mixture was allowed to warm to 25 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 20:1, silica gel) yielded **53a** as a colourless solid (138 mg, 59% yield).

mp (°C): 185–187.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 7.38–7.35 (m, 3 H), 7.48–7.49 (m, 1 H), 7.61–7.65 (m, 2 H), 7.69 (dd, J = 8.16 Hz, J = 0.44 Hz, 1 H).

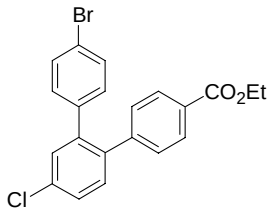
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 109.6, 117.6, 123.9, 128.3 (CH), 130.1 (CH), 130.2 (CH), 132.1 (CH), 134.9 (CH), 135.7, 139.5, 145.8.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3062 (w), 3030 (w), 2222 (m), 1914 (w), 1906 (w), 1592 (m), 1552 (m), 1496 (w), 1470 (s), 1406 (w), 1382 (m), 1304 (w), 1294 (w), 1278 (w), 1256 (m), 1188 (w), 1106 (w), 1096 (m), 1074 (m), 1036 (m), 1028 (m), 1008 (m), 966 (w), 952 (w), 910 (m), 856 (w), 824 (vs), 812 (vs), 742 (m), 730 (m), 712 (m), 656 (m), 620 (s).

MS (EI, 70 eV): *m/z* (%) = 295 (23), 294 (12), 293 (100), 292 (10), 291 (80), 214 (14), 212 (49), 177 (62).

HRMS (EI): calcd. for $C_{13}H_7N^{79}Br^{35}Cl$: 290.9450, found: 290.9451.

Ethyl 4''-bromo-4'-chloro-1,1':2',1''-terphenyl-4-carboxylate (**53b**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of the sulfoxide **47b** (435 mg, 1.00 mmol) in THF (2 mL). The reaction mixture was cooled to –50 °C and *i*PrMgCl·LiCl (0.88 mL, 1.1 mmol, 1.25 M in THF) was added dropwise. After stirring at –50 °C for 5 h $ZnCl_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF) was added. After stirring for 20 min at –50 °C the reaction mixture was allowed to warm to 25 °C and $Pd(PPh_3)_4$ (23 mg, 0.02 mmol) and ethyl 4-iodobenzoate (331 mg, 0.8 mmol) were added and the reaction mixture was stirred for 2 h at 50 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 20:1, silica gel) yielded a colourless solid (210 mg, 50% yield).

mp (°C): 120–123.

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 1.38 (t, J = 7.18 Hz, 3 H), 4.36 (q, J = 7.18 Hz, 2 H), 6.94–6.96 (m, 2 H), 7.14–7.16 (m, 2 H), 7.33–7.35 (m, 3 H), 7.38–7.41 (m, 2 H), 7.90–7.92 (m, 2 H).

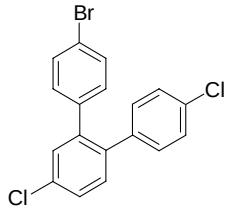
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 14.3 (CH_3), 61.0 (CH_2), 121.6, 127.9 (CH), 129.0, 129.4 (CH), 129.6 (CH), 130.3 (CH), 131.2 (CH), 131.4 (CH), 131.8 (CH), 134.0, 137.9, 138.7, 140.9, 144.6, 166.3.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 1714 (vs), 1608 (m), 1466 (m), 1392 (w), 1378 (m), 1362 (m), 1284 (vs), 1236 (m), 1180 (m), 1120 (s), 1100 (s), 1072 (m), 1034 (m), 1024 (m), 1004 (s), 964 (w), 868 (m), 854 (m), 832 (vs), 814 (s), 774 (s), 748 (m), 734 (m), 714 (m), 702 (m), 690 (m), 650 (m), 628 (w), 604 (w).

MS (EI, 70 eV): *m/z* (%) = 418 (22), 417 (19), 416 (80), 415 (15), 414 (68), 372 (13), 370 (48), 368 (37), 306, 13), 264 (32), 263 (22), 262 (100), 228 (27), 227 (36), 226 (84), 224 (16), 114 (13), 113 838).

HRMS (EI): calcd. for $C_{21}H_{16}O_2{}^{79}Br^{35}Cl$: 414.0022, found: 414.0002.

4''-Bromo-4,4'-dichloro-1,1':2',1''-terphenyl (**53c**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of the sulfoxide **47b** (435 mg, 1.00 mmol) in THF (2 mL). The reaction mixture was cooled to –50 °C and *i*PrMgCl·LiCl (0.88 mL, 1.1 mmol, 1.25 M in THF) was added dropwise. After stirring at –50 °C for 5 h $ZnCl_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF) was added. After stirring for 20 min at –50 °C the reaction mixture was allowed to warm to 25 °C and $Pd(PPh_3)_4$ (23 mg, 0.02 mmol) and 1-iodo-4-chlorobenzene (191 mg, 0.8 mmol) were added and the reaction mixture was stirred for 2 h at 50 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographical purification (pentane, silica gel) yielded a colourless solid (168 mg, 54% yield).

mp (°C): 147–148.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 6.94–7.03 (m, 4 H), 7.18–7.23 (m, 2 H), 7.28–7.32 (m, 1 H), 7.35–7.41 (m, 4 H).

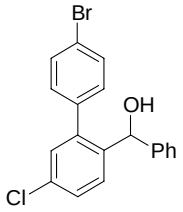
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 121.6, 127.9 (CH), 128.4 (CH), 130.3 (CH), 130.9 (CH), 131.2 (CH), 131.4 (CH), 131.8 (CH), 133.2, 133.8, 137.7, 138.4, 138.8, 140.8.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 1590 (w), 1486 (w), 1472 (m), 1460 (m), 1406 (w), 1394 (w), 1378 (w), 1096 (m), 1070 (m), 1032 (w), 1004 (m), 882 (m), 834 (m), 812 (vs), 754 (w), 744 (m), 722 (m), 710 (w), 698 (m), 650 (w), 636 (w), 628 (w).

MS (EI, 70 eV): *m/z* (%) = 379 (31), 378 (11), 377 (67), 375 (43), 264 (26), 263 (18), 262 (100), 226 (40), 131 (12), 113 (29), 112 (11).

HRMS (EI): calcd. for $C_{18}H_{11}{}^{79}Br^{35}Cl_2$: 375.9421, found: 375.9450.

(4'-Bromo-5-chlorobiphenyl-2-yl)(phenyl)methanol (**53d**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of the sulfoxide **47c** (435 mg, 1.00 mmol) in THF (2 mL). The reaction mixture was cooled to –50 °C and *i*PrMgCl·LiCl (0.88 mL, 1.10 mmol, 1.25 M in THF) was added dropwise. After stirring at –50 °C for 5 h, benzaldehyde (85 mg, 81 µL, 0.80 mmol) was added. After stirring for 20 min at –50 °C the reaction mixture was allowed to warm to 25 °C and stirred for additional 20 min. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 3:1, silica gel) yielded a colourless viscous oil (179 mg, 60% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.36 (s, 1 H), 5.79 (s, 1 H), 7.06–7.12 (m, 4 H), 7.22–7.40 (m, 5 H), 7.50–7.57 (m, 3 H).

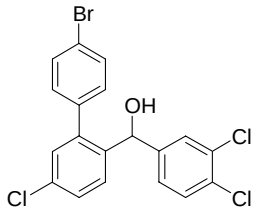
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 72.1 (CH), 121.9, 126.6 (CH), 127.6 (CH), 128.2 (CH), 128.4 (CH), 128.8 (CH), 129.6 (CH), 130.8 (CH), 131.3 (CH), 133.1, 138.3, 139.4, 141.5, 143.1.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2228 (w), 1712 (s), 1608 (m), 1590 (m), 1574 (w), 1472 (m), 1454 (w), 1410 (w), 1390 (m), 1380 (m), 1362 (m), 1284 (vs), 1236 (m), 1198 (m), 1180 (m), 1118 (s), 1102 (vs), 1036 (m), 1018 (m), 1004 (m), 926 (w), 906 (m), 868 (m), 848 (s), 834 (s), 826 (s), 774 (s), 762 (m), 752 (m), 734 (m), 704 (vs), 634 (m).

MS (EI, 70 eV): *m/z* (%) = 373 (75), 371 (60), 321 (56), 319 (54), 277 (79), 276 (42), 275 (80), 239 (40), 181 (44), 152 (57), 150 (18), 105 (100).

HRMS (EI): calcd. for $C_{19}H_{14}O^{79}Br^{35}Cl$: 371.9917, found: 371.9895.

(4'-Bromo-5-chlorobiphenyl-2-yl)(3,4-dichlorophenyl)methanol (**53e**)



According to **TP5** the sulfoxide **47b** (2.17 g, 5.00 mmol) was treated with *i*PrMgCl·LiCl (4.14 mL, 5.50 mmol, 1.20 M in THF) at –50 °C for 5 h. 3,4-dichlorobenzaldehyde (0.70 g, 4.0 mmol) was added and the reaction mixture was stirred for 20 min at –50 °C. The reaction mixture was then allowed to warm to 25 °C and stirred for additional 20 min. Flash chromatographical purification (pentane / ethyl acetate = 3:1, silica gel) yielded a colourless viscous oil (1.11 g, 63% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.08 (s, 1 H), 5.8 (s, 1 H), 6.87–6.91 (m, 2 H), 7.05–7.10 (m, 2 H), 7.18–7.21 (m, 1 H), 7.31 (dd, J = 8.38 Hz, J = 0.85 Hz, 1 H), 7.35–7.39 (m, 1 H), 7.43–7.45 (m, 1 H), 7.51–7.55 (m, 2 H).

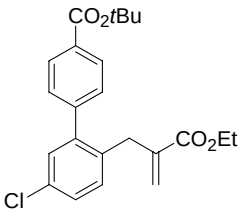
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 71.1 (CH), 122.4, 125.9 (CH), 128.5 (CH), 128.6 (CH), 128.7 (CH), 129.9 (CH), 130.3 (CH), 130.7 (CH), 131.6, 131.7 (CH), 132.6, 133.8, 138.0, 138.6, 141.6, 143.3.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3309 (m), 2975 (w), 2872 (w), 1595 (m), 1465 (s), 1384 (m), 1177 (m), 1094 (m), 1072 (m), 1048 (m), 1026 (s), 1009 (s), 884 (m), 818 (vs), 576 (m).

MS (EI, 70 eV): *m/z* (%) = 446 (17), 444 (60), 442 (95), 439 (50), 389 (44), 347 (35), 345 (100), 342 (98), 295 (26), 215 (33), 214 (26), 177 (32), 175 (61), 173 (34), 152 (32).

HRMS (EI): calcd. for $C_{19}H_{12}{}^{79}Br^{35}Cl_3$: 439.9137 , found: 439.9130.

*t*Butyl 5'-chloro-2'-[2-(ethoxycarbonyl)prop-2-en-1-yl]biphenyl-4-carboxylate (**53f**)



According to **TP5** the sulfoxide **47d** (456 mg, 1.00 mmol) was treated with *i*PrMgCl·LiCl (0.85 mL, 1.10 mmol, 1.30 M in THF) at –50 °C for 7 h. Then CuCN·2LiCl (0.05 mL, 5 mol%, 1.0 M in THF) and ethyl 2-(bromomethyl)acrylate (154 mg, 0.80 mmol) were added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographical purification (pentane / diethyl ether = 12:1, silica gel) yielded a colourless liquid (0.193 g, 60% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) =1.21 (t, J = 7.17 Hz, 3 H), 1.60 (s, 9 H), 3.52 (br, 2 H), 4.12 (q, J = 7.2 Hz, CH_2), 5.19 (br, 1 H), 6.19 (br, 1 H), 7.18 (d, J = 8.26 Hz, 1 H), 7.22 (d, J = 2.19 Hz, 1 H), 7.28 (d, J = 2.19 Hz, 1 H), 7.30–7.33 (m, 2 H), 7.98–8.02 (m, 2 H).

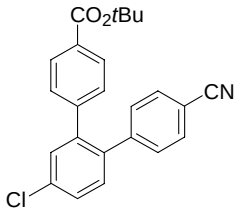
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.1 (CH_3), 28.2 (CH_3), 34.7 (CH_2), 60.8 (CH_2), 81.1, 126.5 (CH_2), 127.9 (CH), 128.8 (CH), 129.4 (CH), 129.7 (CH), 131.2, 131.4 (CH), 132.2, 134.4, 139.9, 143.1, 144.3, 165.5, 166.5.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2977 (w), 1709 (vs), 1609 (w), 1593 (w), 1478 (w), 1391 (w), 1367 (m), 1308 (m), 1293 (s), 1252 (m), 1162 (m), 1142 (m), 1115 (s), 1099 (m), 1030 (m), 1015 (m), 948 (w), 861 (w), 846 (m), 817 (w), 777 (w), 769 (w), 708 (m).

MS (EI, 70 eV): *m/z* (%) = 400 (0.5), 344 (31), 328 (42), 327 (71), 326 (100), 300 (38), 299 (34), 298 (91), 270 (39), 253 (28),

HRMS (EI): calcd. for $C_{23}H_{25}O_4{}^{35}Cl$: 400.1441 , found: 400.1442.

*t*Butyl 5'-chloro-4"-cyano-1,1':2',1"-terphenyl-4-carboxylate (**53g**)



According to **TP5** the sulfoxide **47d** (912 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (1.76 mL, 2.20 mmol, 1.25 M in THF) at –50 °C for 7 h. Then $ZnCl_2$ (2.2 mL, 2.2 mmol, 1.0 M in THF) was added and the reaction mixture was stirred for 20 min. $Pd(dba)_2$ (28 mg, 0.05 mmol), tris-*o*-furylphosphine (23 mg, 0.1 mmol) and 4-iodo-benzobenzonitrile (366 mg, 1.6 mmol) were added and the reaction mixture was stirred for 2 h at 50 °C. Flash chromatographical purification (pentane / diethyl ether = 8:1, silica gel) yielded **53g** as a colourless solid (334 mg, 54% yield).

mp (°C): 171–172.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.58 (s, 9 H), 7.10–7.12 (m, 2 H), 7.17–7.19 (m, 2 H), 7.33 (d, J = 8.11 Hz, 1 H), 7.42–7.45 (m, 2 H), 7.49–7.51 (m, 2 H), 7.84–7.86 (m, 2 H).

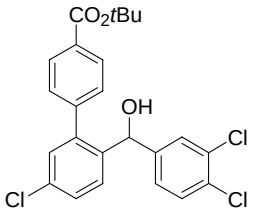
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 28.1 (CH_3), 81.3, 110.9, 118.6, 128.3 (CH), 129.4 (CH), 129.5 (CH), 130.3 (CH), 130.5 (CH), 131.1, 131.6 (CH), 132.0 (CH), 134.6, 137.1, 141.3, 143.5, 144.8, 165.2.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 2226 (w), 1712 (vs), 1604 (w), 1588 (w), 1476 (w), 1464 (w), 1454 (w), 1390 (w), 1368 (m), 1314 (m), 1294 (s), 1278 (s), 1254 (m), 1190 (w), 1164 (s), 1116 (vs), 1104 (s), 1094 (s), 1034 (w), 1016 (w), 1004 (w), 886 (w), 866 (m), 850 (s), 820 (vs), 774 (m), 752 (w), 728 (w), 706 (m).

MS (EI, 70 eV): *m/z* (%) = 391 (10), 389 (28), 335 (33), 334 (23), 333 (100), 318 (11), 316 (32), 289 (16), 288 (23), 254 (33), 253 (50), 252 (17), 251 (20), 57 (33), 43 (25).

HRMS (EI): calcd. for $C_{24}H_{20}O_2N^{35}Cl$: 389.1183, found: 389.1176.

*t*Butyl 5'-chloro-2'-[(3,4-dichlorophenyl)(hydroxy)methyl]biphenyl-4-carboxylate (**53h**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with sulfoxide **47d** (456 mg, 1.0 mmol) dissolved in THF (2 mL). The reaction mixture was cooled to –50 °C and cyclopentyl magnesium bromide (1.15 mL, 1.0 mmol, 0.87 M in THF) was added dropwise. After 7 h of stirring at –50 °C 3,4-dichlorobenzaldehyde (140 mg, 0.80 mmol) was added and the reaction mixture was allowed to warm to 25 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvents were removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 7:2, silica gel) yielded **53h** as a colourless liquid (184 mg, 50% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.63 (s, 9 H), 2.47 (s, 1 H), 5.79 (s, 1 H), 6.88–6.92 (m, 1 H), 7.21–7.25 (m, 2 H), 7.25–7.33 (m, 3 H), 7.39–7.42 (m, 1 H), 7.47–7.50 (m, 1 H), 8.00–8.03 (m, 2 H).

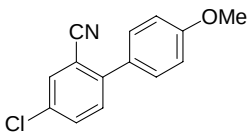
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 28.2 (CH_3), 70.9 (CH), 81.5, 125.8 (CH), 128.5 (CH), 128.7 (CH), 128.8, 129.0 (CH), 129.5 (CH), 129.7 (CH), 130.3 (CH), 131.4, 131.5, 132.5, 133.7 (CH), 138.6, 141.9, 143.3, 143.4, 165.4.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3490 (m), 1692 (vs), 1594 (w), 1470 (m), 1410 (m), 1392 (m), 1380 (m), 1368 (m), 1316 (vs), 1306 (s), 1286 (s), 1250 (m), 1230 (m), 1178 (m), 1158 (s), 1128 (s), 1104 (s), 1094 (s), 1044 (m), 1028 (s), 1014 (m), 878 (m), 860 (m), 838 (s), 824 (s), 784 (m), 776 (m), 752 (s), 734 (m), 708 (m), 692 (w).

MS (EI, 70 eV): *m/z* (%) = 177 (60), 161 (12), 137 (10), 127 (11), 125 (15), 123 (15), 113 (13), 111 (22), 109 (16), 99 (18), 97 (36), 95 (24), 85 (37), 83 (34), 80 (22), 71 (55), 69 (37), 57 (100).

HRMS (EI): calcd. for $C_{24}H_{21}O_3{}^{35}Cl_3$: 462.0556, found: 462.0531.

4-Chloro-4'-methoxybiphenyl-2-carbonitrile (**53i**)



According to **TP5** the sulfoxide **47e** (305 mg, 1.00 mmol) was treated with *i*PrMgCl·LiCl (0.92 mL, 1.10 mmol, 1.20 M in THF) at –50 °C for 5 min. Then $ZnCl_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. $Pd(PPh_3)_4$ (22 mg, 0.02 mmol) was added, followed by 4-iodoanisole (187 mg, 0.80 mmol), and the reaction mixture was stirred for 3 h at 25 °C. Flash chromatographical purification (pentane / diethyl ether = 10:1, silica gel) yielded a colourless solid (164 mg, 84% yield).

mp (°C): 104-106.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 3.86 (s, 3 H), 7.01 (d, J = 8.67 Hz, 2 H), 7.42 (d, J = 8.42 Hz, 1 H), 7.47 (d, J = 8.67 Hz, 2 H), 7.57 (dd, J = 8.42, 1.98 Hz, 1 H), 7.70 (d, J = 1.98 Hz, 1 H).

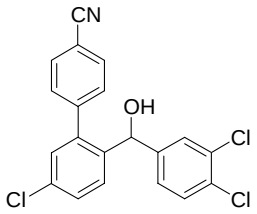
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 55.4 (CH_3), 112.4, 114.3 (CH), 117.7, 129.3, 129.9 (CH), 131.1 (CH), 133.0 (CH), 133.1, 133.2 (CH), 143.7, 160.3.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3067 (w), 2952 (w), 2850 (w), 2227 (m), 1607 (s), 1517 (m), 1481 (s), 1469 (s), 1444 (m), 1386 (m), 1304 (s), 1246 (vs), 1181 (s), 1101 (m), 1030 (s), 1014 (m), 834 (m), 814 (s), 796 (m).

MS (EI, 70 eV): *m/z* (%) = 245 (33), 244 (15), 243 (100), 230 (8), 228 (21), 202 (11), 200 (33), 174 (9), 165 (8), 164 (13).

HRMS (EI): calcd. for $C_{14}H_{10}{}^{35}ClNO$: 243.0451, found: 243.0432.

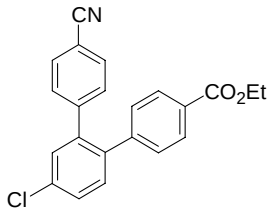
5'-Chloro-2'-[(3,4-dichlorophenyl)(hydroxy)methyl]biphenyl-4-carbonitrile (**53j**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of the sulfoxide **47f** (762 mg, 2.00 mmol) in THF (4 mL). The reaction mixture was cooled to –50 °C and *i*PrMgCl·LiCl (1.60 mL, 2.0 mmol, 1.25 M in THF) was added dropwise. After stirring at –50 °C for 2 h 3,4-dichlorobenzaldehyde (280 mg, 1.60 mmol) was added. After stirring for 20 min at –50 °C the reaction mixture was allowed to warm to 25 °C and stirred for additional 20 min. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 1:1, silica gel) yielded a colourless viscous oil (389 mg, 63% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.26 (s, 1 H), 5.69 (s, 1 H), 6.84–6.87 (m, 1 H), 7.12–7.13 (m, 2 H), 7.29–7.35 (m, 3 H), 7.40–7.51 (m, 2 H), 7.66–7.69 (m, 2 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 71.2 (CH), 112.0, 118.4, 125.8 (CH), 128.5 (CH), 128.9 (CH), 129.1 (CH), 129.7 (CH), 130.0 (CH), 130.4 (CH), 131.8, 132.2 (CH), 132.7, 134.0, 138.4, 140.9, 143.0, 143.9.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3394 (w), 2230 (m), 1608 (w), 1594 (w), 1564 (w), 1468 (s), 1388 (m), 1280 (w), 1260 (w), 1226 (w), 1194 (w), 1178 (m), 1130 (m), 1094 (m), 1028 (s), 1016 (s), 884 (m), 842 (s), 824 (vs), 790 (m), 762 (w), 740 (w), 718 (w), 688 (w), 676 (w).
MS (EI, 70 eV): *m/z* (%) = 334 (10), 178 (60), 176 (94), 175 (23), 147 (29), 143 (31), 141 (100), 120 (31), 113 (49), 111 (65), 105 (71), 77 (97), 75 (29), 70 (34), 61 (58), 51 (26).
HRMS (EI): calcd. for $C_{20}H_{21}ON^{35}Cl_3$: 386.9984, found: 386.9981.

Ethyl 4'-chloro-4"-cyano-1,1':2',1"-terphenyl-4-carboxylate (**53k**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of the sulfoxide **47f** (762 mg, 2.00 mmol) in THF (4 mL). The reaction mixture was cooled to –50 °C and *i*PrMgCl·LiCl (1.54 mL, 2.0 mmol, 1.30 M in THF) was added dropwise. After stirring at –50 °C for 2 h $ZnCl_2$ (2.0 mL, 2.0 mmol, 1.0 M in THF) was added. After stirring for 20 min at –50 °C the reaction mixture was allowed to warm to 25 °C and $Pd(dba)_2$ (57 mg, 0.10 mmol), tris-*o*-furylphosphine (46 mg, 0.2 mmol) and ethyl 4-iodobenzoate (442 mg, 1.6 mmol) were added and the reaction mixture was stirred for 2 h at 50 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 10:1, silica gel) yielded a colourless solid (346 mg, 60% yield).

mp (°C): 158–159.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.41 (t, J = 7.15 Hz, 3 H), 4.39 (q, J = 7.09 Hz, 2 H), 7.13–7.28 (m, 4 H), 7.39–7.55 (m, 5 H), 7.91–7.96 (m, 2 H).

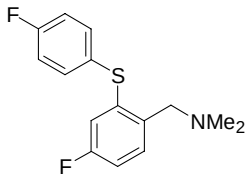
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.3 (CH_3), 61.1 (CH_2), 111.2, 118.5, 128.4, 128.7 (CH), 129.5 (CH), 129.6 (CH), 130.2 (CH), 130.3 (CH), 131.9, 132.0 (CH), 134.3 (CH), 138.1, 140.2, 144.1, 144.5, 166.1.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2228 (w), 1712 (s), 1608 (m), 1590 (m), 1574 (w), 1472 (m), 1454 (w), 1410 (w), 1390 (m), 1380 (m), 1362 (m), 1284 (vs), 1236 (m), 1198 (m), 1180 (m), 1118 (s), 1102 (vs), 1036 (m), 1018 (m), 1004 (m), 926 (w), 906 (m), 868 (m), 848 (s), 834 (s), 826 (s), 774 (s), 762 (m), 752 (m), 734 (m), 704 (vs), 634 (m).

MS (EI, 70 eV): *m/z* (%) = 363 (39), 362 (22), 361 (92), 333 (16), 318 (29), 317 (23), 316 (88), 289 (16), 288 (23), 254 (30), 253 (100), 252 (28), 251 (34), 226 (11), 113 (13).

HRMS (EI): calcd. for $C_{22}H_{16}O_2N^{35}Cl$: 361.0870, found: 361.0859.

{4-fluoro-2-[(4-fluorophenyl)thio]benzyl}dimethylamine (**53l**)



According to **TP5** the sulfoxide **47g** (538 mg, 1.43 mmol) was treated with *i*PrMgCl·LiCl (0.99 mL, 1.57 mol, 1.59 M in THF). After stirring at –50 °C for 1 h a mixture of trifluoroacetic anhydride (0.147 g, 0.70 mol,) and *N,N,N',N'*-tetramethyldiaminomethane (72 mg, 0.70 mol,) which were previously stirred in CH_2Cl_2 at 25 °C for 1 h was added, the reaction mixture was allowed to warm to 25 °C and stirred for additional 2 h. Flash chromatographical purification (diethyl ether, silica gel) yielded a colourless liquid (183 mg, 66% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 2.25 (s, 6 H), 3.48 (s, 2 H), 6.60 (dd, J = 9.54 Hz, J = 2.38 Hz, 1 H), 6.79–6.82 (m, 1 H), 7.04–7.08 (m, 2 H), 7.25–7.28 (m, 1 H), 7.41–7.45 (m, 2 H).

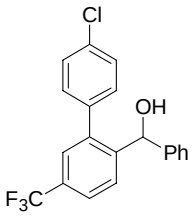
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 45.1 (CH_3), 61.5 (CH_2), 112.5 (d, J = 21.2 Hz, CH), 115.5 (d, J = 24.1 Hz, CH), 116.7 (d, J = 22.0 Hz, CH), 128.8 (d, J = 3.4 Hz), 131.2 (d, J =8.2 Hz, CH), 133.2 (d, J = 3.2 Hz), 135.7 (d, J = 8.5 Hz, CH), 140.3 (d, J = 7.7 Hz), 162.0 (d, J = 246.9 Hz, CF), 162.8 (d, J = 249.0 Hz, CF).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2974 (w), 2944 (m), 2858 (w), 2817 (m), 2770 (m), 1600 (m), 1590 (s), 1576 (m), 1489 (vs), 1479 (vs), 1454 (s), 1397 (w), 1360 (w), 1264 (m), 1250 (m), 1221 (vs), 1174 (m), 1156 (m), 1043 (w), 1025 (m), 1014 (m), 902 (m), 852 (m), 830 (s), 815 (s), 791 (m).

MS (EI, 70 eV): *m/z* (%) = 279 (64), 278 (33), 265 (17), 264 (100), 233 (21), 232 (85), 200 (23), 183 (24), 182 (38), 181 (18), 149 (43), 138 (17), 109 (16), 58 (47).

HRMS (EI): calcd. for $C_{15}H_{15}NF_2{}^{32}S$: 279.0893, found: 279.0884.

[4'-Chloro-5-(trifluoromethyl)biphenyl-2-yl](phenyl)methanol (**53m**)



According to **TP5** the sulfoxide **47h** (424 mg, 1.00 mmol) was treated with *i*PrMgCl·LiCl (0.92 mL, 1.10 mmol, 1.20 M in THF) at –50 °C for 3 h. Then benzaldehyde (85 mg, 81 µL, 0.80 mmol) was added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographical purification (pentane / diethyl ether = 4:1, silica gel) yielded a colourless liquid (198 mg, 68% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.08 (s, 1 H), 5.90 (s, 1 H), 7.07–7.14 (m, 4 H), 7.24–7.28 (m, 3 H), 7.35–7.38 (m, 2 H), 7.46 (s, 1 H), 7.69 (d, J = 8.37 Hz, 1 H), 7.84 (d, J = 8.37 Hz, 1 H).

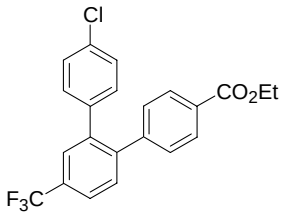
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 72.5 (CH), 123.9 (q, J = 272.4 Hz, CF_3), 124.9 (q, J = 3.6 Hz, CH), 126.8 (q, J = 3.6 Hz, CH), 126.8 (CH), 127.7 (CH), 127.9 (CH), 128.5 (CH), 128.5 (CH), 129.7 (q, J = 32.5 Hz), 130.6 (CH), 134.0, 137.8, 140.5, 142.8, 144.6.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3324 (w), 1485 (m), 1416 (m), 1333 (vs), 1254 (m), 1164 (s), 1119 (vs), 1090 (s), 1075 (s), 1030 (m), 1012 (s), 833 (m), 821 (m), 763 (m), 734 (m), 723 (m), 698 (s).

MS (EI, 70 eV): *m/z* (%) = 364 (10), 362 (26), 310 (20), 309 (100), 283 (13), 249 (10), 105 (13), 77 (10).

HRMS (EI): calcd. for $C_{20}H_{14}O^{35}ClF_3$: 362.0685 , found: 362.0675.

Ethyl 4''-chloro-4'-(trifluoromethyl)-1,1':2',1''-terphenyl-4-carboxylate (**53n**)



According to **TP5** the sulfoxide **47h** (0.424 g, 1.00 mmol,) was treated with *i*PrMgCl·LiCl (1.00 mL, 1.20 mmol, 1.20 M in THF) at –50 °C for 3 h. Then $ZnCl_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. $Pd(dba)_2$ (12 mg, 0.02 mmol) and tris-*o*-furylphosphine (9 mg, 0.04 mmol) were added, followed by ethyl 4-iodobenzoate (221 mg, 0.80 mmol). The reaction mixture was stirred for 3 h at 25 °C. Flash chromatographical purification (pentane / diethyl ether = 12:1, silica gel) yielded **53n** as a yellowish solid (255 mg, 79% yield).

mp (°C): 104–107.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.39 (t, J = 7.15 Hz, 3 H), 4.37 (q, J = 7.15 Hz, 2 H), 7.03–7.06 (m, 2 H), 7.18–7.22 (m, 4 H), 7.53 (d, J = 8.11 Hz, 1 H), 7.66 (d, J = 1.91 Hz, 1 H), 7.69 (dd, J = 8.34, 1.43 Hz, 1 H), 7.93–7.95 (m, 2 H).

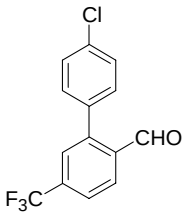
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.3 (CH_3), 61.1 (CH_2), 123.9 (q, J = 271.9 Hz, CF_3), 124.6 (q, J = 3.7 Hz, CH), 127.3 (q, J = 3.7 Hz, CH), 128.5 (CH), 129.4 (CH), 129.5 (CH), 129.6 (CH), 130.4 (q, J =32.7 Hz), 130.9 (CH), 131.0, 133.6, 138.1, 140.0, 143.0, 144.4, 166.2.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2905 (w), 1714 (vs), 1607 (m), 1419 (m), 1389 (m), 1333 (s), 1311 (m), 1284 (s), 1252 (m), 1237 (m), 1180 (m), 1166 (s), 1131 (vs), 1118 (s), 1102 (s), 1092 (s), 1085 (vs), 1033 (m), 1024 (m), 1014 (m), 1006 (m), 913 (m), 839 (s), 831 (s), 778 (m), 758 (m), 744 (m), 719 (m), 704 (m).

MS (EI, 70 eV): *m/z* (%) = 406 (27), 405 (19), 404 (100), 361 (24), 360 (15), 359 (80), 331 (18), 297 (25), 295 (11), 226 (24).

HRMS (EI): calcd. for $C_{22}H_{16}O_2{}^{35}ClF_3$: 404.0791 , found: 404.0793.

4'-Chloro-5-(trifluoromethyl)biphenyl-2-carbaldehyde (**53o**)



According to **TP5** the sulfoxide **47i** (10.3 g, 25.0 mmol) was treated with *i*PrMgCl·LiCl (17.3 mL, 27.5 mmol, 1.59 M in THF) at –50 °C for 30 min. Then DMF (1.56 mL, 20.0 mmol) was added and the reaction mixture was allowed to warm to 25 °C and was stirred for additional 1 h. Flash chromatographical purification (pentane / diethyl ether = 15:1, silica gel) yielded a colourless solid (4.74 g, 83% yield).

mp (°C): 58–60.

^{1}H-NMR (CDCl$_3$, 300 MHz): δ (ppm) = 7.31–7.35 (m, 2 H), 7.47–7.51 (m, 2 H), 7.68 (s, 1 H), 7.74–7.77 (m, 1 H), 8.12 (d, J = 8.17 Hz, 1 H), 9.99 (s, 1 H).

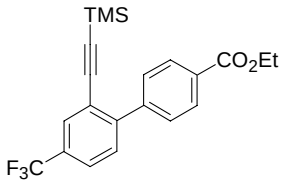
^{13}C-NMR (CDCl$_3$, 75 MHz): δ (ppm) = 123.3 (q, J = 272.0 Hz, CF_3), 124.9 (q, J = 3.6 Hz, CH), 127.7 (q, J = 3.7 Hz, CH), 128.7 (CH), 129.1 (CH), 131.2 (CH), 134.8, 134.9 (q, J = 32.9 Hz), 135.4, 136.0, 144.8, 190.7 (CH).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3098 (vw), 2860 (w), 2360 (vw), 2342 (vw), 1718 (w), 1696 (s), 1662 (w), 1650 (w), 1614 (w), 1594 (w), 1564 (vw), 1498 (w), 1484 (m), 1444 (vw), 1418 (m), 1390 (m), 1364 (w), 1332 (s), 1310 (m), 1298 (m), 1278 (m), 1246 (s), 1200 (m), 1168 (s), 1120 (vs), 1106 (s), 1092 (s), 1074 (vs), 1030 (m), 1012 (m), 982 (m), 968 (w), 950 (w), 910 (m), 858 (s), 852 (s), 838 (s), 822 (s), 790 (s), 742 (m), 718 (m), 682 (m), 656 (m), 626 (m).

MS (EI, 70 eV): *m/z* (%) = 286 (22), 285 (21), 284 (67), 283 (41), 249 (100), 220 (23), 201 (29), 152 (32).

HRMS (EI): calcd. for $C_{14}H_8O^{35}ClF_3$: 284.0216, found: 284.0212.

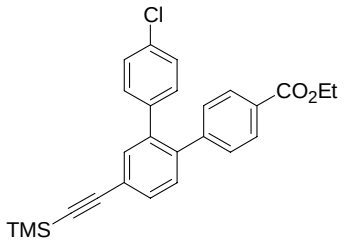
Ethyl 4'-(trifluoromethyl)-2'-[(trimethylsilyl)ethynyl]biphenyl-4-carboxylate (**53p**)



According to **TP5** the sulfoxide **47j** (0.396 g, 1.00 mmol) was treated with *i*PrMgCl·LiCl (0.92 mL, 1.10 mmol, 1.20 M in THF) at –50 °C for 5 min. Then $ZnCl_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. $Pd(dba)_2$ (12 mg, 0.02 mmol) and tris-*o*-furylphosphine (9 mg, 0.04 mmol) were added, followed by ethyl 4-iodobenzoate (221 mg, 0.80 mmol). The reaction mixture was stirred for 3 h at 25 °C. Flash chromatographical purification (pentane / diethyl ether = 16:1, silica gel) yielded a colourless liquid (272 mg, 87% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.13 (s, 9 H), 1.42 (t, J = 7.20 Hz, 3 H), 4.41 (q, J = 7.17 Hz, 2 H), 7.48 (d, J = 8.04 Hz, 1 H), 7.61 (dd, J = 8.23 Hz, 1.12 Hz, 1 H), 7.66 (d, J = 8.6 Hz, 2 H), 7.84 (s, 1 H), 8.10 (d, J = 8.6 Hz, 2 H).
^{13}C-NMR ($CDCl_3$, 300 MHz): δ (ppm) = –0.5 (CH_3), 14.3 (CH_3), 61.1 (CH_2), 100.2, 102.5, 122.4, 123.0 (q, J = 32.7 Hz), 123.6 (q, J = 273.0 Hz, CF_3), 125.2 (q, J = 3.9 Hz, CH), 129.2 (CH), 129.8 (CH), 130.1 (CH), 130.2, 130.3 (q, J = 4.0 Hz, CH), 143.4, 146.2, 168.3.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2960 (w), 2905 (w), 2159 (w), 1717 (s), 1608 (m), 1416 (w), 1396 (m), 1368 (w), 1329 (vs), 1313 (m), 1273 (vs), 1250 (s), 1168 (s), 1125 (vs), 1100 (s), 1080 (s), 904 (s), 834 (s), 778 (m), 755 (m), 745 (m), 704 (m), 648 (m).
MS (EI, 70 eV): *m/z* (%) = 391 (11), 390 (35), 375 (36), 345 (16), 332 (27), 331 (100), 303 (11), 165 (19), 75 (12).
HRMS (EI): calcd. for $C_{21}H_{21}O_2F_3{}^{28}Si$: 390.1263 , found: 390.1260.

Ethyl 4''-chloro-4'-[(trimethylsilyl)ethynyl]-1,1':2',1''-terphenyl-4-carboxylate (**53q**)



According to **TP5** the sulfoxide **47k** (0.439 g, 1.00 mmol,) was treated with *i*PrMgCl·LiCl (0.92 mL, 1.10 mmol, 1.20 M in THF) at –50 °C for 3 h. Then $ZnCl_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. $Pd(dba)_2$ (12 mg, 0.02 mmol) and tris-*o*-furylphosphine (9 mg, 0.04 mmol) were added, followed by ethyl 4-iodobenzoate (221 mg, 0.80 mmol). The reaction mixture was stirred for 3 h at 25 °C. Flash chromatographical purification (pentane / diethyl ether = 15:1, silica gel) yielded a colourless liquid (235 mg, 68% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 0.26 (s, 9 H), 1.38 (t, J = 7.15 Hz, 3 H), 4.35 (q, J = 7.15 Hz, 2 H), 7.01–7.02 (m, 2 H), 7.15–7.18 (m, 4 H), 7.35 (d, J = 8.46 Hz, 1 H), 7.51–7.52 (m, 2 H), 7.90 (d, J = 8.11 Hz, 2 H).

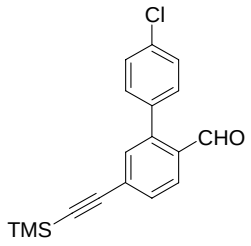
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 0.1 (CH_3), 14.3 (CH_3), 61.0 (CH_2), 95.6, 104.3, 123.1, 128.3 (CH), 128.9, 129.3 (CH), 129.6 (CH), 130.5 (CH), 131.0 (CH), 131.1 (CH), 133.1, 134.0 (CH), 138.7, 139.4, 139.5, 145.1, 166.3.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2980 (w), 2962 (w), 2932 (vw), 2360 (vw), 2342 (vw), 2156 (w), 1710 (s), 1652 (vw), 1608 (w), 1568 (vw), 1558 (vw), 1538 (vw), 1514 (vw), 1494 (w), 1476 (w), 1462 (w), 1408 (w), 1380 (w), 1366 (w), 1308 (w), 1298 (w), 1272 (s), 1250 (s), 1196 (w), 1178 (m), 1124 (m), 1102 (s), 1090 (m), 1044 (w), 1024 (m), 1014 (m), 1004 (m), 944 (vw), 908 (w), 890 (m), 832 (vs), 778 (s), 758 (s), 746 (s), 718 (m), 704 (m), 674 (m), 652 (m), 636 (m), 616 (m).

MS (EI, 70 eV): *m/z* (%) = 434 (33), 433 (28), 432 (100), 419 (62), 418 (50), 417 (26), 389 (32), 186 (13), 154 (16).

HRMS (EI): calcd. for $C_{26}H_{25}O_2{}^{35}Cl^{28}Si$: 432.1312, found: 432.1301.

4'-Chloro-5-[(trimethylsilyl)ethynyl]biphenyl-2-carbaldehyde (**53r**)



According to **TP5** the sulfoxide **47k** (439 mg, 1.00 mmol) was treated with *i*PrMgCl·LiCl (0.92 mL, 1.10 mmol, 1.20 M in THF) at –50 °C for 3 h. Then DMF (62 µL, 0.80 mmol) was added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographical purification (pentane / diethyl ether = 15:1, silica gel) yielded a colourless solid (0.170 g, 68% yield).

mp (°C): 109–110.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.25 (s, 9 H), 7.27–7.31 (m, 2 H), 7.41–7.46 (m, 2 H), 7.49 (dd, J = 1.61, 0.62 Hz, 1 H), 7.53–7.57 (m, 1 H), 7.94 (dd, J = 7.93, 0.50 Hz, 1 H), 9.91 (d, J = 0.74 Hz, 1 H).

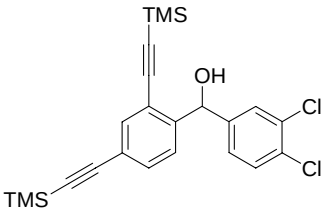
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = –0.3 (CH_3), 99.1, 103.6, 127.8 (CH), 128.6, 128.7 (CH), 131.1 (CH), 131.3 (CH), 132.9, 134.0 (CH), 134.7, 135.4, 144.3, 191.0 (CH).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2956 (m), 2851 (m), 1682 (vs), 1592 (s), 1492 (m), 1476 (m), 1399 (w), 1391 (m), 1248 (s), 1242 (s), 1188 (s), 1091 (s), 1012 (m), 904 (w), 893 (m), 839 (vs), 829 (vs), 824 (s), 802 (s), 757 (s), 663 (m).

MS (EI, 70 eV): *m/z* (%) = 314 (10), 312 (26), 299 (35), 298 (23), 297 (100), 131 (12).

HRMS (EI): calcd. for $C_{18}H_{17}O^{35}Cl^{28}Si$: 312.0737, found: 312.0733.

{2,4-Bis[(trimethylsilyl)ethynyl]phenyl}(3,4-dichlorophenyl)methanol (**53s**)



According to **TP5** the sulfoxide **47m** (425 mg, 1.00 mmol) was treated with *i*PrMgCl·LiCl (0.92 mL, 1.10 mmol, 1.20 M in THF) at –50 °C for 5 min. Then 3,4-dichlorobenzaldehyde (140 mg, 0.80 mmol) was added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographical purification (pentane / diethyl ether = 4:1, silica gel) yielded a colourless oil (257 mg, 72% yield).

^{1}H-NMR ($CDCl_3$, 200 MHz): δ (ppm) = 0.24 (s, 18 H), 2.60 (s, 1H), 6.17 (s, 1 H), 7.20 (dd, J = 8.33 Hz, J = 2.11 Hz, 1 H), 7.37 (d, J = 8.7 Hz, 1 H), 7.41 (s, 1 H), 7.42 (s, 1 H), 7.53 (d, J = 1.83 Hz, 1 H), 7.57–7.58 (m, 1 H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = –0.3 (CH_3), –0.1 (CH_3), 72.6 (CH), 95.5, 101.4, 110.8, 103.5, 121.2, 122.9, 125.9 (CH), 126.1 (CH), 128.1 (CH), 130.3 (CH), 131.5, 132.3 (CH), 132.4, 136.3 (CH), 142.8, 144.8.

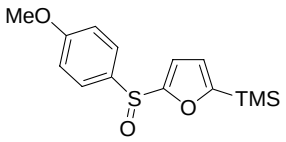
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3326 (w), 2958 (w), 2150 (m), 1483 (w), 1469 (m), 1389 (m), 1248 (s), 1186 (m), 1163 (w), 1131 (w), 1031 (m), 956 (m), 836 (vs), 797 (m), 757 (s), 716 (m), 699 (m), 677 (m), 670 (w), 647 (m), 624 (w), 619 (w), 600 (w), 566 (w).

MS (EI, 70 eV): *m/z* (%) = 446 (11), 444 (14), 429 (19), 409 (16), 375 (15), 374 (17), 373 (73), 372 (25), 371 (100), 358 (26), 357 (15), 356 (38), 336 (16), 75 (12).

HRMS (EI): calcd. for $C_{23}H_{26}O^{35}Cl^{28}Si_2$: 444.0899, found: 444.0887.

4.3.4. Functionalization of the furan ring

{5-[(4-methoxyphenyl)sulfinyl]-2-furyl}(trimethyl)silane (**57**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with 2-furyl(trimethyl)silane (2.10 g, 15.0 mmol) in diethyl ether (45 mL). The reaction mixture was cooled to 0 °C and *n*BuLi (7.4 mL, 17.5 mmol in hexane) was added dropwise. The reaction mixture was allowed to warm to 25 °C and stirred for additional 10 min. In a second dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum 4-methoxybenzene sulfinyl chloride (**38**, 4.2 g, 22.0 mmol) was dissolved in THF (20 mL) and cooled to –50 °C. The lithiated furane was added dropwise and the reaction mixture was allowed to warm to 25 °C and was then stirred for additional 30 min. The reaction mixture was quenched with sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 2:1, silica gel) yielded the **57** as a yellow oil (3.43 g, 78%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.20 (s, 9 H), 3.82 (s, 3 H), 6.56–6.58 (m, 2 H), 6.96–7.01 (m, 2 H), 7.61–7.66 (m, 2 H).

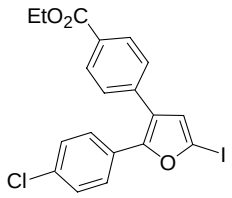
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = –1.9 (CH_3), 55.4 (CH_3), 114.5 (CH), 114.8 (CH), 120.2 (CH), 127.0 (CH), 132.8, 157.5, 162.0, 166.8.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 1716 (m), 1594 (m), 1578 (w), 1494 (m), 1462 (w), 1442 (w), 1410 (w), 1366 (w), 1304 (m), 1248 (s), 1182 (m), 1172 (m), 1140 (w), 1084 (s), 1050 (s), 1024 (m), 920 (m), 830 (vs), 794 (s), 756 (s), 712 (m), 702 (m), 652 (m), 630 (s).

MS (EI, 70 eV): *m/z* (%) = 248 (23), 247 (100), 246 (15), 232 (39), 231 (40), 182 (11), 165 (17), 157 (14), 155 (18), 139 (84), 115 (14), 73 (81).

HRMS (EI): calcd. for $C_{14}H_{18}O_3{}^{32}S^{28}Si$: 294.0766, found: 294.0735.

Ethyl 4-[2-(4-chlorophenyl)-5-iodo-3-furyl]benzoate (**59**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of ethyl 4-[2-(4-chlorophenyl)-5-(trimethylsilyl)-3-furyl] (**61a**; 2.59 g, 6.50 mmol) in CH_3CN (33 mL). The reaction mixture was cooled to 0 °C and ICl (1.57 g, 9.75 mmol) was added dropwise. The reaction mixture was allowed to warm to 25 °C and stirred for additional 1 h. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (10 mL) and a sat. aq $Na_2S_2O_3$ (10 mL) and extracted three times with CH_2Cl_2 (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 25:1, silica gel) yielded **59** as a colourless solid (2.31 g, 79% yield).

mp (°C): 97–98.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.40 (t, J = 7.15 Hz, 3 H), 4.39 (q, J = 7.15 Hz, 2 H), 6.70 (s, 1 H), 7.22–7.26 (m, 2 H), 7.35–7.42 (m, 4 H), 8.00–8.04 (m, 2 H).

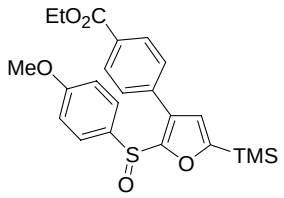
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.3 (CH_3), 61.0 (CH_2), 88.4, 123.8 (CH), 124.5, 127.4 (CH), 128.1, 128.2 (CH), 128.7 (CH), 129.6, 130.0 (CH), 134.1, 137.2, 153.5, 166.1.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3062 (w), 2986 (w), 2942 (w), 2908 (w), 1716 (vs), 1674 (w), 1652 (w), 1644 (w), 1634 (w), 1610 (s), 1568 (w), 1562 (w), 1504 (m), 1476 (m), 1446 (m), 1412 (m), 1392 (m), 1360 (m), 1310 (m), 1292 (s), 1272 (vs), 1252 (s), 1184 (m), 1156 (w), 1126 (s), 1104 (vs), 1094 (s), 1082 (s), 1038 (m), 1020 (s), 1010 (s), 966 (m), 950 (m), 924 (s), 868 (m), 850 (s), 836 (vs), 818 (s), 806 (s), 768 (vs), 740 (s), 718 (m), 704 (s), 684 (s), 638 (m), 630 (m), 614 (m).

MS (EI, 70 eV): *m/z* (%) = 454 (17), 453 (12), 452 (54), 297 (22), 269 (16), 189 (16), 174 (15), 140 (33), 139 (100), 111 (17), 43 (15).

HRMS (EI): calcd. for $C_{19}H_{14}O_3{}^{35}Cl^{127}I$: 451.9676, found: 451.9664.

Ethyl 4-[2-[(4-methoxyphenyl)sulfinyl]-5-(trimethylsilyl)-3-furyl]benzoate (**60a**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with the sulfoxide **57** (5.89 g, 20.0 mmol) dissolved in THF (40 mL). The reaction mixture was cooled to –40 °C and tmpMgCl·LiCl (19.8 mL, 22.0 mmol, 1.11 M in THF) was added dropwise. After 20 min of stirring at –40 °C $ZnCl_2$ (11.0 mL, 11.0 mmol, 1.0 M in THF) was added slowly and the reaction mixture was stirred for 20 min at –40 °C and was then allowed to warm to 25 °C. $Pd(dba)_2$ (115 mg, 0.20 mmol), tris-*o*-furylphosphine (93 mg, 0.40 mmol) and ethyl 4-iodobenzoate (6.63 g, 24.0 mmol) were added and the reaction mixture was stirred for 1 h at 25 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvents were removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 1:1, silica gel) yielded **60a** as a yellow oil (6.52 g, 77% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.22 (s, 9 H), 1.41 (t, J = 7.14 Hz, 3 H), 3.83 (s, 3 H), 4.40 (q, J = 7.14 Hz, 2 H), 6.79 (s, 1 H), 6.94–7.01 (m, 2 H), 7.60–7.67 (m, 4 H), 8.07–8.13 (m, 2 H).

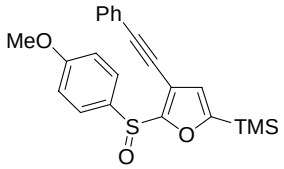
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = –1.98 (CH_3), 14.3 (CH_3), 55.5 (CH_3), 61.1 (CH_2), 114.4 (CH), 121.0 (CH), 127.1 (CH), 128.6 (CH), 129.9 (CH), 130.1, 131.8, 132.2, 135.3, 151.8, 161.9, 161.1, 166.4.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2958 (w), 1594 (m), 1578 (w), 1542 (vw), 1494 (m), 1462 (w), 1442 (w), 1408 (w), 1304 (m), 1248 (s), 1184 (m), 1172 (m), 1140 (w), 1106 (w), 1084 (s), 1050 (s), 1024 (s), 920 (m), 828 (vs), 794 (s), 756 (s), 712 (m), 702 (m), 652 (m), 630 (m).

MS (EI, 70 eV): *m/z* (%) = 428 (5), 427 (12), 426 (37), 397 (5), 396 (9), 395 (29), 394 (100), 291 (5), 275 (5), 139 (8), 73 (34).

HRMS (EI): calcd. for $C_{23}H_{27}O_5{}^{32}S^{28}Si$ (M+H): 443.1348, found: 443.1347.

[5-[(4-methoxyphenyl)sulfinyl]-4-(phenylethynyl)-2-furyl](trimethyl)silane (**60b**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with the sulfoxide **57** (2.94 g, 10.0 mmol) dissolved in THF (20 mL). The reaction mixture was cooled to –40 °C and tmpMgCl·LiCl (9.91 mL, 11.0 mmol, 1.11 M in THF) was added dropwise. After 20 min of stirring at –40 °C iodine (2.79 g, 11.0 mmol) was added and the reaction mixture was allowed to warm to 25 °C. In second dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar ethynylbenzene (1.53 g, 1.65 mL, 15.0 mmol) was added slowly to *i*PrMgCl·LiCl (9.43 mL, 15.0 mmol, 1.59 M in THF). After cessation of gas evolution the reaction mixture was heated to 60 °C for 5 min. After cooling to 25 °C a zinc chloride solution (7.5 mL, 7.5 mmol, 1.0 M in THF) was added slowly. The resulting zinc reagent was transferred to the previously prepared crude iodide. $Pd(dba)_2$ (115 mg, 0.2 mmol), tris-*o*-furylphosphine (93 mg, 0.4 mmol) were added and the reaction mixture was stirred at 50 °C for 2 h. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvents were removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 5:1, silica gel) yielded **60b** as a yellow oil (2.71 g, 69% yield).

^{1}H-NMR (C_6D_6, 300 MHz): δ (ppm) = 0.00 (s, 9 H), 3.15 (s, 3 H), 6.50 (s, 1 H), 6.61–6.65 (m, 2 H), 7.03–7.06 (m, 3 H), 7.46–7.49 (m, 2 H), 7.69–7.73 (m, 2 H).

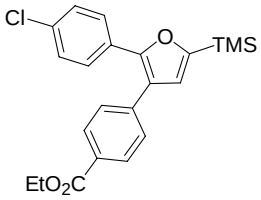
^{13}C-NMR (C_6D_6, 75 MHz): δ (ppm) = –2.2 (CH_3), 54.9 (CH_3), 79.4, 96.2, 112.6, 114.9 (CH), 123.2 (CH), 123.7, 127.0 (CH), 128.7 (CH), 128.9 (CH), 131.9 (CH), 133.9, 160.2, 162.2, 165.9.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3060 (w), 2959 (w), 1737 (w), 1592 (m), 1578 (m), 1493 (s), 1462 (m), 1442 (m), 1303 (m), 1249 (s), 1171 (s), 1140 (m), 1086 (s), 1058 (s), 1044 (s), 1025 (s), 926 (m), 839 (s), 826 (s), 689 (s), 636 (s), 583 (m), 565 (m).

MS (EI, 70 eV): *m/z* (%) = 348 (6), 347 (24), 346 (100), 139 (6), 73 (21).

HRMS (EI): calcd. for $C_{22}H_{22}O_3{}^{32}S^{28}Si$: 394.1059, found: 394.1050.

Ethyl 4-[2-(4-chlorophenyl)-5-(trimethylsilyl)-3-furyl]benzoate (**61a**)



According to **TP6** the sulfoxide **60a** (6.20 g, 14.0 mmol) was treated with *i*PrMgCl·LiCl (9.5 mL, 15.4 mmol, 1.46 M in THF) at –50 °C for 2 h. Then $ZnCl_2$ (16.0 mL, 16.0 mmol, 1.0 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. $Pd(dba)_2$ (81 mg, 0.14 mmol) and tris-*o*-furylphosphine (65 mg, 0.28 mmol) were added, followed by 4-iodo-1-chlorobenzene (2.67 g, 11.2 mmol). After 1 h at 50 °C the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 25:1, silica gel) yielded a colourless solid (3.05 g, 68% yield).

mp (°C): 83–85.

^{1}H-NMR (C_6D_6, 400 MHz): δ (ppm) = –0.28 (s, 9 H), 1.04 (t, J = 7.04 Hz, 3 H), 4.16 (q, J = 7.24 Hz, 2 H), 6.64 (s, 1 H), 6.97–7.00 (m, 2 H), 7.27–7.30 (m, 2 H), 7.33–7.37 (m, 2 H), 8.14–.8.17 (m, 2 H).

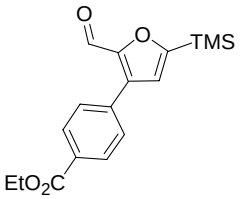
^{13}C-NMR (C_6D_6, 100 MHz): δ (ppm) = –2.0 (CH_3), 13.9 (CH_3), 60.5 (CH_2), 122.3, 123.6, 127.8 (CH), 128.4 (CH), 128.7 (CH), 129.5, 129.6 (CH), 130.0 (CH), 133.7, 138.9, 152.3, 159.7, 165.6.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2990 (vw), 2974 (w), 2956 (w), 2900 (vw), 1710 (s), 1668 (w), 1652 (w), 1608 (m), 1588 (w), 1558 (w), 1510 (w), 1476 (m), 1446 (w), 1414 (w), 1402 (w), 1366 (w), 1312 (w), 1292 (m), 1274 (s), 1248 (s), 1180 (m), 1148 (m), 1126 (m), 1110 (s), 1100 (s), 1090 (s), 1050 (w), 1024 (m), 1014 (m), 982 (w), 972 (w), 954 (m), 940 (m), 876 (w), 828 (vs), 774 (s), 756 (s), 742 (m), 722 (m), 704 (s), 632 (m).

MS (EI, 70 eV): *m/z* (%) = 401 (10), 400 (36), 398 (100), 310 (17), 295 (15), 169 (7), 73 (7).

HRMS (EI): calcd. for $C_{22}H_{23}O_3{}^{35}Cl^{28}Si$: 398.1105, found: 398.1098.

Ethyl 4-[2-formyl-5-(trimethylsilyl)-3-furyl]benzoate (**61b**)



According to **TP6** the sulfoxide **60a** (845 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (1.38 mL, 2.20 mmol, 1.59 M in THF) at –50 °C for 2 h. Then DMF (117 mg, 0.12 mL, 1.60 mmol,) was added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographical purification (pentane / diethyl ether = 8:1, silica gel) yielded **61b** as a yellow oil (384 mg, 76% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 0.35 (s, 9 H), 1.40 (t, J = 7.15 Hz, 3 H), 4.39 (q, J = 7.15 Hz, CH_2), 6.88 (s, 1 H), 7.61–7.63 (m, 2 H), 8.10–8.11 (m, 2 H), 9.75 (s, 1 H).

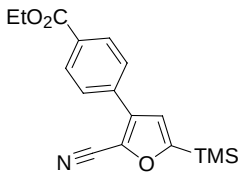
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = –2.0 (CH_3), 14.3 (CH_3), 61.2 (CH_2), 122.5 (CH), 128.9 (CH), 129.9 (CH), 130.7, 135.4, 136.9, 151.2, 166.0, 168.1, 178.0 (CH).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2960 (w), 1714 (s), 1670 (s), 1612 (w), 1578 (w), 1562 (w), 1464 (w), 1414 (w), 1394 (w), 1366 (m), 1310 (w), 1272 (s), 1250 (s), 1180 (m), 1102 (s), 1022 (m), 988 (m), 938 (m), 838 (vs), 794 (s), 772 (s), 756 (s), 734 (m), 704 (s), 648 (w), 630 (m).

MS (EI, 70 eV): *m/z* (%) = 317 (20), 316 (100), 315 (12), 301 (40), 287 (23), 271 (28), 243 (19), 229 (19), 228 (44), 128 (14), 83 (14), 73 (12), 42 (15).

HRMS (EI): calcd. for $C_{17}H_{20}O_4{}^{28}Si$: 316.1131, found: 316.1128.

Ethyl 4-[2-cyano-5-(trimethylsilyl)-3-furyl]benzoate (**61c**)



According to **TP6** the sulfoxide **60a** (845 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (1.38 mL, 2.20 mmol, 1.59 M in THF) at –50 °C for 2 h. Then TosCN (290 mg, 1.60 mmol) was added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographical purification (pentane / diethyl ether = 20:1, silica gel) yielded **61c** as a colourless solid (297 mg, 63% yield).

mp (°C): 73–74.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) = 0.33 (s, 9 H), 1.39 (t, J = 7.14 Hz, 3 H), 4.38 (q, J = 7.14 Hz, 2 H), 6.94 (s, 1 H), 7.71–7.75 (m, 2 H), 8.08–8.12 (m, 2 H).

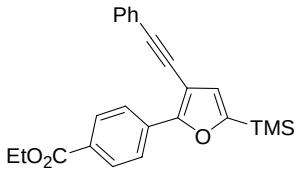
^{13}C-NMR ($CDCl_3$, 100 MHz): δ (ppm) = –2.1 (CH_3), 14.3 (CH_3), 61.1 (CH_2), 112.7, 119.6 (CH), 125.8, 126.8 (CH), 130.3 (CH), 130.8, 133.5, 135.7, 165.9, 168.8.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3112 (vw), 2982 (w), 2960 (w), 2360 (vw), 2342 (vw), 2224 (w), 1716 (s), 1678 (w), 1614 (w), 1474 (w), 1446 (w), 1420 (w), 1410 (w), 1394 (w), 1366 (w), 1318 (w), 1290 (w), 1268 (s), 1250 (s), 1232 (m), 1220 (m), 1190 (m), 1120 (m), 1108 (s), 1024 (w), 992 (w), 938 (m), 842 (vs), 768 (s), 760 (s), 722 (w), 696 (m), 680 (m), 668 (w), 632 (m), 618 (m).

MS (EI, 70 eV): *m/z* (%) = 314 (25), 313 (100), 299 (17), 298 (68), 270 (11), 268 (39), 226 (29), 225 (30), 210 (17), 198 (15), 126 (13), 73 (16), 61 (14), 43 (60).

HRMS (EI): calcd. for $C_{13}H_{17}O_3N^{28}Si$: 313.1134, found: 313.1128.

Ethyl 4-[3-(phenylethynyl)-5-(trimethylsilyl)-2-furyl]benzoate (**61d**)



According to **TP6** the sulfoxide **60b** (395 mg, 1.0 mmol) was treated with *i*PrMgCl·LiCl (0.69 mL, 1.1 mmol, 1.59 M in THF) at –78 °C for 15 min. Then $ZnCl_2$ (1.1 mL, 1.1 mmol, 1.0 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. $Pd(dba)_2$ (12 mg, 0.02 mmol) and tris-*o*-furylphosphine (9 mg, 0.04 mmol) were added, followed by ethyl 4-iodobenzoate (221 mg, 0.8 mmol). After 1 h at 50 °C the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (30 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 6:1, silica gel) yielded **61d** as a brown oil (212 mg, 68% yield).

^{1}H-NMR (C_6D_6, 400 MHz): δ (ppm) = 0.19 (s, 9 H), 1.02 (t, J = 7.14 Hz, 3 H), 4.13 (q, J = 7.14 Hz, 2 H), 6.72 (s, 1 H), 6.99–7.07 (m, 3 H), 7.51–7.55 (m, 2 H), 8.23–8.26 (m, 2 H), 8.37–8.40 (m, 2 H).

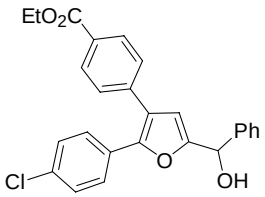
^{13}C-NMR (C_6D_6, 100 MHz): δ (ppm) = –1.9 (CH_3), 14.2 (CH_3), 60.8 (CH_2), 83.4, 95.3, 105.9, 123.9 (CH), 125.0 (CH), 125.4 (CH), 128.6 (CH), 128.8, 130.3, 130.4 (CH), 131.7 (CH), 134.8, 157.8, 160.7, 165.8.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2322 (m), 17011 (m), 1608 (m), 1320 (m), 1281 (s), 1271 (m), 1193 (w), 1138 (w), 1103 (s), 1093 (w), 1040 (w), 1000 (w), 970 (m), 836 (s), 810 (vs), 780 (m), 753 (s), 640 (m).

MS (EI, 70 eV): *m/z* (%) = 388 (100), 345 (1), 344 (1), 300 (3), 285 (1).

HRMS (EI): calcd. for $C_{24}H_{24}O_3{}^{28}Si$: 388.1494, found: 388.1479.

Ethyl 4-{2-(4-chlorophenyl)-5-[hydroxy(phenyl)methyl]-3-furyl}benzoate (**62a**)



According to **TP7** the furan **59** (226 mg, 0.50 mmol) was treated with *i*PrMgCl·LiCl (0.38 mL, 0.55 mmol, 1.46 M in THF) at –40 °C for 20 min. Then benzaldehyde (64 mg, 60µL, 0.60 mmol) was added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographical purification (pentane / diethyl ether = 2:1, silica gel) yielded **62a** as a colourless solid (179 mg, 83% yield).

mp (°C): 65–67.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.42 (t, J = 7.11 Hz, 3 H), 2.63 (s, 1 H), 4.40 (q, J = 7.14 Hz, 2 H), 5.91 (s, 1 H), 6.29 (s, 1 H), 7.24–7.27 (m, 2 H), 7.37–7.45 (m, 7 H), 7.53–7.55 (m, 2 H), 7.97–8.03 (m, 2 H).

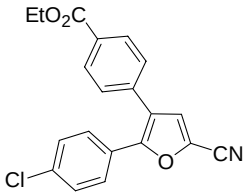
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.3 (CH_3), 61.0 (CH_2), 70.1 (CH), 111.4 (CH), 122.4, 126.6 (CH), 127.7 (CH), 128.3 (CH), 128.3 (CH), 128.6 (CH), 128.7 (CH), 129.0 (CH), 129.3, 129.9, 133.8, 138.4, 140.3, 148.0, 155.6, 166.3.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3418 (w), 2980 (w), 1712 (s), 1694 (s), 1608 (m), 1566 (w), 1552 (w), 1510 (w), 1482 (m), 1464 (w), 1452 (m), 1402 (m), 1392 (m), 1368 (m), 1310 (m), 1272 (vs), 1178 (s), 1094 (vs), 1048 (m), 1012 (s), 974 (m), 952 (s), 918 (m), 862 (m), 830 (s), 774 (s), 750 (m), 728 (s), 722 (s), 698 (vs), 630 (m).

MS (EI, 70 eV): *m/z* (%) = 434 (26), 433 (25), 432 (82), 430 (36), 418 (34), 417 (37), 416 (100), 415 (39), 293 (26), 189 (19), 140 (28), 139 (87), 105 (55).

HRMS (EI): calcd. for $C_{26}H_{21}O_4{}^{35}Cl$: 432.1128, found: 432.1126.

Ethyl 4-[2-(4-chlorophenyl)-5-cyano-3-furyl]benzoate (**62b**)



According to **TP7** the furan **59** (915 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (2.20 mmol, 1.51 mL, 1.46 M in THF) at –40 °C for 20 min. Then TosCN (471 mg, 2.60 mmol) was added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographical purification (pentane / diethyl ether = 2:1, silica gel) yielded **62b** as a colourless solid (539 mg, 77% yield).

mp (°C): 142–144.

^{1}H-NMR (CDCl$_3$, 300 MHz): δ (ppm) = 1.40 (t, J = 7.17 Hz, 3 H), 4.39 (q, J = 7.13 Hz, 2 H), 7.23 (s, 1 H), 7.28–7.32 (m, 2 H), 7.39–7.45 (m, 4 H), 8.04–8.08 (m, 2 H).

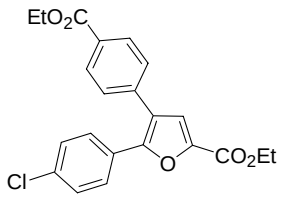
^{13}C-NMR (CDCl$_3$, 75 MHz): δ (ppm) = 14.3 (CH_3), 61.2 (CH_2), 111.3, 122.8, 124.9 (CH), 125.2, 127.0, 128.2 (CH), 128.5 (CH), 129.1 (CH), 130.3 (CH), 130.4, 135.8, 135.9, 152.6, 165.9.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2994 (w), 2228 (m), 1714 (s), 1670 (w), 1610 (m), 1562 (w), 1476 (m), 1448 (w), 1414 (w), 1404 (w), 1388 (w), 1364 (w), 1308 (w), 1290 (m), 1270 (vs), 1178 (m), 1140 (m), 1126 (m), 1096 (s), 1048 (w), 1024 (m), 1014 (m), 976 (m), 954 (m), 870 (m), 854 (m), 834 (vs), 772 (s), 748 (m), 726 (m), 714 (m), 704 (s), 690 (m), 664 (w), 646 (w), 630 (m), 618 (w), 608 (m).

MS (EI, 70 eV): *m/z* (%) = 353 (34), 352 (21), 351 (100), 323 (15), 308 (21), 307 (14), 306 (61), 243 (30), 214 (20), 189 (12).

HRMS (EI): calcd. for $C_{20}H_{14}O_3N^{35}Cl$: 351.0662, found: 351.0658.

Ethyl 5-(4-chlorophenyl)-4-[4-(ethoxycarbonyl)phenyl]-2-furoate (**62c**)



According to **TP7** the furan **59** (814 mg, 1.80 mmol) was treated with *i*PrMgCl·LiCl (1.36 mL, 1.98 mmol, 1.46 M in THF) at –40 °C for 20 min. Then, ethyl cyanoformate (232 mg, 2.34 mmol,) was added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographical purification (pentane / diethyl ether = 2:1, silica gel) yielded **62c** as a colourless solid (614 mg, 86% yield).

mp (°C): 119–120.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.33–1.39 (m, 6 H), 4.32–4.39 (m, 4 H), 7.22–7.26 (m, 3 H), 7.38–7.48 (m, 4), 7.99–8.03 (m, 2 H).

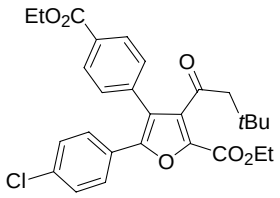
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.3 (2 CH_3), 61.1 (2 CH_2), 120.7 (CH), 123.5, 127.9, 128.3 (CH), 128.4 (CH), 128.9 (CH), 130.1 (CH), 135.1, 137.2, 143.6, 151.4, 158.5, 166.1 (2 C_q).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2986 (w), 2964 (w), 2942 (w), 2904 (w), 1712 (vs), 1614 (w), 1590 (w), 1562 (w), 1536 (w), 1524 (w), 1508 (w), 1474 (m), 1464 (m), 1446 (w), 1414 (w), 1402 (m), 1392 (m), 1366 (m), 1322 (s), 1304 (m), 1288 (m), 1268 (vs), 1252 (s), 1206 (s), 1174 (vs), 1124 (s), 1110 (vs), 1092 (vs), 1050 (m), 1016 (s), 1008 (s), 970 (m), 954 (m), 870 (m), 860 (m), 848 (m), 836 (s), 774 (s), 766 (s), 740 (m), 726 (s), 706 (s), 694 (s), 636 (m), 614 (m).

MS (EI, 70 eV): *m/z* (%) = 400 (38), 399 (28), 398 (100), 370 (18), 353 (27), 325 (15), 269 (16), 189 (29), 57 (12), 44 (37).

HRMS (EI): calcd. for $C_{22}H_{19}O_5{}^{35}Cl$: 398.0921, found: 398.0930.

Ethyl 5-(4-chlorophenyl)-3-(3,3-dimethylbutanoyl)-4-[4-(ethoxycarbonyl)phenyl]-2-furoate (**63**)

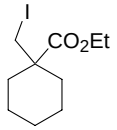


A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum, was charged with a solution of the furan **62c** (359 mg, 0.90 mmol) in THF (2 mL). The reaction mixture was cooled to –40 °C and $tmp_2Mg{\cdot}LiCl$ (2.45 mL, 1.35 mmol, 0.55 M in THF) was added dropwise. The reaction mixture was stirred for 25 min and then $ZnCl_2$ (1.45 mL, 1.35 mmol, 1.0 M in THF) was added, followed by CuCN·2LiCl (1.35 mL, 1.35 mmol, 1.0 M in THF). Then 3,3-dimethylbutanoyl chloride (363 mg, 0.40 mL, 2.70 mmol,) was added dropwise and the reaction mixture was allowed to warm to 25 °C. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (10 mL) and extracted three times with diethylether (30 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 6:1, silica gel) yielded **63** as a colourless oil (414 mg, 93% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 0.86 (s, 9 H), 1.37 (t, J = 7.15 Hz, 3 H), 1.40 (t, J = 7.15 Hz, 3 H), 2.50 (s, 2 H), 4.38 (q, J = 7.15 Hz, 2 H), 4.39 (q, J = 7.15 Hz, 2 H), 7.23–7.25 (m, 2 H), 7.36–7.38 (m, 4 H), 8.05–8.06 (m, 2 H).
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 14.3 (CH_3), 14.3 (CH_3), 29.3 (CH_3), 30.7, 56.9 (CH_2), 61.2 (CH_2), 61.4 (CH_2), 121.6, 127.1, 128.1 (CH), 128.9 (CH), 129.9 (CH), 130.1 (CH), 130.6, 135.4, 135.5, 136.5, 138.6, 151.1, 157.9, 166.1, 199.4.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 1714 (vs), 1478 (m), 1404 (m), 1366 (s), 1324 (m), 1276 (s), 1222 (m), 1176 (s), 1154 (m), 1130 (s), 1110 (s), 1104 (s), 1092 (s), 1074 (m), 1014 (s), 958 (m), 866 (m), 842 (s), 824 (m), 794 (m), 782 (m), 772 (m), 744 (s), 732 (m), 714 (s), 700 (m), 654 (m).
MS (EI, 70 eV): *m/z* (%) = 498 (31), 497 (25), 496 (100), 451 (15), 440 (15), 439 (16), 427 (21), 425 (69), 367 (21), 321 (16), 307 (11), 138 (15).
HRMS (EI): calcd. for $C_{28}H_{29}O_6{}^{35}Cl$: 496.1653, found: 496.1645.

4.3.5. Csp3-I/Mg-exchange

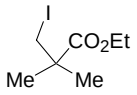
Ethyl 1-(iodomethyl)cyclohexane carboxylate (**64a**)



Diisopropylamine (6.20 mL, 44.0 mmol) was dissolved in 30 mL THF, cooled to –30 °C. *n*BuLi (17.7 mL, 44.0 mmol) was added slowly. After warming up to 0 °C the reaction mixture was cooled to –78 °C and ethyl cyclohexanecarboxylate was added dropwise. After 1 h at –78 °C CH_2I_2 (5.20 mL, 65.0 mmol) was added. The reaction mixture was warmed up to 25 °C overnight and then poured in 100 mL sat. aq. NH_4Cl-solution and extracted three times with ether. The organic phase was dried ($MgSO_4$). After filtration, the solvent was removed under reduced pressure and the crude product was purified by fractionated distillation (bp. 75 °C, 0.5 mbar). A colourless liquid (9.27 g, 68%) was obtained.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.27 (t, J = 7.03, 3 H), 1.58–1.33 (m, 8 H), 3.31 (s, 2 H), 2.13–2.07 (m, 2 H), 4.17 (q, J = 7.13 Hz, 2 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.3 (CH_3), 15.8 (CH_2), 22.9 (CH_2), 25.6 (CH_2), 34.2 (CH_2), 47.1, 60.8 (CH_2), 173.8.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2980 (w), 2932 (s), 2856 (m), 1724 (s), 1448 (m), 1368 (w), 1316 (w), 1280 (w), 1236 (w), 1212 (s), 1168 (m), 1136 (m), 1116 (w), 1096 (w), 1024 (w), 964 (w), 932 (w), 912 (w), 852 (w), 608 (w).
MS (EI, 70 eV), *m/z* (%): 296 (8), 223 (14), 169 (85), 141 (9), 123 (46), 96 (16), 95 (100), 81 (27), 67 (19), 55 (16).
HRMS (EI): calcd. for $C_{16}H_{17}O_2{}^{127}I$: 296.0273, found: 296.0288.

Ethyl 3-iodo-2,2-dimethylpropanoate (**64b**)



Diisopropylamine (15.4 mL, 0.11 mol) was dissolved in 100 mL THF, cooled to –30 °C. *n*-BuLi (44.0 mL, 0.11 mol) was added slowly. After warming up to 0 °C the reaction mixture was cooled to –78 °C and methyl 2-methylpropanoate (13.6 mL, 100 mmol) was added dropwise. After 1 h stirring at –78 °C CH_2I_2 (5.20 mL, 65.0 mmol) was added. The reaction mixture was allowed to warm up to 25 °C, stirred for 14 h and was then poured in 100 mL sat. aq. NH_4Cl-solution and extracted three times with diethyl ether. The organic phase was dried ($MgSO_4$). After filtration the solvent was removed under reduced pressure and the crude product was purified by fractionated distillation (bp. 75 °C, 3 mbar). A slightly yellow liquid (17.7 g, 66%) was obtained.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) =1.27 (t, J = 7.03 Hz, 3 H), 1.32 (s, 6 H), 3.34 (s, 2 H), 4.16 (q, J = 7.3 Hz, 2 H).

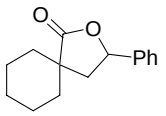
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.2 (CH_3), 16.5 (CH_2), 25.4 (CH_3), 43.2, 61.1 (CH_2), 174.4.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2980 (m), 2936 (w), 2904 (w), 2872 (w), 1728 (s), 1472 (w), 1444 (w), 1384 (w), 1364 (w), 1296 (m), 1232 (w), 1204 (w), 1176 (s), 1160 (m), 1132 (m), 1084 (w), 1024 (w), 960 (w), 940 (w), 912 (w), 864 (w), 804 (w), 760 (w), 620 (w).

MS (EI, 70 eV), *m/z* (%): 256 (21), 211 (5), 184 (2), 183 (62), 155 (2), 130 (6), 129 (100), 101 (2), 101 (9), 87 (8), 83 (5), 73 (49), 59 (9), 57 (12), 56 (17), 55 (54), 45 (6), 43 (12).

HRMS (EI): calcd. for $C_7H_{13}O_2{}^{127}I$: 255.9960, found: 255.9972.

3-Phenyl-2-oxaspiro[4.5]decan-1-one (**66a**)



The alkyl iodide **64a** (296 mg, 1.0 mmol) was dissolved in THF (1 mL) and DMPU (1 mL) and cooled to –10 °C, then *i*Pr_2Mg·LiCl (0.95 ml, 0.8 mmol, 0.84 M in THF) was added and the reaction mixture was stirred for 14 h. The reaction mixture was cooled to –20 °C and benzaldehyde (0.18 g, 0.17 mL, 1.7 mmol) was added. After 30 min of stirring at –20 °C the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution. The aqueous phase was extracted three times with ether (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 6:1, silica gel) afforded colourless crystals[89] (157 mg, 68%).

mp (°C): 59–60.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.15–1.55 (m, 4 H), 1.61–2.00 (m, 7 H), 2.68 (dd, J = 13.1 Hz, 6.7 Hz, 1 H), 5.42 (dd, J = 9.76 Hz, 6.68 Hz, 1 H), 7.29–7.39 (m, 5 H).

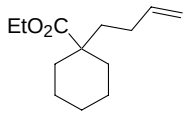
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 22.4 (CH_2), 25.6 (CH_2), 31.8 (CH_2), 34.4 (CH_2), 42.5 (CH_2), 45.5, 78.2 (CH), 125.5 (CH), 128.5 (CH), 128.9 (CH), 140.1, 181.5.

MS (EI, 70 eV), *m/z* (%): 230 (15), 185 (13), 129 (17), 126 (23), 105 (10), 104 (100), 91 (13).

HRMS (EI): calcd. for $C_{15}H_{18}O_2$: 230.1307, found: 230.1302.

[89] Treves, G. R.:; Stange, H.; Olofson, R. A. *J. Am. Chem. Soc.* **1967**, *89*, 6257.

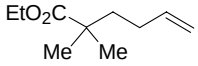
Ethyl 1-but-3-en-1-ylcyclohexanecarboxylate (**66b**)



The alkyl iodide **64a** (296 mg, 1.0 mmol) was dissolved in THF (1 mL) and DMPU (1 mL) and cooled to –10 °C, then *i*Pr_2Mg·LiCl (0.95 ml, 0.7 mmol, 0.74 M in THF) was added and the reaction mixture was stirred for 14 h. Then, the reaction mixture was cooled to –20 °C and CuCN·2LiCl (0.1 mL, 1.0 M in THF) was added followed by allyl bromide (240 mg, 0.17 mL, 2.0 mmol). After 30 min at –20 °C the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution. The aqueous phase was extracted three times with ether (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 10:1, silica gel) afforded a colourless liquid[90] (164 mg, 78%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.81–1.26 (m, 6 H), 1.31–1.37 (m, 2 H), 1.55–1.57 (m, 5 H), 1.93–1.97 (m, 2 H), 2.06–2.08 (m, 2 H), 4.13 (q, J = 7.15 Hz, 2 H), 4.89–4.98 (m, 2 H), 5.71–5.78 (m, 1 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.5 (CH_3), 23.4 (CH_2), 26.2 (CH_2), 28.7 (CH_2), 34.4 (CH_2), 39.9, 46.8 (CH_2), 60.2 (CH_2), 114.6 (CH_2), 138.8, 176.8.
MS (EI, 70 eV), *m/z* (%): 211 $[M+H]^+$ (2), 156 (100), 128 (12), 81 (26), 67 (10).
HRMS (EI): calcd. for $C_{13}H_{23}O_2$ $[M+H]^+$: 211.1698, found: 211.1711.

Ethyl 2,2-dimethylhex-5-enoate (**66c**)



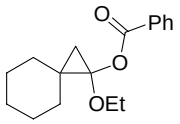
The alkyl iodide **64b** (256 mg, 1.0 mmol) was dissolved in THF (1 mL) and DMPU (1 mL) and cooled to –10 °C, then *i*Pr_2Mg·LiCl (1.02 ml, 0.65 mmol, 0.64 M in THF) was added and the reaction mixture stirred overnight. Then, the mixture was cooled to

[90] a) Nuhrich, A.; Moulines, J. *Tetrahedron* **1991**, *47*, 3075; b) Clive, D. L. J.; Pham, M. P.; Subedi, R. *J. Am. Chem. Soc.* **2007**, *129*, 2713.

–20 °C and CuCN·2LiCl (0.1 mL, 1.0 M in THF) was added followed by allyl bromide (302 mg, 0.22 mL, 2.50 mmol). After 30 min of stirring at –20 °C the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution. The aqueous phase was extracted three times with ether (30 mL). The combined organic layers were dried (MgSO4), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 20:1, silica gel) afforded a colourless liquid[91] (116 mg, 68%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) = 1.16 (s, 6 H), 1.23 (t, J = 7.24 Hz, 3 H), 1.58–1.62 (m, 2 H), 1.95–2.01 (m, 2 H), 4.10 (q, J = 7.24 Hz, 2 H), 4.90–5.01 (m, 2 H), 5.72–5.82 (m, 1 H).
^{13}C-NMR ($CDCl_3$, 100 MHz): δ (ppm) = 14.4 (CH_3), 25.3 (CH_3), 29.6 (CH_2), 40.0 (CH_2), 42.2, 60.4 (CH_2), 114.6 (CH_2), 138.8 (CH), 177.9.
MS (EI, 70 eV), *m/z* (%): 171 $[M+H]^+$ (2), 125 (6), 117 (6), 116 (100), 97 (32), 96 (7), 88 (41), 81 (8), 73 (8), 70 (6), 55 (36).
HRMS (EI): calcd. for $C_{13}H_{23}O_2$ $[M+H]^+$: 171.1385, found: 171.1399.

1-Ethoxyspiro[2.5]oct-1-yl benzoate (**66d**)



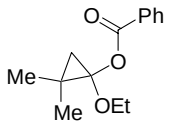
The alkyl iodide **64a** (296 mg, 1.0 mmol) was dissolved in THF (1 mL) and DMPU (1 mL) and cooled to –10 °C, *i*Pr_2Mg·LiCl (0.95 ml, 0.7 mmol, 0.74 M in THF) was added. After 7 h of stirring the mixture was cooled to –20 °C and CuCN·2LiCl (1.40 mmol, 1.40 mL, 1.0 M in THF) was added. After 30 min of stirring, PhCOCl (211 mg, 0.17 mL, 1.50 mmol) was added. After additional 30 min of stirring at –20 °C the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (10 mL). The aqueous phase was extracted three times with ether (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the

[91] a) Ashby, E. C.; Park, B.; Patil, G. S.; Gadru, K.; Gurumurthy, R. *J. Org. Chem.* **1993**, *58*, 424; Juaristi, E.; Jimbnez-Vizquez, H. A. *J. Org. Chem.* **1991**, *56*, 1623; Fehr , C.; Galindo, J .*Helv. Chim. Acta.* **1986**, *69*, 228.

solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 30:1, silica gel) afforded a colourless liquid (194 mg, 71%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.82 (d, J = 6.08 Hz, 1 H), 0.90 (d, J = 6.08 Hz, 1 H), 1.18 (t, J = 7.17 Hz, 3 H), 1.26–1.77 (m, 10 H), 3.68–3.89 (m, 2 H), 7.40–7.46 (m, 2 H), 7.53–7.58 (m, 1 H), 8.03–8.06 (m, 2 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 15.4 (CH_3), 22.6 (CH_2), 24.9 (CH_2), 25.0 (CH_2), 26.3 (CH_2), 30.4 (CH_2), 30.9 (CH_2), 31.1, 64.3 (CH_2), 93.5, 128.4 (CH), 129.7 (CH), 130.3, 133.0 (CH), 165.5.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2976 (w), 2928 (s), 2852 (m), 1732 (s), 1600 (w), 1448 (m), 1380 (w), 1336 (w), 1312 (w), 1272 (s), 1240 (m), 1168 (m), 1120 (m), 1084 (s), 1064 (s), 1024 (s), 992 (w), 912 (w), 708 (s).
MS (EI, 70 eV): *m/z* (%) = 169 (7), 168 (6), 123 (9), 106 (9), 105 (100), 95 (19), 81 (18), 77 (21).
HRMS (EI): calcd. for $C_{17}H_{22}O_3$: 274.1569, found: 274.1590.

1-Ethoxy-2,2-dimethylcyclopropyl benzoate (**66e**)



The alkyl iodide **64b** (768 mg, 3.0 mmol) was dissolved in THF (1 mL) and DMPU (1 mL) and cooled to –10 °C, *i*Pr_2Mg·LiCl (4.40 ml, 1.95 mmol, 0.44 M in THF) was added and the reaction mixture was stirred for 14 h. The reaction mixture was cooled to –20 °C and CuCN·2LiCl (4.50 mmol, 4.50 mL, 1.0 M in THF) was added. After 30 min of stirring PHCOCl (633 mg, 0.52 mL, 4.50 mmol) was added. After additional 30 min of stirring at –20 °C the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution. The aqueous phase was extracted three times with ether (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 30:1, silica gel) afforded a colourless liquid (526 mg, 75%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.84 (d, J = 6.17 Hz, 1 H), 0.90 (d, J = 6.17 Hz, 1 H), 1.14 (s, 3 H), 1.19 (t, J = 7.28 Hz, 3 H), 1.28 (s, 3 H), 3.68–3.85 (m, 2 H), 7.41–7.46 (m, 2 H), 7.54–7.58 (m, 1 H), 8.04–8.08 (m, 2 H).

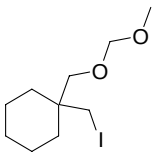
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 15.3 (CH_3), 20.3 (CH_3), 20.9 (CH_3), 23.6 (CH_2), 24.1, 64.2 (CH_2), 93.2, 128.4 (CH), 129.7 (CH), 130.2, 133.0 (CH), 165.4.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2980 (m), 2956 (m), 2928 (m), 2888 (m), 2872 (m), 1732 (s), 1476 (w), 1452 (w), 1372 (w), 1316 (w), 1284 (w), 1260 (m), 1200 (m), 1124 (m), 1084 (s), 1048 (s), 1024 (m), 912 (w), 708 (s).

MS (EI, 70 eV): m/z (%) = 235 (0.01), 113 (2), 106 (6), 105 (100), 77 (10).

HRMS (EI): calcd. for $C_{14}H_{19}O_3$ $[M+H]^+$: 235.1286, found: 235.1286.

1-(Iodomethyl)-1-[(methoxymethoxy)methyl]cyclohexane (**67a**)



Ethyl 1-(iodomethyl)cyclohexanecarboxylate (**64a**) (2.96 g, 10.0 mmol) was dissolved in CH_2Cl_2 (40 mL) and cooled to –78 °C. *i*Bu_2AlH (15 mL, 30 mmol, 2 M in hexane) was added. After 3 h of stirring, methanol (10 mL) was added and the pH was adjusted to 7 using 1M HCl. The aqueous layer was extracted three times with ether. The organic phase was dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. After flash chromatographical purification (pentane/ CH_2Cl_2 5:1, silica gel) a colourless liquid (1.21 g, 85%) was obtained. [1-(Iodomethyl)cyclohexyl]methanol (2.59 g, 10.2 mmol) was dissolved in dimethoxymethane (3.04 g, 3.5 mL, 40.0 mmol) and stirred with Amberlyst-15® (0.2 g) at 25 °C for 18 h. The resin was filtered off and washed three times with ether (30 mL). The solvent was removed under reduced pressure and after flash chromatographical purification (pentane / ethyl acetate = 50:1, silica gel) a colourless liquid (2.09 g, 69%) was obtained.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) =1.60–1.30 (m, 10 H), 3.34–3.36 (m, 7 H), 4.59 (s, 2 H).

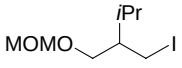
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 19.5 (CH_2), 27.7 (CH_2), 26.0 (CH_2), 32.4 (CH_2), 36.5, 55.3 (CH_3), 72.5 (CH_2), 96.7 (CH_2).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2924 (s), 2882 (m), 2854 (m), 2822 (w), 1450 (w), 1226 (w), 1212 (w), 1182 (w), 1148 (m), 1126 (w), (m), 1070 (w), 1042 (vs), 996 (w), 976 (w), 960 (w), 918 (m).

MS (EI, 70 eV): *m/z* (%) = 298 (1), 139 (10), 125 (9), 109 (56), 97 (11), 75 (11), 67 (10), 45 (100).

HRMS (EI): calcd. for $C_{10}H_{19}{}^{127}I\,O_2$: 298.0430, found: 298.0452.

1-Iodo-2-[(methoxymethoxy)methyl]-3-methylbutane (**67b**)



2-(Bromomethyl)-3-methylbutanoic acid (14.6 g, 75.0 mmol) was dissolved in THF (70 mL) and cooled to –20 °C. Then, borane dimethyl sulfide (7.5 g, 9.5 mL, 100 mmol) in THF (70 mL) was added slowly. After addition the reaction mixture was stirred overnight at 25 °C. The reaction mixture was quenched at 0 °C with potassium carbonate (15 g, 108 mmol) in water (225 mL). The organic layer was separated, and the aqueous layer was extracted three times with ether (100 mL). The combined phases were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. A colourless oil (11.0 g, 81%) was obtained and used without further purification.

Rac-2-(bromomethyl)-3-methylbutan-1-ol (10.9 g, 60.0 mmol) was stirred with Amberlyst 15® (0.70 g) and dimethoxymethane (62 mL, 0.70 mol) for 48 h. The mixture was filtered and after removing of the solvent a colourless oil (12.2 g, 90%) was obtained and used without further purification. 1-Bromo-2-[(methoxymethoxy)methyl]-3-methylbutane (10.0 g, 44.4 mmol) was dissolved in acetone (150 mL) and heated at reflux for 2 h with sodium iodide (46.1 g, 0.15 mol). The mixture was diluted with water (100 mL) and extracted three times with ether (100 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvents were removed under reduced pressure. After flash chromatographical purification (pentane / ethyl acetate = 30:1, silica gel) a pale yellow liquid (11.8 g, 98%, 71% over three steps) was obtained.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.93 (d, J = 6.7 Hz, 6 H), 1.21–1.32 (m, 1 H), 1.62–1.76 (m, 1 H), 3.28–3.49 (m, 3 H), 3.36 (s, 3 H), 3.62 (dd, J = 9.73 Hz, 4.45 Hz, 1 H), 4.60 (s, 2 H).

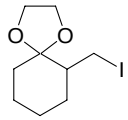
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 10.7 (CH_2), 19.7 (CH_3), 20.2 (CH_3), 29.1 (CH), 46.1 (CH), 55.4 (CH_3), 68.2 (CH_2), 96.7 (CH_2).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2960 (m), 2928 (m), 2880 (m), 2824 (w), 2767 (w), 1464 (w), 1440 (w), 1424 (w), 1412 (w), 1388 (w), 1256 (w), 1196 (w), 1140 (m), 1108 (s), 1040 (s), 944 (w), 932 (w), 916 (m), 876 (w), 864 (w), 848 (w), 772 (w), 632 (w), 604 (w) 584 (w).

MS (EI, 70 eV): *m/z* (%) = 272 (8), 169 (8), 155 (10), 113 (56), 99 (33), 95 (23), 83 (99), 75 (100), 55 (54), 46 (13), 45 (33).

HRMS (EI): calcd. for $C_8H_{17}{}^{127}IO_3$: 272.0273, found: 272.0256.

6-(Iodomethyl)-1,4-dioxaspiro[4.5]decane (**67c**)



Triphenylphosphine (16.3 g, 62.0 mmol) was dissolved in toluene (60 mL) and imidazole (5.58 g, 82.0 mmol) was added. Iodine (20.8 g, 82 mmol) was added and the sluggish stirring mixture was heated at 90 °C for 15 min. Then CH_2Cl_2 (60 mL) was added followed by 1,4-dioxaspiro[4.5]dec-6-ylmethanol (7.05 g, 40.9 mmol) dissolved in a 1:1 mixture of toluene and CH_2Cl_2 (60 mL). The mixture was heated at reflux for 2 h. After cooling to 25 °C, the mixture was extracted with a sat. aq. $Na_2S_2O_3$ solution (25 mL), washed with water (25 mL) and dried ($MgSO_4$). After filtration, the solvents were removed under reduced pressure. The product was purified by a short filter column (pentane / ethyl acetate = 25:1, silica gel) and a colourless light sensitive liquid (10.1 g, 87%) was obtained.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.16–1.72 (m, 7 H), 1.86–1.93 (m, 1 H), 2.07–2.13 (m, 1 H), 2.90 (dd, J = 10.76 Hz, 9.47 Hz, 1 H), 3.52 (dd, J = 9.54 Hz, 2.59 Hz, 1 H), 3.86–3.99 (m, 4 H).

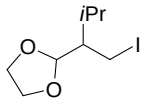
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 7.6 (CH_2), 23.9 (CH_2), 24.4 (CH_2), 30.0 (CH_2), 34.5 (CH_2), 47.8 (CH), 64.8 (CH_2), 110.3.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2932 (s), 2880 (m), 2856 (m), 1476 (w), 1444 (w), 1352 (w), 1320 (w), 1276 (w), 1240 (w), 1176 (m), 1156 (m), 1125 (m), 1084 (s), 1056 (s), 1012 (m), 960 (w), 948 (w), 924 (s), 860(m), 804 (w), 788 (w), 764 (w), 668 (w), 620 (w), 592 (w).

MS (EI, 70 eV): *m/z* (%) = 156 (35), 155 (100), 113 (28), 99 (24), 93 (9), 83 (9), 55 (23).

HRMS (EI): calcd. for $C_9H_{15}O_2{}^{127}I$: 282.0117, found: 282.0131.

2-[1-(Iodomethyl)-2-methylpropyl]-1,3-dioxolane (**67d**)



2-[1-(Bromomethyl)-2-methylpropyl]-1,3-dioxolane[92] (2.58 g, 17.5 mmol) was dissolved in acetone (60 mL) and sodium iodide (8.99 g, 60.0 mmol) was added. The reaction mixture was heated at reflux for 1.5 h and after cooling to room temperature water (150 mL) was added. The water phase was extracted twice with ether (100 mL), and then the combined organic phases were extracted with a sat. aq. sodium thiosulfate solution (50 mL) and with brine (50 mL). The ether phase was dried ($MgSO_4$) and after removal of the solids, the solvent was removed under reduced pressure. After flash chromatographical purification (pentane / diethyl ether = 20:1, silica gel) a colorless liquid (3.85 g, 81%) was obtained.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.97 (d, J = 2.65 Hz, 3 H), 0.99 (d, J = 2.43 Hz, 3 H), 1.68–1.75 (m, 1 H), 1.98–2.07 (m, 1 H), 3.22–3.34 (m, 2 H), 3.80–3.97 (m, 4 H), 4.87 (d, J = 3.53 Hz, 1 H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 4.3 (CH_2), 19.3 (CH_3), 20.4 (CH_3), 28.7 (CH), 48.8 (CH), 64.7 (CH_2), 65.0 (CH_2), 104.6 (CH).

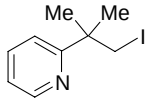
[92] Rrehs,G.; Urban, E. *Tetrahedron*, **1996**, *52*,1221.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2960 (s), 2876 (s), 2764 (w), 2360 (w), 2340 (w), 1740 (w), 1464 (w), 1424 (w), 1388 (m), 1368 (w), 1296 (w), 1280 (w), 1264 (w), 1200 (w), 1176 (w), 1108 (s), 1032 (m), 1012 (m), 964 (m), 952 (m), 856 (w).

MS (EI, 70 eV): *m/z* (%) = 269 (8), 99 (18), 74 (23), 73 (24), 55 (18), 45 (100).

HRMS (EI): calcd. for $C_8H_{15}O_2{}^{127}I$: 270.0117, found: 270.0127.

2-(2-Iodo-1,1-dimethylethyl)pyridine (**67e**)



Triphenylphosphine (16.67 g, 75.0 mmol) was dissolved in toluene (100 mL), imidazole (7.49 g, 110 mmol) was added. Iodine (19.0 g, 75.0 mmol) was added and the sluggish stirring mixture was heated at 90 °C for 15 min. Then CH_2Cl_2 (100 mL) was added, followed by 2-methyl-2-pyridin-2-ylpropan-1-ol (7.40 g, 49.0 mmol) dissolved in a 1:1 mixture of toluene (50 mL) and CH_2Cl_2 (50 mL). The reaction mixture was heated at reflux for 2 h. After cooling to 25 °C, the reaction mixture was extracted with a sat. aq. thiosulfate solution (25 mL), washed with water (25 mL) and dried ($MgSO_4$). After filtration the solvents were removed under reduced pressure. The product was purified by a short filter column (pentane / ethyl acetate = 20:1, silica gel) and a colourless liquid (11.5 g, 90%) was obtained.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.50 (s, 6 H), 3.62 (s, 2 H), 7.10–7.15 (m, 1 H), 7.27–7.30 (m, 1 H), 7.59–7.65 (m, 1 H), 8.56–8.58 (m, 1 H).

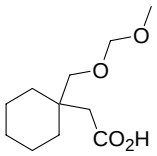
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 23.1 (CH_2), 27.6 (CH_3), 40.9, 119.7 (CH), 121.4 (CH), 136.2 (CH), 149.0 (CH), 164.8.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3088 (w), 3052 (w), 3000 (w), 2964 (s), 2928 (m), 2864 (w), 1588 (s), 1572 (m), 1472 (s), 1432 (s) 1380 (m), 1360 (m), 1300 (w), 1212 (m), 1156 (m), 1108 (w), 1092 (w), 1048 (w) 992 (w), 928 (w), 884 (w), 836 (w), 808 (w), 780 (s), 744 (s), 624 (w), 616 (w).

MS (EI, 70 eV): *m/z* (%) = 261 (2), 135 (10), 134 (100), 120 (7), 119 (12), 118 (18), 93 (12), 92 (8).

HRMS (EI): calcd. for $C_9H_{12}N_1{}^{127}I_1$: 261.0014, found: 261.0025.

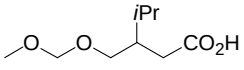
{1-[(Methoxymethoxy)methyl]cyclohexyl}acetic acid (**74a**)



The alkyl iodide **67a** (295 mg, 1.0 mmol) was dissolved in THF (1 mL) and cooled to 0 °C, *i*Pr_2Mg·LiCl (0.93 mL, 0.75 mmol, 0.81 M in THF) was added and the reaction mixture was warmed to 25 °C. After stirring for 5 h the reaction mixture was cooled to –20 °C and carbon dioxide was bubbled through the solution for 10 min. Ethyl acetate (20 mL) was added and the reaction mixture was extracted twice with a sat. aq. sodium carbonate solution (5mL). The combined aqueous layers were neutralised using 2 M HCl and extracted three times with ethyl acetate (15 mL). The solvent was removed under reduced pressure and the product was dried 5 h in high vacuum. A colourless oil (136 mg, 63%) was obtained.

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 1.39–1.47 (m, 10 H), 2.43 (s, 2 H), 3.35 (s, 3 H), 3.48 (s, 2 H), 4.62 (s, 2 H).
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 21.4 (CH_2), 26.6 (CH_2), 33.0 (CH_2), 37.0, 40.3 (CH_2), 55.2 (CH_3), 73.1 (CH_2), 96.7 (CH_2), 177.9.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2926 (vs), 2856 (m), 2826 (w), 1730 (m), 1702 (vs), 1452 (w), 1212 (m), 1148 (m), 1108 (s), 1038 (vs), 918 (m), 900 (w).
MS (EI, 70 eV): *m/z* (%) = 171 (47), 156 (19), 155 (15), 154 (24), 153 (98), 126 (41), 123 (15), 122 (11), 97 (13), 96 (24), 95 (56), 94 (22), 92 (15), 80 (79), 79 (26).
HRMS (EI): calcd. for $C_{11}H_{20}O_4$ $[M-H]^+$: 215.1283, found: 215.1298.

3-[(Methoxymethoxy)methyl]-4-methylpentanoic acid (**74b**)

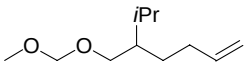


The alkyl iodide **67b** (272 mg, 1.0 mmol) was dissolved in THF (1 mL) and cooled to 0 °C, *i*Pr_2Mg·LiCl (1.36 mL, 1.10 mmol, 0.81 M in THF) was added and the reaction mixture was warmed to 25 °C. After 45 min, the reaction mixture was cooled to –20 °C

and carbon dioxide was bubbled through the solution for 10 min. Ethyl acetate (20 mL) was added and the reaction mixture was extracted twice with a sat. aq. sodium carbonate solution (10 mL). The combined aqueous layers were neutralised using 2 M HCl and extracted three times with ethyl acetate (15 mL). The solvent was removed under reduced pressure and the product was dried 5 h in high vacuum. A yellow oil (139 mg, 73%) was obtained.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.90 (d, J = 3.09 Hz, 3 H), 0.92 (d, J = 3.09 Hz, 3 H), 1.75–1.78 (m, 1 H), 1.99–2.10 (m, 1 H), 2.38 (d, J = 7.06 Hz, 2 H), 3.35 (s, 3 H), 3.45 (dd, J = 9.70 Hz, 7.06 Hz, 1 H), 3.54–3.59 (m, 1 H), 4.59 (s, 2 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 19.4 (CH_3), 19.7 (CH_3), 28.7 (CH), 34.1 (CH_2), 41.2 (CH), 55.3 (CH_3), 68.6 (CH_2), 96.5 (CH_2), 179.2.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2960 (s), 2932 (s), 2880 (m), 2828 (w), 2772 (w), 1704 (s), 1468 (w), 1440 (w), 1412 (w), 1388 (w), 1280 (w), 1216 (w), 1148 (m), 1108 (s), 1036 (s), 944 (w), 916 (m).
MS (EI, 70 eV): *m/z* (%) = 145 (24), 129 (30), 128 (24), 127 (100), 100 (50), 85 (20), 83 (16), 70 (17), 69 (61), 45 (46).
HRMS (ESI): calcd. for $C_9H_{19}O_4[M+H]^+$: 191.1283, found: 191.1281.

5-[(Methoxymethoxy)methyl]-6-methylhept-1-ene (**74c**)



The alkyl iodide **67b** (0.41 g, 1.50 mmol) was dissolved in THF (1.5 mL) and cooled to 0 °C, $ClMg(CH_2)_5MgCl{\cdot}2LiCl$ (2.68 ml, 1.65 mmol, 0.62 M in THF) was added and the temperature was raised to 25 °C. After 2 h the reaction mixture was cooled to –30 °C and CuCN·2LiCl (0.08 mL, 5 mol %, 1 M in THF) and allyl bromide (0.363 g, 0.26 mL, 3.0 mmol) was added. The reaction mixture was stirred for additional 30 min, then the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (10 mL). The aqueous phase was extracted three times with ether (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 40:1, silica gel) afforded a colourless liquid (198 mg, 71%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.88 (d, J = 7.06 Hz, 6 H), 1.31–1.47 (m, 3 H), 1.76–1.87 (m, 1 H), 1.99–2.16 (m, 2 H), 3.35 (s, 3 H), 3.40–3.50 (m, 2 H), 4.59 (s, 2 H), 4.91–5.03 (m, 2 H), 5.73–5.83 (m, 1 H).

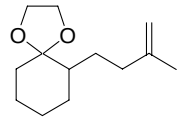
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 19.2 (CH_3), 19.6 (CH_3), 27.6 (CH_2), 28.2 (CH), 32.0 (CH_2), 43.6 (CH), 55.2 (CH_3), 68.7 (CH_2), 96.6 (CH_2), 114.3 (CH_2), 139.1 (CH).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3076 (w), 2956 (s), 2928 (s), 2876 (s), 2768 (w), 1640 (w), 1463 (w), 1440 (w), 1388 (w), 1368 (w), 1216 (w), 1152 (m), 1108 (m), 1044 (s), 996 (w), 912 (m), 644 (w).

MS (EI, 70 eV): *m/z* (%) = 124 (4), 123 (10), 81 (12), 69 (34), 67 (11), 55 (19), 45 (100).

HRMS (EI): calcd. for $C_{11}H_{22}O_2$: 186.1620, found: 186.1652

6-(3-Methylbut-3-en-1-yl)-1,4-dioxaspiro[4.5]decane (**74d**)



The alkyl iodide **67c** (564 mg, 2.0 mmol) was dissolved in THF (2 mL) and cooled to –15 °C, $ClMg(CH_2)_5MgCl{\cdot}2LiCl$ (2.8 ml, 2.2 mmol, 0.79 M in THF) was added. After 3 h, the reaction mixture was cooled to –30 °C and CuCN·2LiCl (0.1 mL, 1M in THF) and 3-bromo-2-methylprop-1-ene (324 mg, 0.25 mL, 2.4 mmol) was added. The reaction mixture was stirred for additional 30 min, then the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (10 mL). The aqueous phase was extracted three times with ether (30 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 20:1, silica gel) afforded a colourless liquid (302 mg, 72%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.16–1.36 (m, 4 H), 1.44–1.54 (m, 2 H), 1.58–1.62 (m, 2 H), 1.70 (s, 3 H), 1.72–1.81 (m, 3 H), 1.90–1.95 (m, 1 H), 2.04–2.09 (m, 1 H), 3.89–3.97 (m, 4 H), 4.66–4.67 (m, 2 H).

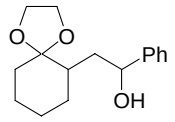
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 22.4 (CH_3), 23.9 (CH_2), 24.5 (CH_2), 26.1 (CH_2), 29.0 (CH_2), 34.7 (CH_2), 35.6 (CH_2), 44.1 (CH), 64.7 (CH_2), 64.8 (CH_2), 109.6 (CH_2), 110.9, 146.4.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3072 (w), 2932 (s), 2876 (m), 2864 (m), 1648 (w), 1448 (m), 1372 (w), 1352 (w), 1280 (w), 1188 (w), 1156 (m), 1140 (w), 1088 (s), 1060 (m), 1028 (w), 948 (w), 924 (m), 884 (m), 800 (w), 768 (w), 664 (w).

MS (EI, 70 eV): *m/z* (%) = 210 (30), 156 (8), 142 (6), 125 (12), 113 (21), 99 (100), 86 (10), 55 (16), 41 (10).

HRMS (EI): calcd. for $C_{13}H_{22}O_3$: 210.1620, found: 210.1633.

2-(1,4-Dioxaspiro[4.5]dec-6-yl)-1-phenylethanol (**74e**)



The alkyl iodide **67c** (564 mg, 2.0 mmol) was dissolved in THF (2 mL) and cooled to –15 °C, $ClMg(CH_2)_5MgCl{\cdot}2LiCl$ (3.3 ml, 2.2 mmol, 0.79 M in THF) was added. After 3 h the reaction mixture was cooled to –30 °C and benzaldehyde (318 mg, 0.30 mL, 3.0 mmol) was added. The reaction mixture was stirred for additional 60 min, then the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution. The aqueous phase was extracted three times with ether (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 3:1, silica gel) afforded a colourless liquid (378 mg, 72%). The diastereomeric ratio was determined by ^{1}H-NMR (3:1). NMR-Data is given for the main diastereomer.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.14–2.14 (m, 11 H), 3.05 (s, 1 H), 3.96–4.05 (m, 4 H), 4.83–4.87 (m, 1 H), 7.24–7.37 (m, 5 H).

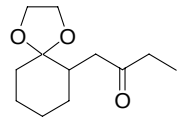
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 23.6 (CH_2), 24.6 (CH_2), 31.1 (CH_2), 38.5 (CH_2), 40.4 (CH_2), 42.3 (CH), 64.3 (CH_2), 64.6 (CH_2), 72.4 (CH), 110.7, 125.8 (CH), 127.1 (CH), 129.3 (CH), 144.9.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3420 (w), 3060 (w), 3028 (w), 2932 (s), 2884 (m), 2860 (m), 1492 (w), 1448 (w), 1352 (w), 1336 (w), 1284 (w), 1156 (w), 1088 (s), 1056 (m), 1016 (w), 924 (m), 888 (s), 864 (w), 800 (w), 756 (m), 700 (s).

MS (EI, 70 eV): *m/z* (%) = 262 (15), 200 (11), 156 (18), 155 (100), 133 (13), 120 (23), 113 (19), 105 (15), 99 (64), 77 (8).

HRMS (EI): calcd. for $C_{16}H_{22}O_3$: 262.1567, found: 262.1567.

1-(1,4-Dioxaspiro[4.5]dec-6-yl)butan-2-one (**74f**)



The alkyl iodide **67c** (0.564 g, 2.0 mmol) was dissolved in THF (2 mL) and cooled to –15 °C, $ClMg(CH_2)_5MgCl{\cdot}2LiCl$ (2.8 ml, 2.2 mmol, 0.79 M in THF) was added. After 3 h the reaction mixture was cooled to –30 °C and CuCN·2LiCl (2.5 mL, 2.5 mmol, 1.0 M in THF) was added. After stirring for 30 min at –30 °C propanoyl chloride (231 mg, 0.22 mL, 2.50 mmol) was added and the reaction mixture was stirred for additional 30 min. The temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution. The aqueous phase was extracted three times with ether (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether 3:1, silica gel) afforded a colourless liquid (268 mg, 63%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.02 (t, J = 7.28 Hz, 3 H), 1.27–1.37 (m, 3 H), 1.4–1.50 (m, 1 H), 1.55–1.56 (m, 2 H), 1.68–1.78 (m, 2 H), 2.14 (dd, J = 16.10 Hz, 7.94 Hz, 1 H), 2.24–2.29 (m, 1 H), 2.37–2.42 (m, 2 H), 2.60 (dd, J = 15.88 Hz, 5.29 Hz, 2 H), 3.63–3.95 (m, 4 H).

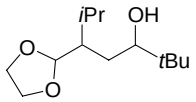
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 7.9 (CH_3), 23.8 (CH_2), 24.5 (CH_2), 30.2 (CH_2), 34.2 (CH_2), 36.1 (CH_2), 40.6 (CH), 42.4 (CH_2), 64.4 (CH_2), 64.5 (CH_2), 110.0, 211.1.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2972 (m), 2936 (s), 2884 (m), 2860 (m), 1708 (s), 1460 (w), 1448 (w), 1376 (w), 1352 (w), 1276 (w), 1256 (w), 1220 (w), 1156 (m), 1108 (m), 1092 (s), 1064 (w), 1032 (m), 948 (w), 924 (s), 876 (w), 800 (w), 768 (w), 628 (w).

MS (EI, 70 eV): *m/z* (%) = 212 (10), 183 (6), 156 (10), 155 (84), 141 (12), 113 (26), 100 (12), 99 (100), 86 (15), 57 (19), 55 (46).

HRMS (EI): calcd. for $C_{12}H_{21}O_3[M+H]^+$: 213.1491, found: 213.1477.

4-(1,3-Dioxolan-2-yl)-2,2,5-trimethylhexan-3-ol (**74g**)



The alkyl iodide **67d** (540 mg, 2.0 mmol) was dissolved in THF (2 mL) and cooled to –20 °C, $ClMg(CH_2)_5MgCl{\cdot}2LiCl$ (3.3 ml, 2.2 mmol, 0.67 M in THF) was added. After 3 h *t*BuCHO (215 mg, 0.27 mL, 2.5 mmol) was added. After 30 min of stirring at –20 °C the temperature was raised to 25 °C and the reaction mixture was stirred for additional 30 min. Then, the reaction mixture was quenched with a sat. aq. NH_4Cl-solution. The aqueous phase was extracted three times with ethyl acetate (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 20:1, silica gel) afforded a colourless liquid (333 mg, 72%). The diastereomeric ratio was determined by ^{1}H-NMR (4:1). NMR data is given for the main diastereomer.

^{1}H-NMR (C_6D_6, 400 MHz): δ (ppm) = 0.89–1.06 (m, 15 H), 1.45–1.52 (m, 1 H), 1.59–1.64 (m, 1 H), 1.70–1.77 (m, 1 H), 1.9–2.03 (m, 1 H), 3.17–3.43 (m, 5 H), 3.58 (m, 1 H), 4.65 (d, J = 4.65 Hz, 1 H).

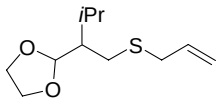
^{13}C-NMR (C_6D_6, 100 MHz): δ (ppm) = 18.9 (CH_3), 20.7 (CH_3), 26.1 (CH_3), 27.7 (CH_2), 30.0 (CH), 35.5, 46.9 (CH), 64.5 (CH_2), 64.3 (CH_2), 80.4 (CH), 106.2 (CH).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3476 (m), 2956 (s), 2872 (m), 1480 (w), 1468 (w), 1388 (w), 1316 (w), 1244 (w), 1220 (w), 1156 (w), 1116 (m), 1080 (m), 1060 (m), 1008 (m), 948 (m), 812 (w).

MS (EI, 70 eV): *m/z* (%) = 174 (11), 173 (16), 144 (21), 130 (15), 129 (51), 111 (100), 101 (49), 83 (32), 74 (10), 73 (28), 69 (22), 57 (16), 45 (29).

HRMS (EI): calcd. for $C_{13}H_{26}O_3$: 230.1882, found: 230.1865.

2-{1-[(Allylthio)methyl]-2-methylpropyl}-1,3-dioxolane (**74h**)



The alkyl iodide **67d** (540 mg, 2.0 mmol) was dissolved in THF (2 mL) and cooled to –20 °C, $ClMg(CH_2)_5MgCl{\cdot}2LiCl$ (3.31 ml, 2.20 mmol, 0.66 M in THF) was added. After 2.5 h *S*-allyl benzenesulfonothioate (563 mg, 2.50 mmol) was added. After 30 min of stirring at –20 °C the temperature was raised to 25 °C and the reaction mixture was stirred for additional 30 min. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (10 mL). The aqueous phase was extracted three times with ethyl acetate (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether = 20:1, silica gel) afforded a yellow liquid (251 mg, 58%).

^{1}H-NMR (C_6D_6, 400 MHz): δ (ppm) = 1.01–1.04 (m, 6 H), 1.93–1.96 (m, 1 H), 2.22–2.27 (m, 1 H), 2.58 (dd, *J* = 12.91 Hz, 7.43 Hz, 1 H), 2.82 (dd, *J* = 13.01 Hz, 5.38 Hz, 1 H), 2.93–2.98 (m, 2 H), 3.28–3.20 (m, 2 H), 3.45–3.48 (m, 2 H), 4.90–5.02 (m, 3 H), 5.70–5.78 (m, 1 H).

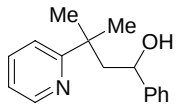
^{13}C-NMR (C_6D_6, 100 MHz): δ (ppm) = 20.0 (CH_3), 20.6 (CH_3), 27.8 (CH), 28.5 (CH_2), 35.8 (CH_2), 47.6 (CH), 64.5 (CH_2), 64.9 (CH_2), 104.9 (CH), 116.5 (CH_2), 135.2 (CH).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3080 (w), 2956 (s), 2876 (s), 1636 (w), 1468 (w), 1424 (w), 1400 (w), 1368 (w), 1300 (w), 1228 (w) 1176 (w), 1144 (m), 1108 (s), 1048 (m), 1020 (m), 988 (w), 944 (m), 916 (s), 760 (w), 744 (w), 592 (w).

MS (EI, 70 eV): *m/z* (%) = 175 (10), 154 (9), 143 (4), 111 (5), 99 (25), 85 (5), 73 (100), 55 (9).

HRMS (EI): calcd. for $C_{11}H_{20}O_2{}^{32}S$: 216.1184, found: 216.1182.

3-Methyl-1-phenyl-3-pyridin-2-ylbutan-1-ol (**74i**)



The alkyl iodide **67e** (0.522 g, 2.0 mmol) was dissolved in THF (1.5 mL) and cooled to 0 °C, *i*Pr_2Mg·LiCl (2.13 ml, 1.40 mmol, 0.66 M in THF) was added and the reaction mixture was warmed to 25 °C. After 1.5 h of stirring the reaction mixture was cooled to –20 °C and benzaldehyde (0.31 mL, 0.32 g, 3.0 mmol) was added. After 30 min at –20 °C the temperature was raised to 25 °C and the reaction was quenched with a sat. aq. NH_4Cl-solution (10 mL). The aqueous phase was extracted three times with ethyl acetate (30 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 15:2, silica gel) afforded a pale yellow liquid (270 mg, 56%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.46 (s, 3 H), 1.55 (s, 3 H), 1.88 (dd, J = 15.00 Hz, 2.21 Hz, 1 H), 2.42 (dd, J = 15.00 Hz, 2.21 Hz, 1 H), 4.94 (dd, J = 10.14 Hz, 2.21 Hz, 1 H), 6.91 (s, 1 H), 7.18–7.45 (m, 6 H), 7.70–7.76 (m, 1 H), 8.56–8.59 (m, 1 H).

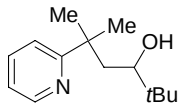
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 28.3 (CH_3), 31.5 (CH_3), 41.3, 52.0 (CH_2), 71.2 (CH), 120.6 (CH), 121.3 (CH), 125.8 (CH), 126.7 (CH), 128.2 (CH), 137.3(CH), 146.9, 147.5 (CH), 168.1.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3360 (m), 3088 (w), 3060 (w), 3028 (w), 2964 (s), 2928 (m), 2908 (m), 2684 (w), 1592 (s), 1572 (m), 1476 (s), 1432 (s), 1388 (w), 1364 (w), 1292 (w), 1200 (w), 1156 (w), 1120 (w), 1064 (m), 1052 (m), 1024 (w), 1004 (w), 912 (w), 788 (m), 748 (m), 727 (m), 700 (s), 636 (w), 564 (w).

MS (EI, 70 eV): *m/z* (%) = 240 (12), 208 (8), 135 (41), 134 (43), 122 (10), 121 (100), 120 (95), 106 (19), 93 (27), 79 (14), 77 (14).

HRMS (EI): calcd. for $C_{16}H_{18}N_1O_1$ $[M-H]^+$: 240.1388, found: 240.1392.

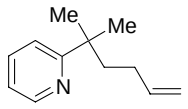
2,2,5-Trimethyl-5-pyridin-2-ylhexan-3-ol (**74j**)



The alkyliodide **67e** (522 mg, 2.0 mmol) was dissolved in THF (1.5 mL) and cooled to 0 °C, *i*Pr_2Mg·LiCl (2.13 ml, 1.40 mmol, 0.66 M in THF) was added and the reaction mixture was warmed to 25 °C. After 1.5 h of stirring the mixture was cooled to –20 °C and pivaldehyde (0.26 g, 0.33 mL, 3.0 mmol) was added. After stirring 30 min at –20 °C the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (10 mL). The aqueous phase was extracted three times with ethyl acetate (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 15:2) afforded a slightly yellowish liquid (275 mg, 61%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.89 (s, 9 H), 1.37 (d, J = 7.5 Hz, 6 H) 1.71–1.73 (m, 1 H) 1.99–2.07 (m, 1 H) 3.32–3.35 (m, 1 H), 5.36 (s, 1 H), 7.08–7.12 (m, 1 H), 7.35–7.39 (m, 1 H), 7.61–7.67 (m, 1 H), 8.45–8.49 (m, 1 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 25.8 (CH_3), 27.8 (CH_3), 32.3 (CH_3), 35.0, 40.8 (CH_2), 44.0, 75.8 (CH), 120.8 (CH), 121.1 (CH), 137.0 (CH), 147.5 (CH), 168.5.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3224 (m), 3088 (w), 3060 (w), 3032 (w), 2952 (s), 2864 (m), 1592 (m), 1568 (w), 1492 (w), 1476 (w), 1428 (w), 1360 (w), 1244 (w), 1156 (w), 1096 (w), 1076 (w), 1036 (w), 1016 (w), 944 (w), 756 (w), 700 (m).
MS (EI, 70 eV): *m/z* (%) = 206 (5), 165 (10), 164 (100), 134 (22), 121 (66), 119 (96), 118 (6), 106 (8), 93 (7), 92 (7).
HRMS (EI): calcd. for $C_{14}H_{22}O_1N_1$ $[M-H]^+$: 220.1780, found: 220.1771.

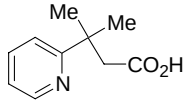
2-(1,1-Dimethylpent-4-en-1-yl)pyridine (**74k**)



The alkyl iodide **67e** (522 mg, 2.0 mmol) was dissolved in THF and cooled to 0 °C, *i*Pr_2Mg·LiCl (2.12 ml, 1.4 mmol, 0.66 M in THF) was added. Then solution was warmed to 25 °C and stirred for 1 h. After cooling to –20 °C CuCN·2LiCl (0.1 mL, 1.0 M in THF) was added followed by allyl bromide (363 mg, 0.26 mL, 3.00 mmol). After stirring for 30 min at –20 °C the temperature was raised to 25 °C and after additional 30 min of stirring the reaction mixture was quenched with a sat. aq. NH_4Cl-solution. The aqueous phase was extracted twice with ethyl acetate (30 mL), and two times with ether (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvents were removed under reduced pressure. Flash chromatographical purification (silica gel, pentane/diethyl ether 22:1) afforded a colourless liquid[93] (226 mg, 64%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.31 (s, 6 H), 1.75–1.77 (m, 4 H), 4.79–4.90 (m, 2 H), 5.65–5.75 (m, 1 H), 7.00–7.04 (m, 1 H), 7.21–7.25 (m, 1 H), 7.52–7.57 (m, 1 H), 8.51–8.53 (m, 1 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 28.1 (CH_3), 29.5 (CH_2), 40.1, 42.8 (CH_2), 114.1 (CH_2), 120.1 (CH), 120.8 (CH), 136.2 (CH), 139.5 (CH), 148.9 (CH), 168.2.

3-Methyl-3-pyridin-2-ylbutanoic acid (**74l**)



The alkyl iodide **67e** (522 mg, 2.0 mmol) was dissolved in THF (1.5 mL) and cooled to 0 °C, *i*Pr_2Mg·LiCl (2.13 ml, 1.40 mmol, 0.66 M in THF) was added and the reaction mixture was warmed to 25 °C. After 1.5 h of stirring the reaction mixture was cooled to –20 °C and carbon dioxide was bubbled through the solution for 10 min. Ethyl acetate

[93] Pasquinet, E.; Rocca,P.; Godard, A.; Marsais, F.; Quéguiner, G. *J. Chem. Soc*., *Perkin Trans. 1* **1998**, 3807.

(20 mL) was added and the reaction mixture was extracted twice with 2 M NaOH (10 mL). The combined aqueous layers were neutralised using 2 M aq. HCl and extracted three times with ethyl acetate (20 mL). The solvent was removed under reduced pressure and the product was dried 5 h in high vacuum. A yellow solid (268 mg, 75%) was obtained.

mp (°C): 68–69.

^{1}H-NMR (DMSO-d6, 400 MHz): δ (ppm) = 1.36 (s, 6 H), 2.69 (s, 2 H), 7.16 (dd, J = 7.41 Hz, 4.79 Hz, 1 H), 7.40 (d, J = 8.61 Hz, 1 H), 7.64–7.71 (m, 1 H), 8.47–8.48 (m, 1 H), 11.90 (s, 1 H).

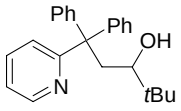
^{13}C-NMR (DMSO-d6, 75 MHz): δ (ppm) = 28.0 (CH_3), 39.1, 45.8 (CH_2), 119.5 (CH), 120.9 (CH), 136.4 (CH), 148.0 (CH), 166.7, 172.6.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3084 (w), 2972 (m), 2935 (w), 2880 (w), 2472 (m), 1956 (m), 1708 (s), 1600 (s), 1572 (m), 1480 (m), 1436 (m), 1368 (m), 1344 (m), 1304 (m), 1228 (s), 1212 (m), 1168 (s), 1144 (s), 1096 (w), 1048 (w), 1008 (s), 936 (w), 892 (w), 792 (s), 760 (s), 696 (w), 636 (m).

MS (EI, 70 eV): *m/z* (%) = 179 (4), 146 (19), 135 (12), 134 (100), 129 (11), 120 (33), 41 (4).

HRMS (EI): calcd. for $C_{10}H_{13}NO_2$: 179.0946, found: 179.0936.

4,4-Dimethyl-1,1-diphenyl-1-pyridin-2-ylpentan-3-ol (**74m**)



The alkyl iodide **67f** (578 mg, 1.5 mmol) was dissolved in THF (1.5 mL) and cooled to 0 °C, *i*Pr$_2$Mg·LiCl (2.01 ml, 0.9 mmol, 0.45 M in THF) was added and the reaction mixture was warmed to 25 °C. After 2.5 h of stirring the reaction mixture was cooled to –20 °C and pivalaldehyde (194 mg, 0.24 mL, 2.25 mmol) was added. After additional 30 min of stirring at –20 °C the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (10 mL). The aqueous phase was extracted three times with ethyl acetate (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure.

Flash chromatographical purification (pentane / ethyl acetate gradient from 15:1 to 1:1, silica gel) afforded pale yellow crystals (304 mg, 59%).

mp (°C): 158–160.

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 0.83 (s, 9 H), 2.53 (dd, J = 14.77 Hz, 1.10 Hz, 1 H), 2.68 (dd, J = 8.60 Hz, 0.88 Hz, 1 H), 3.10 (dd, J = 14.77 Hz, 8.60 Hz, 1 H), 6.83 (d, J = 9.70 Hz, 2 H), 6.88 (d, J = 10.14 Hz, 1 H), 7.17–7.19 (m, 1 H), 7.21–7-30 (m, 8 H), 7.51–7.54 (m, 1 H), 7.93 (s, 1 H), 8.56–8.58 (m, 1 H).

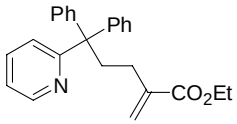
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 25.9 (CH_3), 35.3, 44.6 (CH_2), 60.8, 74.6 (CH), 121.5 (CH), 126.4 (CH), 126.5 (CH), 127.2 (CH), 127.8 (CH), 128.2 (CH), 128.6 (CH), 130.0 (CH), 136.6 (CH), 144.6 (CH), 146.6 (CH), 150.3, 165.4.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3196 (s), 3056 (m), 2960 (s), 2946 (s), 2868 (s), 1591 (s), 1564 (m), 1481 (m), 1469 (s), 1423 (m), 1389 (w), 1358 (w), 1289 (w), 1244 (w), 1159 (w), 10897 (m), 1082 (m), 1063 (m), 1049 (w), 788 (w), 756 (s), 701 (s), 635 (m).

MS (EI, 70 eV): *m/z* (%) = 345 (3), 289 (19), 288 (100), 259 (12), 258 (54), 245 (30), 244 (40), 243 (17), 167 (18).

HRMS (EI): calcd. for $C_{24}H_{27}NO$: 345.2093, found: 345.2106.

Ethyl 2-(3,3-diphenyl-3-pyridin-2-ylpropyl)acrylate (**74n**)



The alkyl iodide **67f** (578 mg, 2.0 mmol) was dissolved in THF (1.5 mL) and cooled to 0 °C, *i*Pr_2Mg·LiCl (2.01 ml, 0.9 mmol, 0.45 M in THF) was added and the reaction mixture was warmed to 25 °C. After 2.5 h the reaction mixture was cooled to –20 °C and ethyl 2-(bromomethyl)acrylate (386 mg, 2.9 mmol) and CuCN·2LiCl (0.1 mL, 1.0 M in THF) was added. After 5 min of stirring at –20 °C the temperature was raised to 25 °C and the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (10 mL). The aqueous phase was extracted three times with ether (30 mL). The combined organic layers were dried ($MgSO_4$), and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / ethyl acetate = 20:1, silica gel) afforded a colourless liquid (328 mg, 59%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.30 (t, J = 7.06, 3 H), 2.09–2.15 (m, 2 H), 2.86–2.92 (m, 2 H), 4.20 (q, J = 7.06, 2 H), 5.53 (s, 1 H), 6.13 (s, 1 H), 7.08–7.12 (m, 1 H), 7.19–7.21 (m, 11 H), 7.54–7.59 (m, 1 H), 8.60–8.62 (m, 1 H).

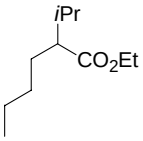
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.2 (CH_3), 28.4 (CH_2), 39.0 (CH_2), 59.0, 60.5 (CH_2), 120.9 (CH), 124.2 (CH_2), 124.2 (CH), 124.8 (CH), 126.1 (CH), 127.8 (CH), 129.4 (CH), 141.3, 146.2, 148.5 (CH), 166.0, 167.3.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3085 (w), 3055 (w), 3030 (w), 2979 (w), 2936 (w), 1710 (s), 1628 (w), 1585 (m), 1567 (w), 1368 (w), 1326 (m), 1304 (w), 1257 (m), 1231 (m), 1180 (s), 1133 (s), 1029 (m), 941 (m), 787 (w), 747 (s), 698 (s), 614 (m), 589 (m).

MS (EI, 70 eV): *m/z* (%) = 371 (5), 259 (18), 258 (100), 245 (25), 244 (20), 243 (14), 167 (13).

HRMS (EI): calcd. for $C_{25}H_{25}O_2N_1$: 371.1885, found: 371.1875.

Ethyl-2-*iso*propylhexanoate



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar and a septum was charged with THF (70 mL) and diisopropylamine (7.08 g, 9.84 mL, 70.0 mmol). The solution was cooled to –40 °C and *n*BuLi (29.5 mL, 70.0 mmol, 2.37 M in hexane) was added slowly. The reaction mixture was allowed to reach 0 °C, and was then transferred slowly into a cooled solution (–78 °C) of ethyl 3-methylbutanoate (8.55 g, 65.7 mmol) in THF (35 mL). The reaction mixture was stirred for 1 h at –78 °C, and then 1-iodo-butane (27.6 g, 17.0 mL, 150 mmol) was added dropwise. The reaction mixture was allowed to reach 25 °C over night and was then poured into a sat. aq. NH_4Cl–solution (70 mL). The aqueous layer was extracted three times with dietyl ether (100 mL). The combined organic layers were dried ($MgSO_4$), and after removal of the solids, the solvent was removed under reduced pressure. A distillation (5.5 mbar, 70–72 °C) yielded ethyl-*iso*propylhexanoate as a colorless liquid (9.59 g, 78%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.83–0.91 (m, 9 H), 1.25–1.31 (m, 7 H), 1.40–1.62 (m, 2 H), 1.74–1.86 (m, 1 H), 2.01–2.08 (m, 1 H), 4.11 (q, J = 7.15 Hz, 2 H).

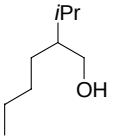
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 13.9 (CH_3), 14.4 (CH_3), 20.2 (CH_3), 20.5 (CH_3), 22.7 (CH_2), 29.4 (CH), 30.0 (CH_2), 30.6 (CH_2), 52.8 (CH), 59.8 (CH_2), 175.9.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2960 (m), 2936 (m), 2874 (w), 2226 (m), 2214 (m), 2184 (m), 2160 (m), 2098 (m), 2064 (m), 2030 (m), 2022 (m), 1974 (m), 1918 (w), 1732 (vs), 1466 (m), 1448 (m), 1388 (m), 1370 (m), 1316 (m), 1278 (m), 1256 (m), 1222 (m), 1178 (s), 1162 (s), 1144 (s), 1122 (m), 1036 (m).

MS (EI, 70 eV): *m/z* (%) = 144 (100), 143 (24), 141 (25), 130 (94), 129 (20), 115 (26), 113 (21), 101 (17), 87 (24), 73 (55), 71 (45), 57 (47), 55 (16), 42 (26).

HRMS (EI): calcd. for $C_{11}H_{22}O_2$: 186.1620, found: 186.1631.

2-Isopropylhexanol



A dry and argon-flushed three necked *Schlenk*-flask, equipped with a stirring bar, a dropping funnel and a reflux condenser was charged with dry diethyl ether (240 mL) and $LiAlH_4$ (7.59 g, 200 mmol). The reaction mixture was cooled to 0 °C and ethyl-2-*iso*propylhexanoate (9.57 g, 51.4 mmol in 120 mL diethyl ether) was added dropwise. The ice bath was removed and the reaction mixture was heated at reflux for 1.5 h. The reaction mixture was cooled to 0 °C, and $Na_2SO_4 \cdot 10H_2O$ was added until cessation of gas evolution. After filtration, the solvent was removed under reduced pressure. A colorless liquid (6.95 g, 94%) was obtained which was used without further purification.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.85–0.89 (m, 9 H), 1.16–1.39 (m, 8 H), 1.76–1.78 (m, 1 H), 3.54–3.58 (m, 2 H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.1 (CH_3), 13.1 (CH_3), 19.8 (CH_3), 23.1 (CH_2), 27.3 (CH_2), 27.8 (CH_2), 30.1 (CH), 46.5 (CH), 63.7 (CH_2).

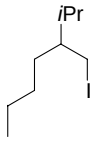
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2956 (s), 2930 (s), 2872 (m), 2226 (m), 2214 (m), 2190 (s), 2160 (s), 2098 (m), 2030 (s), 2018 (s), 1976 (s), 1910 (m), 1750 (m), 1718 (vs),

1498 (m), 1466 (s), 1386 (m), 1368 (s), 1316 (m), 1278 (m), 1222 (m), 1126 (m), 1042 (s), 700 (m).

MS (EI, 70 eV): *m/z* (%) = 84 (4), 83 (5), 71 (42), 70 (9), 69 (16), 57 (100), 56 (19), 55 (23), 43 (34), 41 (18).

HRMS (EI): calcd. for $C_9H_{19}O$: 143.1436 (M-H): , found: 143.1356.

1-Iodo-2-isopropylhexane (**79a**)



A dry and argon-flushed three necked *Schlenk*-flask, equipped with a stirring bar, a dropping funnel and a reflux condenser was charged with dry toluene (100 mL) and triphenylphosphine (18.9 g, 72.0 mmol). Imidazole (6.54 g, 96.0 mmol) and iodine (24.37 g, 96.0 mmol) were added. The reaction mixture was heated at 90 °C for 10 min. Then CH_2Cl_2 (100 mL) was carefully added, followed by 2-isopropylhexanol (6.88 g, 47.7 mmol in 50 mL CH_2Cl_2/toluene 1:1). The reaction mixture was heated at reflux for 1.5 h, and was then cooled to 25 °C. The excess of iodine was removed with a sat. aq. $Na_2S_2O_3$-solution (50 mL). The aqueous layer was extracted three times with diethyl ether (100 ml), and dried ($MgSO_4$). After removal of the solids, the solvent was removed under reduced pressure. The residue was taken up in diethyl ether and filtered over a short pad of silica gel. **79a** was obtained as a colorless liquid (7.87 g, 64%) which was used without further purification.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.85–0.92 (m, 9 H), 0.97–1.02 (m, 1 H), 1.13–1.49 (m, 6 H), 1.68–1.73 (m, 1 H), 3.27 (d, J = 5.01 Hz, 2 H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.1 (CH_3), 14.2 (CH_2), 19.1 (CH_3), 19.8 (CH_3), 22.8 (CH_2), 29.5 (CH_2), 30.6 (CH_2), 30.7 (CH), 45.6 (CH).

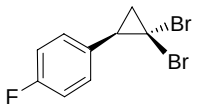
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2958 (s), 2932 (s), 2872 (m), 2226 (m), 2214 (s), 2184 (s), 2160 (s), 2098 (m), 2064 (m), 2030 (s), 2018 (s), 1976 (s), 1910 (m), 1890 (m), 1750 (m), 1718 (vs), 1496 (m), 1464 (s), 1428 (m), 1386 (m), 1368 (s), 1316 (m), 1278 (s), 1222 (s), 1192 (m), 1180 (m), 1158 (m), 1126 (m), 728 (m), 698 (m).

MS (EI, 70 eV): *m/z* (%) = 169 (4), 155 (6), 127 (32), 85 (52), 72 (4), 71 (100), 69 (11), 57 (75), 55 (22), 43 (91), 41 (32).

HRMS (EI): calcd. for $C_9H_{19}{}^{127}I$: 254.0531, found: 254.0523.

4.3.6. Cyclopropanes

1-(2,2-Dibromocyclopropyl)-4-fluorobenzene (**86**):



A round bottom flask equipped with a stirring bar was charged with 1-fluoro-4-vinylbenzene (6.11 g, 50.0 mmol), $CHBr_3$ (50.5 g, 0.20 mol), pinacol (0.768 g, 6.50 mmol) and triethylbenzylammonium chloride (0.569 g, 2.50 mmol). NaOH (8.00 g, 0.20 mol in 8mL H_2O) was added dropwise and the reaction mixture stirred vigorously for 16 h. Then the solids were filtered off and washed with CH_2Cl_2 (50 mL). The aqueous layer was extraxted with CH_2Cl_2 (50 mL) and the combined organic phases were dried ($MgSO_4$). After filtration the solvent was removed under reduced pressure and the crude product was purified by distillation (100 °C, 2.5 mbar), furnishing a colourless liquid (10.2 g, 70%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.98 (t, J = 8.0 Hz, 1 H), 2.16 (dd, J = 10.5 Hz, 7.8 Hz, 1 H), 2.94 (dd, J = 10.2 Hz, 8.6 Hz, 1 H), 7.04–7.11 (m, 2 H), 7.22–7.28 (m, 2 H).

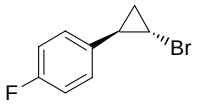
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 27.9 (CH_2), 28.5, 35.6 (CH), 115.7 (d, J = 21.6 Hz, CH), 130.9 (d, J = 8.2 Hz, CH), 132.2 (d, J = 3.1 Hz), 162.6 (d, J = 246.7 Hz, CF).

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 1606 (m), 1510 (vs), 1434 (w), 1228 (s), 1220 (s), 1158 (m), 1102 (m), 1052 (m), 1038 (m), 1014 (w), 926 (w), 860 (m), 830 (vs), 818 (s), 730 (m), 676 (s), 634 (w).

MS (EI, 70 eV): *m/z* (%) = 215 (24), 213 (26), 135 (8), 134 (100), 133 (88), 107 (7), 67 (12), 57 (6).

HRMS (EI): calcd. for $C_9H_9{}^{79}Br_2F$: 291.8899, found: 291.8898.

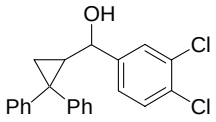
E-1-(2-Bromocyclopropyl)-4-fluorobenzene (**83c**):



A dry and argon-flushed two necked *Schlenk*-flask, equipped with a stirring bar and a septum was charged with LiBr (3.02 g, 34.8 mmol). The salt was dried in high vac. (5h, 150 °C) and then dissolved in THF (30 mL) and diethyl ether (30 mL). The solution was cooled to –80 °C and *n*BuLi (14.4 mL, 34.8 mmol, 2.42 M in hexane) was added, and the reaction mixture was cooled to –110 °C. The dibromide **86** (9.23 g, 31.6 mmol) was added dropwise and the reaction mixture was stirred for 1 h at –100 °C. Then ethanol (15 mL) was added the reaction mixture was warmed to 25 °C. The reaction mixture was quenched with a sat. aq. NH_4Cl-solution (50 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration the solvent was removed under reduced pressure. Flash chromatographical purification (pentane, silica gel) furnished a colourless liquid (3.37 g, 50%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.37–1.55 (m, 2 H), 2.34–2.41 (m, 1 H), 2.94–2.99 (m, 1 H), 6.94–7.05 (m, 4 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 18.7 (CH_2), 21.3 (CH), 26.2 (CH), 115.3 (d, J = 21.3 Hz, CH), 127.5 (d, J = 8.3 Hz, CH), 135.3 (d, J = 3.2 Hz), 161.5 (d, J = 244.3 Hz, CF).
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 1608 (w), 1600 (w), 1510 (vs), 1444 (w), 1226 (vs), 1180 (w), 1160 (m), 1104 (m), 1070 (w), 1042 (w), 1014 (w), 982 (w), 934 (m), 890 (m), 860 (m), 818 (vs), 718 (m), 702 (m), 634 (w), 612 (s).
MS (EI, 70 eV): *m/z* (%) = 136 (8), 135 (100), 134 (7), 133 (26), 115 (13), 109 (14), 107 (4), 83 (4), 67 (2), 56 (3).
HRMS (EI): calcd. for $C_9H_8{}^{79}BrF$: 213.9793, found: 213.9777.

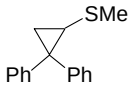
(3,4-Dichlorophenyl)(2,2-diphenylcyclopropyl)methanol (**85a**)



According to **TP8** the cyclopropane **83a** (456 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (4.40 mL, 4.40 mmol, 1.00 M in THF) at 25 °C for 2 d. The reaction mixture was cooled to –30 °C and 3,4-dichlorobenzaldehyde (770 mg, 4.40 mmol) was added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographical purification (pentane / diethyl ether = 2:1, silica gel) yielded **85a** as a colourless solid (473 mg, 64% yield) as a single diastereomer.

^{1}H-NMR ($CDCl_3$, 200 MHz): δ (ppm) = 1.36 (dd, J = 8.70 Hz, 5.04 Hz, 1 H), 1.70 (s, 1 H), 1.81–1.86 (m, 1 H), 2.06–2.18 (m, 1 H), 3.95 (d, J = 8.61 Hz, 1 H), 7.03–7.31 (m, 12 H), 7.41 (d, J = 8.24, 1 H).
^{13}C-NMR (C_6D_6, 100 MHz): δ (ppm) = 17.8 (CH_2), 33.0 (CH), 36.1, 73.2 (CH), 126.1 (CH), 126.5 (CH), 126.9 (CH), 128.4 (CH), 128.5 (CH), 128.6 (CH), 129.3 (CH), 130.3 (CH), 130.5 (CH), 131.6, 132.5, 140.8, 144.6, 146.2.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 3320 (w), 1494 (m), 1468 (m), 1446 (m), 1414 (w), 1390 (w), 1198 (w), 1132 (m), 1072 (m), 1030 (s), 986 (m), 968 (m), 882 (m), 846 (w), 820 (m), 768 (m), 756 (s), 736 (m), 698 (vs), 670 (m), 636 (m), 618 (m).
MS (EI, 70 eV): *m/z* (%) = 352 (22), 350 (37), 194 (28), 193 (90), 191 (76), 189 (30), 188 (44), 183 (44), 181 (36), 180 (100), 179 (40), 178 (49), 167 (32), 165 (68), 115 (72), 91 (35), 44 (52).
HRMS (EI): calcd. for $C_{22}H_{18}O^{35}Cl$: 368.0735, found: 368.0719.

2,2-Diphenylcyclopropyl methyl sulfide (**85b**)



According to **TP8** the cyclopropane **83a** (456 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (4.40 mL, 4.40 mmol, 1.00 M in THF) at 25 °C for 2 d. The reaction mixture was cooled to –30 °C and *S*-methyl benzenesulfonothioate (829 mg, 4.40 mmol) was added and the reaction mixture was allowed to warm to 25 °C and

stirred for additional 2.5 h. Flash chromatographical purification (pentane / diethyl ether = 9:1, silica gel) yielded **85b** as a colourless solid (351 mg, 73% yield).

mp (°C): 64–65.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.49 – 1.56 (m, 2 H), 2.03 (s, 3 H), 2.66 (dd, J = 7.9 Hz, 5.7 Hz, 1 H), 7.05 – 7.29 (m, 10 H).

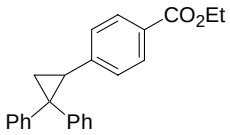
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 16.9 (CH_3), 23.0 (CH_2), 30.6 (CH), 39.3, 126.8 (CH), 127.2 (CH), 128.5 (CH), 128.6 (CH), 128.8 (CH), 130.5 (CH), 141.2, 146.0.

IR (KBr): $\tilde{\nu}$ / cm^{-1} = 3057 (m), 3025 (m), 2015 (m), 1599 (m), 1495 (m), 1446 (s), 1023 (m), 764 (s), 698 (vs), 610 (s).

MS (EI, 70 eV): *m/z* (%) = 240 (4), 194 (10), 193 (67), 192 (100), 191 (32), 189 (11), 178 (35), 165 (28), 116 (10), 115 (96), 91 (24).

HRMS (EI): calcd. for $C_{16}H_{16}{}^{32}S$: 240.0973, found: 240.0985.

Ethyl 4-(2,2-diphenylcyclopropyl)benzoate (**85c**)



According to **TP8** the cyclopropane **83a** (456 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (4.40 mL, 4.40 mmol, 1.00 M in THF) at 25 °C for 2 d. The reaction mixture was cooled to –30 °C and $ZnCl_2$ (2.20 ml, 2.20 mmol, 1 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. Then $Pd(dba)_2$ (46 mg, 0.08 mmol), tris-*o*-furylphosphine (38 mg, 0.16 mmol) and ethyl 4-iodobenzoate (1.21 g, 4.40 mmol) were added and the reaction mixture was stirred for 2 h at 25 °C. Flash chromatographical purification (pentane / diethyl ether = 15:1, silica gel) yielded **85c** as a colourless solid (423 mg, 62% yield).

mp (°C): 68–70.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.35 (t, J = 7.18 Hz, 3 H), 1.88 (dd, J = 8.92 Hz, 5.45 Hz, 1 H), 2.02–2.05 (m, 1 H), 2.89 (dd, J = 8.92 Hz, 6.69 Hz, 1 H), 4.31 (q, J = 7.18 Hz, 2 H), 6.90 (d, J = 8.17 Hz, 2 H), 7.07–7.21 (m, 6 H), 7.28–7.29 (m, 4 H), 7.74–7.78 (m, 2 H).

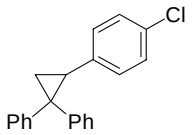
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 14.3 (CH_3), 21.5 (CH_2), 32.4 (CH), 40.3, 60.7 (CH_2), 126.1 (CH), 126.5 (CH), 127.3 (CH), 127.7 (CH) 127.8 (CH), 128.1 (CH), 128.4 (CH), 128.9 (CH), 131.1, 139.6, 144.4, 146.5, 166.6.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 2206 (w), 2190 (m), 2184 (m), 2160 (m), 2030 (m), 2024 (m), 2018 (m), 1974 (m), 1708 (s), 1608 (m), 1498 (m), 1442 (m), 1366 (m), 1314 (m), 1276 (s), 1222 (m), 1184 (m), 1158 (m), 1126 (s), 1116 (s), 1104 (s), 1076 (m), 1052 (m), 1026 (m), 966 (m), 866 (m), 856 (m), 834 (w), 780 (m), 768 (m), 758 (m), 740 (s), 694 (vs), 608 (m).

MS (EI, 70 eV): *m/z* (%) = 343 (15), 342 (60), 313 (23), 297 (19), 270 (22), 269 (100), 264 (24), 192 (46), 191 (82), 179 (21), 178 (30), 165 (39), 115 (18), 91 (29).

HRMS (EI): calcd. for $C_{24}H_{22}O_3$: 342.1620, found: 342.1616.

1-Chloro-4-(2,2-diphenylcyclopropyl)benzene (**85d**)



According to **TP8** the cyclopropane **83a** (456 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (4.40 mL, 4.40 mmol, 1.00 M in THF) at 25 °C for 2 d. The reaction mixture was cooled to –30 °C and $ZnCl_2$ (2.20 ml, 2.20 mmol, 1 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. Then $Pd(OAc)_2$ (4.0 mg, 0.02 mmol), S-Phos (12 mg, 0.03 mmol) and 1-bromo-4-chlorobenzene (881 mg, 4.60 mmol) were added and the reaction mixture was stirred for 2 h at 25 °C. Flash chromatographical purification (pentane / diethyl ether = 40:1, silica gel) yielded **85d** as a colourless liquid (406 mg, 67% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.82 (dd, J = 8.99 Hz, 5.59 Hz, 1 H), 1.94 (dd, J = 6.44 Hz, 5.47 Hz, 1 H), 2.81 (dd, J = 8.99 Hz, 6.56 Hz, 1 H), 6.75–6.80 (m, 2 H), 7.03–7.20 (m, 8 H), 7.25–7.28 (m, 4 H).

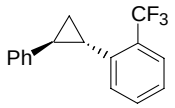
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 21.1 (CH_2), 31.7 (CH), 39.5, 126.0 (CH), 126.4 (CH), 127.3 (CH), 127.7 (CH), 128.1 (CH), 128.4 (CH), 129.1 (CH), 131.1, 131.2 (CH), 137.3, 139.8, 146.6.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2226 (w), 2190 (m), 2158 (m), 2098 (w), 2064 (w), 2032 (m), 2018 (m), 1974 (m), 1718 (m), 1598 (w), 1494 (s), 1444 (m), 1366 (m), 1316 (m), 1278 (m), 1222 (w), 1130 (w), 1092 (m), 1078 (w), 1022 (w), 1012 (m), 908 (m), 836 (m), 818 (m), 768 (m), 748 (s), 732 (m), 718 (m), 696 (vs), 648 (m), 610 (w).

MS (EI, 70 eV): *m/z* (%) = 306 (26), 304 (91), 269 (72), 226 (49), 192 (62), 191 (100), 179 (28), 178 (46), 165 (53), 115 (16), 91 (17).

HRMS (EI): calcd. for $C_{21}H_{17}{}^{35}Cl$: 304.1019, found: 304.1019.

E-1-[2-phenylcyclopropyl]-2-(trifluoromethyl)benzene (**85e**)



According to **TP9** the cyclopropane **83b** (456 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (2.20 mL, 2.20 mmol, 1.00 M in THF) at 25 °C for 8 h. The reaction mixture was cooled to –30 °C and $ZnCl_2$ (1.10 ml, 1.10 mmol, 1 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. Then $Pd(dba)_2$ (23 mg, 0.04 mmol), tris-*o*-furylphosphine (38 mg, 0.08 mmol) and 1-iodo-2-trifluoromethylbenzene (653 mg, 2.40 mmol) were added and the reaction mixture was stirred for 2 h at 25 °C. Flash chromatographical purification (pentane / diethyl ether = 20:1, silica gel) yielded **85e** as a colourless liquid (244 mg, 46% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 1.45–1.55 (m, 2 H), 2.20–2.24 (m, 1 H), 2.51–2.52 (m, 1 H), 7.17–7.21 (m, 4 H), 7.27–7.31 (m, 3 H), 7.47–7.50 (m, 1 H), 7.63 (d, *J* = 7.63 Hz, 1 H).

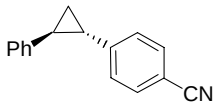
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 17.5 (CH), 23.6 (CH_2), 27.4 (CH), 124.6 (q, *J* = 273.9 Hz, CF_3), 125.7 (CH), 125.8 (q, *J* = 5.7 Hz, CH), 126.0 (CH), 126.1 (CH), 126.2 (CH), 128.4 (CH), 129.5 (q, *J* = 30.2 Hz), 131.9 (q, *J* = 1.8 Hz), 140.6 (CH), 141.7.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2190 (m), 2184 (m), 2160 (m), 2030 (m), 2018 (m), 1976 (m), 1718 (m), 1606 (m), 1496 (m), 1458 (m), 1312 (vs), 1278 (m), 1222 (w), 1180 (m), 1154 (s), 1114 (vs), 1076 (m), 1060 (m), 1034 (s), 764 (s), 752 (s), 732 (m), 696 (vs), 652 (s).

MS (EI, 70 eV): *m/z* (%) = 263 (17), 262 (100), 261 (24), 221 (11), 193 (50), 184 (13), 183 (13), 178 (20), 117 (29), 116 (12), 115 (47), 97 (12), 91 (39), 83 (10), 71 (11), 69 (11), 57 (18), 44 (16).

HRMS (EI): calcd. for $C_{16}H_{13}F_3$: 262.0969, found: 262.0969.

E-4-[2-phenylcyclopropyl]benzonitrile (**85f**)



According to **TP9** the cyclopropane **83b** (456 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (2.20 mL, 2.20 mmol, 1.00 M in THF) at 25 °C for 8 h. The reaction mixture was cooled to –30 °C and $ZnCl_2$ (1.10 ml, 1.10 mmol, 1 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. Then $Pd(OAc)_2$ (4 mg, 0.02 mmol), S-Phos (12 mg, 0.03 mmol) and 4-bromobenzonitrile (256 mg, 2.40 mmol) were added and the reaction mixture was stirred for 2 h at 25 °C. Flash chromatographical purification (pentane / diethyl ether = 40:1, silica gel) yielded **85f** as a colourless liquid (256 mg, 58% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.46–1.62 (m, 2 H), 2.15–2.25 (m, 2 H), 7.12–7.15 (m, 2 H), 7.17–7.24 (m, 3 H), 7.27–7.33 (m, 2 H), 7.54–7.58 (m, 2 H).

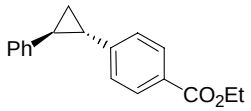
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 19.0 (CH_2), 28.1 (CH), 29.3 (CH), 109.2, 119.1, 125.8 (CH), 126.2 (2 CH), 128.5 (CH), 132.2 (CH), 141.3, 148.4.

IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2226 (m), 2190 (m), 2160 (m), 2030 (m), 2024 (m), 1992 (m), 1974 (m), 1718 (m), 1604 (s), 1510 (m), 1496 (m), 1462 (m), 1366 (w), 1316 (m), 1278 (m), 1222 (m), 1180 (m), 1120 (m), 906 (m), 898 (m), 850 (m), 820 (m), 762 (m), 750 (s), 732 (m), 696 (vs).

MS (EI, 70 eV): *m/z* (%) = 220 (16), 219 (100), 218 (91), 217 (12), 204 (36), 203 (20), 141 (19), 140 (21), 117 (12), 116 (12), 115 (20), 91 (19).

HRMS (EI): calcd. for $C_{16}H_{13}N$: 219.1048, found: 219.1042.

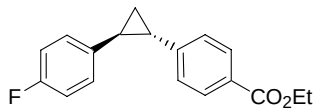
E-Ethyl 4-[2-phenylcyclopropyl]benzoate (**85g**)



According to **TP9** the cyclopropane **83b** (456 mg, 2.00 mmol) was treated with *i*PrMgCl·LiCl (2.20 mL, 2.20 mmol, 1.00 M in THF) at 25 °C for 8 h. The reaction mixture was cooled to –30 °C and $ZnCl_2$ (1.10 ml, 1.10 mmol, 1 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. Then $Pd(OAc)_2$ (4 mg, 0.02 mmol), S-Phos (12 mg, 0.03 mmol) and ethyl 4-bromobenzoate (596 mg, 2.60 mmol) were added and the reaction mixture was stirred for 2 h at 25 °C. Flash chromatographical purification (pentane / diethyl ether = 10:1, silica gel) yielded **85g** as a colourless liquid (271 mg, 51% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 1.39 (t, J = 7.15 Hz, 3 H), 1.49–1.56 (m, 2 H), 2.19–2.25 (m, 2 H), 4.37 (q, J = 6.84 Hz, 2 H), 7.14–7.21 (m, 5 H), 7.29–7.32 (m, 2 H), 7.96–7.98 (m, 2 H).
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 14.3 (CH_3), 18.8 (CH_2), 28.1 (CH), 28.9 (CH), 60.8 (CH_2), 125.4 (CH), 125.8 (CH), 126.0 (CH), 127.9, 128.4 (CH), 129.7 (CH), 141.8, 148.1, 166.5.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2160 (w), 2030 (w), 1974 (w), 1712 (s), 1608 (m), 1366 (m), 1270 (vs), 1180 (s), 1106 (s), 1098 (s), 1020 (s), 850 (m), 778 (s), 764 (s), 740 (s), 696 (vs).
MS (EI, 70 eV): *m/z* (%) = 266 (27), 237 (14), 221 (20), 194 (15), 193 (100), 192 (11), 191 (10), 177 (26), 114 (48), 91 (12).
HRMS (EI): calcd. for $C_{18}H_{18}O_2$: 266.1307, found: 266.1303.

E-Ethyl 4-[2-(4-fluorophenyl)cyclopropyl]benzoate (**85h**)



A dry and argon-flushed *Schlenk*-flask, equipped with a stirring bar was charged with *i*PrMgCl·LiCl (2.20 ml, 2.20 mmol, 1 M in THF) and dioxane (0.2 mL). *E*-1-(2-bromocyclopropyl)-4-fluorobenzene (**83c**) (394 mg, 2.00 mmol) was added and the reaction mixture was stirred at 25 °C for 12 h. The reaction mixture was cooled to –30 °C and $ZnCl_2$ (1.1 mL, 1.1 mmol, 1 M in THF) was added. The reaction mixture was allowed to warm to 25 °C and $Pd(OAc)_2$ (4 mg, 0.02 mmol), S-Phos (12 mg, 0.03 mmol) and ethyl 4-bromobenzoate (596 mg, 2.60 mmol) were added. The reaction mixture was stirred at 25°C for 2 h. Then the reaction mixture was quenched with a sat. aq. NH_4Cl-solution (20 mL) and extracted three times with ethyl acetate (50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographical purification (pentane / diethyl ether 10:1, silica gel) yielded a colourless liquid (307 mg, 54% yield).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ (ppm) = 1.39 (t, J = 7.15 Hz, 3 H), 1.47–1.49 (m, 2 H), 2.12–2.15 (m, 1 H), 2.19–2.22 (m, 1 H), 4.36 (q, J = 7.15 Hz, 2 H), 6.96–6.99 (m, 2 H), 7.08–7.11 (m, 2 H), 7.15–7.17 (m, 2 H), 7.96–7.97 (m, 2 H).
^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) = 14.3 (CH_3), 18.7 (CH_2), 27.9 (CH), 28.1 (CH), 60.8 (CH_2), 115.2 (d, J = 21.5 Hz, CH), 125.4, (CH), 127.3, (d, J = 8.1 Hz, CH), 128.0, 129.7 (CH), 137.4, 147.8, 161.3 (d, J = 244.0 Hz, CF), 166.5.
IR (ATR): $\tilde{\nu}$ / cm^{-1} = 2184 (m), 2158 (m), 2030 (m), 2018 (m), 1976 (m), 1712 (s), 1608 (s), 1510 (s), 1366 (m), 1316 (m), 1272 (vs), 1226 (s), 1210 (m), 1180 (s), 1158 (m), 1106 (s), 1020 (m), 816 (s), 770 (s), 698 (m).
MS (EI, 70 eV): *m/z* (%) = 284 (21), 255 (12), 239 (30), 212 (19), 211 (100), 210 (10), 209 (11), 196 (25), 133 (21), 115 (23), 109 (17).
HRMS (EI): calcd. for $C_{18}H_{17}O_2F$: 284.1213, found: 284.1209

5. Curriculum Vitae

Christian Bernhard Rauhut

Personal Information:

Address:	Straubinger Str. 14
	D-80687 Munich
	Germany
Telephone:	+49-89-57081286 / +49-176-21135498
E-Mail:	christian.rauhut@cup.uni-muenchen.de
Date of Birth:	February 8th 1977
Place of Birth:	Munich, Germany
Nationality:	German

Education and work experience:

11/2005-12/2008	PhD student in organic chemistry in the group of Prof. Dr. Paul Knochel: "Preparation of Functionalized Organo-magnesium Reagents by *ortho*-Magnesiation, Sulfoxide-, Iodine- and Bromine-Magnesium Exchange Reactions." at the Ludwig-Maximilians-University, Munich
3/2005-9/2005	Diploma thesis in organic chemistry in the group of Prof. Dr. Thomas Lindel: "Synthesis of the frame of the marine natural product Bastadin 5 through macrocyclizing etherification" at the Ludwig-Maximilians-University, Munich
2/2004-3/2004	Dye synthesis, LambdaChem GmbH & Co. KG, Munich
10/2000-2/2005	Undergraduate studies (Vordiplom) and Graduate studies (Diplom) at the Department of Chemistry and Biochemistry, Ludwig-Maximilians-University, Munich
6/1998-8/2000	Certified chemical technical assistant at the Chemistry Academy Dr. Erwin Elhardt, Munich
4/1998-6/1998	Practical training in a laboratory for waste water treatment AVA, Fuerstenfeldbruck
1/1997-2/1998	Alternative civilian service, Munich
6/1996	Abitur at the Max-Born-Gymnasium, Germering

Language Skills:

German:	mother-tongue
English:	fluent
French:	basic education

Publications:

- Christian B. Rauhut, Viet Anh-Vu, Frasier F. Fleming, Paul Knochel, „Preparation of Functionalized Alkylmagnesium Derivatives Using an I/Mg-Exchange", *Org. Lett.* **2008**, *10*, 1187.
- Christian B. Rauhut, Laurin Melzig, Paul Knochel, „*Meta*- and *Para*-Difunctionalization of Arenes via a Sulfoxide-Magnesium Exchange Reaction"**,** *Org. Lett.* **2008**, *10*, 3891.
- Laurin Melzig, Christian B. Rauhut, Paul Knochel, „ *Meta*-and *Para*-Difunctionalization of Arenes via a *Ortho*-Magnesiation and a Subsequent Sulfoxide-Magnesium Exchange", *Synthesis* **2009***, in press*.
- Christian B. Rauhut, Christian Cervino, Arkady Krasovskiy, Paul Knochel, „Stereoselective Preparation of Cyclopropylmagnesium Reagents via Br/Mg-exchange using *i*PrMgCl·LiCl in the Presence of Dioxane", *Synlett* ***2009****,* 67.
- Christian B. Rauhut, Laurin Melzig, Paul Knochel, „Functionalization of Furan, Benzofuran and Thiophene via *ortho*-Magnesiation and Subsequent Sulfoxide-Magnesium Exchange Reaction", *manuscript in preparation*.

Additional experience:

- Tutorials for undergraduates supporting the lecture "Organische Chemie I" in 2003, 2004 and 2005.
- Organization of the "Münchner Industrie-Tag 2006" at the LMU Munich, Germany.
- Organization of the "5th Asian-European Symposium on Metal Mediated Efficient Organic Synthesis", 2008 in Obernai, France.
- Poster presentation at 5th Asian-European Symposium on Metal Mediated Efficient Organic Synthesis, 2008 in Obernai, France.

Personal Skills and Interests:

- Hiking
- Diving (Open water diver & Advanced open water diver)
- Travelling (Discovering other cultures and meet interesting people)