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Generation of Aryl and Heteroaryl Magnesium and Zinc Reagents in Toluene by Br/Mg and I/Zn Exchange Reactions
- and -
New Iron-Catalyzed Cross-Couplings of Organomanganese Species

von

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aus

Arpajon, Frankreich

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ERKLÄRUNG

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EIDESSTATTLICHE VERSICHERUNG

Diese Dissertation wurde eigenständig und ohne unerlaubte Hilfe erarbeitet.

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……

(Alexandre Desaintjean)

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List of Publications

A) Communications

1) "Preparation of Polyfunctional Arylzinc Organometallics in Toluene by Halogen/Zinc Exchange Reactions"
M. Balkenhohl, D. S. Ziegler, A. Desaintjean, L. J. Bole, A. R. Kennedy, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2019**, *58*, 12898; *Angew. Chem.* **2019**, *131*, 13030.

2) "Iron-Catalyzed Cross-Coupling of Functionalized Benzylmanganese Halides with Alkenyl Iodides, Bromides, and Triflates"
A. Desaintjean, S. Belrhomari, L. Rousseau, G. Lefèvre, P. Knochel, *Org. Lett.* **2019**, *21*, 8684.

3) "Iron-Catalyzed Cross-Coupling of Bis-(aryl)manganese Nucleophiles with Alkenyl Halides: Optimization and mechanistic investigations"
L. Rousseau, A. Desaintjean, P. Knochel, G. Lefèvre, *Molecules* **2020**, *25*, 723.

4) "Regioselective Bromine/Magnesium Exchange for the Selective Functionalization of Polyhalogenated Arenes and Heterocycles"
A. Desaintjean, T. Haupt, L. J. Bole, N. R. Judge, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2021**, *60*, 1513; *Angew. Chem.* **2021**, *133*, 1536.

5) "Preparation of Functionalized Diorganomagnesium Reagents in Toluene *via* Bromine or Iodine/Magnesium Exchange Reactions"
A. Desaintjean,[+] F. Danton,[+] P. Knochel, *Synthesis* **2021**, *ahead of print*, 10.1055/a-1551-4093.

6) "Regioselective Iodine/Zinc Exchange for the Selective Functionalization of Polyiodinated Arenes and Heterocycles in Toluene"
A. Desaintjean,[+] F. Sanchez,[+] F. Danton, P. Knochel, *Synthesis* **2021**, *ahead of print*, 10.1055/a-1559-3384.

[+] These authors contributed equally to the work.

B) Review

7) "Preparation of Polyfunctional Zinc and Magnesium Organometallic Species"
F. Danton, C. Hamze, A. Desaintjean, P. Knochel, *L'Act. Chim.* **2020**, 22.

Pour ma famille

“On ne va pas à l’école pour travailler… On y va pour réussir !”

Maurice Pajadon, Papi

Abbreviations

Ac	Acetyl
acac	acetylacetonate
aq.	aqueous
Ar	undefined aryl substituent
ATR	Attenuated Total Reflection
Bn	Benzyl
Boc	*tert*-Butyloxycarbonyl
BOM	Benzyloxymethyl
Bu	Butyl
ca.	*circa*
calc.	calculated
cat.	catalytic (amount)
CIPE	Complex-Induced Proximity Effect
conc.	concentrated
Cy	Cyclohexyl
δ	chemical shift in ppm
d	doublet (NMR)
dba	*trans*,*trans*-dibenzylideneacetone
DCC	*N,N'*-Dicyclohexylcarbodiimide
DCM	Dichloromethane
DG	Directing group
DIBAL-H	Diisobutylaluminium hydride
DMAP	4-Dimethylaminopyridine
DME	Dimethoxyethane
DMF	*N*,*N*-Dimethylformamide
DMPU	*N,N'*-Dimethylpropyleneurea
DMSO	Dimethylsulfoxide
DoI	Directed *ortho*insertion
dppp	propane-1,3-diyl*bis*(diphenylphosphane)
E	*Entgegen*
E^+	Electrophile
EI	Electron ionization (MS)
ee	*enantiomeric excess*
e.g.	*exempli gratia*
equiv	equivalents

ESI	Electrospray ionization (MS)
Et	Ethyl
etc.	*et cetera*
FG	Functional group
GC	Gas Chromatography
h	hour
Het	undefined heteroaryl substituent
Hex	Hexyl
HRMS	High Resolution Mass Spectroscopy
i	*iso*
IR	Infrared
J	coupling constant in Hz (NMR)
m	multiplet (NMR)
m	*meta*
M	$mol.L^{-1}$
M	Metal
M_n	number average molar mass
Me	Methyl
Mes	Mesityl
min	minutes
M.p.	melting point
MS	Mass Spectrometry
MTBE	Methyl *tert*-butyl ether
n	*normal*
Nf	Nonaflate
NHC	*N*-Heterocyclic Carbene
NMP	1-Methylpyrrolidin-2-one
NMR	Nuclear Magnetic Resonance
o	*ortho*
Oct	Octyl
p	*para*
PDI	Polydispersity index
Pent	Pentyl
Ph	Phenyl
Piv	Pivaloyl
PMA	Phosphomolybdic acid
PMB	*p*-Methoxybenzyl

PMDTA	*N*,*N*,*N*',*N*'',*N*''-Pentamethyldiethylenetriamine
ppm	parts per million
Pr	Propyl
q	quartet (NMR)
R	undefined organic substituent
R	*rectus*
s	*sec*
s	singulet (NMR)
S	*sinister*
sat.	saturated
SPhos	2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl
t	triplet (NMR)
t	*tert*
TBAF	Tetra-*n*-butylammonium fluoride
TBS	*tert*-Butyldimethylsilyl
TBDMS	alternative abbreviation of TBS
Tf	Triflate
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
THP	Tetrahydropyran
TIPS	Triisopropylsilyl
TLC	Thin layer chromatography
TMEDA	*N,N,N′,N′*-tetramethylethylenediamine
TMP	2,2,6,6-Tetramethylpiperidyl
TMS	Trimethylsilyl
Tol	Toluene
TP	Typical procedure
Ts	Tosyl
vol	volume
X	halogen atom
Z	*Zusammen*
χ	electronegativity

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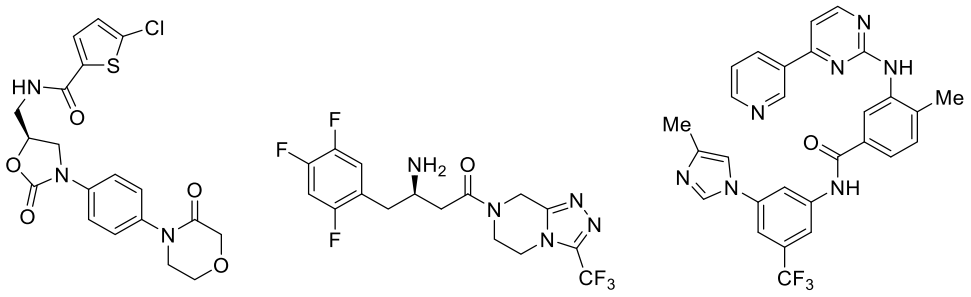
A. INTRODUCTION

1 Overview

Over the last decades, industry's interest in organometallic chemistry has never ceased growing as it represents a preponderant tool for the formation of carbon-carbon bonds.[1] Indeed, organometallics have been widely used since the early 1950s to help with the formation of complex structures in the agrochemical and medicinal industries as well as in many other fields.[2] For instance, chemical crop protection has been greatly improved by the use of synthetic insecticides, fungicides and herbicides[3] as an answer to the raising need for food production resulting from a steadily growing population (2019: approx. 7.7 billion)[4] and however limited resources on Earth.[5] This rise of world population being accompanied by an increase of life expectancy,[6] an increasing number of diseases such as cancer should be expected. While not less than 19 million new cases and almost 10 million cancer-related deaths have been recorced in 2020,[7] scientists have been attempting to find new ways of designing and preparing target molecules.



Rivaroxaban **Sitagliptin** **Nilotinib**

Figure 1: Examples for top-selling drugs synthesized using organometallic reagents.

As a matter of fact, many of the 200 top-selling drugs[8] are small molecules which can be prepared involving organometallics, proving that organometallic chemistry is nowadays widely needed in modern drug discovery and organic chemistry. Examples for those compounds (Figure 1) are

[1] a) *Transition Metals for Organic Synthesis* (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **2004**; b) *Handbook of Functionalized Organometallics: Applications in Synthesis* (Ed.: P. Knochel), Wiley-VCH, Weinheim, **2005**; c) *Generation and Trapping of Functionalized Aryl- and Heteroarylmagnesium and –Zinc Compounds*, F. H. Lutter, M. S. Hofmayer, J. M. Hammann, V. Malakhov, P. Knochel. In *Organic Reactions*, Wiley-VCH, Weinheim, **2019**.

[2] a) G. W. Parshall, *Organometallics* **1987**, *6*, 687; b) *Applications of Organometallic compounds* (Ed.: I. Omae), Wiley-VCH, Weinheim, **1998**.

[3] P. A. Urech, *Plant Pathol.* **1999**, *48*, 689.

[4] United Nations, Department of Economic and Social Affairs, Population Division (2019). *World Population Prospects 2019, Online Edition*.

[5] Food and Agriculture Organization of the United Nations (FAO), World Agriculture Towards 2030/2050. The 2012 Revision.

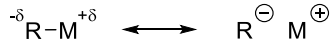
[6] V. Kontis, J. E. Bennett, C. D. Mathers, G. Li, K. Foreman, M. Ezzati, *Lancet* **2017**, *389*, 1323.

[7] H. Sung, J. Ferlay, R. L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, F. Bray, *CA-Cancer J. Clin.* **2021**, *71*, 209.

[8] N. A. McGrath, M. Brichacek, J. T. Njardarson, *J. Chem. Educ.* **2010**, *87*, 1348.

Rivaroxaban[9] (cardiovascular diseases), Sitagliptin[10] (diabetes) and Nilotinib[11] (oncology). Thus, the development of new organometallic reagents is of great importance for the chemical industry.

When developing an organometallic reagent, the choice of the metal remains crucial: not only the price and the toxicity of the metal matter, but also its own unique properties and reactivity. In general, they directly rely on the nature of the carbon-metal bond. The most common way to study this bond is to consider the difference in electronegativity between carbon and the metal attached to it. Starting from here, chemists can choose from a whole range of different compromises located between two extremes. Due to this fact, a carbon-metal bond which is very polarized (almost considered ionic) will be mighty but will only reach a low functional group tolerance whereas an almost covalent carbon-metal bond (slightly polarized) will display an enhanced functional group compatibility but inhibited reactivity. That way, well differentiable and fine-tuned reactivities can be achieved through a broad range of organometallic species (Figure 2).



χ(C) = 2.55

Metal (M)	Li	Mg	Sc	Mn	Al	Zn	Cu	Sn	B
Electronegativity (χ)	0.98	1.31	1.36	1.55	1.61	1.65	1.90	1.96	2.04

Figure 2: Electronegativity scale of selected metals compared to carbon (Pauling scale).[12]

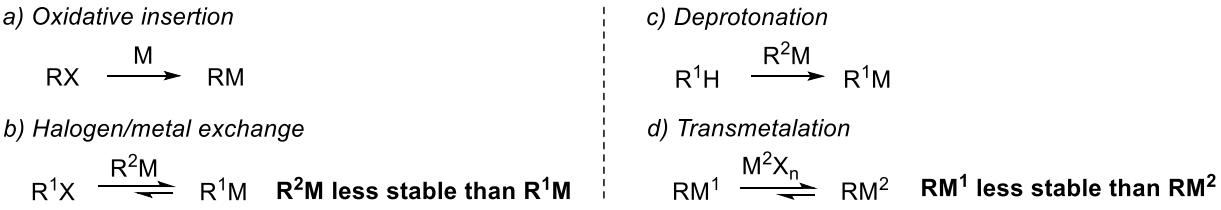
Based on Figure 2, organolithium reagents exhibit a highly polarized carbon-metal bond. They are therefore amongst the most reactive organometallic derivatives while having a low functional group tolerance: esters and nitriles are for example not compatible. In contrast, organomagnesium, organomanganese and especially organozinc or even organoboron compounds possess a relatively more covalent carbon-metal bond. They are shown to be less reactive but can often be used in the presence of various substituents at the appropriate low – or even sometimes at ambient – temperatures. With this high versatility in hand, various synthetic problems can be solved using organometallics. This is also one of the reasons why organometallic chemistry plays an important role in modern synthetic chemistry.

[9] X. Berzosa Rodríguez, F. Marquillas Olondriz, A. Llebaria Soldevilla, C. Serra Comas US2014/128601, **2014**.
[10] S. G. Davies, A. M. Fletcher, L. Lv, P. M. Roberts, J. E. Thomson, *Tetrahedron Lett.* **2012**, *53*, 3052.
[11] M. D. Hopkin, I. R. Baxendale, S. V. Ley, *Org. Biomol. Chem.* **2013**, *11*, 1822.
[12] L. Pauling, *J. Am. Chem. Soc.* **1932**, *54*, 3570.

2 Preparation of Polyfunctional Magnesium, Zinc and Manganese Organometallic Reagents

With an increasing interest for organometallics,[13] the use of magnesium[1b] and zinc[14] derivatives is well established in modern organic synthesis. Those metals are therefore of high interest for the development of new organometallic reagents. Also, an important point for chemical industry is to look for the most sustainable, atom-economic[15] and eco-friendly synthetic solutions to waste as little as possible. As an alternative to those metals, manganese can be considered. Indeed, organomanganese species have a slightly more polarized carbon-metal bond than organozinc compounds (χ(Mn) = 1.55 and χ(Zn) = 1.65). Being more reactive than organozincs but less reactive than organomagnesiums, organomanganese species display an intermediate reactivity with interesting properties. Thus, they also possess a well-balanced reactivity and compatibility towards sensitive functional groups. Noteworthy, manganese is an abundant, relatively cheap metal and is toxicologically benign. From this point of view, the only transition metal which is better is iron.[16]

To generate organometallics, a first pathway consists of the oxidative insertion of a metal into a carbon-halogen bond. The second major method is the halogen/metal exchange reaction, in which a thermodynamically less stable organometallic reacts with an organic halide to form a more stable species. The stability is in pair with the one of the corresponding carbanions: it is directly related to the hybridization of the carbon atom bearing the metal but also depends on the conjugation and inductive effects present in the molecule.[17] The third method is called deprotonation and consists of the abstraction of a proton by a base, forming a "metalated" species. The last one, transmetalation, is also an equilibrium process during which an existing metal species reacts with another one, often a metal salt, generating more stable (and more covalent in the case of a metal salt) carbon-metal bond (Scheme 1).



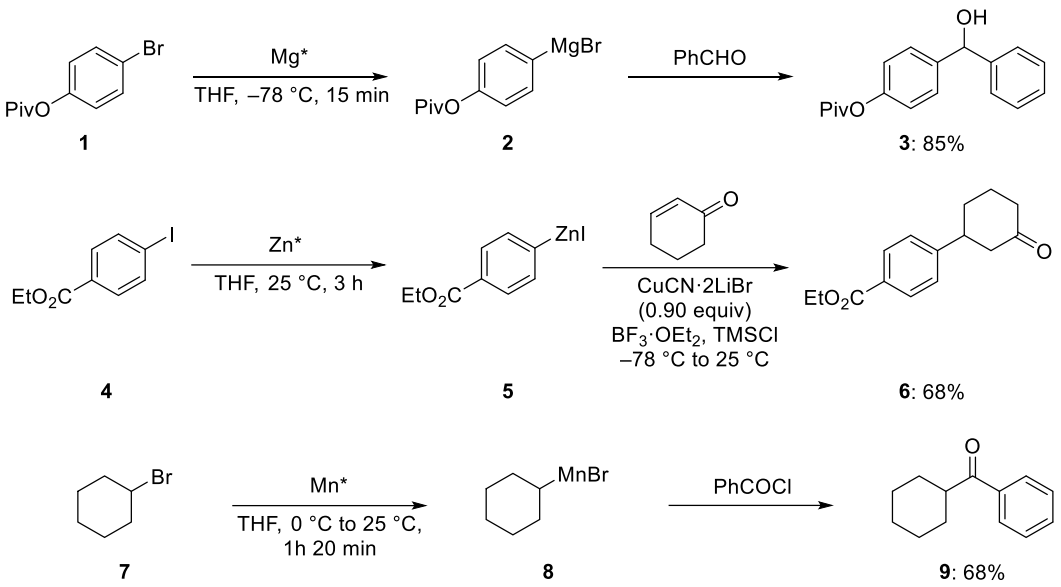
Scheme 1: Preparation of organometallic reagents *via* different pathways.

[13] *Comprehensive Organometallic Chemistry III: From Fundamentals to Applications* (Eds.: R. Crabtree, M. Mingos), Elsevier Ltd., Oxford, **2007**.
[14] *The Chemistry of Organozinc Compounds* (Eds.: Z. Rappoport, I. Marek), John Wiley & Sons Ltd., Chichester, **2006**.
[15] B. M. Trost, *Science* **1991**, *254*, 1471.
[16] C. Duplais, J. Buendia, G. Cahiez, *Chem. Rev.* **2009**, *109*, 1434.
[17] D. E. Applequist, D. F. O'Brien, *J. Am. Chem. Soc.* **1963**, *85*, 743.

2.1 Oxidative Insertion

The first oxidative insertion was realized by Frankland in 1849, who prepared diethylzinc by the reaction of granulated zinc with ethyliodide.[18] Another pioneer work was the one of Grignard on organomagnesium reagents. Based on the first findings of Barbier in 1899 (*in situ* formation and consumption of the organomagnesium, also known as *Barbier-type* conditions),[19] he generated and isolated the first organomagnesium compound by reaction of methyliodide with magnesium turnings in diethylether.[20] For his work, he got the Nobel Prize in Chemistry in 1912. In the 1980s, *Hiyama et al.*[21] and Cahiez[22] described the first *Barbier-type* reactions with organomanganese compounds starting from commercially available manganese powder. Since then, numerous investigations have been made as the rise of organometallic chemistry occurred. Most of those were conducted to activate the zerovalent metal, which normally possesses an oxide layer at its surface, reducing its reactivity. Different solutions were found: amongst them, addition of iodine, trimethylsilyl chloride or 1,2-dibromoethane, grinding or sonification of the metal or even the use of a Zn(Cu) couple can be cited.[23] Rieke has made huge improvements when he prepared the so-called activated Rieke magnesium (Mg*),[24] Rieke zinc (Zn*)[25] and Rieke manganese (Mn*)[26] by reduction of metal salts with lithium or potassium. As an example, bromoarene **1** reacts with Mg* to form the magnesium compound **2**, which is quenched with benzaldehyde to yield the corresponding alcohol **3** in 85% yield.[24] Additionally, ethyl 4-iodobenzoate (**4**) reacts with Zn* within 3 h at room temperature to give the corresponding zinc reagent **5**, which provides **6** in 68% yield after subsequent copper-mediated 1,4-addition on cyclohex-2-en-1-one.[27] Analogically, Bromocyclohexane (**7**) reacts with Mn* within 1 h 20 min to form the corresponding organomanganese bromide **8** which can be quenched by benzoyl chloride to give the ketone **9** in 68% yield (Scheme 2).[26]

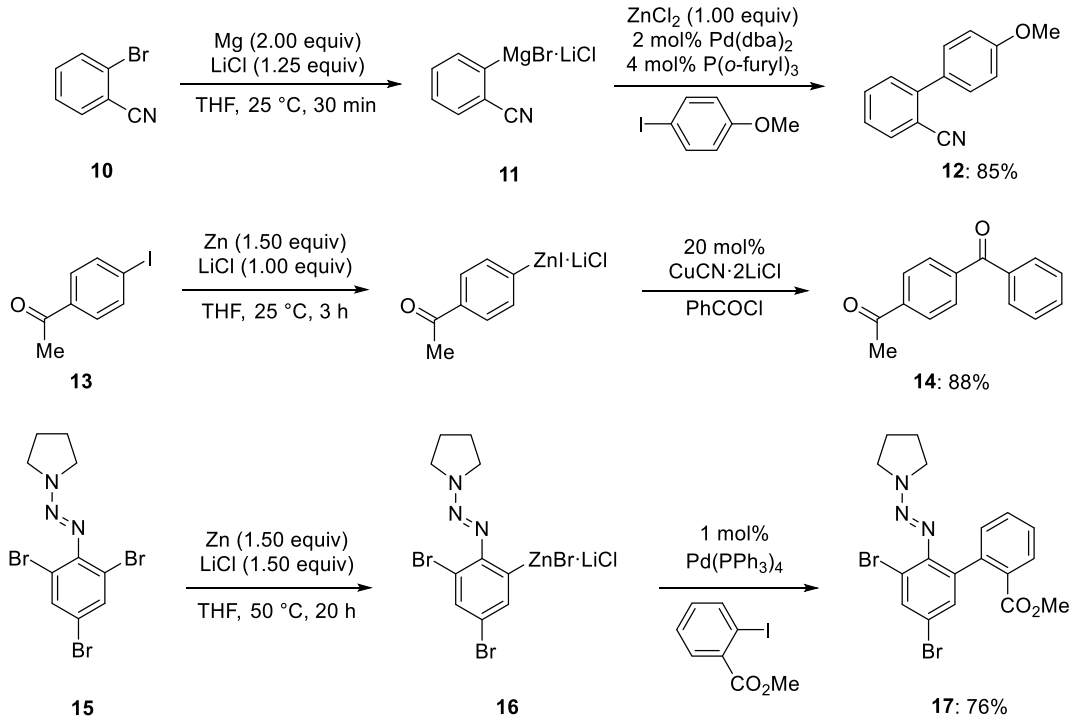
[18] E. Frankland, *Liebigs Ann. Chem.* **1849**, *71*, 171.
[19] P. Barbier, *Compt. Rend. Acad. Sci. Paris* **1899**, *128*, 110.
[20] V. Grignard, *Compt. Rend. Acad. Sci. Paris* **yOS**, *130*, 1322.
[21] T. Hiyama, M. Sawahata, M. Obayashi, *Chem. Lett.* **1983**, *8*, 1237.
[22] G. Cahiez, P.-Y. Chavant, *Tetrahedron Lett.* **1989**, *30*, 7373.
[23] a) R. D. Rieke, *Acc. Chem. Res.* **1977**, *10*, 301; b) Y. Tamaru, H. Ochiai, T. Nakamura, K. Tsubaki, Z.-I. Yoshida, *Tetrahedron Lett.*, **1985**, *26*, 5559; c) M. Gaudemar, *Bull. Soc. Chim. Fr.* **1962**, 974; d) T. Kentaro, *Chem. Lett.* **1993**, *22*, 469; e) K. Takai, T. Ueda, T. Hayashi, T. Moriwake, *Tetrahedron Lett.* **1996**, *37*, 7049.
[24] R. D. Rieke, S. E. Bales, P. M. Hudnall, T. P. Burns, G. S. Poindexter, *Org. Synth.* **1979**, *59*, 85.
[25] R. D. Rieke, P. T.-J. Li, T. P. Burns, S. T. Uhm, *J. Org. Chem.* **1981**, *46*, 4323.
[26] S.-H. Kim, M. V. Hanson, R. D. Rieke, *Tetrahedron Lett.* **1996**, *37*, 2197.
[27] a) J.-S. Lee, R. Velarde-Ortiz, A. Guijarro, R. D. Rieke, *J. Org. Chem.* **2000**, *65*, 5428; b) L. Zhu, R. M. Wehmeyer, R. D. Rieke, *J. Org. Chem.* **1991**, *56*, 1445.



Scheme 2: Oxidative insertion of Rieke magnesium, zinc and manganese into organic halides.

Later, in 2006, Knochel and co-workers showed that the use of LiCl as an additive led to improved results in the formation of sensitive organometallics. They were able to prepare a wide variety of organomagnesium and zinc species bearing sensitive functional groups.[28] The magnesium insertion to 2-bromobenzonitrile (**10**) in the presence of lithium chloride proceeds smoothly, producing the magnesium species **11** which, after transmetallation to zinc, undergoes a Pd-catalyzed Negishi cross-coupling[29] with 4-iodoanisole, giving the arylated benzonitrile **12** in 85% yield.[28] Zinc insertion to 1-(4-iodophenyl)ethan-1-one (**13**) followed by quenching with benzoyl chloride in the presence of 20 mol% CuCN·2LiCl gives the benzophenone derivative **14** in 88% yield.[28] Interestingly, in the case of the di-iodo substituted arene **15**, only the halogen which is positioned *ortho* to a directing group is reacting. This phenomenon is known as the directed *ortho*insertion (DoI).[30] The zinc species **16** prepared *via* DoI readily reacts with methyl 2-iodobenzoate in the presence of $Pd(PPh_3)_4$ (1 mol%) to give the product **17** in 76% yield (Scheme 3).[30] In 2016, *Blum et al.* studied the role of LiCl during oxidative insertions thanks to fluorescence microscopy.[31] They found that LiCl actually helps to solubilize the newly formed organometallic generated at the surface of the metal, providing a constantly clean metal surface.[32]

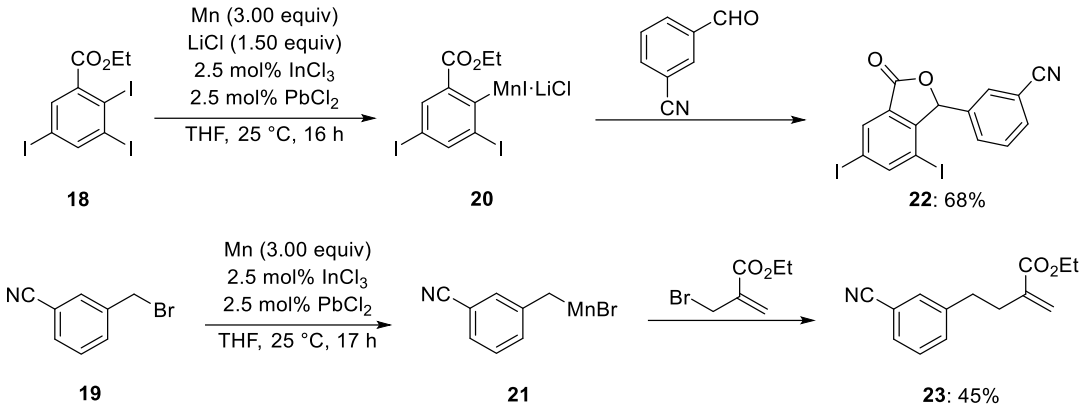
[28] a) A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040; b) F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 6802; c) A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1107.
[29] E. Negishi, S. Baba, *J. Am. Chem. Soc.* **1976**, *98*, 6729.
[30] N. Boudet, S. Sase, P. Sinha, C.-Y. Liu, A. Krasovskiy, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 12358.
[31] C. Feng, D. W. Cunningham, Q. T. Easter, S. A. Blum, *J. Am. Chem. Soc.* **2016**, *138*, 11156.
[32] C. Feng, Q. T. Easter, S. A. Blum, *Organometallics* **2017**, *36*, 2389.



Scheme 3: Preparation of organomagnesium and organozinc reagents by metal insertion in the presence of LiCl.

While LiCl alone is not sufficient to activate powdered manganese, prior reports have shown that combinations of Lewis-acids ($TiCl_4$, $PbCl_2$, $InCl_3$ or $BiCl_3$) with LiCl are beneficial for the oxidative insertion of aluminum into organic halides.[33] Based on those observations, Knochel and co-workers reported in 2011 the preparation of functionalized aryl and benzyl manganese reagents by manganese insertion in the presence of LiCl and catalytic amounts of $InCl_3$ and $PbCl_2$.[34] Thus, the oxidative insertion of manganese into an aryl or benzyl halide **18** and **19** proceeded under the above mentioned conditions, leading to the corresponding functionalized manganese halides **20** and **21**. Trapping with 3-formylbenzonitrile and ethyl 2-(bromomethyl)acrylate gave the desired products **22** and **23** in 45–68% yield. It is worth stating that in the case of benzyl halides, the insertion was performed without LiCl. In fact, this salt favoured the formation of undesired homocoupling (Scheme 4). Due to their exceptional reactivity, organomanganese species do not need any transition-metal catalysts for many further transformations (acylations, allylic substitutions and 1,4-additions).[34]

[33] T. Blümke, Y.-H. Chen, Z. Peng, P. Knochel, *Nat. Chem.* **2010**, *2*, 313.
[34] Z. Peng, P. Knochel, *Org. Lett.* **2011**, *13*, 3198.



Scheme 4: Preparation of organomanganese species by manganese insertion promoted by $InCl_3$ and $PbCl_2$.

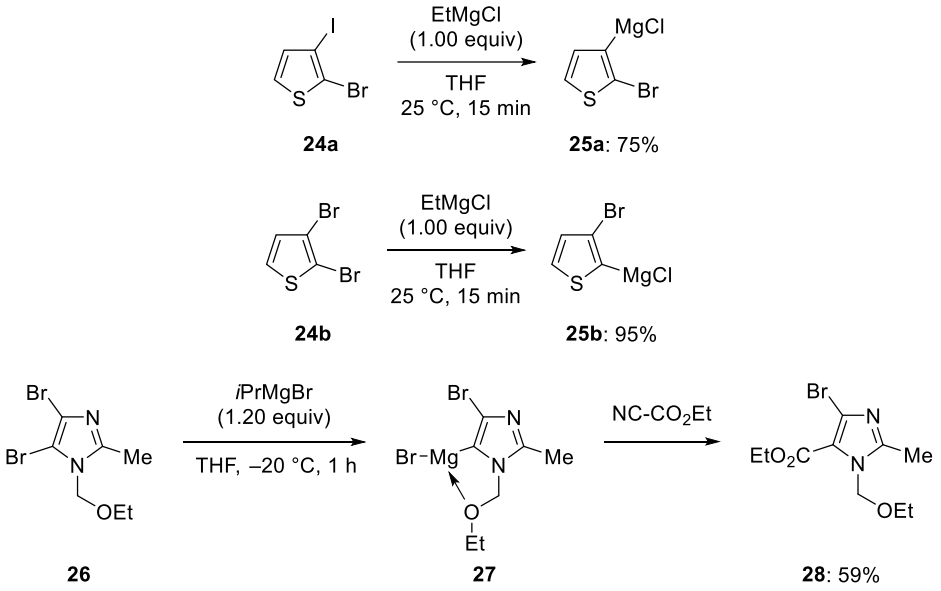
2.2 Halogen/Metal Exchange

Another commonly used method for the preparation of organometallics is the halogen/metal exchange. In general, the driving force for this reaction type is the formation of a more stable organometallic species compared to the exchange reagent itself. As said before, the stability of the organometallic reagent decreases that way: $C(sp) > C(sp^2_{vinyl}) > C(sp^2_{aryl}) > C(sp^3_{primary}) > C(sp^3_{secondary}) > C(sp^3_{tertiary})$.[17,35] The halogen/lithium exchange was discovered by Gilman[36] and Wittig[37] and has proven its synthetic utility over the last decades for preparing a wide range of organometallic species derived from lithium.[38] Still, the high reactivity of the carbon-lithium bond has limited the use of this method for preparing polyfunctional lithium compounds at convenient reaction temperatures.[39] For that reason, halogen/metal exchange reagents with a more covalent carbon-metal bond like organo-magnesium, -zinc or -manganese should be more advantageous. Nevertheless, the halogen/lithium exchange is one of the fastest reactions in organic synthesis,[40] especially compared to the other halogen/metal exchange reactions like halogen/magnesium,[41] which are considered to be relatively slow.

[35] D. Hauk, S. Lang, A. Murso, *Org. Process Res. Dev.* **2006**, *10*, 733.
[36] a) H. Gilman, W. Langham, A. L. Jacoby, *J. Am. Chem. Soc.* **1939**, *61*, 106; b) R. G. Jones, H. Gilman, *Org. React.* **1951**, *6*, 339.
[37] G. Wittig, U. Pockels, H. Dröge, *Ber. dtsch. Chem. Ges.* **1938**, *71*, 1903.
[38] a) J. Clayden, *Organolithiums: Selectivity for Synthesis* (Ed.: J. Clayden), Pergamon, Oxford, **2002**; b) C. Nájera, J. M. Sansano, M. Yus, *Tetrahedron* **2003**, *59*, 9255.
[39] Remarkable exceptions: a) A. Nagaki, H. Kim, H. Usutani, C. Matsuo, J.-i. Yoshida, *Org. Biomol. Chem.* **2010**, *8*, 1212; b) H. Kim, A. Nagaki, J.-i. Yoshida, *Nat. Comm.* **2011**, *2*, 264; c) A. Nagaki, K. Imai, S. Ishiuchi, J.-i. Yoshida, *Angew. Chem. Int. Ed.* **2015**, *54*, 1914; d) H. Kim, H.-J. Lee, D.-P. Kim, *Angew. Chem. Int. Ed.* **2015**, *54*, 1877.
[40] W. F. Bailey, J. J. Patricia, T. T. Nurmi, W. Wang, *Tetrahedron Lett.* **1986**, *27*, 1861.
[41] a) L. Shi, Y. Chu. P. Knochel, H. Mayr, *Angew. Chem. Int. Ed.* **2008**, *47*, 202; b) L. Shi, Y. Chu, P. Knochel, H. Mayr, *Org. Lett.* **2009**, *11*, 3502; c) L. Shi, Y. Chu, P. Knochel, H. Mayr, *J. Org. Chem.* **2009**, *74*, 2760; d) L. Shi, Y. Chu, P. Knochel, H. Mayr, *Org. Lett.* **2012**, *14*, 2602.

2.2.1 Halogen/Magnesium Exchange

In 1931, Prévost observed the first example of a bromine/magnesium exchange.[42] Even if he obtained really low conversions of starting material, this technique could be used by others on some electron-deficient substrates such as heteroaromatic rings and/or electro-deficient aromatics. Köbrich[43] and Villieras[44] used the halogen/magnesium exchange to generate magnesium carbenoids. In 2003, Christophersen produced the 3-magnesiated bromothiophene **25a** *via* an iodine/magnesium exchange on 2-bromo-3-iodothiophene (**24a**) while he obtained the 2-magnesiated bromothiophene **25b** when 2,3-dibromothiophene (**24b**) was used as starting material (Scheme 5).[45] The formation of **25a** can be explained by the increased exchange rate of iodine towards bromine. Indeed, the reactivity order of the halogen (I>Br>Cl>>F) is influenced by the bond strength of the carbon-halogen bond and the halide's electronegativity and polarizability.[46] The generation of **25b** can be explained by the improved stability – due to the close proximity of a heteroatom[47] – of this one compared to the corresponding 3-magnesiated bromothiophene **24a**.

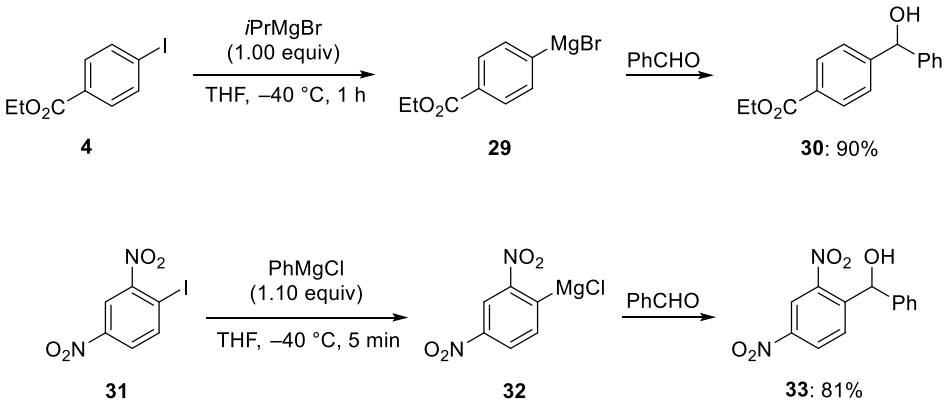


Scheme 5: Regioselectivity of the halide/magnesium exchange on electron poor heteroaromatic halides.

A regioselectivity can also sometimes be triggered by the presence of a strong directing group. When in proximity of the halogen, this last one coordinates the exchange reagent, directs the exchange reaction and stabilizes the newly formed carbon-magnesium bond. For example, the ethoxy group of the

[42] Prévost, C. *Bull. Soc. Chim. Fr.* **1931**, *49*, 1372
[43] G. Köbrich, P. Buck, *Chem. Ber.* **1970**, *103*, 1412.
[44] J. Villieras, B. Kirschleger, R. Tarhouni, M. Rambaud, *Bull. Soc. Chim. Fr.* **1986**, 470.
[45] C. Christophersen, M. Begtrup, S. Ebdrup, H. Petersen, P. Vedso, *J. Org. Chem.* **2003**, *68*, 9513.
[46] C. Tamborski, G. J. Moore, *J. Organomet. Chem.* **1971**, *26*, 153.
[47] P. Beak, D. B. Reitz, *Chem. Rev.* **1978**, *78*, 275.

dibromoimidazole derivative **26** complexed *i*PrMgBr, producing the very stable Grignard reagent **27** which, after trapping with NC-CO_2Et provided the bromoimidazole **28** in 59% yield.[48] As already stated, apart from heterocycles, the presence of an electron-withdrawing substituent can help getting suitable conversions during a halogen/magnesium exchange. Around 2000, for the first time, access to arylmagnesium reagents bearing an ester or a nitro group was enabled.[49] Indeed, previous attempts through oxidative insertion of magnesium resulted in a total reaction inhibition and only led to reduced products.[50] Thus, ethyl 4-iodobenzoate (**4**) reacted with *i*PrMgBr at –40 °C within 1 h, providing the functionalized arylmagnesium bromide **29**. After addition of benzaldehyde, the expected alcohol **30** was obtained in 90% yield.[49a] Similarly, the reaction of 2-iodo-1,5-dinitrobenzene (**31**) with PhMgCl at –40 °C for 5 min provided the corresponding Grignard reagent **32**. After reaction with PhCHO, the alcohol **33** was obtained in 81% yield (Scheme 6).[51]

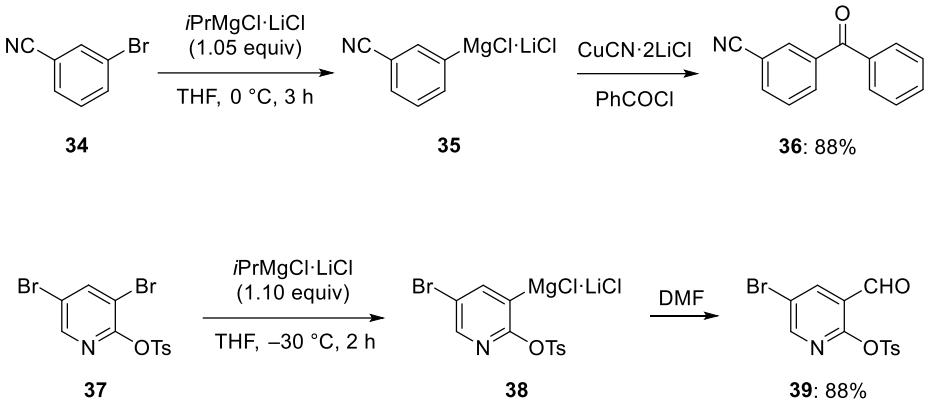


Scheme 6: Chemoselective iodine/magnesium exchange reaction.

Thanks to this kind of exchange reagents, alkaloids such as kealiinines A–C have been synthesized.[52] However, as said earlier, a general methodology for aryl and heteroaryl halides was not always possible[53] and the use of lithium trialkylmagnesiates[54] was often required, reducing the chemoselectivity of this type of exchange. Fortunately, in 2004, *Knochel et al.* found that the use of LiCl was enhancing

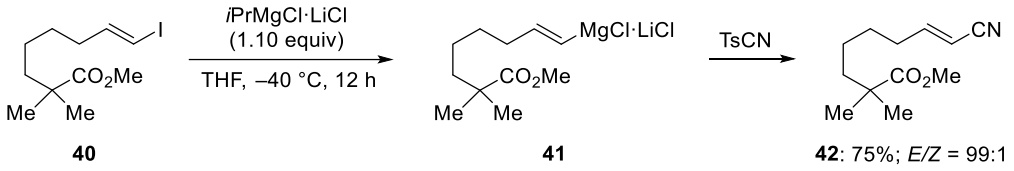
[48] a) M. Abarbri, F. Dehmel, P. Knochel, *Tetrahedron Lett.* **1999**, *40*, 7449; b) M. Abarbri, J. Thibonnet, L. Berillon, F. Dehmel, M. Rottlaender, P. Knochel, *J. Org. Chem.* **2000**, *65*, 4618.
[49] a) L. Boymond, M. Rottländer, G. Cahiez, P. Knochel, *Angew. Chem. Int. Ed.* **1998**, *37*, 1701; b) G. Varchi, A. Ricci, G. Cahiez, P. Knochel, *Tetrahedron* **2000**, *56*, 2727; c) W. Dohle, D. M. Lindsay, P. Knochel, *Org. Lett.* **2001**, *3*, 2871; d) Y. Nakamura, S. Yoshida, T. Hosoya, *Chem. Lett.* **2017**, *46*, 858.
[50] a) T. Severin, D. Bätz, H. Krämer, *Chem. Ber.* **1971**, *104*, 950; b) G. Bartoli, G. Palmieri, M. Bosco, R. Dalpozzo, *Tetrahedron Lett.* **1989**, *30*, 2129; c) M. Bosco, R. Dalpozzo, G. Bartoli, G. Palmieri, M. Petrini, *J. Chem. Soc.* **1991**, 657.
[51] a) I. Sapountzis, P. Knochel, *Angew. Chem. Int. Ed.* **2002**, *41*, 1610; b) I. Sapountzis, H. Dube, R. Lewis, N. Gommermann, P. Knochel, *J. Org. Chem.* **2005**, *70*, 2445.
[52] J. Das, P. B. Koswatta, J. D. Jones, M. Yousufuddin, C. J. Lovely, *Org. Lett.* **2012**, *14*, 6210.
[53] a) J. Thibonnet, P. Knochel, *Tetrahedron Lett.* **2000**, *41*, 3319; b) O. Ryabtsova, T. Verhelst, M. Baeten, C. M. L. Vande Velde, B. U. W. Maes, *J. Org. Chem.* **2009**, *74*, 9440.
[54] a) K. Kitagawa, A. Inoue, H. Shinokubo, K. Oshima, *Angew. Chem. Int. Ed.* **2000**, *39*, 2481; b) A. Inoue, K. Kitagawa, H. Shinokubo, K. Oshima, *J. Org. Chem.* **2001**, *66*, 4333; c) A. Inoue, J. Kondo, H. Shinokubo, K. Oshima, *Chem. - Eur. J.* **2002**, *8*, 1730; d) L. Struk, J. G. Sosnicki, *Synthesis* **2012**, *44*, 735.

the kinetic activity of this type of exchange reagents. The development of the reagent *i*PrMgCl·LiCl – also known as "*turbo*-Grignard" – made accessible the preparation of a wide range of functionalized magnesium organometallics.[55] For example, 3-bromobenzonitrile (**34**) was converted by *i*PrMgCl·LiCl to the corresponding Grignard reagent **35** at 0 °C within 3 h. Quenching with benzoyl chloride led to the benzophenone derivative **36** in 88% yield.[55a] Polybromides such as the dibromopyridine **37** underwent an exchange at position C(3), since this position leads to the most stabilized Grignard reagent **38**. After addition of *N*,*N*-dimethylformamide (DMF), the aldehyde **39** was obtained in 88% yield (Scheme 7).[56]



Scheme 7: Bromine/magnesium exchange reaction triggered by *i*PrMgCl·LiCl.

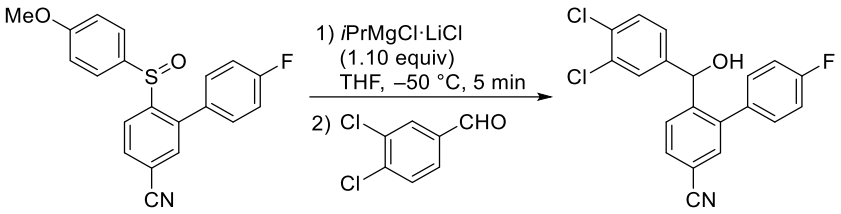
Thanks to the *turbo*-Grignard, alkenyl magnesium derivatives could also be obtained. For example, the polyfunctional alkenyl iodide **40** reacted with *turbo*-Grignard at –40 °C furnishing (*E*)-alkenylmagnesium derivative **41**. After reaction with TsCN, the product **42** was obtained in 75% yield (Scheme 8).[57]



Scheme 8: Preparation of alkenylmagnesium reagents using *i*PrMgCl·LiCl.

[55] a) A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333; b) A. Krasovskiy, B. F. Straub, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 159; c) T. Kunz, P. Knochel, *Angew. Chem. Int. Ed.* **2012**, *51*, 1958; d) J. Nickel, M. Fernandez, L. Klier, P. Knochel, *Chem. - Eur. J.* **2016**, *22*, 14397; e) C.-Y. Liu, P. Knochel, *Org. Lett.* **2005**, *7*, 2543.
[56] H. Ren, P. Knochel, *Chem. Commun.* **2006**, 726.
[57] H. Ren, A. Krasovskiy, P. Knochel, *Org. Lett.* **2004**, *6*, 4215.

Interestingly, the sulfoxide/magnesium exchange, which was well studied by Satoh[58] and Hoffmann,[59] could also be performed by *i*PrMgCl·LiCl. Remarkably, the polyfunctional sulfoxide **43** underwent a fast sulfoxide/magnesium exchange at −50 °C within 5 min, producing an intermediate Grignard reagent. By addition of 3,4-dichlorobenzaldehyde, benzonitrile **44** was furnished in 88% yield (Scheme 9).[60]



43 **44**: 88%

Scheme 9: Preparation of polyfunctional arenes using a sulfoxide/magnesium exchange.

Since its initial report,[55a] *turbo*-Grignard has become very popular and numerous applications have been reported.[61] It was also for example used for natural product synthesis.[62] Gosselin also used it to synthesize a selective estrogen receptor degrader. In the presence of *bis*(2-dimethylaminoethyl)ether, he converted the aryl iodide **45** into the corresponding Grignard **46** and made it react on the ketone **47** to obtain the alcohol **48** as a single diastereoisomer (Scheme 10).[63] Halide/magnesium exchanges with *turbo*-Grignard were also performed with microreactors in flow chemistry.[64]

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[58] a) T. Satoh, T. Oohara, Y. Ueda, K. Yamakawa, *J. Org. Chem.* **1989**, *54*, 3130; b) T. Satoh, K. Horiguchi, *Tetrahedron Lett.* **1995**, *36*, 8235; c) T. Satoh, K. Takano, H. Ota, H. Someya, K. Matsuda, M. Koyama, *Tetrahedron* **1998**, *54*, 5557.

[59] a) R. W. Hoffmann, P. G. Nell, *Angew. Chem. Int. Ed.* **1999**, *38*, 338; b) R. W. Hoffmann, B. Hölzer, O. Knopff, K. Harms, *Angew. Chem. Int. Ed.* **2000**, *39*, 3072; c) R. W. Hoffmann, B. Hölzer, O. Knopff, *Org. Lett.* **2001**, *3*, 1945; d) B. Holzer, R. W. Hoffmann, *Chem. Commun.* **2003**, 732; e) R. W. Hoffmann, *Chem. Soc. Rev.* **2003**, *32*, 225.

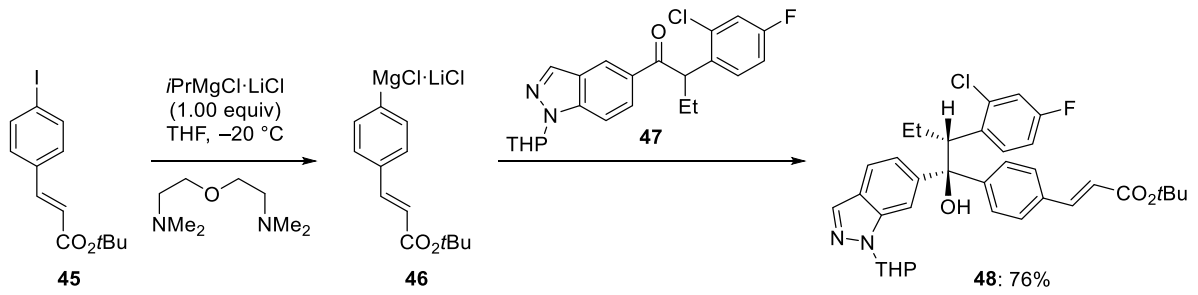
[60] a) C. B. Rauhut, L. Melzig, P. Knochel, *Org. Lett.* **2008**, *10*, 3891; b) L. Melzig, C. B. Rauhut, P. Knochel, *Synthesis* **2009**, 1041; c) L. Melzig, C. B. Rauhut, N. Naredi-Rainer, P. Knochel, *Chem. - Eur. J.* **2011**, *17*, 5362; d) N. M. Barl, E. S. Sansiaume-Dagousset, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2013**, *52*, 10093; e) D. Nath, F. F. Fleming, *Chem. - Eur. J.* **2013**, *19*, 2023; f) M. Hughes, T. Boultwood, G. Zeppetelli, J. A. Bull, *J. Org. Chem.* **2013**, *78*, 844; g) C. Sämann, E. Coya, P. Knochel, *Angew. Chem. Int. Ed.* **2014**, *53*, 1430.

[61] a) T. Leermann, F. R. Leroux, F. Colobert, *Org. Lett.* **2011**, *13*, 4479; b) E. Demory, V. Blandin, J. Einhorn, P. Y. Chavant, *Org. Process Res. Dev.* **2011**, *15*, 710; c) X.-F. Duan, Z.-Q. Ma, F. Zhang, Z.-B. Zhang, *J. Org. Chem.* **2009**, *74*, 939; d) K. C. Nicolaou, A. Krasovskiy, V. É. Trépanier, D. Y. K. Chen, *Angew. Chem. Int. Ed.* **2008**, *47*, 4217; e) K. C. Nicolaou, A. Krasovskiy, U. Majumder, V. É. Trépanier, D. Y. K. Chen, *J. Am. Chem. Soc.* **2009**, *131*, 3690; f) J. T. Reeves, K. Camara, Z. S. Han, Y. Xu, H. Lee, C. A. Busacca, C. H. Senanayake, *Org. Lett.* **2014**, *16*, 1196; g) M. Döbele, M. S. Wiehn, S. Bräse, *Angew. Chem. Int. Ed.* **2011**, *50*, 11533; h) V. Diemer, F. R. Leroux, F. Colobert, *Eur. J. Org. Chem.* **2011**, 327.

[62] A. O. Termath, S. Ritter, M. König, D. P. Kranz, J. M. Neudörfl, A. Prokop, H. G. Schmalz, *Eur. J. Org. Chem.* **2012**, 4501.

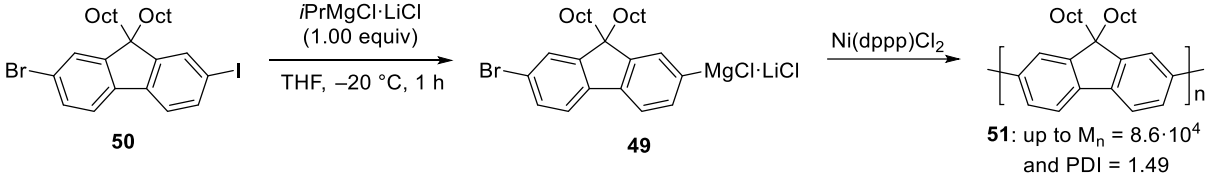
[63] N.-K. Lim, T. Cravillion, S. Savage, A. McClory, C. Han, H. Zhang, A. Di Pasquale, F. Gosselin, *Org. Lett.* **2018**, *20*, 1114.

[64] a) H. Wakami, J.-i. Yoshida, *Org. Process Res. Dev.* **2005**, *9*, 787; b) T. Tricotet, D. F. O'Shea, *Chem. - Eur. J.* **2010**, *16*, 6678; c) T. Brodmann, P. Koos, A. Metzger, P. Knochel, S. V. Ley, *Org. Process Res. Dev.* **2012**, *16*, 1102; d) Q. Deng, R. Shen, Z. Zhao, M. Yan, L. Zhang, *Chem. Eng. J.* **2015**, *262*, 1168; e) S. Korwar, S. Amir, P. N. Tosso, B. K. Desai, C. J. Kong, S. Fadnis, N. S. Telang, S. Ahmad, T. D. Roper, B. F. Gupton, *Eur. J. Org. Chem.* **2017**, 6495.



Scheme 10: Preparation of drug intermediate **48** using *i*PrMgCl·LiCl.

Furthermore, polymers could also be prepared using *turbo*-Grignard.[65] For instance, the Grignard reagent **49** could be selectively prepared by treatment of the dihalogenofluorene derivative **50** with *i*PrMgCl·LiCl at −20 °C in THF, which polymerized at 0 °C in the presence of catalytic amounts of Ni(dppp)Cl_2, leading to poly(9,9-dioctylfluorene) (**51**) with a high M_n of $8.6 \cdot 10^4$ and a polydispersity index (PDI) of 1.49. Interestingly, without LiCl, the polymerization afforded a lower molecular weight product (Scheme 11).[66]



Scheme 11: LiCl-promoted polymerization using *turbo*-Grignard reagent.

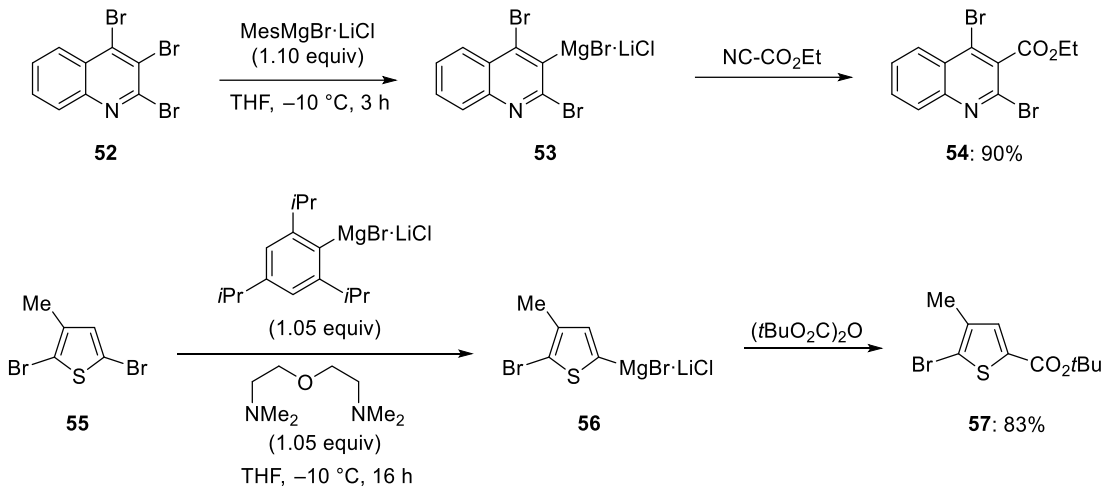
When replacing the secondary alkyl chain of the *turbo*-Grignard by a mesityl moiety, affording MesMgBr·LiCl, Knochel and co-workers could increase the bulkiness of this type of exchange reagents. They could selectively exchange the bromine at the position C(3) on 2,3,4-tribromoquinoline (**52**) to afford the corresponding Grignard **53**, which gave in presence of NC-CO_2Et the ester **54** in 90% yield.[67] Interestingly, when replacing the methyl groups of the mesityl moiety by isopropyl chains, a selective bromine/magnesium exchange could be performed on the thiophene **55** in the presence of *bis*(2-dimethylaminoethyl)ether, affording the Grignard **56** which provided the ester **57** in 83% yield upon reaction with (tBuO_2C)$_2$O (Scheme 12).[68]

[65] a) S. Wu, L. Huang, H. Tian, Y. Geng, F. Wang, *Macromolecules* **2011**, *44*, 7558; b) Y. Nanashima, A. Yokoyama, T. Yokozawa, *Macromolecules* **2012**, *45*, 2609; c) Y. Takeoka, K. Umezawa, T. Oshima, M. Yoshida, M. Yoshizawa-Fujita, M. Rikukawa, *Polym. Chem.* **2014**, *5*, 4132; d) F. Pammer, U. Passlack, *ACS Macro Lett.* **2014**, *3*, 170; e) Z.-K. Yang, N.-X. Xu, R. Takita, A. Muranaka, C. Wang, M. Uchiyama, *Nature Comm.* **2018**, *9*, 1587.

[66] a) L. Huang, S. Wu, Y. Qu, Y. Geng, F. Wang, *Macromolecules* **2008**, *41*, 8944; b) E. L. Lanni, A. J. McNeil, *J. Am. Chem. Soc.* **2009**, *131*, 16573; c) M. C. Stefan, A. E. Javier, I. Osaka, R. D. McCullough, *Macromolecules* **2009**, *42*, 30.

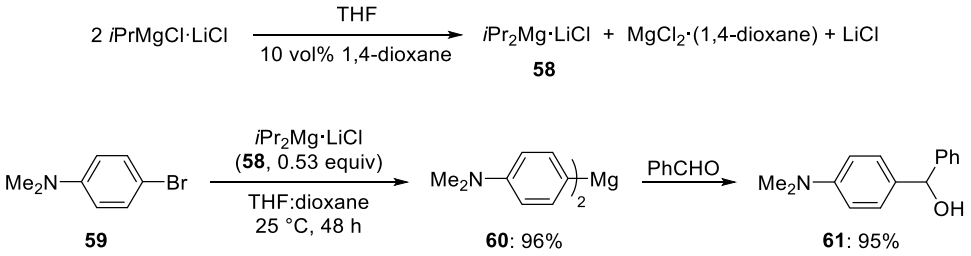
[67] N. Boudet, J. R. Lachs, P. Knochel, *Org. Lett.* **2007**, *9*, 5525.

[68] C. Sämann, B. Haag, P. Knochel, *Chem. Eur. J.* **2012**, *18*, 16145.



Scheme 12: Regioselective bromine/magnesium exchange by the use of bulky exchange reagents.

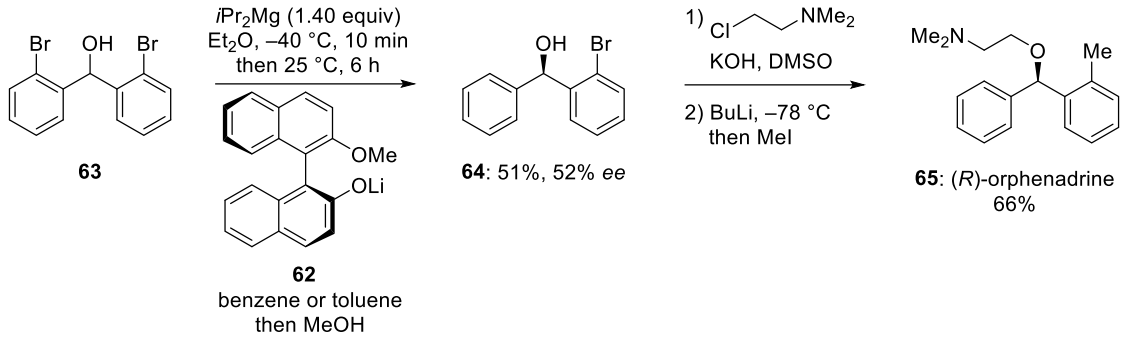
Although it was stated in the original patent that anion donor ligands such as alkoxides and amides could enhance the rate of exchange,[69] efforts were made to improve the *turbo*-Grignard by synthesizing dialkylmagnesium species complexed with LiCl, for example by treating *s*BuMgCl with *s*BuLi.[55b] Also, the treatment of two equivalents of *i*PrMgCl·LiCl with 10 vol% of 1,4-dioxane displaced the *Schlenk*-equilibrium towards the formation of **58**. The reaction of the electron-rich aryl bromide 4-bromo-*N*,*N*-dimethylaniline (**59**) with *turbo*-Grignard produced the corresponding Grignard species with only 16% conversion, whereas the reagent **58** led to the di(4-dimethyl,aminophenyl)magnesium (**60**) complexed with LiCl with 96% conversion after 48 h at 25 °C. Addition of benzaldehyde provided the alcohol **61** in 95% yield (Scheme 13).[55b]



Scheme 13: Preparation of magnesium reagents using *i*Pr$_2$Mg·LiCl (**58**).

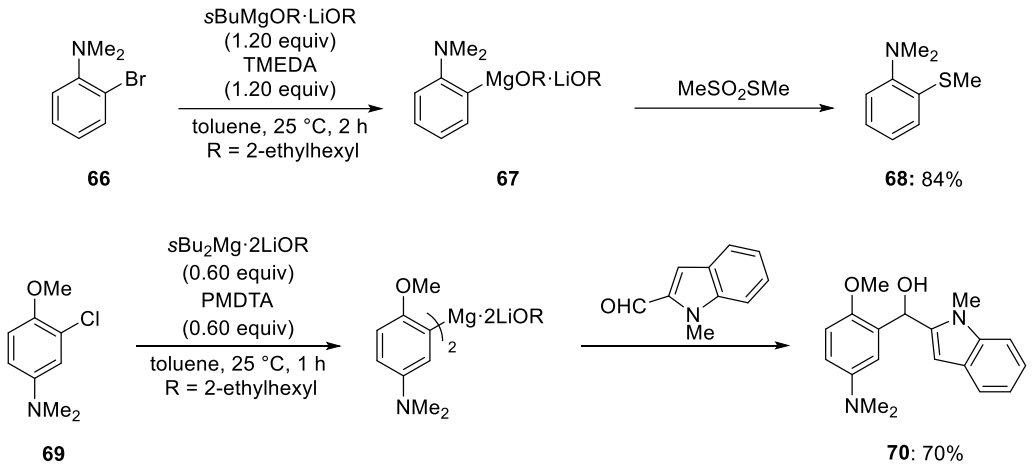
Brückner showed that in the presence of various additives like the binol-derivative **62**, *i*Pr$_2$Mg underwent a complete bromine/magnesium exchange on *bis*(2-bromophenyl)methanol (**63**) within 6 h at 25 °C in ether. After solvent switch to toluene, he obtained the chiral alcohol **64** in 51% yield and 52% *ee*. After *o*-alkylation and methylation, (*R*)-orphenadine (**65**) was obtained (Scheme 14).[70]

[69] a) J. Farkas, S. J. Stoudt, E. M. Hanawalt, A. D. Pajerski, H. G. Richey, *Organometallics* **2004**, *23*, 423; b) P. Knochel, A. Krasovskiy, *EP1582523A1* **2005**.
[70] D. Sälinger, R. Brückner, *Chem. - Eur. J.* **2009**, *15*, 6688.



Scheme 14: Desymmetrization of benzhydryl alcohol **57** *via* an enantioselective bromine/magnesium exchange.

Recently, in 2018, a new class of exchange reagents has been developed.[71] Using lithium alkoxides, for the first time, organomagnesium species could be prepared in apolar solvents. The use of this new type of reagents induced an extremely fast bromine/magnesium as well as, in some cases, a chlorine/magnesium exchange. For instance, the electron-rich 2-bromo-*N*,*N*-dimethylaniline (**66**) was converted into the corresponding magnesium species **67** using *s*BuMgOR·LiOR (R = 2-ethylhexyl, 1.20 equiv) in the presence of TMEDA at room temperature within 2 h. When $MeSO_2SMe$ was added, it provided the product **68** in 84% yield. Also, in combination with PMDTA, the dialkylmagnesium reagent *s*Bu_2Mg·2LiOR (R = 2-ethylhexyl, 0.60 equiv) reacts with an electron-rich aryl chloride **69** bearing a methoxy group in ortho position, to afford, after quenching with 1-methyl-1*H*-indole-2-carbaldehyde, the functionalized anisole **70** in 70% yield (Scheme 15).

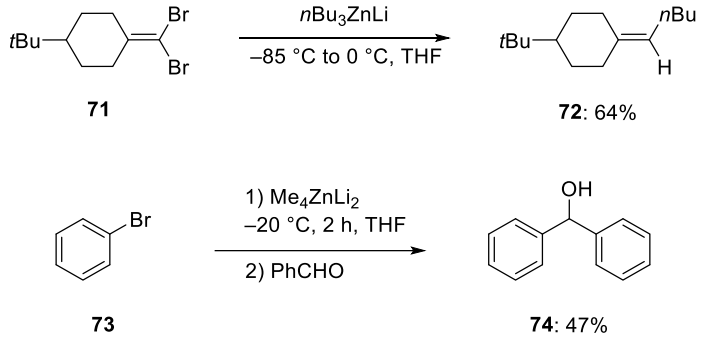


Scheme 15: Halogen/magnesium exchange on aryl bromides and chlorides in toluene.

[71] D. S. Ziegler, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 6701.

2.2.2 Halogen/Zn and Halogen/Mn Exchange Reactions

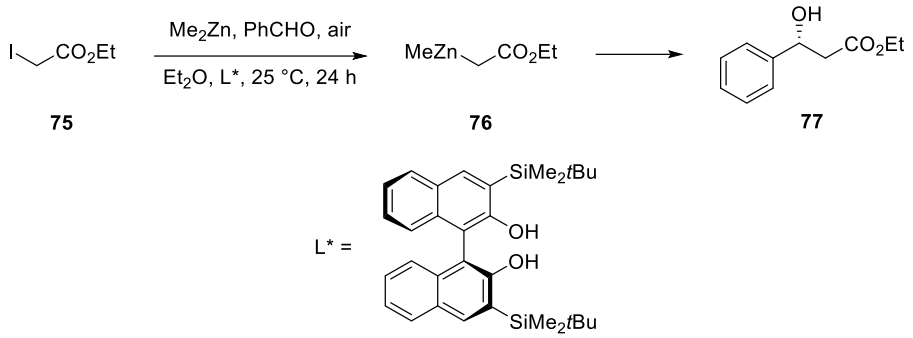
In 1988, for the first time, lithium zincates of the type R_3ZnLi have been used to perform a bromine/zinc exchange on alkenyl bromides.[72] Those species could then undergo alkylation when warming up the reaction mixture to 0 °C. It was attempted by Kondo and Sakamoto[73] to generalize this approach with the use of R_4ZnLi_2, but unfortunately, those lithium zincates behaving more or less like the corresponding lithium derivatives, the scope of the reaction remained unsatisfactory. As an example, when **71** was put in the presence of nBu$_3$ZnLi at −85 °C and warmed to 0 °C, the alkylated product **72** was obtained in 64% yield. Also, bromobenzene (**73**) reacted with Me_4ZnLi_2 in THF at −20 °C within 2 h to provide after quenching with benzaldehyde diphenylmethanol (**74**) in 47% yield (Scheme 16).



Scheme 16: Bromine/zinc exchange using lithium zincates.

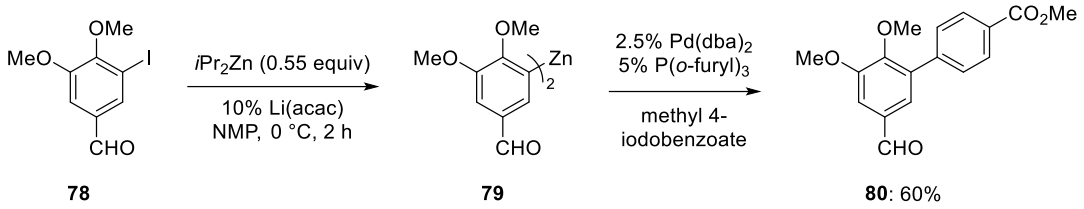
A few years later, in the mid-1990s, huge improvements have been made. Knochel reported the iodine/zinc exchange of primary and secondary alkyl iodides based on the use of R_2Zn.[74] For the first time, those mild conditions allowed the preparation of highly functionalized organozinc species by exchange reactions, which have for example been used to perform *Reformatsky-type* reactions.[75] For instance, when the α-iodo ester **75** was put in presence of Me_2Zn, a chiral binol derivative and benzaldehyde, the zinc species **76** was formed and reacted *in situ* to give the chiral alcohol **77** (Scheme 17).[76]

[72] a) T. Harada, D. Hara, K. Hattori, A. Oku, *Tetrahedron Lett.* **1988**, *29*, 3821; b) T. Harada, T. Katsuhira, A. Oku, *J. Org. Chem.* **1992**, *57*, 5805.
[73] M. Uchiyama, M. Koike, M. Kameda, Y. Kondo, T. Sakamoto, *J. Am. Chem. Soc.* **1996**, *118*, 8733.
[74] a) M. J. Rozema, S. AchyuthaRao, P. Knochel, *J. Org. Chem.* **1992**, *57*, 1956; b) M. J. Rozema, C. Eisenberg, H. Lütjens, K. Belyk, P. Knochel, *Tetrahedron Lett.* **1993**, *34*, 3115; c) P. Knochel, *Synlett* **1995**, 393; d) L. Micouin, P. Knochel, *Synlett* **1997**, 327.
[75] a) S. Reformatskii, *J. Russ. Phys. Chem. Soc.* **1890**, *22*, 44; b) S. Miki, K. Nakamoto, J.-I. Kawakami, S. Handa, S. Nuwa, *Synthesis* **2008**, 409.
[76] a) M. A. Fernández-Ibáñez, B. Maciá, A. J. Minnaard, B. L. Feringa, *Angew. Chem. Int. Ed.* **2008**, *47*, 1317; b) E. Mileo, F. Benfatti, P. G. Cozzi, M. Lucarini, *Chem. Commun.* **2009**, 469.



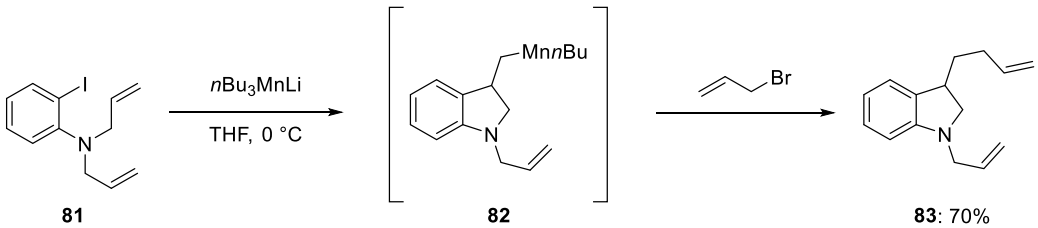
Scheme 17: Use of Me_2Zn for generating a Reformatsky reagent.

Later, in 2004, Knochel and co-workers found that 10% of Li(acac) associated with *i*Pr_2Zn and NMP could perform iodine/zinc exchange on aryl iodides with an outstanding scope, since the carbon-zinc bond is quite covalent.[77] The polyfunctional aldehyde **78** reacts under the previously stated conditions to give the zinc species **79**, which underwent a Pd-catalyzed Negishi cross-coupling with methyl 4-iodobenzoate to give the product **80** in 60% yield (Scheme 18).



Scheme 18: Iodine/zinc exchange reaction catalyzed by Li(acac) in NMP.

Sadly, studies on the halogen/manganese exchange are scarce. In 1997, Hosomi[78] and Oshima[79] both reported a case of halogen/manganese exchange by using an aryl iodide **81** and lithium tri- or tetraalkylmanganates of type R_3MnLi or R_4MnLi_2. Unfortunately, the manganese species such as **82** are rarely stable, suffering from β-hydride elimination. For that reason, reactive electrophiles like allyl bromide must be used right away to give, for instance, the desired product **83** (Scheme 19).

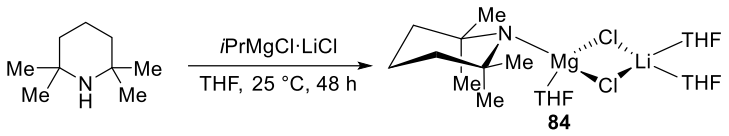


Scheme 19: Iodine/manganese exchange reaction.

[77] a) F. F. Kneisel, M. Dochnahl, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 1017; b) L.-Z. Gong, P. Knochel, *Synlett* **2005**, 267.
[78] a) M. Hojo, H. Harada, H. Ito, A. Hosomi, *Chem. Commun.* **1997**, 2077; b) M. Hojo, H. Harada, H. Ito, A. Hosomi, *J. Am. Chem. Soc.* **1997**, *119*, 5459; c) M. Hojo, R. Sakuragi, Y. Murakami, Y. Baba, A. Hosomi, *Organometallics* **2000**, *19*, 4941.
[79] J. Nakao, R. Inoue, H. Shinokubo, K. Oshima, *J. Org. Chem.* **1997**, *62*, 1910.

2.3 Deprotonation

A third approach towards organometallics, the deprotonation, was originally discovered in the late 1920s by Schlenk when he prepared 9-fluorenyllithium by using EtLi and fluorene.[80] This has led other chemists like Gilman[81] and Wittig[82] to work on deprotonations. Pioneered by Snieckus,[83] Quéguiner[84] and Schlosser,[85] lithium dialkylamides (R_2NLi) have been widely used for low-temperature metalations of organic compounds. Once again, the high reactivity of those lithium reagents was not compatible with functionalized substrates and other bases had to be developed. Despite the work of Mulvey, Mongrin, Uchiyama and Kondo since 1999 on lithium magnesiates and zincates which considerably broadened the scope of metalations,[86] magnesium amides, developed by Hauser (R_2NMgX or $(R_2N)_2Mg$) and Eaton (TMP_2Mg), provided higher tolerance towards sensitive functional groups.[87] For instance, Mulzer demonstrated their use for natural product synthesis. However, due to their low kinetic basicity and solubility, a large excess of magnesium bases and electrophiles were required.[88] These limitations have hampered their use until Knochel and co-workers developed in 2006 a highly reactive metal amide base, TMPMgCl·LiCl (**84**), by mixing TMPMgCl with one equivalent of lithium chloride in THF (Scheme 20). The resulting base exhibited an excellent solubility in common organic solvents (*ca.* 1.4 M in THF) as well as improved kinetic basicity.[89]



Scheme 20: Preparation of TMPMgCl·LiCl (**84**) using *i*PrMgCl·LiCl and TMP-H.

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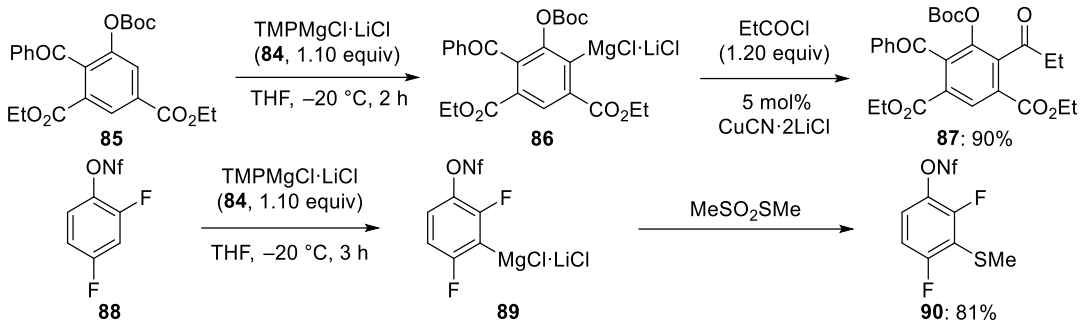
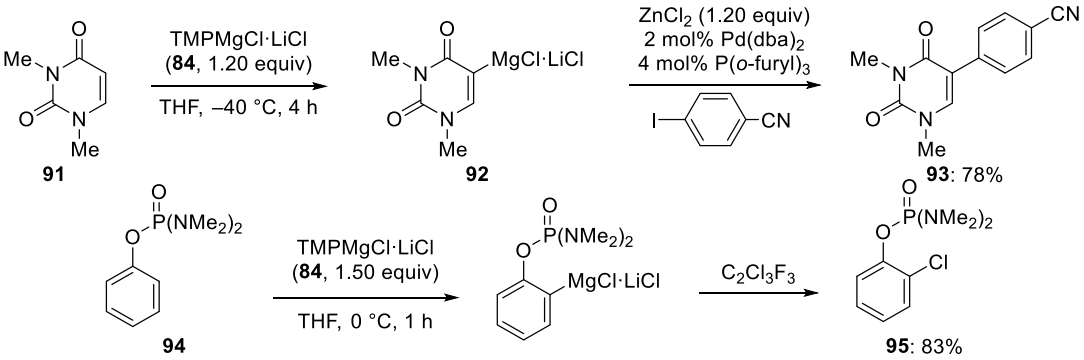
[80] W. Schlenk, E. Bergmann, *Justus Liebigs Ann. Chem.* **1928**, *463*, 98.
[81] H. Gilman, R. L. Bebb, *J. Am. Chem. Soc.* **1939**, *61*, 109.
[82] G. Wittig, G. Fuhrmann, *Ber. Dtsch. Chem. Ges.* **1940**, *73*, 1197.
[83] a) P. Beak, V. Snieckus, *Acc. Chem. Res.* **1982**, *15*, 306; b) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879; c) L. Green, B. Chauder, V. Snieckus, *J. Heterocyclic Chem.* **1999**, *36*, 1453; d) K. R. Campos, *Chem. Soc. Rev.* **2007**, *36*, 1069.
[84] a) A. Turck, N. Plé, F. Mongin, G. Quéguiner, *Tetrahedron* **2001**, *57*, 4489; b) F. Mongin, G. Quéguiner, *Tetrahedron* **2001**, *57*, 4059.
[85] a) M. Schlosser, *Angew. Chem. Int. Ed.* **2005**, *44*, 376; b) M. Schlosser, F. Mongin, *Chem. Soc. Rev.* **2007**, *36*, 1161.
[86] a) R. E. Mulvey, *Organometallics* **2006**, *25*, 1060; b) R. E. Mulvey, F. Mongin, M. Uchiyama, Y. Kondo, *Angew. Chem. Int. Ed.* **2007**, *46*, 3802; c) R. E. Mulvey, *Acc. Chem. Res.* **2009**, *42*, 743; d) S. D. Robertson, M. Uzelac, R. E. Mulvey, *Chem. Rev.* **2019**, *119*, 8332; e) Y. Kondo, H. Shilai, M. Uchiyama, T. Sakamoto, *J. Am. Chem. Soc.* **1999**, *121*, 3539; f) T. Imahori, M. Uchiyama, Y. Kondo, *Chem. Commun.* **2001**, 2450; g) M. Uchiyama, T. Miyoshi, Y. Kajihana, T. Sakamoto, Y. Otami, T. Ohwada, Y. Kondo, *J. Am. Chem. Soc.* **2002**, *124*, 8514; h) M. Uchiyama, Y. Kobayashi, T. Furuyama, S. Nakamura, Z. Kajihara, T. Miyoshi, T. Sakamoto, Y. Kondo, K. Morokuma, *J. Am. Chem. Soc*. **2008**, *130*, 472.
[87] a) C. R. Hauser, H. G. Walker, *J. Am. Chem. Soc.* **1947**, *69*, 295; b) P. E. Eaton, C. H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016; c) P. E. Eaton, K. A. Lukin, *J. Am. Chem. Soc.* **1993**, *115*, 11370.
[88] W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *J. Org. Chem.* **1995**, *60*, 8414.
[89] a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958; b) P. García-Álvarez, D. V. Graham, E. Hevia, A. R. Kennedy, J. Klett, R. E. Mulvey, C. T. O'Hara, S. Weatherstone, *Angew. Chem. Int. Ed.* **2008**, *47*, 8079; c) S. H. Wunderlich, C. J. Rohbogner, A. Unsinn, P. Knochel, *Org. Process Res. Dev.* **2010**, *14*, 339; d) G. Monzón, I. Tirotta, Y. Nishii, P. Knochel, *Angew. Chem. Int. Ed.* **2012**, *51*, 10624.

The high functional group tolerance of TMPMgCl·LiCl (**84**) allowed a huge variety of polyfunctional aromatics and heteroaromatics to be magnesiated.[89] For example, the magnesiation with TMPMgCl·LiCl (**84**) of the highly functionalized ketone **85** by using an OBoc as a directing group smoothly generated the magnesium derivative **86** which was converted into **87** in 90% yield.[90] Moreover, electron-deficient substrates such as the nonaflate-substituted derivative **88** were magnesiated with **84** providing the Grignard reagent **89**. Addition of $MeSO_2SMe$ led to the expected methyl thioether **90** in 81% yield (Scheme 21).[91]



Scheme 21: Metalation of polyfunctional aromatics using TMPMgCl·LiCl (**84**).

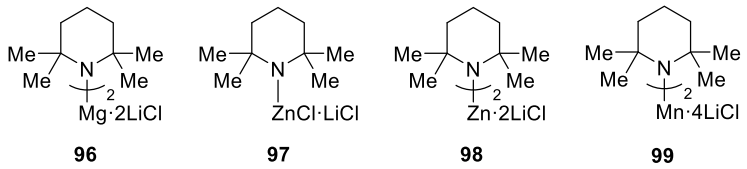
Furthermore, various electron-poor and -rich heteroaromatics was magnesiated with TMPMgCl·LiCl (**84**). Thus, protected uracil **91** reacted regioselectively with TMPMgCl·LiCl (**84**) at –40 °C in 4 h and provided the C(5) metalated heterocycle **92**. Transmetalation with $ZnCl_2$, followed by a Pd-catalyzed Negishi cross-coupling with 4-iodobenzonitrile led to the arylated methyl protected uracil **93** in 78% yield (Scheme 22).[92] Interestingly, *N*-heterocycles such as the pyridine **94** bearing a *N*,*N*,*N*',*N*'-tetramethyldiaminophosphorodiamidate directing group were metalated at 0 °C within 1 h. By using **84**, the desired product **95** was afforded in 83% yield after quench with $C_2Cl_3F_3$ (Scheme 22).[93]



Scheme 22: Metalation of heteroaromatics using TMPMgCl·LiCl (**84**).

[90] W. Lin, O. Baron, P. Knochel, *Org. Lett.* **2006**, *8*, 5673.
[91] G. Monzon, P. Knochel, *Synlett* **2010**, 304.
[92] L. Klier, E. Aranzamendi, D. Ziegler, J. Nickel, K. Karaghiosoff, T. Carell, P. Knochel, *Org. Lett.* **2016**, *18*, 1068.
[93] C. J. Rohbogner, S. Wirth, P. Knochel, *Org. Lett.* **2010**, *12*, 1984.

In the following years, a number of new TMP-bases were established[94] like $TMP_2Mg·2MgCl_2·2LiCl$ (**96**),[95] TMPZnCl·LiCl (**97**),[96] $TMP_2Zn·2MgCl_2·2LiCl$ (**98**)[97] and $TMP_2Mn·2MgCl_2·4LiCl$ (**99**)[98] (Figure 3). Since then, the metalation scope of unsaturated substrates has been considerably expanded. Thanks to their high kinetic basicity, TMP-bases offered the possibility to metalate chemo- and regioselectively a wide range of aromatic systems, as well as highly functionalized heterocycles and non-aromatic, unsaturated systems under practical conditions.[94]

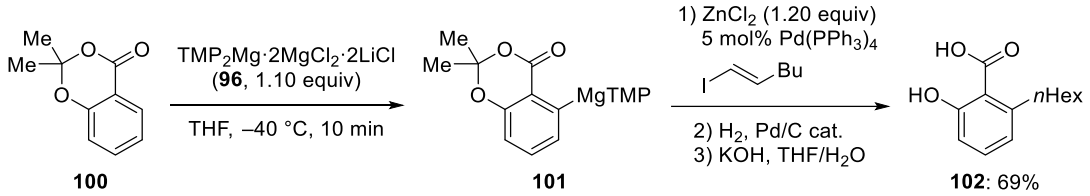


96 **97** **98** **99**

Note: For clarity reasons, the metal salts are not always fully written.

Figure 3: TMP-derived, mixed metal/lithium amide bases.

Aromatic substrates bearing electron-donating or weakly-accepting substituents were difficult to magnesiate with **84**. The higher reactivity of $TMP_2Mg·2MgCl_2·2LiCl$ (**96**) solved this problem by enabling the magnesiation of moderately activated aromatics and heteroraromatics. For instance, $TMP_2Mg·2MgCl_2·2LiCl$ (**96**) allowed the magnesiation of dimethyl-1,3-benzodioxan-4-one (**100**) at **–** 40 °C in 10 min. After transmetalation with $ZnCl_2$ and Pd-catalyzed Negishi cross-coupling with (*E*)-1-hexenyl iodide, the magnesiated species **101** was converted into the corresponding 6-substituted benzodioxane. Subsequent hydrogenation and deprotection gave the natural product found in the essential oil of *Pelargonium sidoides DC* **102** in 69% yield (Scheme 23).[95]



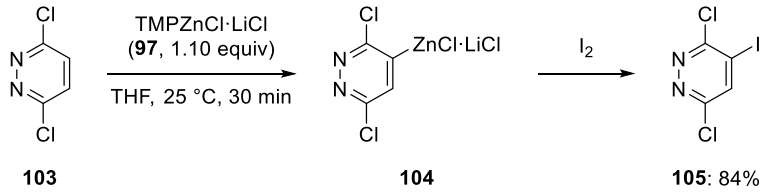
100 **101** **102**: 69%

Scheme 23: Magnesiation of dimethyl-1,3-benzodioxan-4-one (**100**) using $TMP_2Mg·2MgCl_2·2LiCl$ (**96**).

On the one hand, TMPMgCl·LiCl (**84**) and $TMP_2Mg·2MgCl_2·2LiCl$ (**96**) were unfortunately not adapted for the metalation of several sensitive aromatics and heterocyclic substrates such as electron-poor *N*-heterocycles. On the other hand, they could smoothly be metalated with TMPZnCl·LiCl (**97**). Consequently, **97** tolerates more sensitive functional groups such as nitro, aldehyde or methyl ketone

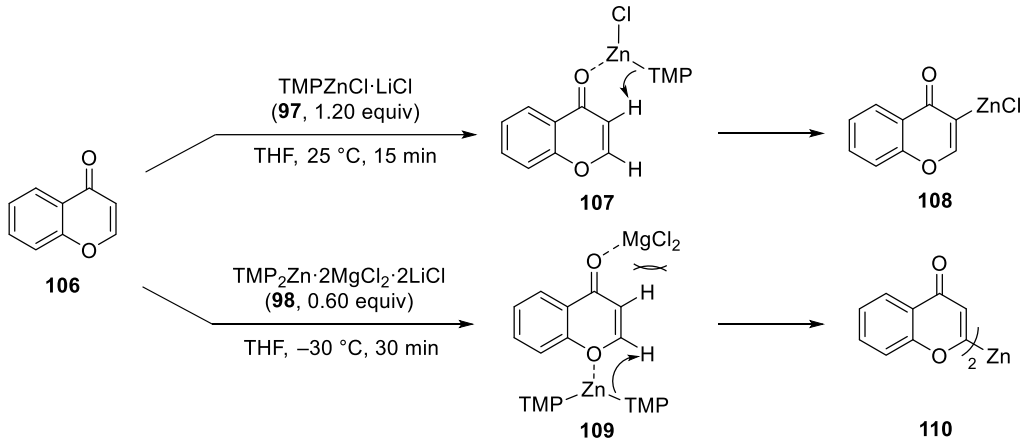
[94] B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9794.
[95] G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7681.
[96] M. Mosrin, P. Knochel, *Org. Lett.* **2009**, *11*, 1837.
[97] S. H. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7685.
[98] S. H. Wunderlich, M. Kienle, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 7256.

groups and the high thermal stability of these zinc organometallics (up to 120 °C) enabled the directed metalation under a wide range of conditions.[94,96] For instance, the sensitive pyridazine heterocycle **103**, which previously could only be metalated at low temperatures in moderate yields,[84a] was zincated to give **104** at 25 °C within 30 min. An iodination led to the trihalogenated pyridazine **105** in 84% yield (Scheme 24).[96]



Scheme 24: Zincation of sensitive pyrazine **103** using TMPZnCl·LiCl (**97**).

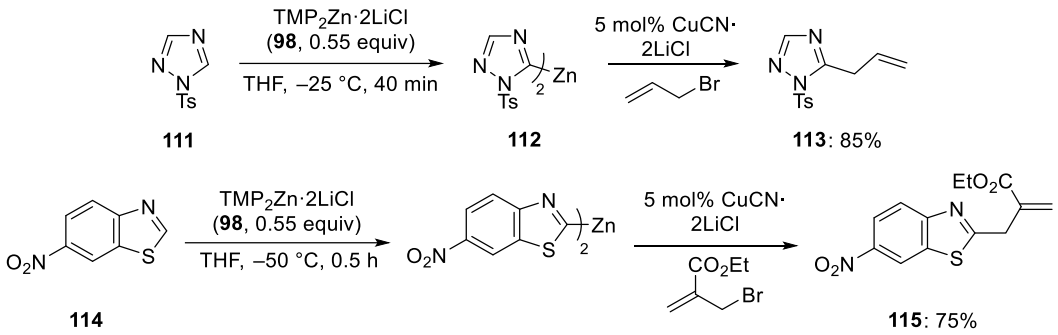
Furthermore, TMPZnCl·LiCl (**97**) allowed the coordination-induced regioselective zincation of chromones of type **106** at the position C(3) through the intermediate **107**, giving the organozinc **108**. Interestingly, the regioselectivity of those bases can be modulated by the presence of Lewis acids. Although $BF_3 \cdot OEt_2$ has been frequently selected,[99] milder Lewis acids such as $MgCl_2$ can also be employed.[92,99d,100] The C(2)-selective zincation was then achieved using the more powerful zinc base $TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (**98**). The coordination of $MgCl_2$ to the most basic oxygen provided the intermediate **109,** triggering by Complex-Induced Proximity Effect (CIPE)[101] the formation of the *bis*-heterocyclic zinc reagent **110** (Scheme 25).[100]



Scheme 25: Regioselective zincation of chromone **106** using TMPZnCl·LiCl (**97**) and $TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (**98**).

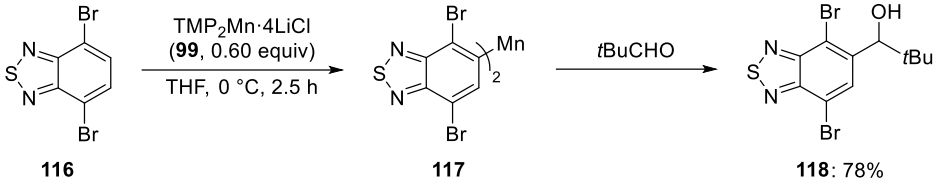
[99] a) M. Jaric, B. A. Haag, A. Unsinn, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2010**, *49*, 5451; b) M. Jaric, B. A. Haag, S. M. Manolikakes, P. Knochel, *Org. Lett.* **2011**, *13*, 2306; c) S. M. Manolikakes, M. Jaric, K. Karaghiosoff, P. Knochel, *Chem. Commun.* **2013**, *49*, 2124; d) T. Klatt, D. S. Roman, T. Léon, P. Knochel, *Org. Lett.* **2014**, *16*, 1232; e) see: M. Balkenhohl, Ph.D. Dissertation, LMU München, **2019**.
[100] L. Klier, T. Bresser, T. A. Nigst, K. Karaghiosoff, P. Knochel, *J. Am. Chem. Soc.* **2012**, *134*, 13584.
[101] M. C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem. Int. Ed.* **2004**, *43*, 2206.

The zinc base **98** was also used for the metalation of sensitive heterocycles such as triazole **111**, which was prone to undergo fragmentation during metalation process.[97,102] After transmetalation of **112** to copper and allylation, the product **113** was obtained in 85% yield. Also, **98** could tolerate various sensitive functional groups. Thus, 6-nitrobenzo[*d*]thiazole (**114**) was zincated at −50 °C within 0.5 h, leading to benzothiazole **115** in 75% yield after copper catalyzed allylation (Scheme 26).[97]



Scheme 26: Zincation of sensitive heterocycles using $TMP_2Zn·2MgCl_2·2LiCl$ (**98**).

Although directed manganation has been rarely studied, $TMP_2Mn·2MgCl_2·4LiCl$ (**99**) has been proven to be a base of choice for the metalation of a variety of functionalized arenes and heteroarenes under mild conditions.[98] Thus, **99** was used for the functionalization of the benzothiadiazole scaffold, which possesses potential applications in the preparation of new materials.[103] Indeed, 3,6-dibromobenzothiadiazole (**116)** was metalated by **99** at 0 °C within 2.5 h to give the manganese species **117**. After pivaldehyde was added, the alcohol **118** was isolated in 78% yield (Scheme 27).[98]



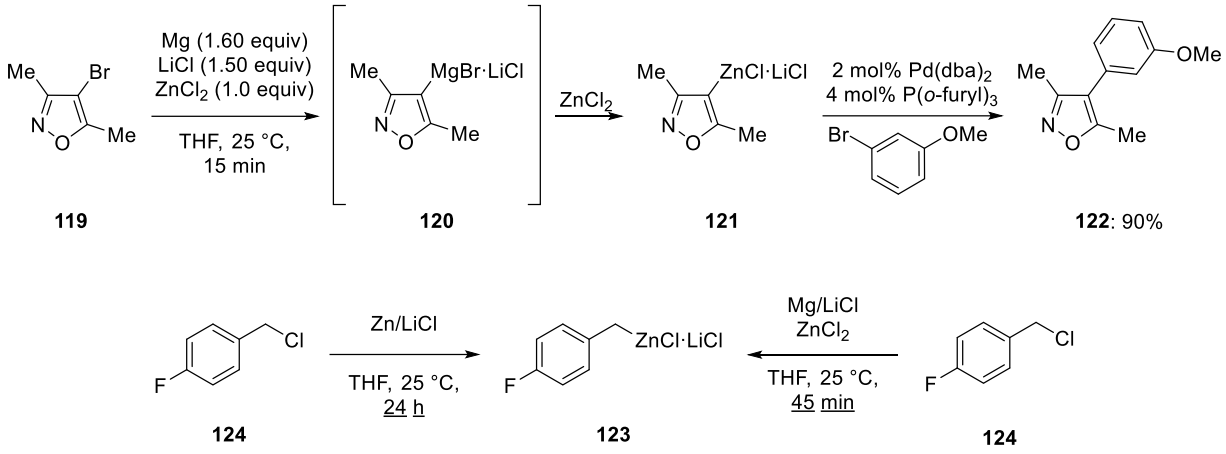
Scheme 27: Manganation of 3,6-dibromobenzothiadiazole (**116**) using $TMP_2Mn·2MgCl_2·4LiCl$ (**99**).

2.4 Transmetalation

The transmetalation of organometallic compounds offers another approach for the preparation of organozinc, organomagnesium and organomanganese compounds by addition of an inorganic metal salt such as $ZnCl_2$. It has been found to be useful for the preparation of sensitive reagents and allowed the

[102] a) A. Turck, N. Plé, L. Mojovic, G. Quéguiner, *J. Heterocycl. Chem.* **1990**, *27*, 1377; b) L. Mojovic, A. Turck, N. Plé, M. Dorsy, B. Ndzi, G. Quéguiner, *Tetrahedron* **1996**, *52*, 10417.
[103] a) J. Y. Kim, K. Lee, N. E. Coates, D. Moses, T.-C. Nguyen, M. Dante, A. J. Heeger, *Science* **2007**, *317*, 222; b) T. Clarke, A. Ballantyne, F. Jamieson, C. Brabec, J. Nelson, J. Durrant, *Chem. Commun.* **2009**, 89.

metalation of certain scaffolds with new selectivies.[104] Furthermore, this transmetalation process is used for many reactions with electrophiles *e.g.* cross-coupling, acylation or allylation reactions where the organometallic species must be either a zinc or a copper species.[105] As exposed earlier, the driving force for the transmetalation reaction is the formation of a more covalent carbon-metal bond and along with it the formation of a more stable reagent. For example, the sensitive isoxazole **119** was prepared by a magnesium insertion in the presence of $ZnCl_2$. Thereby, the unstable magnesium reagent **120** was directly transmetalated using $ZnCl_2$ to form the comparatively stable zinc reagent **121**. After a Negishi cross-coupling, the arylated product **122** was obtained in 90% yield. Transmetalation can also accelerate the generation of an organometallic species compared to the oxidative insertion. For instance, the fluorated benzylic zinc species **123** can be generated from **124** by oxidative zinc insertion in the presence of LiCl within 24 h at 25 °C while the magnesium insertion in the presence of LiCl and $ZnCl_2$ provides **123** within 45 min (Scheme 28).[106]

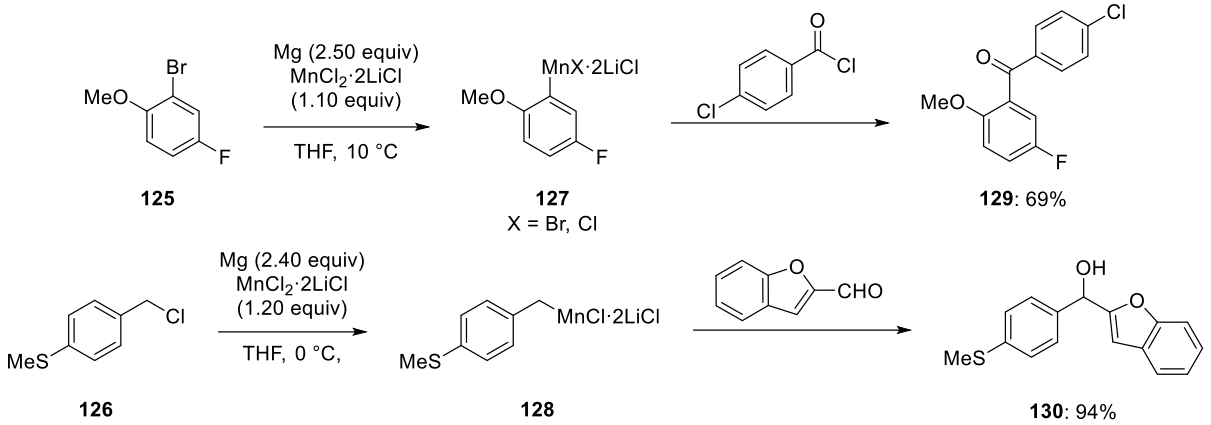


Scheme 28: Preparation of the functionalized isoxazole **122** *via* an *in situ* generated zinc reagent.

Although not being common, transmetalation from magnesium to manganese was already described in 1937 by Gilman and Bailie.[107] During the rest of the 20th century, further reports remained sporadic until the pioneer work of *Cahiez et al.* on organomanganese chemistry. He described, amongst other methods,[16] the transmetalation of already prepared Grignard reagents when mixed with $MnCl_2 \cdot 2LiCl$ in THF.[108] Later, a more practical version of this method using *in situ* generation of Grignards in the

[104] A. Frischmuth, M. Fernández, N. M. Barl, F. Achrainer, H. Zipse, G. Berionni, H. Mayr, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2014**, *53*, 7928.
[105] a) T. Klatt, J. T. Markiewicz, C. Sämann, P. Knochel, *J. Org. Chem.* **2014**, *79*, 4253; b) M. Balkenhohl, P. Knochel, *SynOpen* **2018**, *2*, 78.
[106] F. M. Piller, A. Metzger, M. A. Schade, B. A. Haag, A. Gavryushin, P. Knochel, *Chem. - Eur. J.* **2009**, *15*, 7192.
[107] a) H. Gilman, J. C. Bailie, *J. Org. Chem.* **1937**, *2*, 84; b) H. Gilman, R. Kirby, *J. Am. Chem. Soc.* **1941**, *63*, 2046.
[108] G. Friour, G. Cahiez, J. F. Normant, *Synthesis* **1984**, 37.

presence of $MnCl_2 \cdot 2LiCl$ has been developed.[109] Indeed, the aryl or benzyl halide **125** or **126** underwent smooth magnesium insertion and were successfully *in situ* transmetalated to manganese to furnish **127** and **128**. Subsequent trapping reactions with either an acyl chloride or an aldehyde could be performed, yielding the desired products **129** and **130** (Scheme 29).[109]



Scheme 29: Direct insertion of magnesium into aryl and benzyl halides in the presence of $MnCl_2 \cdot 2LiCl$.

2.5 Transition-Metal-Catalyzed Cross-Coupling Reactions of Organomanganese Reagents

Transition-metal-catalyzed cross-couplings are of great interest and play an important role for organometallic chemistry.[110] Many metals have been applied to such transformations and a variety of catalysts have been developed. So far, *Kumada-Corriu* (organomagnesium),[111] *Negishi* (organozinc),[29] *Stille* (organotin),[112] and *Suzuki-Miyaura* (organoboron)[113] cross-couplings are well established and found numerous applications. In 2013, Feringa described a Pd-catalyzed cross-coupling of organolithium reagents in toluene.[114] Regarding organomanganese reagents, the first palladium-catalyzed cross-coupling reaction with aryl halides and triflates was performed by Cahiez and co-workers in 1997. As an exemple, the functionalized arylmanganese chloride **131** underwent a fast coupling with ethyl 4-bromobenzoate in the presence of $Pd(PPh_3)_2Cl_2$, leading to the unsymmetrical biaryl **132** in 91% yield (Scheme 30).[115]

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[109] a) Z. Peng, N. Li, X. Sun, F. Wang, L. Xu, C. Jiang, L. Song, Z.-F. Yan, *Org. Biomol. Chem.* **2014**, *12*, 7800; b) P. Quinio, A. D. Benischke, A. Moyeux, G. Cahiez, P. Knochel, *Synlett* **2015**, *26*, 514.

[110] a) *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**; b) *Metal-Catalyzed Cross-Coupling Reactions and More* (Eds.: A. de Meijere, S. Bräse, M. Oestreich), Wiley-VCH, Weinheim, **2014**.

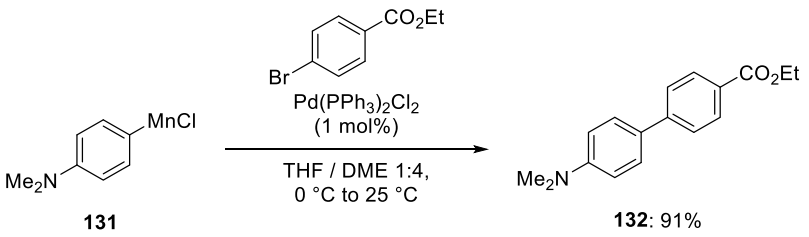
[111] a) K. Tamao, K. Sumitani, M. Kumada, *J. Am. Chem. Soc.* **1972**, *94*, 4374; b) C. E. I. Knappe, A. J. von Wangelin, *Chem. Soc. Rev.* **2011**, *40*, 4948.

[112] a) J. K. Stille, *Angew. Chem. Int. Ed.* **1986**, *25*, 508; b) P. Espinet, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2004**, *43*, 4704.

[113] a) N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Lett.* **1979**, *20*, 3437; b) A. Suzuki, *Angew. Chem. Int. Ed.* **2011**, *50*, 6722.

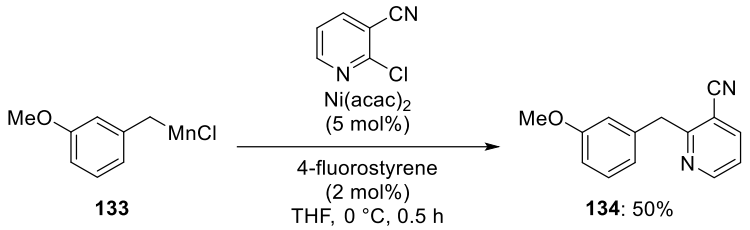
[114] M. Giannerini, M. Fananás-Mastral, B. L. Feringa, *Nat. Chem.* **2013**, *5*, 667.

[115] E. Riguet, M. Alami, G. Cahiez, *Tetrahedron Lett.* **1997**, *38*, 4397.



Scheme 30: Pd-catalyzed cross-coupling of arylmanganese chlorides and aryl halides or triflates.

Besides palladium, nickel catalysts are considered to be powerful and cheap alternatives. In 2006, Schneider reported a catalytic system involving $Ni(acac)_2$ and a NHC ligand, which allowed couplings of arylmanganese chlorides with aryl halides.[116] In 2012, *Wang et al.* developed a nickel-catalyzed cross-coupling procedure of arene- or heteroarenecarbonitriles with aryl- and heteroarylmanganese reagents.[117] In 2017 was reported a nickel-catalyzed cross-coupling of functionalized benzyl- and arylmanganese reagents with aryl- and heteroaryl halides promoted by 4-fluorostyrene. For instance, 3-methoxybenzylmanganese chloride (**133**) underwent a cross-coupling with 2-chloronicotinonitrile in the presence of $Ni(acac)_2$ and 4-fluorostyrene in THF to yield within 30 min the corresponding product **134** (Scheme 31).



Scheme 31: Ni-catalyzed cross-coupling of benzyl- and arylmanganese chlorides with (hetero)aryl halides promoted by 4-fluorostyrene.

In addition, several cross-coupling methodologies of organomanganese reagents involving iron,[118] copper[119] or cobalt[120] catalysts have been studied. Since it allows to replace palladium or nickel catalysts with inexpensive and non-toxic iron salts, iron-catalyzed cross-couplings are really crucial in a perspective of an always greener chemistry. For that matter, since recently, many extensive studies were carried out on the catalytic activity of iron catalysts and their application in organometallic chemistry.[121]

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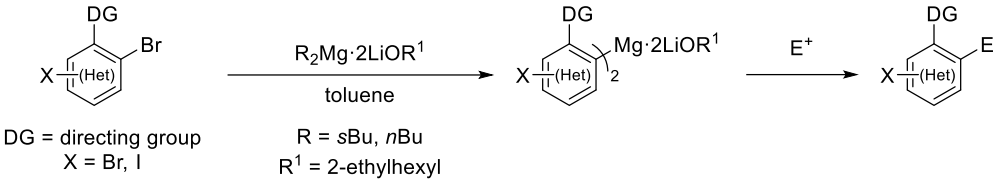
[116] A. Leleu, Y. Fort, R. Schneider, *Adv. Synth. Catal.* **2006**, *348*, 1086.
[117] N. Liu, Z.-X. Wang, *Adv. Synth. Catal.* **2012**, *354*, 1641.
[118] a) G. Cahiez, S. Marquais, *Tetrahedron Lett.* **1996**, *37*, 1773; b) G. Cahiez, S. Marquais, *Pure Appl. Chem.* **1996**, *68*, 53; c) M. S. Hofmayer, J. M. Hammann, G. Cahiez, P. Knochel, *Synlett* **2018**, *29*, 65; d) A. D. Benischke, A. J. A. Breuillac, A. Moyeux, G. Cahiez, P. Knochel, *Synlett* **2016**, *27*, 471.
[119] a) J. G. Donkervoort, J. L. Vicario, J. T. B. H. Jastrzebski, R. A. Gossage, G. Cahiez, G. van Koten, *Recl. Trav. Chim. Pays-Bas Belg.* **1996**, *115*, 547; b) J. G. Donkervoort, J. L. Vicario, J. T. B. H. Jastrzebski, R. A. Gossage, G. Cahiez, G. van Koten, *J. Organomet. Chem.* **1998**, *558*, 61.
[120] M. S. Hofmayer, J. M. Hammann, D. Haas, P. Knochel, *Org. Lett.* **2016**, *18*, 6456.
[121] a) C. Bolm, J. Legros, J. Le Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217; b) B. D. Sherry, A. Fürstner, *Acc. Chem. Res.* **2008**, *41*, 1500; c) W. M. Czaplik, M. Mayer, J. Cvengros, A. J. von Wangelin, *ChemSusChem* **2009**, *2*, 396.

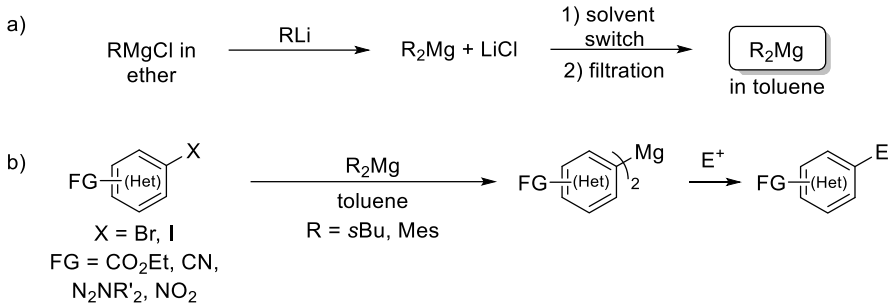
3 Objectives

Based on previous results on halogen/magnesium exchange in apolar solvents, the aim of the first project was the development of a method for the regioselective bromine/magnesium exchange on polyhalogenated (hetero)arenes in toluene using lithium alkoxide complexed alkyl magnesium reagents. It was anticipated that due to the lack of coordination of the magnesium species in toluene, these exchange reagents would display unprecedented regioselectivities. The resulting halogenated (hetero)aryl magnesium species should then give access to new building blocks for the functionalization of (hetero)aromatic compounds of interest in an industrial friendly solvent (Scheme 32).



Scheme 32: Regioselective bromine/magnesium exchange on polyhalogenated (hetero)arenes using lithium alkoxide complexed alkylmagnesium reagents.

In addition, it was also envisioned for this thesis to design a complementary halogen/magnesium exchange reagent in toluene that would not require the use of any lithium alkoxides nor magnesiates.[122] This kind of milder reagent allowed a greater functional group tolerance compared with the powerful halogen/magnesium exchange reagents that were previously reported in toluene (Scheme 33).

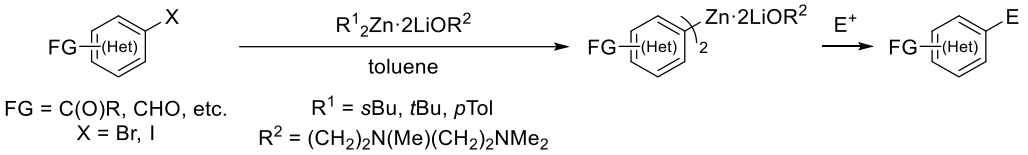


Scheme 33: a) Preparation of new magnesium exchange reagents in toluene. b) Halogen/magnesium exchange on sensitive (hetero)aryl halides in toluene.

Another objective was the development of a halogen/zinc exchange reaction using lithium alkoxide complexed dialkyl or diarylzinc reagents.[123] It was anticipated that these reagents are suitable for the preparation of organometallic species in toluene. Since zinc organometallics are very mild compared to

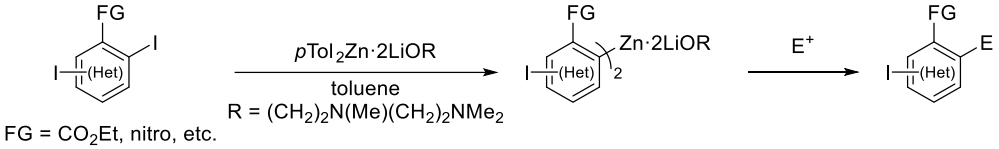
[122] This project was developed in cooperation with Dr. F. Danton.
[123] This project was developed in cooperation with Dr. D. S. Ziegler and Dr. M. Balkenhohl, see: M. Balkenhohl, Dissertation, **2019**, LMU München.

organomagnesium species, sensitive functional groups such as ketones or aldehydes were tolerated by these novel exchange reagents (Scheme 34).



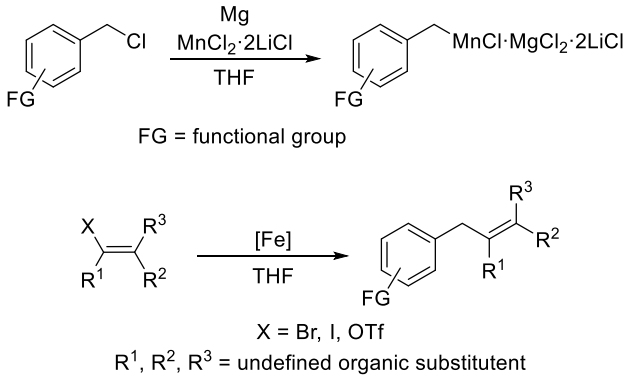
Scheme 34: The halogen/zinc exchange reaction using lithium alkoxide complexed dialkyl or diarylzinc reagents.

With analogy to the first topic of this thesis, we aimed at performing regioselective I/Zn exchanges on polyiodinated hetero(arenes). The advantage of using Zn instead of Mg laid in the fact that organozincs can tolerate more functional groups than Grignard reagents, allowing us to prepare functionalized (hetero)aryl iodides bearing more sensitive functions (Scheme 35).[124]



Scheme 35: Regioselective iodine/zinc exchange on polyiodinated (hetero)arenes using lithium alkoxide complexed arylzinc reagents.

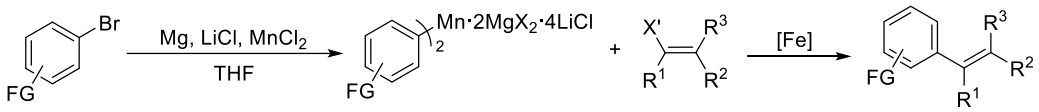
A further topic of interest for this thesis involved the preparation of functionalized benzylic manganese reagents from the corresponding benzylic chlorides, which underwent novel Fe-catalyzed cross-coupling reactions with alkenyl halides and triflates, leading to polyfunctionalized alkenes while promoting greener chemistry (Scheme 36).



Scheme 36: Preparation of benzylic manganese reagents followed by iron-catalyzed cross-couplings with alkenyl halides and triflates.

[124] This project was developed in cooperation with F. Sanchez under the guidance of A. Desaintjean.

The last study of this thesis was meant to develop a new one-pot preparation method of functionalized *bis*-(aryl)manganese reagents from the corresponding aryl bromides, followed by an iron-catalyzed cross-coupling with various alkenyl halides (Scheme 37).



X = Br, Cl; FG = functional group; X' = Br, I; R^1, R^2, R^3 = undefined organic substituents

Scheme 37: One-pot preparation of *bis*-(aryl)manganese reagents by *in situ* transmetalation, followed by Fe-catalyzed cross-couplings with various alkenyl halides.

B. RESULTS AND DISCUSSION

1 Regioselective Bromine/Magnesium Exchange for the Selective Functionalization of Polyhalogenated Arenes and Heterocycles

1.1 Introduction

Functionalized halogenated arenes and heteroarenes constitute key tools for building pharmaceuticals, materials and natural products.[8,125] A few metal-mediated methods such as regioselective zinc insertion in the presence of LiCl on dihalogenated (hetero)arenes[30] have been developed to access these valuable molecules.[126] Although being one of the most powerful approaches to functionalize haloarenes, halogen/magnesium exchange has shown limited success for this type of substrates in terms of versatility and regioselective tunability. Some exceptions include the use of the *turbo*-Grignard,[55a,127] which can trigger selective Br/Mg exchanges in THF.[56,128] Bulkier variations of *i*PrMgCl·LiCl containing mesityl or 2,4,6-triisopropylphenyl substituents have displayed improved regioselectivities.[67,68] It was recently shown by *Knochel et al.* that mixed-metal compositions *s*BuMgOR·LiOR (**134a**) and to a greater extent the stoichiometric variant *s*Bu_2Mg·2LiOR (R = 2-ethylhexyl, **134b**) can promote Br/Mg and in a few cases Cl/Mg exchanges in toluene or other non-polar solvents with an excellent substrate scope at room temperature.[71] Expanding further the synthetic utility of these alkyl/alkoxide s-block metal combinations, herein, we report fast and highly regioselective Br/Mg exchanges on various dibromo(hetero)arenes using **134b** in the industrially friendly solvent toluene. In addition, the use of Lewis donors such as PMDTA activates in some cases a regioselectivity switch.

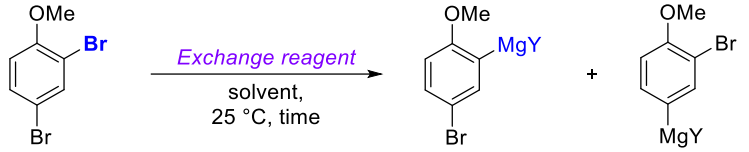
1.2 Optimization and Scope of the Regioselective Br/Mg Exchange on Polybrominated Arenes and Heteroarenes

We commenced our studies evaluationg the regioselectivity of the Br/Mg exchange on 2,4-dibromoanisole (**135a**) with several mixed Li/Mg combinations (Table 1). We first treated **135a** with the *turbo*-Grignard in THF at 25 °C and obtained within 2 h an 85:15 ratio of the two regioisomeric Grignard species **136a** and **137a** respectively (87% conversion, entry 1). The preferential formation of

[125] a) D. G. Brown, J. Boström, *J. Med. Chem.* **2016**, *59*, 4443; b) J. H. Koo, H. D. Maynard, *Chem. Soc. Rev.* **2018**, *47*, 8998.
[126] a) I. J. S. Fairlamb, *Chem. Soc. Rev.* **2007**, *36*, 1036; b) Y. Garcia, F. Schoenebeck, C. Y. Legault, C. A. Merlic, K. N. Houk, *J. Am. Chem. Soc.* **2009**, *131*, 6632; c) C. J. Diehl, T. Scattolin, U. Englert, F. Schoenebeck, *Angew. Chem. Int. Ed.* **2019**, *58*, 211; d) T. Bach, M. Bartels, *Synlett* **2001**, 1284.
[127] a) A. Murso, P. Rittmeyer, *Spec. Chem. Mag.* **2006**, *26*, 40; b) C. Schnegelsberg, S. Bachmann, M. Kolter, T. Auth, M. John, D. Stalke, K. Koszinowski, *Chem. Eur. J.* **2016**, *22*, 7752.
[128] a) S. Gross, S. Heuser, C. Ammer, G. Heckmann, T. Bach, *Synthesis* **2011**, 199; b) C. Stock, F. Höfer, T. Bach, *Synlett* **2005**, 511.

136a may be rationalized by assuming a coordination of the exchange reagent to the neighboring methoxy substituent, reminiscent of the CIPE in aromatic *ortho*-lithiations.[101]

Table 1: Screening of the regioselective Br/Mg exchange on 2,4-dibromoanisole (**135a**).



135a **136a**[a],[b],[c] **137a**[a],[b],[c]

Entry	Exchange reagent[d]	Solvent	Time (min)	Ratio **136a**:**137a**	Conv. [%][e]
1	*i*PrMgCl·LiCl	THF	120	85:15	87[a]
2	*s*BuMgOR·LiOR (**134a**)	toluene	30	99:1	75[b]
3	*s*Bu_2Mg·2LiOR (**134b**)	toluene	5	99:1	99[c]

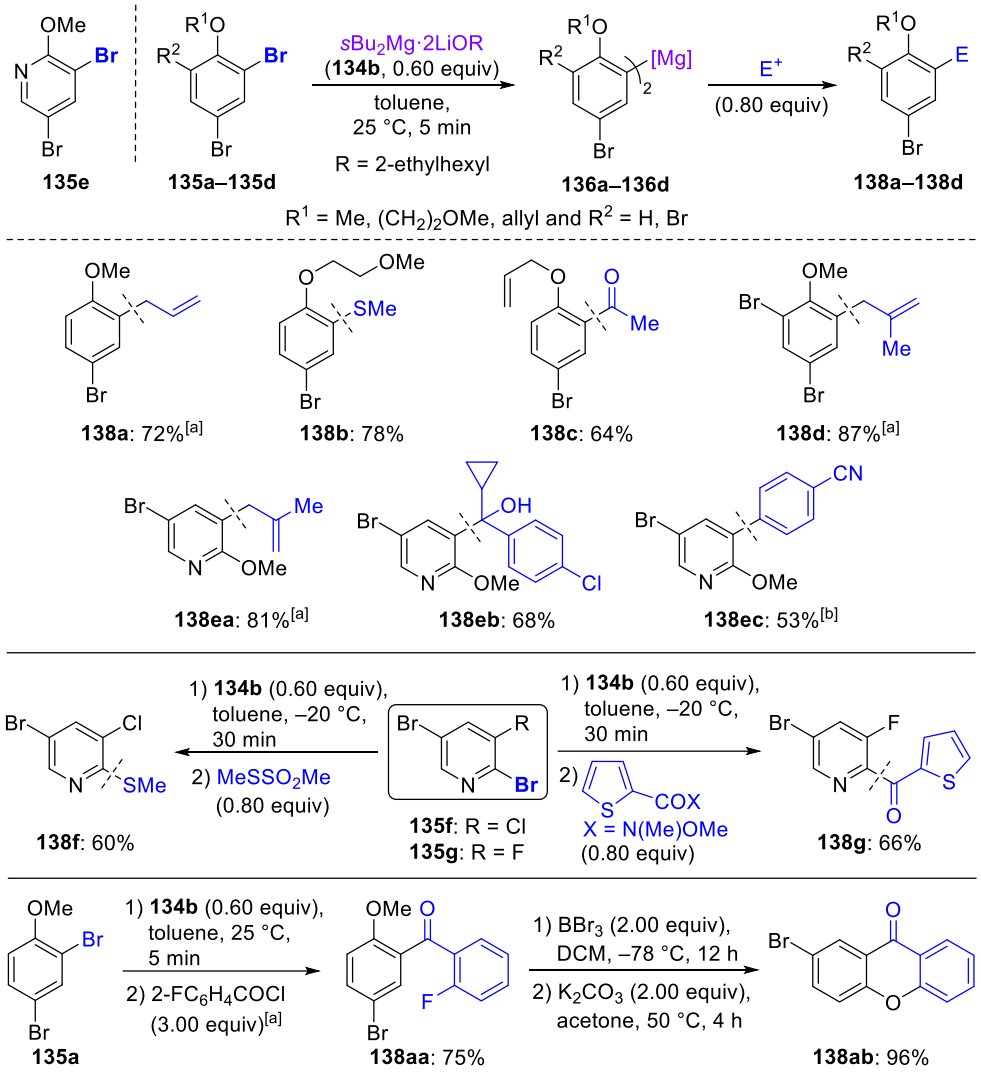
[a] Y = Cl·LiCl. [b] Y = OR·LiOR. [c] Y = anisyl·2LiOR. [d] R = 2-ethylhexyl, these reactions were carried out at 0.50 M using 1.20 equiv of alkylmagnesium species. Reagents are displayed accordingly to their stoichiometry and not their actual structure. [e] Conversion determined by GC-analysis of reaction aliquots after aqueous quench.

In an attempt to maximize coordination effects between the substrate and the exchange reagent to improve the regioselectivity, ethereal THF was replaced by non-polar toluene[129] and *s*BuMgOR·LiOR (R = 2-ethylhexyl, **134a**) was used as exchange reagent. Thus, treatment of **135a** with **134a** generated the 2-anisylmagnesium species **136a** solely (**136a**:**137a** = 99:1) within 30 min of reaction, however with a lower conversion than with *i*PrMgCl·LiCl (75%, entry 2). To our delight, the more activated reagent *s*Bu_2Mg·2LiOR (**134b**, 0.60 equiv), which was readily prepared by mixing *s*BuLi (2.00 equiv) with $Mg(OR)_2$,[71] completed the magnesiation of **135a** after just 5 min affording **136a** (99% conversion, **136a**:**137a** = 99:1, entry 3).

Different sets of substrates and electrophiles were investigated next. Thus, Cu-catalyzed allylation[130] of **136a** furnished **138a** in 72% yield (Scheme 38). Similarly, electron-rich 2-bromoaryl ethers **135b–135d** underwent complete Br/Mg exchange at C(2) position upon treatment with **134b** (25 °C, 5 min). The corresponding diarylmagnesium (**136b–136d**) were smoothly thiomethylated with $MeSO_2SMe$, acylated with *N*-methoxy-*N*-methylacetamide or allylated with methallyl bromide, producing the bromoaryl ethers **138b–138d** in 64–87% yield. Analogously, 3,5-dibromo-2-methoxypyridine (**135e**) was regioselectively converted into the *ortho*-methalated compound **136e**. After allylation with

[129] Regioselective lithiation in non-polar solvents: a) P. C. Gros, F. Elaachbouni, *Chem. Commun.* **2008**, 4813; b) A. Doudouh, C. Woltermann, P. C. Gros, *J. Org. Chem.* **2007**, *72*, 4978; c) W. E. Parham, R. M. Piccirilli, *J. Org. Chem*. **1977**, *42*, 257.
[130] P. Knochel, M. C. P. Yeh, S. C. Berk, J. Talbert, *J. Org. Chem.* **1988**, *53*, 2390.

methallyl bromide, addition to a ketone, or transmetalation with $ZnCl_2$,[131] followed by Pd-catalyzed Negishi cross-coupling with 4-iodobenzonitrile,[132] the functionalized bromopyridines **138ea–138ec** were isolated in 53–81% yield. In addition, 2-bromopyridines (**135f–135g**) led to the corresponding 2-magnesiated pyridines (**136f–136g**), which gave after thiomethylation or acylation with a Weinreb amide[133] the products **138f–138g** in 60–66% yield.



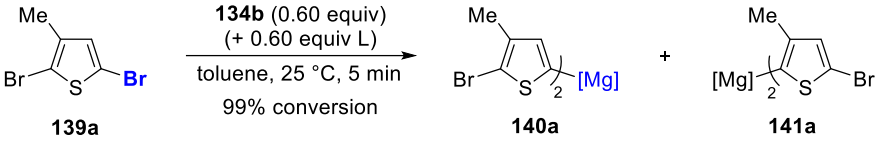
[a] CuCN·2LiCl cat. was used. [b] $ZnCl_2$ (1.30 equiv), $Pd(OAc)_2$ (4 mol%) and SPhos (8 mol%) were used.

Scheme 38: Reaction of various polybrominated (hetero)aromatics with *s*Bu_2Mg·2LiOR (**134b**), followed by electrophilic functionalization.

[131] A. Metzger, F. M. Piller, P. Knochel, *Chem. Commun.* **2008**, 5824.
[132] E. Negishi, Z. Huang, G. Wang, S. Mohan, C. Wang, H. Hattori, *Acc. Chem. Res.* **2008**, *41*, 1474.
[133] S. M. Weinreb, S. Nahm, *Tetrahedron Lett.* **1981**, *22*, 3815.

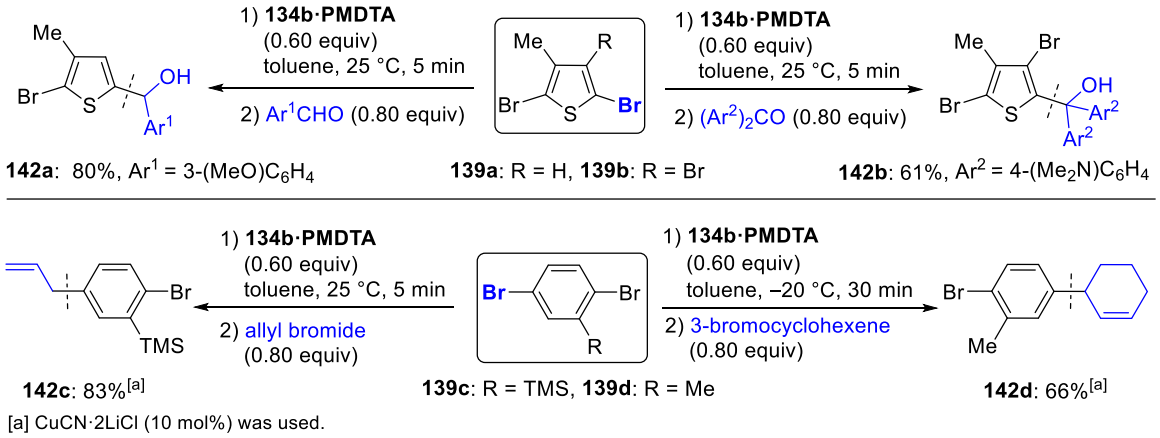
As an application, we have prepared the xanthone **138ab**, a precursor of a type II dehydroquinase inhibitor (antibacterial properties).[134] Thus, the selective magnesiation of **135a** followed by a Cu-catalyzed acylation with 2-fluorobenzoyl chloride produced the benzophenone **138aa** in 75% yield. BBr_3-deprotection of the methoxy group and mild K_2CO_3-mediated ring closure furnished the target xanthone in 96% yield (Scheme 38).[135]

We next got interested in 2,5-dibromo-3-methylthiophene (**139a**), for which the exchange reagent **134b** did not provide satisfactory regioselectivity (99% conversion, **140a**:**141a** = 90:10, Scheme 39). Since previous works have shown that, used as additives, Lewis donors[68,129] can enhance regioselectivities in halogen/metal exchange processes, we next probed the effect of adding TMEDA[136] or PMDTA (0.60 equiv) to **134b**, which led to the formation of **140a** with a better control of regioselectivity (96:4, 99% conversion for TMEDA, and 99:1, 99% conversion for PMDTA).



Scheme 39: Screening of the regioselective Br/Mg exchange on 2,5-dibromo-3-methylthiophene (**139a**).

Trapping of **140a** with 3-methoxybenzaldehyde afforded the alcohol **142a** in 80% yield (Scheme 40).



Scheme 40: Reaction of various polybrominated (hetero)aromatics with *s*Bu_2Mg·2LiOR in the presence of PMDTA (**134b·PMDTA**), followed by electrophilic functionalization.

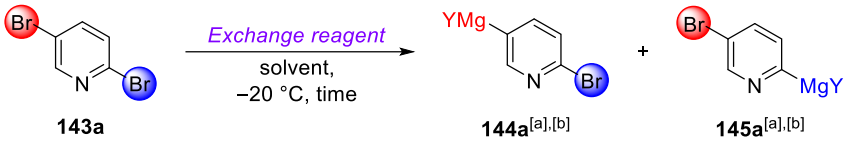
[134] a) P. J. Ballester, M. Mangold, N. I. Howard, R. L. Marchese Robinson, C. Abell, J. Blumberger, J. B. O. Mitchell, *J. R. Soc. Interface* **2012**, *9*, 3196; b) D. A. Robinson, K. A. Stewart, N. C. Price, P. A. Chalk, J. R. Coggins, A. J. Lapthorn, *J. Med. Chem.* **2006**, *49*, 1282.
[135] C. Zhou, R. C. Larock, *J. Org. Chem.* **2006**, *71*, 3551.
[136] F. M. Perna, A. Salomone, M. Dammacco, S. Florio, V. Capriati, *Chem. Eur. J.* **2011**, *17*, 8216.

This donor effect was quite general and the same procedure was extended to other polyhalogenated (hetero)arenes. Thus, **140b–140d** underwent complete Br/Mg exchange upon treatment with **134b·PMDTA**, leading to the less sterically hindered Grignard species. After allylation or addition to Michler's ketone, the polyfunctionalized products **142b–142d** were isolated in 61–83% yield.

1.3 Tunable Regioselectivity of the Br/Mg Exchange on Dibrominated Pyridines and Quinolines

Interestingly, investigating the reactivity of **134b** towards 2,5-dibromopyridine (**143a**)[129] established that the regioselectivity of the Br/Mg exchange can be finely tuned, changing from C(2) to C(5) in the presence of a Lewis donor such PMDTA (Table 2).

Table 2: Br/Mg exchange on 2,5-dibromopyridine (**143a**) using various exchange reagents.



143a **144a**[a],[b] **145a**[a],[b]

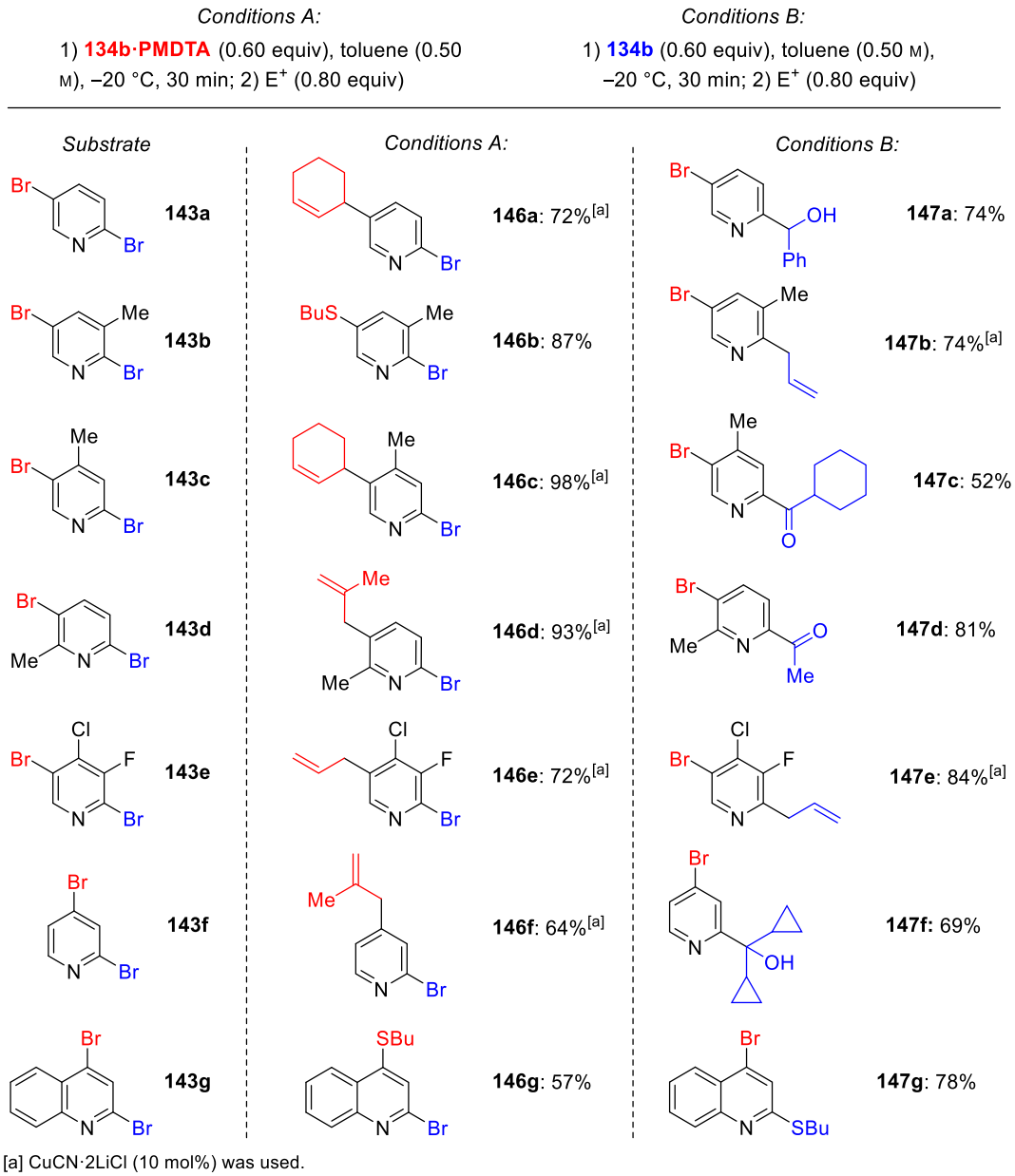
Entry	Exchange reagent[c]	Solvent	Time (min)	Ratio **144a**:**145a**	Conv. [%][d]
1	*i*PrMgCl·LiCl	THF	120	99:1	94[a]
2	*s*Bu$_2$Mg·2LiOR (**134b**)	toluene	30	1:99	99[b]
3	**134b·PMDTA**	toluene	30	99:1	99[b]

[a] Y = Cl·LiCl. [b] Y =pyridyl·2LiOR(·PMDTA). [c] R = 2-ethylhexyl, these reactions were carried out at 0.50 M using 1.20 equiv of alkylmagnesium species. Reagents are displayed accordingly to their stoichiometry and not their actual structure. [d] Conversion determined by GC-analysis of reaction aliquots after aqueous quench.

Thus, **143a** underwent selective Br/Mg exchange with *turbo*-Grignard *i*PrMgCl·LiCl at C(5) position to give the thermodynamically more favored product **144a** (entry 1). Alternatively, using *s*Bu$_2$Mg·2LiOR (**134b**) in neat toluene furnished the kinetic C(2)-magnesiation product **145a** (entry 2). While this regioselectivity is unprecedented for Br/Mg exchanges,[137] previous studies using organolithium reagents have shown that the C(2)-lithiation product isomerizes quickly to the more stable C(5)-lithiated species.[129] Furthermore this unusual regioselectivity can be switched to C(5)-magnesiation by adding PMDTA (0.60 equiv) to **134b** (entry 3). *Conditions A* and *B* described

[137] Song has reported C(2)-functionalization of **143a**, by replacing the Br at the C(2) position by I, followed by an I/Mg exchange step using *i*PrMgCl: J. J. Song, N. K. Yee, Z. Tan, J. Xu, S. R. Kapadia, C. H. Senanayake, *Org. Lett.* **2004,** *6*, 4905.

respectively in entries 3 and 2 of Table 2 were then applied to various dibromo-pyridines and -quinolines (Scheme 41).



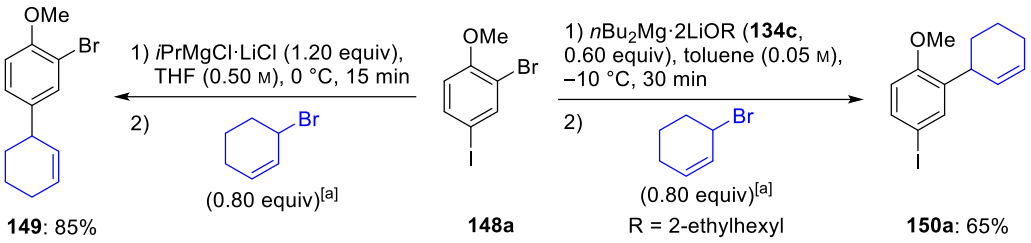
Scheme 41: Reaction of various dibrominated heteroaromatics with *s*Bu_2Mg·2LiOR·PMDTA (**134b·PMDTA**, *Conditions A*) or **134b** alone (*Conditions B*), followed by electrophilic quench.

Thus, following *Conditions A* (**134b·PMDTA**, 0.60 equiv, toluene, –20 °C, 30 min), **143a** was regioselectively converted into **144a** which was trapped with 3-bromocyclohexene, affording the C(5)-allylated product **146a** in 72% yield. Using *Conditions B* (**134b**, 0.60 equiv, toluene, –20 °C, 30 min), **143a** was regioselectively converted into **145a**, which was quenched with benzaldehyde, leading to the alcohol **147a** in 74% yield. Analogously, the methyl-substituted pyridines **143b–143d** produced either using *Conditions A* or *B* the expected regioisomeric pyridylmagnesium derivatives which were trapped by allylation, thioalkylation or acylation, affording **146b–146d** and **147b–147d** in 52–98% yield. The

electron-deficient 2,5-dibromo-4-chloro-3-fluoropyridine (**143e**) underwent smooth Br/Mg exchange under *Conditions A* or *B*, forming after addition of allyl bromide the allylated compounds **146e–147e** in 72–84% yield. This Br/Mg exchange was extended to 2,4-dibromopyridine (**143f**) and 2,4-dibromoquinoline (**143g**). The expected regioisomeric products **146f–146g** and **147f–147g** were isolated after thioalkylation, allylation or addition of dicyclopropyl ketone in 57–78% yield.

1.4 Competition between Br/Mg and I/Mg exchanges

Building on these findings we next assessed the reactivities of *i*PrMgCl·LiCl and *n*Bu_2Mg·2LiOR (**134c**) towards 2-bromo-4-iodoanisole (**148a**, Scheme 42).[138] For this substrate, Li-directing effects should favor the Br/Mg exchange *ortho* to the donating OMe group, whereas considering purely the activation of the C-halogen bond, functionalization at the C(4) position *via* I/Mg exchange should be preferred. Unsurprisingly, *turbo*-Grignard in neat THF reacts with the most activated site of **148a**, undergoing exclusively I/Mg exchange, affording, after allylation, the anisole derivative **149** in 85% yield. However, a completely different scenario plays out for **134c** in toluene, where coordination effects dominate, encouraging reactivity *ortho* to the directing OMe group and hence triggering a Br/Mg exchange with a selectivity of 4:1. Subsequent allylation and chromatographical separation furnished **150a** in 65% yield (Scheme 42). Supporting this interpretation, and demonstrating the importance of non-coordinating solvent toluene, addition of polydentate donor PMDTA which can chelate Li, switches off this Br/Mg exchange preference, offering an I/Mg exchange only.[138]



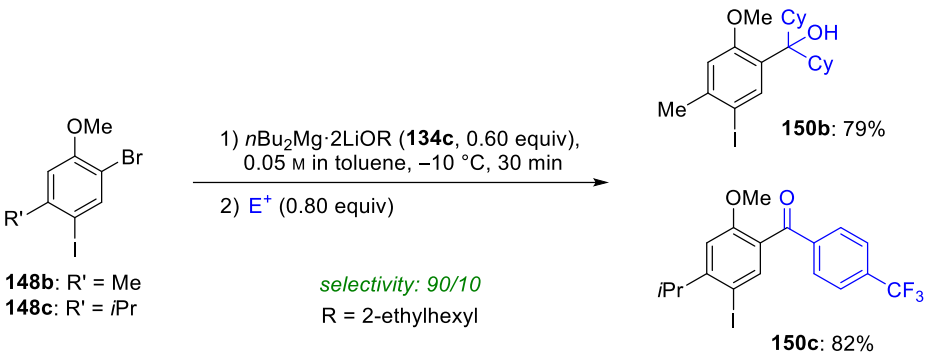
149: 85% **148a** **150a**: 65%

[a] CuCN·2LiCl (10 mol%) was used.

Scheme 42: Selective Br/Mg exchange on 2-bromo-4-iodoanisole (**148a**) with *n*Bu_2Mg·2LiOR (**134c**) followed by allylation reaction: comparison with *i*PrMgCl·LiCl.

Finally, replacing 2-bromo-4-iodoanisole (1**48a**) with 2-bromo-4-iodo-5-methylanisole (**148b**) or 2-bromo-4-iodo-5-isopropylanisole (**148c**) allowed an improvement of selectivity to 9:1 when using **134c**. After reaction with dicyclohexyl ketone or *N*-methoxy-*N*-methyl-4-(trifluoromethyl)benzamide followed by chromatographical separation, the alcohol **150b** and ketone **150c** could be isolated in 79–82% yield (Scheme 43).

[138] See Experimental Part (p. 95–98) for a complete table of optimization as well as additional results.

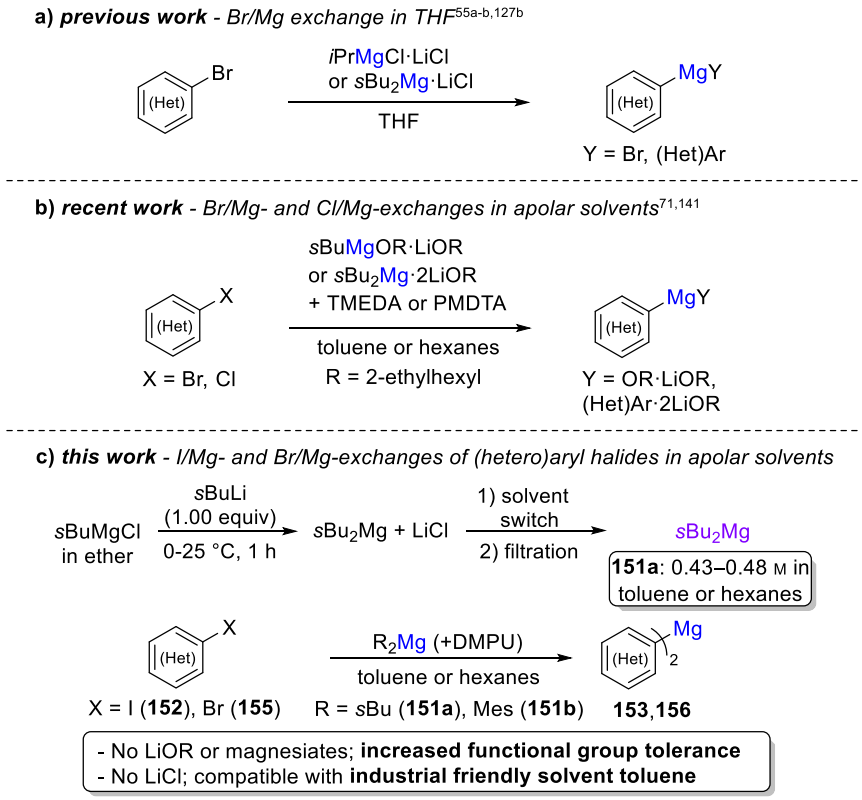


Scheme 43: Selective Br/Mg exchange on 2-bromo-4-iodo-5-methylanisole (**148b**) and 2-bromo-4-iodo-5-isopropylanisole (**148c**) with *n*Bu_2Mg·2LiOR (**134c**) followed by electrophilic quench.

2 Preparation of Functionalized Diorganomagnesium Reagents in Toluene *via* Bromine or Iodine/Magnesium Exchange Reactions

2.1 Introduction

Polyfunctionalized organometallic reagents are essential intermediates in modern organic chemistry.[1b,8,125a,139] Furthermore, organomagnesium reagents are ideal for industrial applications as they combine excellent functional group tolerance with high reactivity while being available at moderate cost and having moderate toxicity.[1c,140] One of the best methods for preparing Grignard reagents in ethereal solvents is the halogen/magnesium exchange, which has been well-established since the development of *i*PrMgCl·LiCl (*turbo*-Grignard; Scheme 44a).[55a-b,127b]



Scheme 44: Current halogen/magnesium exchange reagents, preparation and use of *s*Bu_2Mg (**151a**) in apolar solvents.

[139] a) R. H. V. Nishimura, N. Weidmann, P. Knochel, *Synthesis* **2020**, *52*, 3036; b) C. P. Tüllmann, S. Steiner, P. Knochel, *Synthesis* **2020**, *52*, 2357; c) J. Skotnitzki, A. Kremsmair, B. Kicin, R. Saeb, V. Ruf, P. Knochel, *Synthesis* **2020**, *52*, 873; d) J. Skotnitzki, A. Kremsmair, P. Knochel, *Synthesis* **2020**, *52*, 189; e) N. Weidmann, R. H. V. Nishimura, J. H. Harenberg, P. Knochel, *Synthesis* **2021**, *53*, 557; f) A. Kremsmair, S. Graßl, C. J. B. Seifert, E. Godineau, P. Knochel, *Synthesis* **2021**, *ahead of print*, 10.1055/a-1534-0624.
[140] A. Kremsmair, J. H. Harenberg, K. Schwärzer, A. Hess, P. Knochel, *Chem. Sci.* **2021**, *12*, 6011.

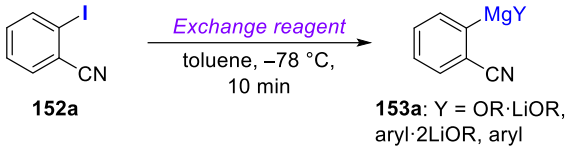
Recently, we have reported a halogen/magnesium exchange in apolar solvents using new reagents of the type *s*BuMgOR·LiOR (**134a**, R = 2-ethylhexyl) and *s*Bu_2Mg·2LiOR (**134b**; Scheme 44b).[71,141,142] The use of toluene or related hydrocarbon solvents was attractive for industrial applications and deserved further investigation.[143]

Herein, we now report new I/Mg- and Br/Mg-exchange reactions on various (hetero)aryl halides in apolar solvents using *s*Bu_2Mg (**151a**),[144] which was readily prepared by reaction of *s*BuMgCl in diethyl ether with *s*BuLi (1.00 equiv) in cyclohexane at 25 °C (2 h). After a solvent switch to toluene and filtration, *s*Bu_2Mg was obtained in 96% yield as a 0.43–0.48 M solution in toluene (Scheme 44c).[145] This method was successfully extended to alkenyl iodides to provide dialkenylmagnesium species in toluene that reacted well with various electrophiles.

2.2 Optimization and Scope of the I/Mg Exchange on Aryl and Heteroaryl Iodides

First, we investigated the I/Mg exchange on 2-iodobenzonitrile (**152a**) in toluene using various exchange reagents (Table 3).

Table 3: Optimization of the I/Mg exchange on 2-iodobenzonitrile (**152a**), leading to magnesium reagents of type **153**.



152a **153a**: Y = OR·LiOR, aryl·2LiOR, aryl

Entry	Exchange reagent (equiv)[a]	Yield [%][b]
1	*s*BuMgOR·LiOR (**134a**, 1.20 equiv)	42
2	*s*Bu_2Mg·2LiOR (**134b**, 0.60 equiv)	61
3	*s*Bu_2Mg (**151a**, 0.60 equiv)	98

[a] R = 2-ethylhexyl, these reactions were carried out at a concentration of 0.50 M. All reagents were displayed accordingly to their stoichiometry and not their actual structure. [b] Calibrated yields determined by GC-analysis of reaction aliquots after Cu-catalyzed allylation.

[141] a) D. S. Ziegler, B. Wei, P. Knochel, *Chem. Eur. J.* **2019**, *25*, 2695; b) A. Desaintjean, T. Haupt, L. J. Bole, N. R. Judge, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2021**, *60*, 1513; c) L. J. Bole, N. R. Judge, E. Hevia, *Angew. Chem. Int. Ed.* **2021**, *60*, 7626.
[142] For a related halogen/zinc exchange, see: M. Balkenhohl, D. S. Ziegler, A. Desaintjean, L. J. Bole, A. R. Kennedy, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2019**, *58*, 12898.
[143] a) *Solvent Recovery Handbook* (Ed.: I. M. Smallwood), Blackwell Science Ltd., Oxford, **2002**; b) L. Delhaye, A. Ceccato, P. Jacobs, C. Köttgen, A. Merschaert, *Org. Process Res. Dev.* **2007**, *11*, 160.
[144] This reagent still contained 0.50 equiv of Et_2O, having the formula *s*Bu_2Mg·0.5Et_2O (determined by ^{1}H-NMR analysis) that we abbreviated *s*Bu_2Mg for the sake of clarity: A. Hess, J. P. Prohaska, S. B. Doerrich, F. Trauner, F. H. Lutter, S. Lemaire, S. Wagschal, K. Karaghiosoff, P. Knochel, *Chem. Sci.* **2021**, *12*, 8424.
[145] The same reactivity was observed after 5 days of storage of the *s*Bu_2Mg toluene solution at –20 °C.

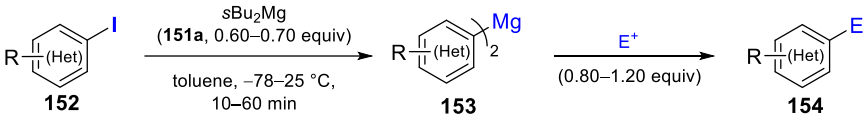
We treated **152a** with *s*BuMgOR·LiOR (R = 2-ethylhexyl, **134a**)[71,141] in toluene at −78 °C for 10 min, which led to the organomagnesium species **153a** (Y = OR·LiOR) in 42% yield (Table 3, entry 1). In an attempt to improve the yield of this exchange reaction, **134a** was replaced with *s*Bu_2Mg·2LiOR (**134b**).[71,141] Thus, treatment of **152a** with **134b** at −78 °C led after 10 min to the magnesium reagent **153a** (Y = aryl·2LiOR) in 61% yield (Table 3, entry 2). However, using *s*Bu_2Mg (**151a**, 0.60 equiv), the magnesiation of **152a** was complete after 10 min at −78 °C, affording **153a** (Y = aryl) in 98% yield (Table 3, entry 3).

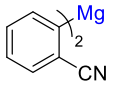
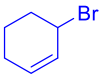
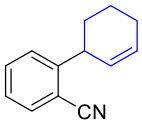
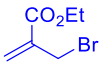
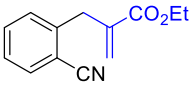
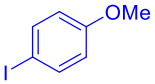
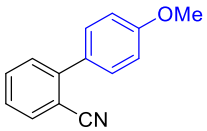
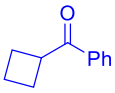
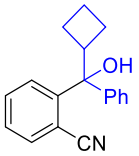
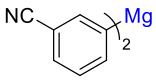
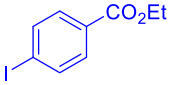
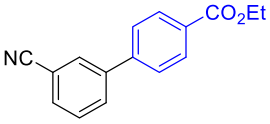
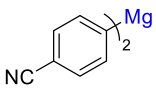
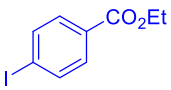
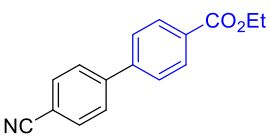
Subsequently, after Cu(I)-catalyzed allylation[130] of **153a** with 3-bromocyclohexene and ethyl 2-(bromomethyl)acrylate, transmetalation with $ZnCl_2$[131] followed by Pd-catalyzed Negishi cross-coupling with 4-iodoanisole,[132] or addition to a ketone, the functionalized benzonitriles **154aa**–**154ad** were isolated in 55–98% yield (Table 4, entries 1–4). Similarly, the iodobenzonitrile derivatives **152b**–**152d** underwent a complete I/Mg exchange upon treatment with **151a** (−78 °C, 10 min). The corresponding diarylmagnesium reagent (**153b**–**153d**) underwent Pd-catalyzed cross-couplings with ethyl 4-iodobenzoate, or a Cu-mediated acylation with 4-chlorobenzoyl chloride, producing the biaryl compounds **154b**–**154d** in 70–76% yield (entries 5–7). Analogously, ethyl 2-iodobenzoate (**152e**) was converted into the corresponding organomagnesium compound **153e**, which gave after allylation with methallyl bromide the ester **154e** in 92% yield (entry 8). Also, the reaction of *s*Bu_2Mg (**151a**, 0.60 equiv) with the halogenated iodopyridines **152f**–**152g** generated within 15 min the corresponding heteroaryl organomagnesium compounds **153f**–**153g**. After acylation or addition to 2-adamantanone, the polyfunctionalized heterocycles **154fa**–**154fb** and **154g** were obtained in 73–75% yield (entries 9–11). The diiodoanisole derivatives **152h**–**152i** reacted smoothly with **151a** and provided after allylation and addition to benzaldehyde the products **154h**–**154i** in 51–53% yield (entries 12–13). Electron-rich substrates such as the anisole derivatives **152j**–**152l** and the silyl ether **152m** were quantitatively converted into the corresponding diorganomagnesium reagents **153j**–**153m**. They reacted with a range of electrophiles to afford **154ja**–**154jb**, **154ka**–**154kc** and **154l**–**154m** in 60–94% yield (entries 14–20). Interestingly, 2-bromo-4-iodotoluene (**152n**) underwent selective I/Mg exchange to provide, after reaction with a ketone, the alcohol **154n** in 53% yield (entry 21). In addition, aryl polyiodides (**152o**–**152q**) led to the corresponding mono-magnesiated aryl iodides **153o**–**153q** when the exchange was performed in the presence of DMPU (*N*,*N*′-dimethylpropyleneurea, 1.00 equiv),[146] which furnished after allylation, addition to benzaldehyde derivatives or to ethyl cyanoformate the products **154oa**–**154ob**, **154pa**–**154pb**, and **154q** in 45–73% yield (entries 22–26). An extension of this method was possible by switching from *s*Bu_2Mg (**151a**) to Mes_2Mg (**151b**, Mes = mesityl) in the case of particularly sensitive

[146] When used in association with R_2Mg (**151a**, R = *s*Bu; **151b**, R = Mes), DMPU increases the exchange rate, thus improving conversions and diminishing side reactions: a) T. Mukhopadhyay, D. Seebach, *Helv. Chim. Acta* **1982**, *65*, 385; b) A. D. Benischke, G. Le Corre, P. Knochel, *Chem. Eur. J.* **2017**, *23*, 778; c) M. Bengtsson, T. Liljefors, *Synthesis* **1988**, 250; d) E. Riguet, I. Klement, C. K. Reddy, G. Cahiez, P. Knochel, *Tetrahedron Lett.* **1996**, *37*, 5865; e) M. Ellwart, I. S. Makarov, F. Achrainer, H. Zipse, P. Knochel, *Angew. Chem. Int. Ed.* **2016**, *55*, 10502.

aryl iodides.[147] This exchange reagent was prepared analogously to *s*Bu_2Mg (**151a**). Thus, mixing the aryl iodide bearing a triazine moiety (**152r**) with **151b** in the presence of DMPU (1.00–4.00 equiv)[146] afforded after allylation with allyl bromide the arene **154r** in 79% yield (entry 27). Under similar conditions, the diarylmagnesium species generated from 2-iodo-nitrobenzene derivatives **152s**–**152t** were allylated, providing the nitro-substituted compounds **154s**–**154t** in 60–71% yield (entries 28–29).

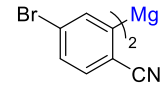
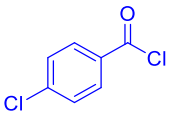
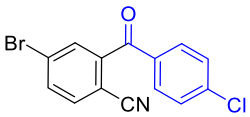
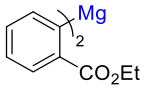
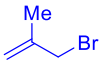
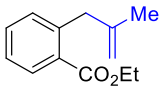
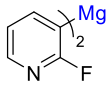
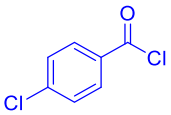
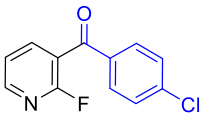
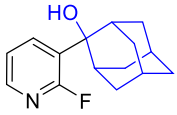
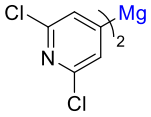
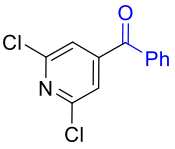
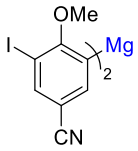
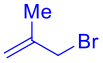
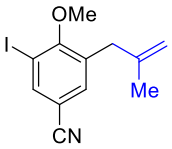
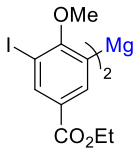
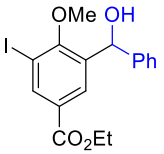
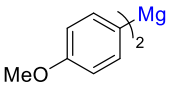
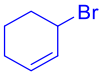
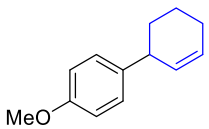
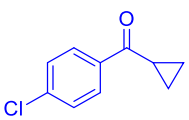
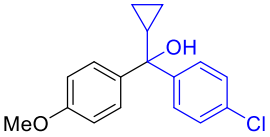
Table 4: Reaction of various aryl iodides with R_2Mg (**151a**, R = sBu; **151b**, R = Mes), followed by electrophilic functionalization.[148]

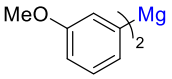
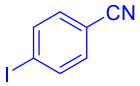
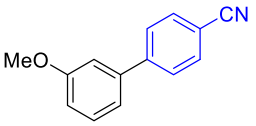
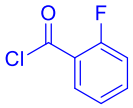
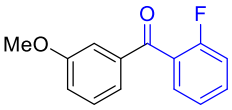
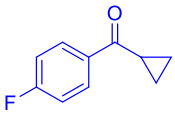
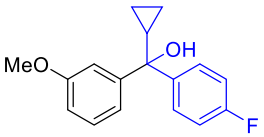
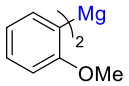
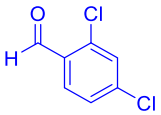
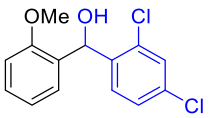
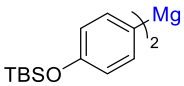
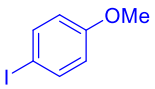
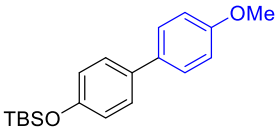
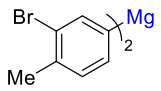
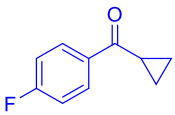
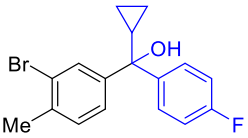
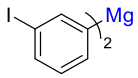
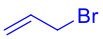
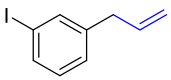
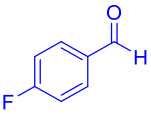
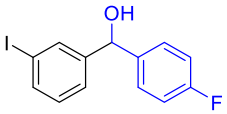
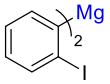
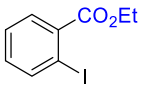
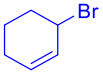
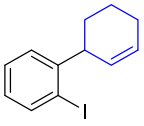


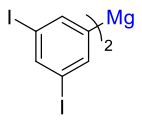
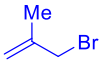
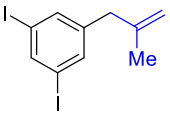
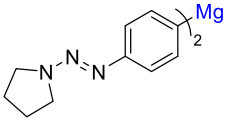
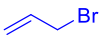
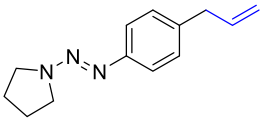
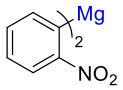
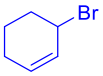
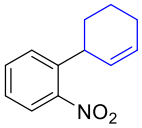
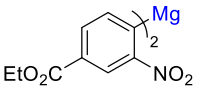
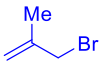
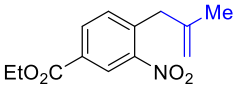
Entry	Magnesium reagent (°C, min)	Electrophile[a] (0.80–1.20 equiv)	Product, yield [%][b]
1	 **153a** (–78, 10)		 **154aa**: 98
2	**153a** (–78, 10)		 **154ab**: 88
3	**153a** (–78, 10)		 **154ac**: 73
4	**153a** (–78, 10)		 **154ad**: 55
5	 **153b** (–78, 10)		 **154b**: 72
6	 **153c** (–78, 10)		 **154c**: 70

[147] Arylmetal reagents tolerate more functional groups than their alkyl counterparts: A. D. Benischke, L. Anthore-Dalion, F. Kohl, P. Knochel, *Chem. Eur. J.* **2018**, *24*, 11103.

[148] The synthesis of all starting materials as well as the corresponding literature were depicted in the Experimental Part (p. 127–134).

7	 **153d** (–78, 10)		 **154d**: 76
8	 **153e** (–78, 15)		 **154e**: 92
9	 **153f** (–78, 15)		 **154fa**: 73
10[c]	**153f** (–78, 15)	adamantanone	 **154fb**: 74
11	 **153g** (–78, 15)	benzoyl chloride	 **154g**: 75
12	 **153h** (–78, 15)		 **154h**: 51
13	 **153i** (–78, 15)	PhCHO	 **154i**: 53
14[c]	 **153j** (25, 30)		 **154ja**: 78
15[c]	**153j** (25, 30)		 **154jb**: 63

16[c]	 **153k** (25, 30)		 **154ka**: 88
17[c]	**153k** (25, 30)		 **154kb**: 60
18[c]	**153k** (25, 30)		 **154kc**: 94
19[c]	 **153l** (25, 30)		 **154l**: 75
20[c]	 **153m** (25, 30)		 **154m**: 65
21[c]	 **153n** (25, 30)		 **154n**: 53
22[d]	 **153o** (–20, 60)		 **154oa**: 65
23[d]	**153o** (–20, 60)		 **154ob**: 73
24[d]	 **153p** (–20, 60)		 **154pa**: 45
25[d]	**153p** (–20, 60)		 **154pb**: 64

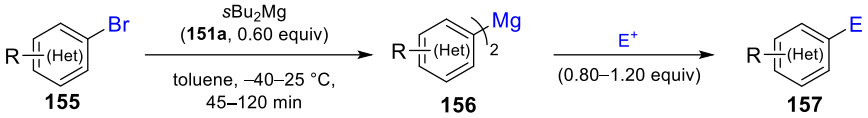
26[d]	 **153q** (–20, 60)		 **154q**: 66
27[e]	 **153r** (–20, 60)		 **154r**: 79
28[e]	 **153s** (–50, 60)		 **154s**: 71
29[e]	 **153t** (–70, 60)		 **154t**: 60

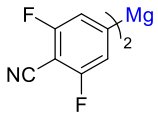
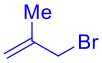
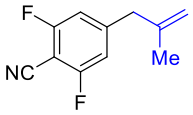
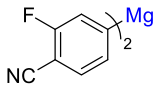
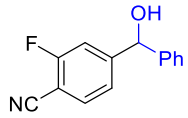
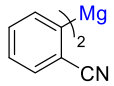
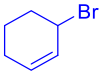
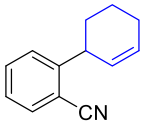
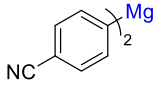
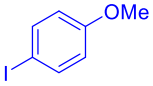
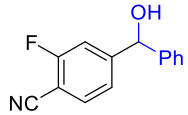
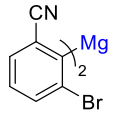
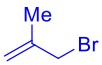
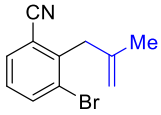
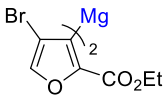
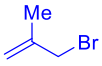
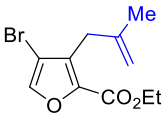
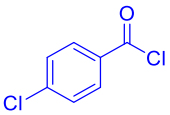
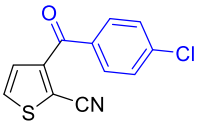
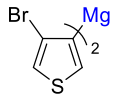
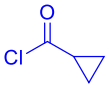
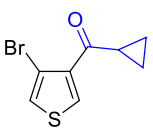
[a] See Experimental Part (p. 135–154) for detailed electrophilic trappings. [b] Isolated yield of analytically pure product. [c] THF (1.20 equiv) was used. [d] DMPU (1.00 equiv) was used. [e] Mes_2Mg (0.60 equiv) in the presence of DMPU (1.00–4.00 equiv) were used.

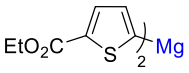
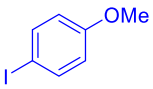
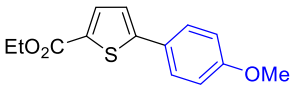
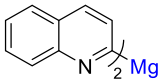
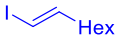
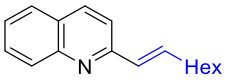
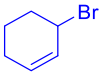
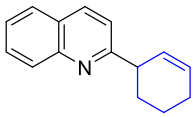
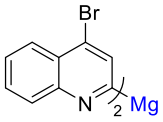
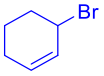
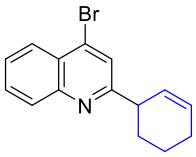
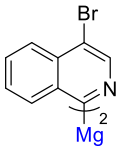
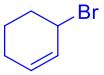
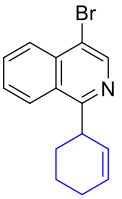
2.3 Optimization and Scope of the Br/Mg Exchange on Aryl and Heteroaryl Bromides

We next turned our attention to (hetero)aryl bromides (Table 5). Thus, the bromobenzonitrile derivatives **155a**–**155e** underwent smooth Br/Mg exchanges with *s*Bu_2Mg in the presence of DMPU (1.00 equiv)[146] within 2 h at −20 °C, generating the diarylmagnesium reagents **156a**–**156e**. After allylation, addition to benzaldehyde or transmetalation with $ZnCl_2$ followed by Pd-catalyzed Negishi cross-coupling with 4-iodoanisole, the corresponding products (**157a**–**157e**) were obtained in 55–98% yield (entries 1–5). Under similar conditions, the dibromofuran **155f** led within 90 min at −20 °C to the di(bromofuryl)magnesium species **156f**, which furnished, after allylation with methallyl bromide, the alkylated furan **157f** in 51% yield (entry 6). More electron-poor thiophenes **155g**–**155i** reacted quantitatively with **151a** solely, providing the magnesiated thiophenes **156g**–**156i**. After acylation or cross-coupling with 4-iodoanisole, the functionalized thiophenes **157g**–**157i** were isolated in 63–91% yield (entries 7–9). Analogously, the bromoquinolines **155j**–**155k** and bromoisoquinoline **155l** underwent complete Br/Mg exchange upon treatment with **151a** (25 °C, 60 min). The corresponding diheteroarylmagnesium compound (**156j**–**156l**) were smoothly engaged in a Pd-catalyzed cross-coupling with (*E*)-1-iodooct-1-ene or a Cu-catalyzed allylation with 3-bromocyclohexene, producing the functionalized (iso)quinolines **157ja**–**157jb** and **157k**–**157l** in 70–79% yield (entries 10–13).

Table 5: Reaction of various aryl- and heteroaryl- bromides with *s*Bu$_2$Mg (**151a**), followed by trapping with electrophiles leading to products of type **157**.[148]



Entry	Magnesium reagent (°C, min)	Electrophile[a] (0.80–1.20 equiv)	Product, yield [%][b]
1[c]	 **156a** (–20, 120)		 **157a**: 98
2[c]	 **156b** (–20, 120)	PhCHO	 **157b**: 62
3[c]	 **156c** (–20, 120)		 **157c**: 79
4[c]	 **156d** (–20, 120)		 **157d**: 55
5[c]	 **156e** (–20, 120)		 **157e**: 85
6[c]	 **156f** (–20, 90)		 **157f**: 51
7	 **156g** (–20, 45)		 **157g**: 91
8	 **156h** (–20, 45)		 **157h**: 63

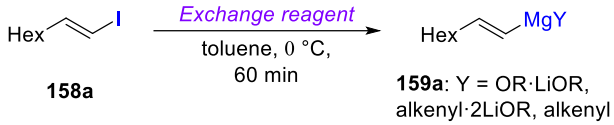
9	 **156i** (–40, 45)		 **157i**: 72
10	 **156j** (25, 60)		 **157ja**: 78
11	**156j** (25, 60)		 **157jb**: 70
12[d]	 **156k** (25, 60)		 **157k**: 71
13	 **156l** (25, 60)		 **157l**: 79

[a] See Experimental Part (p. 154–163) for detailed electrophilic trappings. [b] Isolated yield of analytically pure product. [c] DMPU (1.00 equiv) was used. [d] A 97:3 ratio of the regioisomers was obtained.

2.4 Optimization and Scope of the I/Mg Exchange on Alkenyl Iodides

We further studied the reactivity of the exchange reagents with alkenyl iodides in toluene (Table 6). First, we treated (*E*)-1-iodooct-1-ene (**158a**) with the previously described *s*BuMgOR·LiOR (R = 2-ethylhexyl, **134a**) and *s*Bu_2Mg·2LiOR (**134b**) in toluene at 0 °C for 60 min, which both led to a total decomposition of **158a** (entries 1–2). In an attempt to achieve a full exchange reaction, we mixed **158a** with **151a** under various conditions. Thus, treatment of **158a** with **151a** at 0 °C led after 60 min to **159a** (Y = alkenyl) in 6% yield (entry 3). However, using *s*Bu_2Mg (**151a**, 0.60 equiv) in the presence of DMPU (1.00 equiv)[146] led to a complete magnesiation of **158a** after 60 min at 0 °C, affording **159a** (Y = alkenyl) in 99% yield (entry 4).

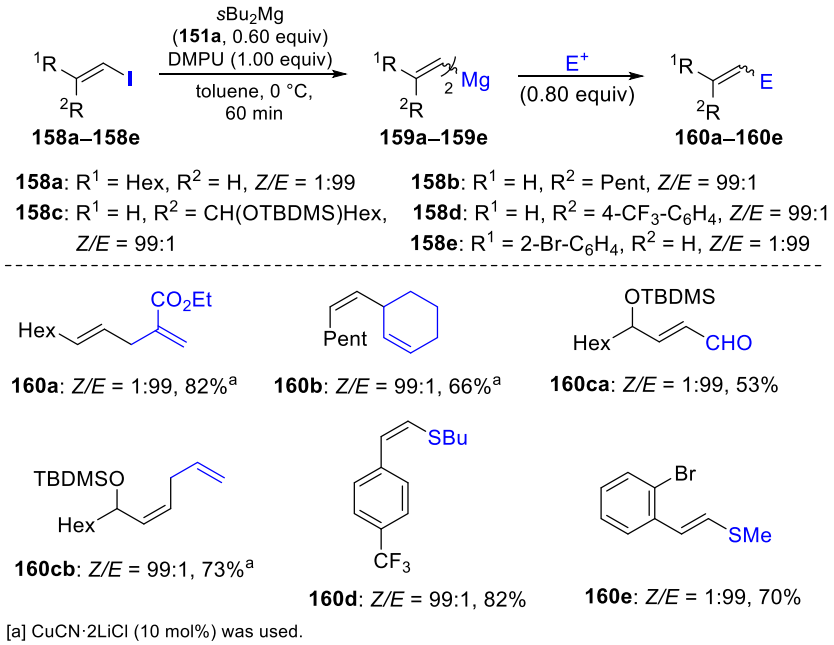
Table 6: Screening of the I/Mg exchange on (*E*)-1-iodooct-1-ene (**158a**).



Entry	Exchange reagent (equiv)[a]	Yield [%][b]
1	*s*BuMgOR·LiOR (**134a**, 1.20 equiv)	0
2	*s*Bu$_2$Mg·2LiOR (**134b**, 0.60 equiv)	0
3	*s*Bu$_2$Mg (**151a**, 0.60 equiv)	6
4	*s*Bu$_2$Mg (**151a**, 0.60 equiv) + DMPU (1.00 equiv)	99

[a] R = 2-ethylhexyl, these reactions were carried out at a concentration of 0.50 M. All reagents were displayed accordingly to their stoichiometry and not their actual structure. [b] Calibrated yields determined by GC-analysis of reaction aliquots quenched with water. 0% yield indicates that full decomposition was observed.

The newly formed dialkenylmagnesium reagent **159a** smoothly reacted in toluene with ethyl 2-(bromomethyl)acrylate in the presence of copper to provide the allylated (*E*)-alkene **160a** in 82% yield (Scheme 45).



Scheme 45: Reaction of various alkenyl iodides with *s*Bu$_2$Mg (**151a**) in the presence of DMPU, followed by electrophilic functionalization.[148]

The exchange on (*Z*)-1-iodohept-1-ene (**158b**) followed by allylation proceeded with retention of the configuration, affording the (*Z*)-alkene **160b** in 66% yield and *Z*/*E* = 99:1. In addition, the protected allylic alcohol **158c** underwent retentive I/Mg exchange with **151a** within 60 min at 0 °C, providing the

(*Z*)-dialkenyl magnesium species **159c** (*Z*/*E* = 99:1). On the one hand, when **159c** reacted with DMF, the unsaturated aldehyde was fully isomerized to its (*E*)-isomer, providing **160ca** in 53% yield. On the other hand, an allylation with allyl bromide generated the *Z*-alkene **160cb** in 73% yield. Finally, the (*Z*)-alkene **158d** and *E*-alkene **158e** furnished after thioalkylation the corresponding alkenes **160d** and **160e** with retention of configuration in 70–82% yield.

3 Preparation of Polyfunctional Arylzinc Organometallics in Toluene *via* Halogen/Zinc Exchange Reactions

3.1 Introduction

Organozinc reagents represent key intermediates in organic synthesis as they are mild and they tolerate many functional groups. For that reason, they widely participate in transition-metal-catalyzed C-C bond forming reactions.[149] Especially, (hetero)aryl zinc halides have been readily used for accessing complex organic molecules.[150] Organozinc compounds can be generated by directed insertion of zinc powder to organic halides[27b,28a,30,151] but also by directed metalation using TMP-zinc bases.[94,96,105] Halogen/zinc exchange using lithium organozincates of type R_3ZnLi or R_4ZnLi_2 have also been reported.[152] Moreover, a Li(acac)-catalyzed I/Zn exchange has been performed on (hetero)aryl iodides using pyrophoric and light sensitive *i*Pr_2Zn in NMP.[77a] Unfortunately, the corresponding less expensive aryl or heteroaryl bromides are not reactive enough to be used as substitutes. The exchange reagent *i*PrMgCl·LiCl (*turbo*-Grignard) has been extensively used to prepare related organomagnesium species, since it allows high reaction rates for the Br/Mg exchange reaction.[55a] This exchange can be further accelerated by using a stronger donor such as a lithium alkoxide (ROLi; R = 2-ethylhexyl) instead of LiCl.[71] This exchange could even be performed in the industrially friendly solvent toluene. Herein, we report a new I/Zn exchange and firstly, a Br/Zn exchange using a bimetallic exchange reagent of type *s*Bu_2Zn·2LiOR (**161**), which allows the preparation of a wide range of polyfunctional (hetero)arylzinc reagents.[123,153]

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[149] a) E. Negishi, *Acc. Chem. Res*. **1982**, *15*, 340; b) P. Knochel, R. D. Singer, *Chem. Rev.* **1993**, *93*, 2117; c) P. Knochel, N. Millot, A. L. Rodriguez, C. E. Tucker, in *Preparation and Applications of Functionalized Organozinc Compounds. Organic Reactions. Vol. 58*, Wiley-VCH, Weinheim, **2004**, 417; d) E. Negishi, *Angew. Chem. Int. Ed*. **2011**, *50*, 6738; e) *Metal-Catalyzed Cross-Coupling Reactions, Second Edition* (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2008**; f) Y.-H. Chen, M. Ellwart, V. Malakhov, P. Knochel, *Synthesis* **2017**, *49*, 3215.

[150] a) T. J. Greshock, K. P. Moore, R. T. McClain, A. Bellomo, C. K. Chung, S. D. Dreher, P. S. Kutchukian, Z. Peng, I. W. Davies, P. Vachal, M. Ellwart, S. M. Manolikakes, P. Knochel, P. G. Nantermet, *Angew. Chem. Int. Ed.* **2016**, *55*, 13714; b) Y. H. Chen, M. Ellwart, G. Toupalas, Y. Ebe, P. Knochel, *Angew. Chem. Int. Ed.* **2017**, *56*, 4612; c) Y. H. Chen, C. P. Tüllmann, M. Ellwart, P. Knochel, *Angew. Chem. Int. Ed.* **2017**, *56*, 9236.

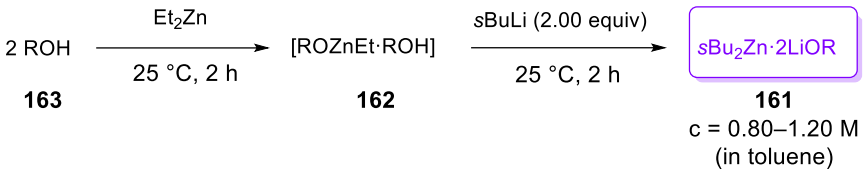
[151] a) C. Y. Liu, X. Wang, T. Furuyama, S. Yasuike, A. Muranaka, K. Morokuma, M. Uchiyama, *Chem. Eur. J.* **2010**, *16*, 1780; b) R. D. Rieke, *Science* **1989**, *246*, 1260; c) R. D. Rieke, M. V. Hanson, *Tetrahedron* **1997**, *53*, 1925.

[152] a) M. Uchiyama, T. Furuyama, M. Kobayashi, Y. Matsumoto, K. Tanaka, *J. Am. Chem. Soc.* **2006**, *128*, 8404; b) T. Furuyama, M. Yonehara, S. Arimoto, M. Kobayashi, Y. Matsumoto, M. Uchiyama, *Chem. Eur. J.* **2008**, *14*, 10348; c) L. Melzig, C. R. Diène, C. J. Rohbogner, P. Knochel, *Org. Lett.* **2011**, *13*, 3174; d) D. Tilly, F. Chevallier, F. Mongin, P. C. Gros, *Chem. Rev.* **2014**, *114*, 1207.

[153] The compounds **166d**–**166g**,**166j**,**166q**,**166s**–**166u**, **169c**–**169d**,**169l**–**169q** and **170a**–**170m** were prepared by Dr. M. Balkenhohl and Dr. D.S. Ziegler and will be shown for the sake of completeness. See: M. Balkenhohl, Dissertation, **2019**, LMU München.

3.2 Optimization and Scope of the I/Zn Exchange on Aryl and Heteroaryl Iodides

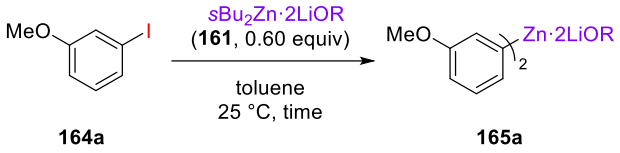
Thus, we have prepared several zinc alkoxides ROZnEt·ROH of type **162** by treating Et_2Zn (25 °C, 2 h) with various alcohols (2.00 equiv, **163**) in toluene.[154] These zinc alkoxides (**162**) further reacted with *s*BuLi (2.00 equiv, in cyclohexane) within 2 h at 25 °C to generate the bimetallic reagent tentatively represented as $sBu_2Zn{\cdot}2LiOR$ (**161**). Removal of the solvents and further redissolution in toluene provided a light-yellow solution of **161** (c = 0.80–1.20 M in toluene; Scheme 46) which can be stored at 25 °C over months without significant loss of reactivity.

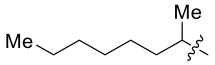
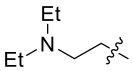
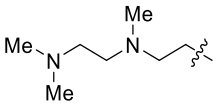


Scheme 46: Preparation of bimetallic exchange reagents of type **161**.

First, the complex $sBu_2Zn{\cdot}2LiOR$ (R = 2-octyl; **161a**) reacted in toluene[155] with 3-iodoanisole (**164a**) within 30 min at 25 °C, producing bis-anisylzinc (**165a**) in 23% yield, as determined by GC-analysis of reaction aliquots (Table 7, entry 1).

Table 7: Optimization of the reaction conditions for the I/Zn exchange using dialkylzinc reagents of type **161**.

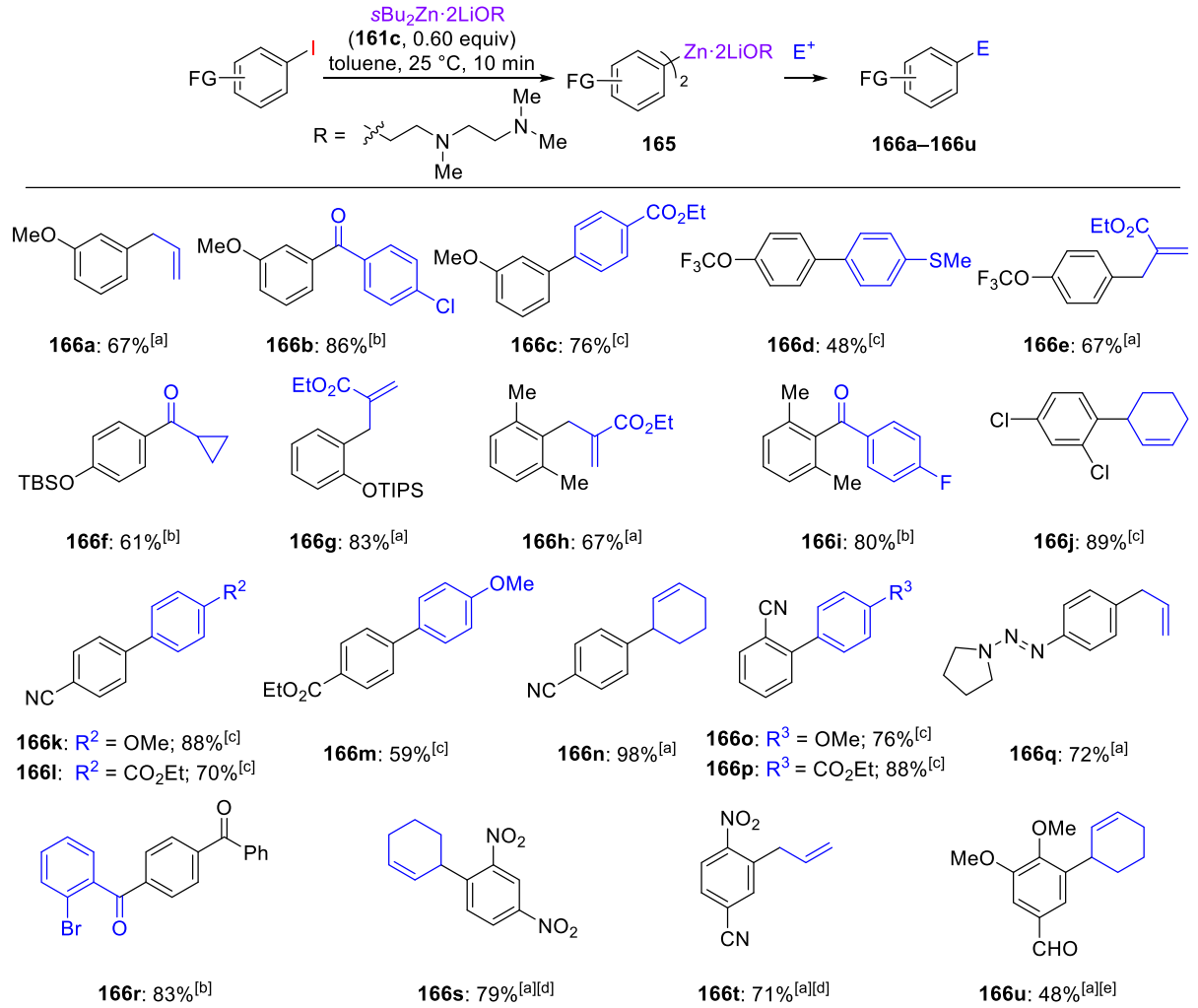


Entry	*s*$Bu_2Zn{\cdot}2LiOR$ (**161**)	Time (min)	Yield [%][a]
1	**161a**; R = 	30	23
2	**161b**; R = 	30	95
3	**161c**; R = 	30	99
4	**161c**	1	99

[a] Yield of **165a** determined by GC-analysis of reaction aliquots quenched with water.

[154] a) R. L. Geerts, J. C. Huffman, K. G. Caulton, *Inorg. Chem.* **1986**, *25*, 1803; b) S. C. Goel, M. Y. Chiang, W. E. Buhro, *Inorg. Chem.* **1990**, *29*, 4646; c) K. Merz, S. Block, R. Schoenen, M. Driess, *Dalton Trans.* **2003**, 3365.
[155] A solvent screening showed, that the halogen/zinc exchange can not only be performed in hydrocarbons such as toluene or hexane, but also in other industrially friendly ethereal solvents such as 2-methyl-THF or MTBE.

The use of alcohols bearing *N*-coordination sites further improved the I/Zn exchange.[70] Indeed, the complex **161b** (R = -$CH_2CH_2N(Et)_2$) led to the diarylzinc **165a** in 95% yield (entry 2). A great improvement was made by using an alcohol bearing a second *N*-coordination site. Thus, the new reagent **161c** (R = -$CH_2CH_2N(CH_3)CH_2CH_2N(CH_3)_2$) led to the formation of **165a** in 99% yield (entry 3). In fact, after 1 min reaction time, the I/Zn exchange was already complete (entry 4). The resulting bis-anisylzinc reagent **165a** reacted with allyl bromide in the presence of CuI (20 mol%) to give the allylated arene **166a** in 67% yield (Scheme 47). Transmetalation of **165a** to copper using CuI (0.60 equiv) followed by addition of 4-chlorobenzoyl chloride provided the acylated anisole **166b** in 86% yield.



[a] CuI (20 mol%) was used. [b] CuI (0.60 equiv) was used. [c] $Pd(OAc)_2$ (3 mol%) and SPhos (6 mol%) was used. [d] *p*Tol_2Zn·2LiOR (**167**, 0.60 equiv, –15 °C, 15 min) was used. [e] *t*Bu_2Zn·2LiOR (**168**, 0.80 equiv, 0 °C, 10 min) was used.

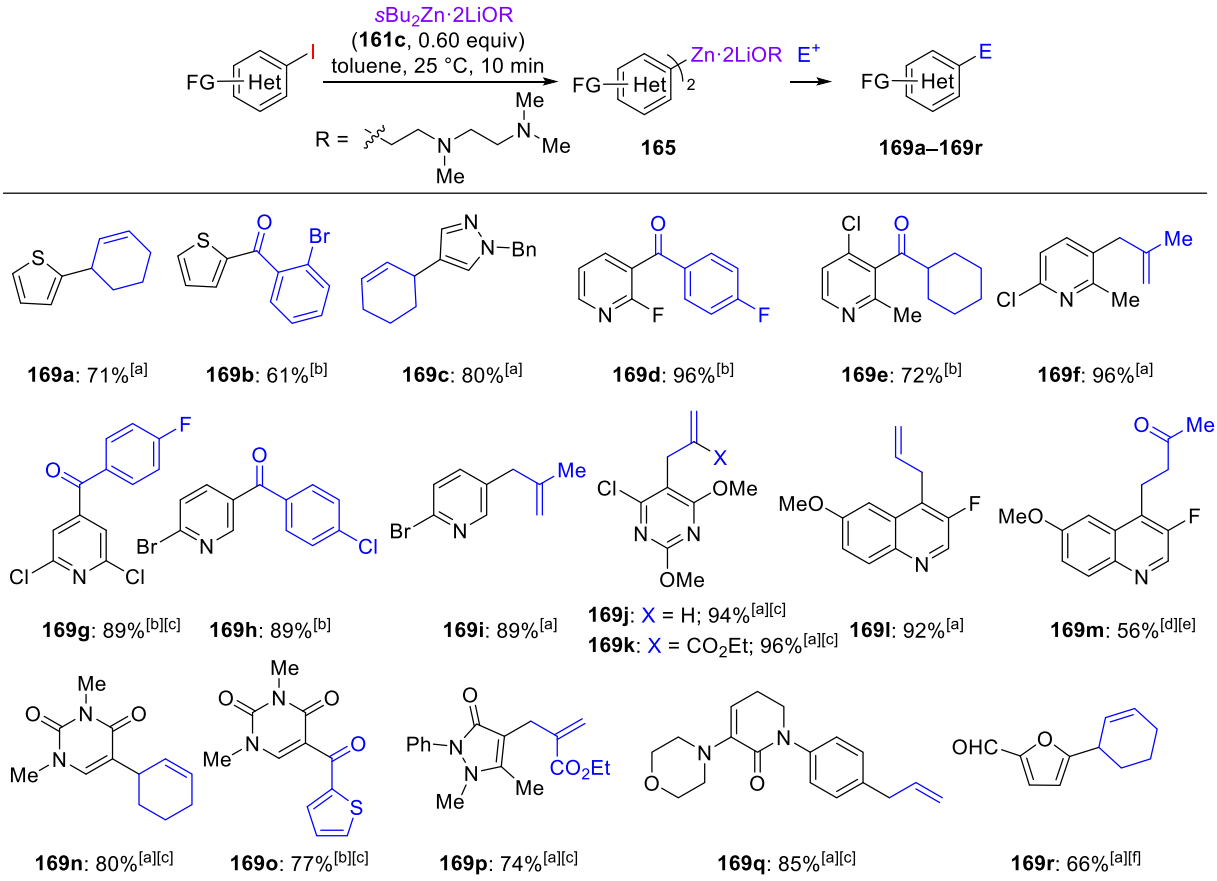
Scheme 47: Reaction of various aryl iodides with *s*Bu_2Zn·2LiOR (**161c**), followed by electrophilic functionalization.

When the zinc species **165a** was mixed with ethyl 4-iodobenzoate, $Pd(OAc)_2$ (3 mol%), and SPhos (6 mol%),[156] a palladium-catalyzed Negishi cross-coupling[157] took place, leading to the biaryl **166c** in 76% yield. 4-Iodobenzotrifluoride underwent a smooth I/Zn exchange using **161c**, leading to the corresponding diarylzinc reagent **165b**. Reaction of **165b** with ethyl 2-(bromomethyl)acrylate or a palladium-catalyzed cross-coupling with 4-iodothioanisole gave functionalized arenes **166d**–**166e** in 48–67% yield (Scheme 47). TBS- or TIPS-protected iodophenols were treated with **161c** and the resulting zinc organometallic was allylated or acylated, providing **166f**–**166g** in 61–83% yield. The zinc reagent obtained from sterically demanding 2-iodo-1,3-dimethylbenzene was quenched with ethyl 2-(bromomethyl)acrylate and 4-fluorobenzoyl chloride to give the 2-substituted *m*-xylenes **166h**–**166i** in 67–80% yield. Various electron-poor aryl iodides bearing ester or nitrile groups readily reacted with **161c** and quenching of the zinc reagent of type **165** with various electrophiles gave products **166j**–**166p** in 59–98% yield. Exchange on an aryl iodide bearing a triazine moiety, followed by allylation, gave **166q** in 72% yield. Next, the diaryl zinc species generated from 4-iodobenzophenone was allylated, providing ketone **166r** in 83% yield. Also, the I/Zn exchange could also be extended to nitro-substituted aryl iodides. In this case, $p Tol_2Zn \cdot 2LiOR$ (**167**) gave the best result.[158] Hence, the milder exchange reagent $p Tol_2Zn \cdot 2LiOR$ (**167**, R = $-CH_2CH_2N(CH_3)CH_2CH_2N(CH_3)_2$) was prepared by mixing the akoxide **162c** with *p*tolyllithium (2.00 equiv).[159] Treatment of 2,4-dinitroiodobenzene or 3-iodo-4-nitrobenzonitrile with **167** (0.60 equiv) at –15 °C for 15 min, followed by a copper-mediated allylation reaction, afforded nitroarenes **166s**–**166t** in 71–79% yield. For converting an iodo-benzaldehyde to the corresponding zinc species, a short screening showed, that the best exchange reagent was $t Bu_2Zn \cdot 2LiOR$ (**168**). Thus, the alkoxide **162c** was treated with *t*BuLi (2.00 equiv) and the resulting less nucleophilic reagent $t Bu_2Zn \cdot 2LiOR$ (**168**, R = $-CH_2CH_2N(CH_3)CH_2CH_2N(CH_3)_2$) was obtained as a 1.00 M solution in toluene. Reaction of 5-iodo-veratraldehyde with **168** (0.80 equiv, 0 °C, 10 min) afforded a diarylzinc organometallic of type **165**, which, after allylation, provided the vanillin derivative **166u** in 48% yield (Scheme 47).

Various aryl- and heteroaryl iodides reacted smoothly with **161c**, to give a range of functionalized bis-arylzinc organometallics. Thus, bis-thienylzinc either reacted with 3-bromocyclohexene or 2-bromobenzoyl chloride to provide **169a**–**169b** in 61–71% yield (Scheme 48). Benzyl-protected 3-iodopyrazole reacted with **161c** to give, after allylation, **169c** in 80% yield. Also, various iodopyridines, -pyrimidines and -quinoline were converted into the corresponding zinc reagents using **161c** and quenched with several acid chlorides and allyl bromides, producing **169d**–**169l** in 72–96% yield. The

[156] a) R. A. Altman, S. L. Buchwald, *Nat. Protoc.* **2007**, *2*, 3115; b) T. E. Barder, S. D. Walker, J. R. Martinelli, S. L. Buchwald, *J. Am. Chem. Soc.* **2005**, *127*, 4685.
[157] a) A. O. King, N. Okukado, E. Negishi, *J. Chem. Soc., Chem. Commun.* **1977**, 683; b) D. Haas, J. M. Hammann, R. Greiner, P. Knochel, *ACS Catal.* **2016**, *6*, 1540.
[158] When 2,4-dinitroiodobenzene was treated with **161c**, decomposition of the starting material was observed.
[159] *p*Tolyllithium was prepared by a direct lithium insertion to 4-chlorotoluene, see: C. G. Screttas, B. R. Steele, M. Micha-Screttas, G. A. Heropoulos, *Org. Lett.* **2012**, *14*, 5680.

organometallic obtained from an iodoquinoline underwent a copper-mediated 1,4-addition to methyl vinyl ketone in the presence of TMSCl. Subsequent enol ether cleavage using TBAF (1.10 equiv, 25 °C, 1 h) gave ketone **169m** in 56% yield over two steps. Reaction of more complex iodinated *N*-heterocycles namely pyrazolone, uracil or 5,6-dihydropyridone gave the expected bis-zinc reagents of type **165**, which, after allylation or acylation provided **169n**–**169q** in 74–85% yield.[160] 4-Iodofuraldehyde was treated with *t*Bu$_2$Zn·2LiOR (**168**) and the resulting zinc reagent reacted with 3-bromocyclohexene in the presence of CuI to give the furfural derivative **169r** in 66% yield (Scheme 48).



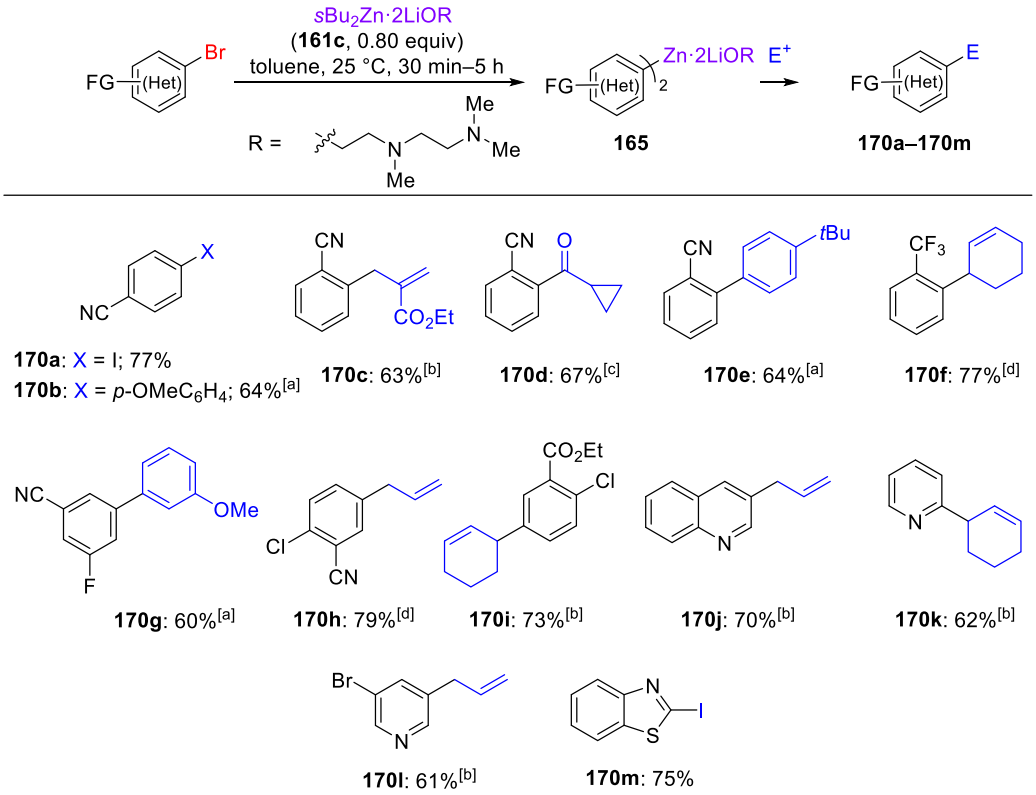
[a] CuI (20 mol%) was used. [b] CuI (0.60 equiv) was used. [c] The reaction was run in THF. [d] Yield over two steps.
[e] Reaction conditions: 1) CuI, methyl vinyl ketone, TMSCl 2) TBAF. [f] *t*Bu$_2$Zn·2LiOR (**168**, 0.80 equiv, 0 °C, 10 min) was used.

Scheme 48: Reaction of various heteroaryl iodides with *s*Bu$_2$Zn·2LiOR (**161c**), followed by electrophilic functionalization.

[160] Due to poor solubility of the aryl iodides, the reactions leading to **169g**,**169j**,**169k**,**169n**–**169q** were performed in THF.

3.3 The Br/Zn Exchange on Aryl and Heteroaryl Bromides

The impressive reactivity of these bimetallic exchange reagents led us to examine the Br/Zn exchange reaction. Thus, treatment of 4-bromobenzonitrile with **161c** (0.80 equiv) at 25 °C for 5 h in toluene, provided the desired bis-arylzinc of type **165**, which, after quenching with iodine, gave 4-iodobenzonitrile (**170a**) in 77% yield (Scheme 49). Reaction of the same zinc reagent with 4-iodoanisole under palladium-catalysis gave the desired biaryl **170b** in 64% yield.[161] Allylation, acylation and cross-coupling of the zinc reagents obtained from 2-bromobenzonitrile and 2-bromobenzotrifluoride gave **170c**–**170e** in 63–67% yield. Various bromoarenes bearing e.g. an ester functional group underwent a smooth Br/Zn exchange, which, after allylation or cross-coupling, produced the arenes **170f**–**170i** in 60–79% yield. Additionally, bromopyridines and a bromoquinoline were treated with **161c**. Allylation of the resulting zinc reagents gave the functionalized heteroarenes **170j**–**170l** in 61–70% yield. Finally, 2-bromobenzothiazole was mixed with **161c** and the obtained metal species reacted with iodine to give **170m** in 75% yield (Scheme 49).



[a] $Pd(OAc)_2$ (3 mol%), SPhos (6 mol%) and TMSCl (0.80 equiv) were used. [b] CuI (20 mol%) was used. [c] CuI (0.60 equiv) was used. [d] A 1.00 M CuCN·2LiCl solution in THF (20 mol%) was used.

Scheme 49: Reaction of various aryl bromides with *s*Bu_2Zn·2LiOR (**161c**), followed by electrophilic functionalization.

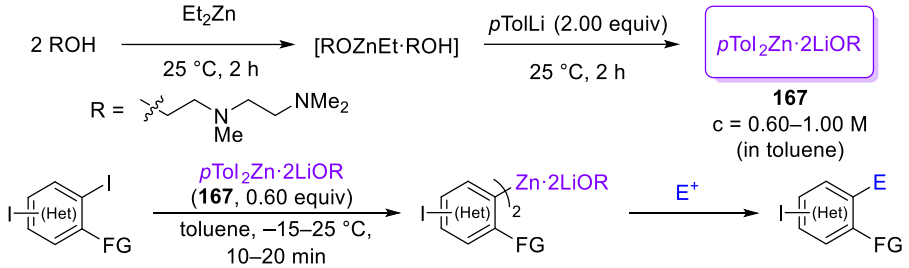
[161] Prior to the addition of the catalyst system and aryl iodide, TMSCl (0.80 equiv, 0 °C, 10 min) was added in order to quench the excess of alkoxide.

4 Regioselective Iodine/Zinc Exchange for the Selective Functionalization of Polyiodinated Arenes and Heterocycles in Toluene

4.1 Introduction

The regioselective functionalization of polyhalogenated arenes and heteroarenes[61h,126a-c,162] is an excellent method for the preparation of various functionalized halogenated aromatics and heterocycles of interest as agrochemicals, pharmaceuticals or new organic materials.[8,125] The functionalization of halogenated (hetero)arenes was best performed by their conversion to organometallics followed by various quenching reactions with electrophiles.[1a-b] Organozinc intermediates were usually preferred over organolithium and organomagnesium species as they tolerate most functional groups.[1c,132,149c,e,163] The selective zinc dust insertion in the presence of LiCl on dihalogenated (hetero)arenes led to such organometallic species with remarkable regioselectivities.[28a,30,146b] Although regioselective iodine or bromine/magnesium-exchanges have been reported in THF[55a,67,68,128,164] and more recently in non-polar solvents such as toluene,[141b,c] no selective I/Zn exchanges on polyiodoarenes have been described yet.[165] Recently, we have reported that reagents of the type *s*$Bu_2Zn{\cdot}2LiOR$ (R = $(CH_2)_2N(CH_3)(CH_2)_2N(CH_3)_2$; **161c**, 0.60–1.00 M in toluene) allowed iodine/zinc exchanges in toluene, displaying a good functional group tolerance.[142]

Herein, we report fast and highly regioselective I/Zn exchanges on various polyiodo-arenes and -heteroarenes using *p*$Tol_2Zn{\cdot}2LiOR$ (R = $(CH_2)_2N(CH_3)(CH_2)_2N(CH_3)_2$; **167**, 0.60–1.00 M in toluene), which was readily prepared from *p*TolLi (2.00 equiv), ROH (R = $(CH_2)_2N(CH_3)(CH_2)_2N(CH_3)_2$, 2.00 equiv) and Et_2Zn (1.00 equiv) in toluene (Scheme 50).[142]



Scheme 50: Preparation of *p*$Tol_2Zn{\cdot}2LiOR$ (**167**) in toluene.

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[162] a) S. Schröter, C. Stock, T. Bach, *Tetrahedron* **2005**, *61*, 2245; b) C. Y. Legault, Y. Garcia, C. A. Merlic, K. N. Houk, *J. Am. Chem. Soc.* **2007**, *129*, 12664; c) S. T. Keaveney, G. Kundu, F. Schoenebeck, *Angew. Chem. Int. Ed.* **2018**, *57*, 12573.

[163] P. Knochel, H. Leuser, L.-Z. Cong, S. Perrone, F. F. Kneisel In *Handbook of Functionalized Organometallics*, Wiley-VCH, Weinheim, **2008**.

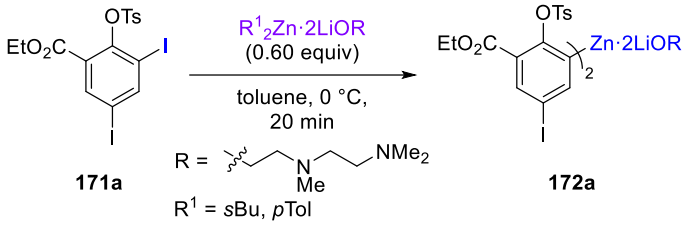
[164] a) O. Baron, P. Knochel, *Angew. Chem. Int. Ed.* **2005**, *44*, 3133; b) S. Bruña, A. R. Kennedy, M. Fairley, C. T. O'Hara, *Chem. Eur. J.* **2021**, *27*, 4134.

[165] a) T. D. Blümke, T. Klatt, K. Koszinowski, P. Knochel, *Angew. Chem. Int. Ed.* **2012**, *51*, 9926; b) M. Balkenhohl, P. Knochel, *Chem. Eur. J.* **2020**, *26*, 3688.

4.2 Optimization and Scope of the Regioselective I/Zn Exchange on Polyiodinated Arenes and Heteroarenes in Toluene

In preliminary experiments, we have studied the I/Zn exchange on ethyl 3,5-diiodo-2-(tosyloxy)benzoate (**171a**) in toluene (Table 8). First, the diiodoarene **171a** was treated with 0.60 equiv of sBu$_2$Zn·2LiOR (R = $(CH_2)_2N(CH_3)(CH_2)_2N(CH_3)_2$; **161c**)[142] in toluene at 0 °C for 20 min, generating regioselectively the organozinc species **172a** in 63% yield (Table 8, entry 1).[166]

Table 8: Screening of the I/Zn exchange on ethyl 3,5-diiodo-2-(tosyloxy)benzoate (**171a**).



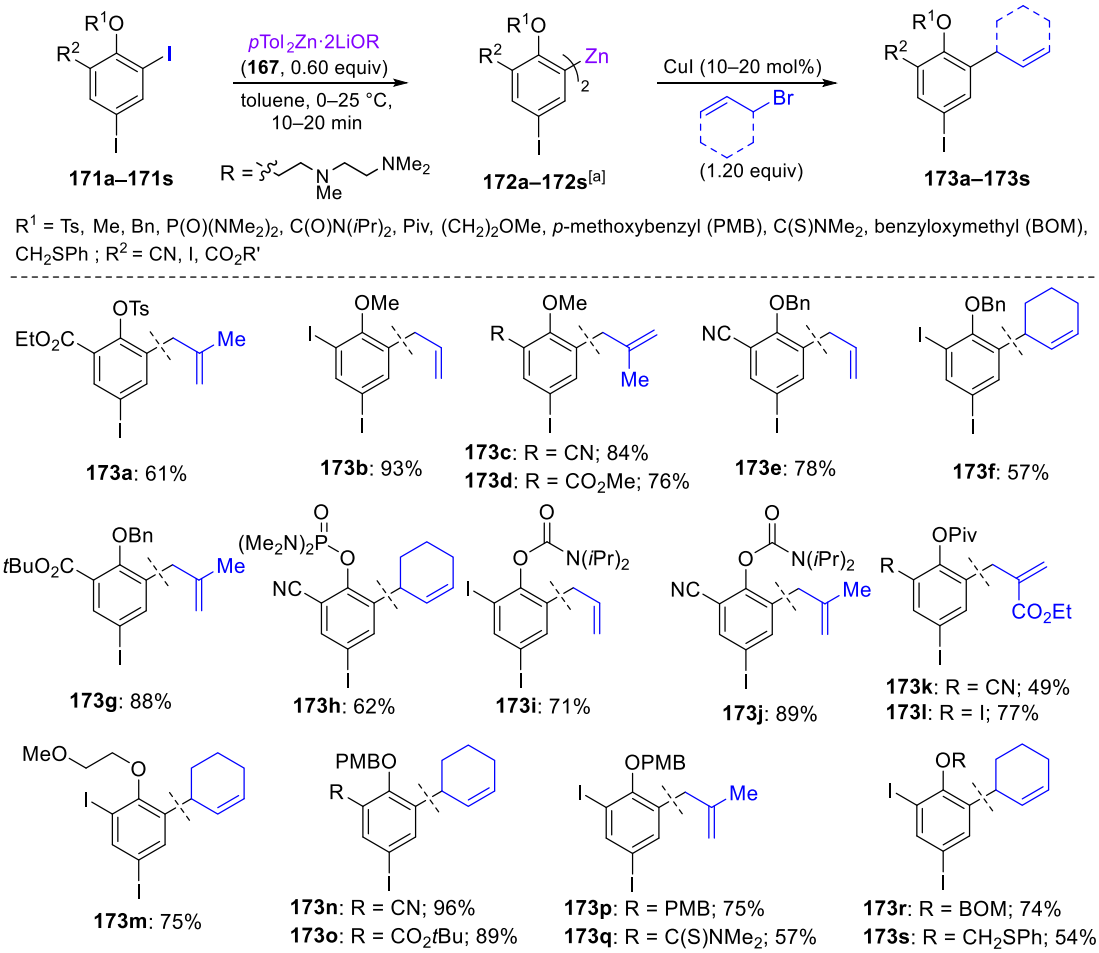
Entry	Exchange reagent[a]	Regioselectivity [%][b]	Yield [%][b]
1	sBu$_2$Zn·2LiOR (**161c**)	99	63
2	pTol$_2$Zn·2LiOR (**167**)	99	99

[a] These reactions were carried out at 0.50 M. All organometallic reagents were displayed accordingly to their stoichiometry and not their actual structure. [b] Yield and regioselectivity were determined by GC-analysis of reaction aliquots quenched with water.

As arylmetal reagents have proven to tolerate more functional groups,[147] the dialkylzinc reagent **161c** was replaced by the diarylzinc exchange reagent pTol$_2$Zn·2LiOR (R = $(CH_2)_2N(CH_3)(CH_2)_2N(CH_3)_2$; **167**). Thus, treatment of the diiodoarene **171a** with **167** at 0 °C led after 20 min to the diarylzinc **172a** in 99% yield (Table 8, entry 2). After a Cu-catalyzed allylation of **172a** with methallyl bromide, the functionalized tosylate **173a** was isolated in 61% yield (Scheme 51). Similarly, 2,4,6-triiodoanisole (**171b**) regioselectively underwent complete I/Zn exchange upon treatment with **167** (0 °C, 20 min). The corresponding diarylzinc (**172b**) was smoothly allylated, producing the allylated product **173b** in 93% yield. Analogously, the diiodinated anisole **171c**–**171d** were both converted into the corresponding organozinc compounds (**172c**–**172d**), which gave after copper-catalyzed (CuI, 0.10 equiv) reaction with methallyl bromide the nitrile and ester **173c**–**173d** in 76–84% yield. In addition, the benzylic ethers **171e**–**171g** led to the corresponding zincated aryl iodides **172e**–**172g**, which furnished after trapping with allyl bromide or 3-bromocyclohexene the iodinated products **173e**–**173g** in 57–88% yield. Also, when reacted with the *bis*-tolylzinc reagent **167**, the phosphoramide **171h** generated the corresponding diorganozinc species **172h**. After allylation, the polyfunctionalized arene **173h** was obtained in 62%

[166] 37% of the corresponding carboxylic acid were obtained after hydrolysis.

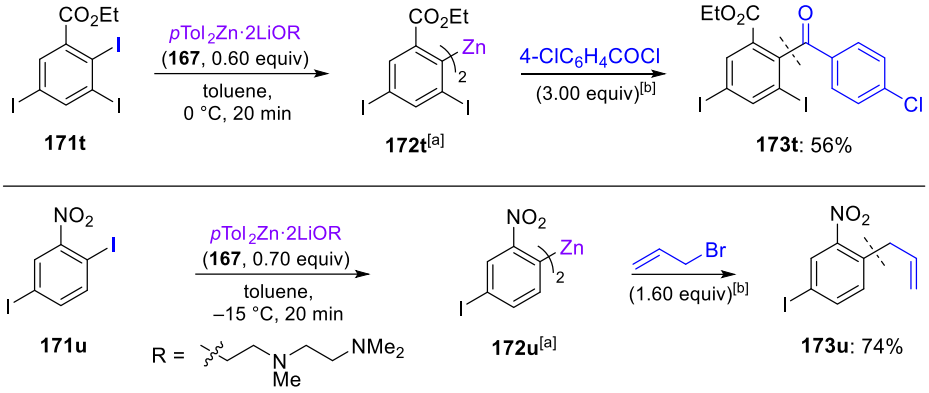
yield. Next, the two carbamates **171i**–**171j** successfully afforded the corresponding organozinc species (**172i**–**172j**), which furnished after allylation the products **173i**–**173j** in 71–89% yield. Pivalate derivatives **171k**–**171l** were also tolerated and produced after I/Zn exchange and allylation with ethyl 2-(bromomethyl)acrylate the esters **173k**–**173l** in 49–77% yield. The 2-methoxyethylether **171m** underwent smooth exchange to generate the organozinc **172m**. It reacted with 3-bromocyclohexene in the presence of a copper catalyst to yield **173m** in 75% yield. Additionally, the para-methoxybenzyl derivatives **171n**–**171p** were subjected to the same conditions, leading after allylation to the iodinated products **173n**–**173p** in 75–96% yield. The dimethylcarbamothioic acid derivative **171q** was furthermore successfully used and produced after allylation **173q** in 57% yield. Afterwards, the triiodoaryl ether **171r** reacted with **167** to give the corresponding diarylzinc (**172r**). This species smoothly reacted with 3-bromocyclohexene furnishing **173r** in 74% yield. Finally, the thioether **171s** was successfully converted to the corresponding organozinc reagent (**172s**) which provided after allylation the diiodoarene **173s** in 54% yield.



[a] 2LiOR was omitted for the sake of clarity.

Scheme 51: Zincation of various polyiodinated aromatics with *p*Tol$_2$Zn·2LiOR (**167**), followed by a copper-catalyzed allylation.

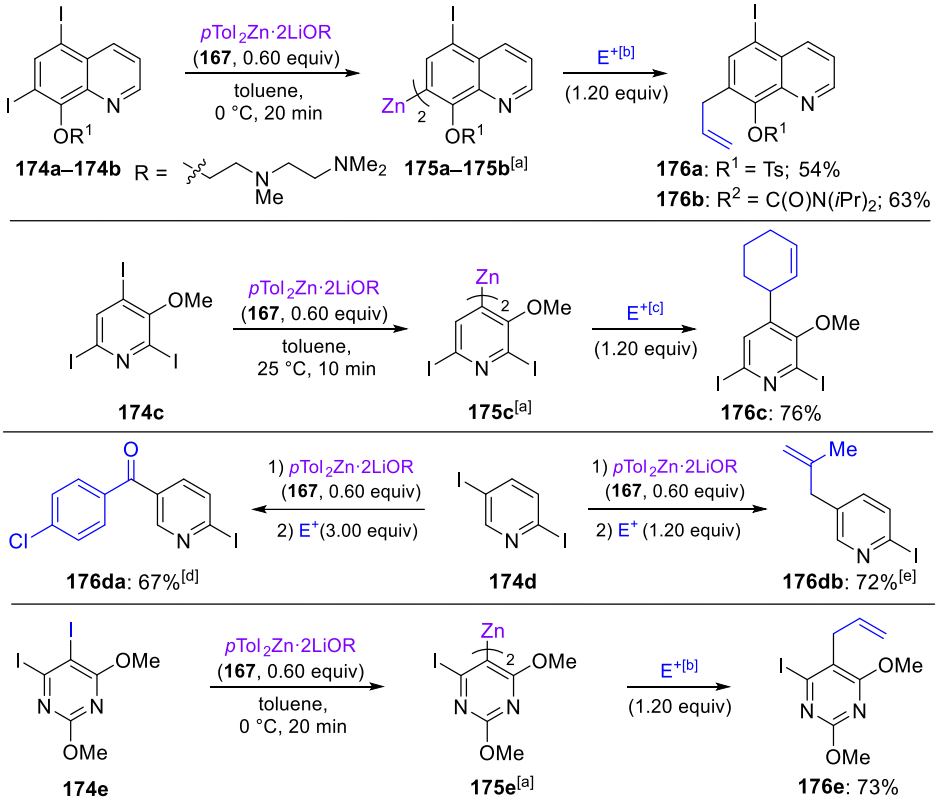
Extending further the scope of this regioselective I/Zn exchange reaction, ethyl 2,3,5-triiodobenzoate (**171t**) led to the regioselective formation of **172t** (Scheme 52). After transmetallation with CuI and acylation with 4-chlorobenzoyl chloride (3.00 equiv), the ketone **173t** was isolated in 56% yield. To our delight, the I/Zn exchange could be extended to 1,4-diiodo-2-nitrobenzene (**171u**), which resulted in the regioselective generation of the diorganozinc **172u**. After a copper-catalyzed reaction with allyl bromide, the allylated aryl iodide bearing a nitro group **173u** was obtained in 74% yield.



[a] 2LiOR was omitted for the sake of clarity. [b] CuI (10-60 mol%) was used.

Scheme 52: Reaction of various polyiodinated aromatics with *p*Tol$_2$Zn·2LiOR (**167**), followed by a copper-catalyzed allylation or acylation.

The extension to iodinated heterocycles (**174a**–**174e**) was then evaluated (Scheme 53). Thus, the tosylated diiodoquinoline **174a** underwent a selective I/Zn exchange with **167** at 0 °C within 20 min. The resulting diarylzinc (**175a**) was allylated with allyl bromide in the presence of CuI (10 mol%) and the desired product **176a** was isolated in 54% yield. Similarly, the carbamate **174b** was converted into the corresponding diheteroarylzinc species (**175b**), which provided after allylation the allylated iodoquinoline **176b** in 63% yield. In addition, the triiodomethoxypyridine **174c** successfully generated the organometallic **175c** upon addition of **167**. After allylation with 3-bromocyclohexene, **175c** gave the allylated pyridine **176c** in 76% yield. 2,5-Diiodopyridine (**174d**) regioselectively led to the corresponding zincated heterocycle (**175d**) using diarylzinc reagent **167**. After transmetallation to copper (0.60 equiv) and reaction with 4-chlorobenzoyl chloride (3.00 equiv) or Cu-catalyzed (CuI, 0.10 equiv) allylation with methallyl bromide, the ketone **176da** and allylated pyridine **176db** were obtained in 67–72% yield. Finally, the scope of this I/Zn exchange was extended to the diiodopyrimidine **174e**. Thus, after mixing the diiodouracil derivative **174e** with **167** for 20 min at 0 °C, the zincated pyrimidine **175e** was formed. After allylation with allyl bromide, the iodopyrimidine **176e** was obtained in 73% yield.



[a] 2LiOR was omitted for the sake of clarity. [b] CuI (10 mol%) and allyl bromide (1.20 equiv) were used. [c] CuI (10 mol%) and 3-bromocyclohexene (1.20 equiv) were used. [d] CuI (60 mol%) and 4-chlorobenzoylchloride (3.00 equiv) were used. [e] CuI (10 mol%) and methallyl bromide (1.20 equiv) were used.

Scheme 53: Reaction of various polyiodinated heteroaromatics with *p*Tol$_2$Zn·2LiOR (**167**), followed by a copper-catalyzed allylation or acylation.

5 Iron-Catalyzed Cross-Coupling of Functionalized Benzylmanganese Halides with Alkenyl Iodides, Bromides and Triflates

5.1 Introduction

Transition-metal catalyzed cross-couplings are of great importance for generating C─C bonds with diverse electrophiles.[110b] Although palladium- and nickel-catalyzed cross-couplings[167] are amongst the most versatile, tolerating various functionalities on both electrophiles and nucleophiles, these metals have drawbacks including high prices for palladium[168] and acute toxicity in the case of nickel.[169] Alternative metal-catalyses have been developed and include the use of copper,[170] iron[171] or cobalt.[172] Organomagnesium[111a] and organozinc[157b] reagents have mostly been used as organometallic reaction partners.[173] Pioneered by Cahiez, organomanganese reagents have proven to be remarkable nucleophiles in various cross-coupling reactions, including those catalyzed by iron salts.[16,118a,171b] Unfortunately, these reactions often required the use of N-methylpyrrolidinone (NMP)[174,175] and exhibited a limited functional group tolerance. The low price and toxicity of these metals being considered, such cross-coupling methodologies represent attractive alternatives compared to organo-boronic esters which may have genotoxic properties.[176]

We have recently described an effective preparation of functionalized benzylic manganese reagents of type **177** starting from benzylic chlorides of type **178**.[109b,118d,177] Herein, we report an iron-catalyzed cross-coupling of functionalized benzylic manganese reagents (**177**) with alkenyl iodides, bromides and triflates of type **179** providing a range of polyfunctionalized alkenes of type **180** (Scheme 54).

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[167] a) *Cross-Coupling Reactions. A Practical Guide* (Eds.: N. Miyaura), Springer, Berlin, **2002**; b) *Organotransition Metal Chemistry* (Ed.: J. F. Hartwig), University Science Books: Sausalito, CA, **2010**; c) R. Jana, T. P. Pathak, M. S. Sigman, *Chem. Rev.* **2011**, *111*, 1417; d) V. B. Phapale, D. J. Cárdenas, *Chem. Soc. Rev.* **2009**, *38*, 1598.

[168] $FeCl_2$ ca. 332 €/mol, $PdCl_2$ ca. 6164 €/mol; prices retrieved from Alfa Aesar in August 2019.

[169] a) $LD_{50}(FeCl_2$, rat oral) = 900 mg/kg; $LD_{50}(NiCl_2$, rat oral) = 186 mg/kg; b) K. S. Egorova, V. P. Ananikov, *Angew. Chem. Int. Ed.* **2016**, *55*, 12150.

[170] S. Thapa, B. Shrestha, S. K. Gurung, R. Giri, *Org. Biomol. Chem.* **2015**, *13*, 4816.

[171] a) G. Cahiez, A. Moyeux, J. Cossy, *Adv. Synth. Catal.* **2015**, *357*, 1983; b) A. Fürstner, A. Leitner, M. Méndez, H. Krause, *J. Am. Chem. Soc.* **2002**, *124*, 13856; c) R. B. Bedford, P. B. Brenner, In *Iron Catalysis II* (Eds.: E. Bauer), Springer, Berlin, **2015**; d) I. Bauer, H.-J. Knölker, *Chem. Rev.* **2015**, *115*, 3170.

[172] a) G. Cahiez, A. Moyeux, *Chem. Rev.* **2010**, *110*, 1435; b) C. Gosmini, J.-M. Bégouin, A. Moncomble, *Chem. Commun.* **2008**, 3221.

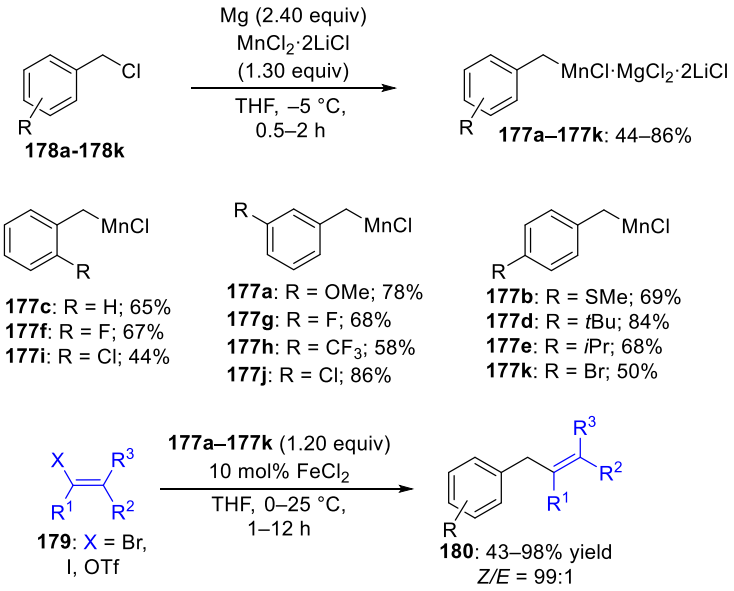
[173] K. Groll, T. D. Blümke, A. Unsinn, D. Haas, P. Knochel, *Angew. Chem. Int. Ed.* **2012**, *51*, 11157.

[174] a) G. Cahiez, H. Avedissian, *Synthesis* **1998**, 1199; b) Reprotoxic Category 2, R61, Official Journal of the European Union, December 31, **2008**, European regulation No. 1272/2008.

[175] For a recent report on the role of NMP in Fe-catalyzed coupling methodologies, see: S. B. Muñoz III, S. L. Daifuku, J. D. Sears, T. M. Baker, S. H. Carpenter, W. W. Brennessel, M. L. Neidig, *Angew. Chem. Int. Ed.* **2018**, *57*, 6496.

[176] a) M. R. O'Donovan, C. D. Mee, S. Fenner, A. Teasdale, D. H. Phillips, *Mutat. Res.* **2011**, *724*, 1; b) M. M. Hansen, R. A. Jolly, R. J. Linder, *Org. Process Res. Dev.* **2015**, *19*, 1507.

[177] A. D. Benischke, A. Desaintjean, T. Juli, G. Cahiez, P. Knochel, *Synthesis* **2017**, *49*, 5396.



[a] For clarity reasons, the magnesium salt has been omitted. Yields were determined by titration against iodine in THF.

Scheme 54: Preparation of benzylic manganese reagents[a] by *in situ* transmetalation followed by iron-catalyzed cross-couplings with alkenyl iodides, bromides and triflates.

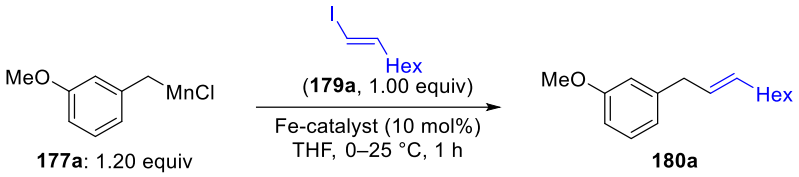
5.2 Optimization and Scope of the Iron-Catalyzed Cross-Coupling of Functionalized Benzylmanganese Halides with Alkenwl Iodides, Bromides and Triflates

In preliminary experiments, we have prepared various benzylic organometallics derived from 3-methoxybenzyl chloride (**178a**). Thus, the benzylic manganese reagent **177a** was conveniently prepared by treating **178a** (1.00 equiv) in THF at −5 °C with magnesium turnings (2.40 equiv) and $MnCl_2$·2LiCl (1.30 equiv) for 1 h. Titration[178] with iodine led to a yield for **177a** of 78%. We also prepared the corresponding benzylic magnesium (**181**; 48% yield) and zinc (**182**; 42% yield) chlorides.[179]

In the absence of any iron-catalyst, the cross-coupling of **177a** with (*E*)-1-iodooctene (**179a**; 25 °C, 1 h) produced the desired cross-coupling product **180a** in 65% yield (Table 9, entry 1). Under these conditions, **181** and **182** gave lower yields (respectively 47% and 14%). Although the cross-coupling performed with $FeBr_2$ gave a moderate yield of 63%, the use of $Fe(acac)_2$, $Fe(acac)_3$ or $FeBr_3$ afforded **180a** in 74–80% yield (entries 2−5). Using $FeCl_3$ proved to be even more effective as the yield increased to 96% (entry 6). Our best result was obtained with $FeCl_2$ as catalyst, producing **180a** in 97% yield. Moreover, the use of 99.99% pure $FeCl_2$ similarly gave **180a** in 98% yield, showing that it is unlikely that metal impurities are responsible for this catalysis (entries 7−8).

[178] A. Krasovskiy, P. Knochel, *Synthesis* **2006**, 890.
[179] For more details, see the Experimental Part (p. 249).

Table 9: Catalyst screening of the reaction between the benzylic manganese chloride **177a**[a] and (*E*)-1-iodooctene (**179a**).



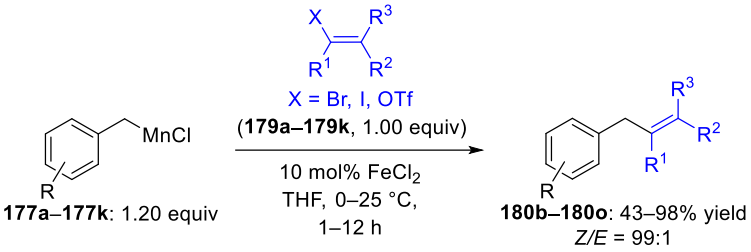
Entry	Catalyst (10 mol%)	Yield [%][b]
1	none	65
2	$FeBr_2$	63
3	$Fe(acac)_2$	75
4	$Fe(acac)_3$	74
5	$FeBr_3$	80
6	$FeCl_3$	96
7	$FeCl_2$ (99.5% purity)	97
8	$FeCl_2$ (99.99% purity)	98

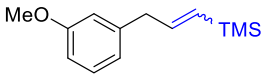
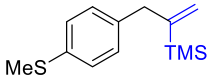
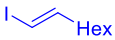
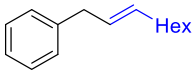
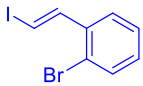
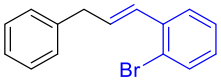
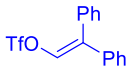
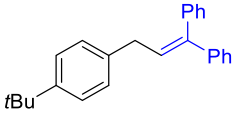
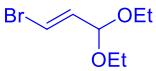
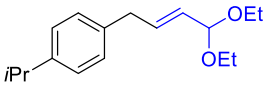
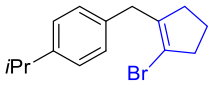
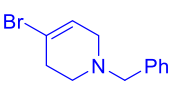
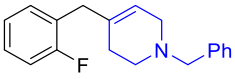
[a] For clarity reasons, the magnesium salt has been omitted. [b] Yield of analytically pure product.

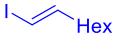
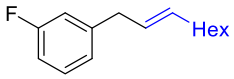
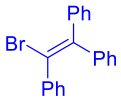
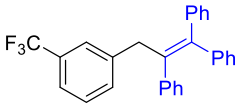
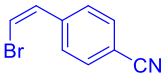
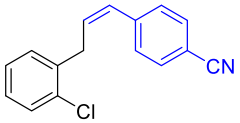
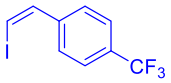
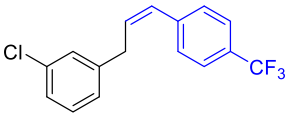
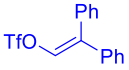
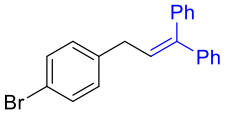
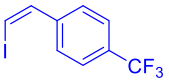
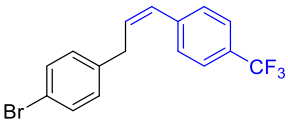
We noticed that the reprotoxic cosolvent NMP[174,175] did not positively influence the reaction.[179] However, the amount of $FeCl_2$ could be reduced to 2.5 mol% without significantly decresing the yield.[179] We also observed that the benzylic magnesium and zinc species (**181** and **182**) were less efficient reagents and reacted with **179a** in the presence of 10 mol% $FeCl_2$ (25 °C, 1 h) to give **180a** in 66–68% yield.

Furthermore, the cross-couplings of **177a** with (2-bromovinyl)trimethylsilane (**179b**; *Z*/*E* = 10:90) gave the olefin **180b** in 92% yield with retention of stereochemistry (*Z*/*E* = 6:94) whereas the yield without iron salt was of 0% (Table 10, entry 1). When the electron-rich 4-(methylthio)benzylmanganese chloride (**177b**) was mixed with (1-bromovinyl)trimethylsilane (**179c**), alkenylsilane **180c** was generated in 92% yield and no product was observed without iron catalyst (entry 2). Benzylmanganese chloride (**177c**) underwent smooth cross-couplings with **179a** and (*E*)-1-bromo-2-(2-iodovinyl)benzene (**179d**) to afford *E*-alkenes **180d** and **180e** in 77% and 87% yield. In comparison, 7% and 52% were obtained without catalyst (entries 3–4). Also, 4-(tert-butyl)benzylmanganese chloride (**177d**) reacted with 2,2-diphenylvinyl trifluoromethanesulfonate (**179e**) to give **180f** in 95% yield (entry 5).

Table 10: Iron-catalyzed cross-couplings of benzylmanganese reagents (**177a**–**177k**)[a] with alkenyl iodides, bromides and triflates (**179a**–**179k**).[b]



Entry	Benzylic manganese reagent	Electrophile	Product, yield [%][c]
1	**177a**	 **179b**: *Z*/*E* = 10:90	 **180b**: 92 (0)[d] *Z*/*E* = 6:94
2	**177b**	 **179c**	 **180c**: 92 (0)[d]
3	**177c**	 **179a**: *Z*/*E* = 1:99	 **180d**: 77 (7)[d] *Z*/*E* = 1:99
4	**177c**	 **179d**: *Z*/*E* = 1:99	 **180e**: 87 (52)[d] *Z*/*E* = 1:99
5	**177d**	 **179e**	 **180f**: 95 (74)[d]
6	**177e**	 **179f**: *Z*/*E* = 1:99	 **180g**: 79 (0)[d] *Z*/*E* = 1:99
7[e]	**177e**	 **179g**	 **180h**: 57 (8)[d]
8	**177f**	 **179h**	 **180i**: 84 (0)[d]

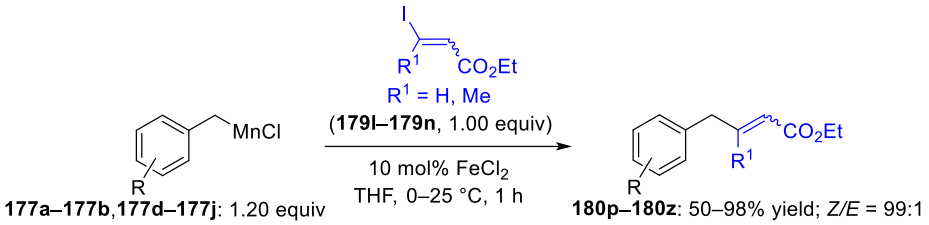
9	**177g**	 **179a**: *Z*/*E* = 1:99	 **180j**: 94 (0)[d] *Z*/*E* = 1:99
10	**177h**	 **179i**	 **180k**: 87 (7)[d]
11	**177i**	 **179j**: *Z*/*E* = 99:1	 **180l**: 98 (21)[d] *Z*/*E* = 99:1
12	**177j**	 **179k**: *Z*/*E* = 99:1	 **180m**: 98 (58)[d] *Z*/*E* = 99:1
13	**177k**	 **179e**	 **180n**: 43 (20)[d]
14	**177k**	 **179k**: *Z*/*E* = 99:1	 **180o**: 53 (12)[d] *Z*/*E* = 99:1

[a] For clarity reasons, the magnesium salt has been omitted. [b] Reaction time: 1 h for iodides, 12 h for bromides and triflates. [c] Isolated yield of analytically pure product. [d] In parentheses, yield obtained without catalyst. [e] For this reaction, 1.00 equiv of **177e** were used.

Very interestingly, 4-isopropylbenzylmanganese chloride (**177e**) reacted with the acid-sensitive (*E*)-1-bromo-3,3-diethoxyprop-1-ene (**179f**) and 1,2-dibromocyclopent-1-ene (**179g**, 1.00 equiv of **177e**) to provide the acetal **180g** (*Z*/*E* = 1:99) and the bromopentene derivative **180h** in 79% and 57% yield. The reaction without $FeCl_2$ gave almost no product (0–8%, entries 6–7). Electron-deficient fluorine-containing benzylmanganese reagents (**177f**–**177h**) also reacted with various cross-coupling partners (**179a,179h**–**179i**) producing **180i**–**180k** in 84–94% yield (0–7% were obtained without $FeCl_2$, entries 8–10). The analogous chlorine-containing benzylmanganese species (**177i**–**177j**) reacted with the functionalized alkenyl halides (*Z*)-4-(2-bromovinyl)benzonitrile (**179j**) and (*Z*)-1-(2-iodovinyl)-4-

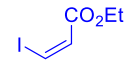
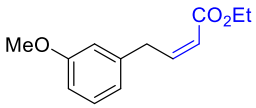
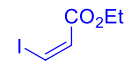
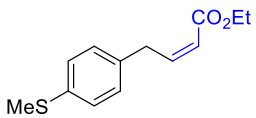
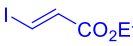
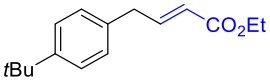
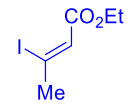
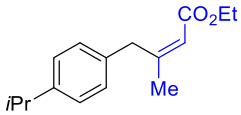
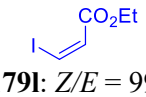
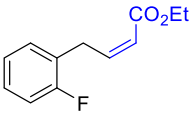
(trifluoromethyl)benzene (**179k**) to yield 98% of **180l** and **180m** (21% and 58% were obtained without any catalyst, entries 11–12). Finally, 4-bromobenzylmanganese chloride (**177k**) reacted with the alkenyl triflate **179e** and iodostyrene **179k** produced the expected alkenes **180n** and **180o** in 43–53% yield (12–20% were obtained without $FeCl_2$, entries 13–14). Generally, we have observed that alkenyl bromides and electron-poor benzylmanganese reagents only gave traces of product in the absence of $FeCl_2$.

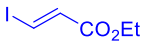
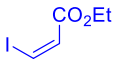
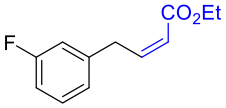
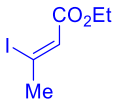
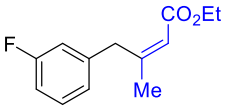
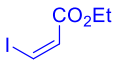
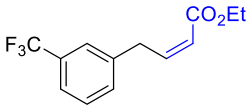
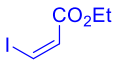
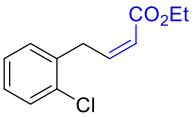
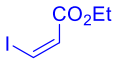
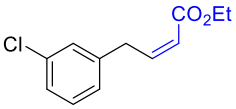
Table 11: Iron-catalyzed cross-couplings of benzylmanganese reagents (**177a**–**177b**,**177d**–**177j**)[a] with iodoacrylates (**179l–179n**).



177a–177b,**177d–177j**: 1.20 equiv

180p–180z: 50–98% yield; *Z*/*E* = 99:1

Entry	Benzylic manganese reagent	Electrophile	Product, yield [%][b]
1	**177a**	 **179l**: *Z*/*E* = 99:1	 **180p**: 98 (73)[c] *Z*/*E* = 99:1
2	**177b**	 **179l**: *Z*/*E* = 99:1	 **180q**: 78 *Z*/*E* = 99:1
3	**177d**	 **179m**: *Z*/*E* = 1:99	 **180r**: 55 (44)[c] *Z*/*E* = 1:99
4	**177e**	 **179n**: *Z*/*E* = 99:1	 **180s**: 78, *Z*/*E* = 99:1 (60, *Z*/*E* = 44:56)[c]
5	**177f**	 **179l**: *Z*/*E* = 99:1	 **180t**: 97 *Z*/*E* = 99:1

6	**177f**	 **179m**: *Z*/*E* = 1:99	 **180u**: 66 (41)[c] *Z*/*E* = 1:99
7	**177g**	 **179l**: *Z*/*E* = 99:1	 **180v**: 71 *Z*/*E* = 99:1
8	**177g**	 **179n**: *Z*/*E* = 99:1	 **180w**: 69, *Z*/*E* = 99:1 (83, *Z*/*E* = 67:33)[c]
9	**177h**	 **179l**: *Z*/*E* = 99:1	 **180x**: 50 *Z*/*E* = 99:1
10	**177i**	 **179l**: *Z*/*E* = 99:1	 **180y**: 50 *Z*/*E* = 99:1
11	**177j**	 **179l**: *Z*/*E* = 99:1	 **180z**: 73 *Z*/*E* = 99:1

[a] For clarity reasons, the magnesium salt has been omitted. [b] Isolated yield of analytically pure product. [c] In parentheses, yield obtained without catalyst.

These benzylic manganese species also undergo cross-couplings with iodoacrylate derivatives (**179l**–**179n**). Thus, the benzylic manganese chloride **177a** reacted with ethyl (*Z*)-3-iodoacrylate (**179l**) to provide the *Z*-acrylate **180p** in 98% yield (73% were obtained without catalysis). In the same conditions, 4-(methylthio)benzylmanganese chloride (**177b**) afforded the acrylate **180q** in 78% yield (Table 11, entries 1–2). Moreover, 4-alkylated benzylic manganese chlorides **177d**–**177e** respectively reacted with (*E*)-3-iodoacrylate (**179m**) and ethyl (*Z*)-3-iodobut-2-enoate (**179n**) to give the acrylates **180r** and **180s** in 55% and 78% yield, whereas the reactions without $FeCl_2$ gave 44% and 60% yield (*Z*/*E* = 44:56, entries 3–4). Also, 2-fluorobenzylman-ganese chloride (**177f**) reacted with both *Z* and *E* isomers of ethyl-3-iodoacrylate (**179l**–**179m**) to yield the corresponding *Z* and *E* acrylates **180t** in 97% and **180u**

in 66% yield (41% were obtained without catalysis, entries 5–6). The two other fluorine-containing benzylic manganese species **177g**–**177h** also underwent smooth cross-couplings with **179l**,**179n** to yield 50–71% of **180v**–**180x** (**180w**: 83%, *Z/E* = 67:33 were obtained without $FeCl_2$; entries 7–9). The chloro-substituted benzylic manganese species **177i**–**177j** were treated with **179l** and 10 mol% $FeCl_2$ to give the *Z*-acrylates **180y**–**180z** in 50–73% yield (entries 10–11).[180]

[180] Interestingly, partial isomerization of the double bond was observed when reactions of unsymmetrically substituted substrates were carried out without $FeCl_2$.

6 Iron-Catalyzed Cross-Coupling of Functionalized *Bis*-(aryl)manganese Nucleophiles with Alkenyl Halides

6.1 Introduction

Transition-metal catalyzed cross-couplings are widely used in the development and production of pharmaceutical compounds.[181] Since they tolerate a great variety of functionalities on both coupling partners, palladium-catalyzed and nickel-catalyzed cross-couplings are the most versatile ones.[167c-d,182] Yet, these metals have drawbacks such as toxicity[169] and high prices in the case of palladium.[168] That is one of the reasons why copper,[170] iron,[171] or cobalt[172a] have been developed as alternative metal-catalysts.

Pioneered by Cahiez,[16] organomanganese species often considerably reduce the amount of side reactions such as homo-coupling[109a,183] and have proven to be excellent nucleophiles in various types of reactions,[109a,184] including cross-couplings.[118a] Organomanganese compounds thus constitute an interesting alternative to usual cross-coupling partners such as organomagnesium,[111a] organozinc,[157b] and organo-boronic esters, which may have genotoxic properties.[176]

Recently, we have developed a two-step preparation of functionalized *bis*-(aryl)manganese reagents by oxidative insertion of magnesium into the C-Br bond of aryl bromides, which is followed by a transmetalation with $MnCl_2 \cdot 2LiCl$.[177] Herein, we wish to report an effective one-pot preparation of those functionalized *bis*-(aryl)manganese reagents ($Ar_2Mn \cdot 2MgX_2 \cdot 4LiCl$, denoted as Ar_2Mn (**181**), Scheme 55) starting from aryl bromides, which are followed by an iron-catalyzed cross-coupling of **181** with alkenyl iodides and bromides, and provide a range of polyfunctionalized alkenes (**184**, Scheme 55). These *bis*-(aryl)manganese reagents are generally stable at 25 °C for several hours, which makes them suitable reagents for mild cross-coupling reactions.[185]

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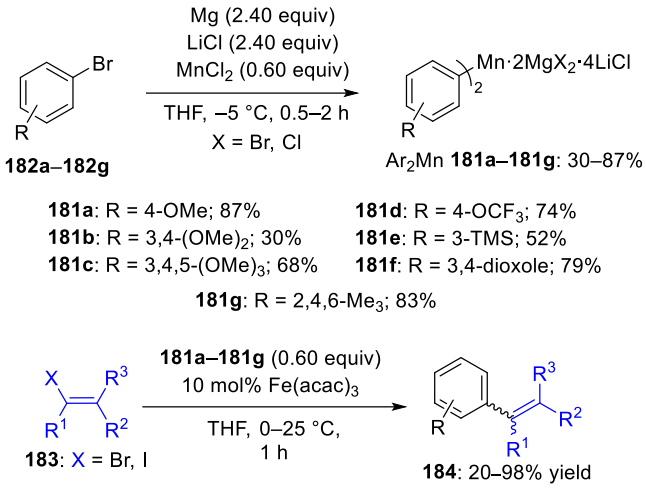
[181] *Applications of Transition Metal Catalysis in Drug Discovery and Development: An Industrial Perspective* (Eds.: M. L. Crawley, B. M. Trost), John Wiley & Sons: New Jersey, **2012**.
[182] a) N. Miyaura, *Org. Process Res. Dev.* **2003**, *7*, 1084; b) J. F. Hartwig, *Angew. Chem. Int. Ed.* **2010**, *49*, 7622.
[183] D. Haas, J. M. Hammann, A. Moyeux, G. Cahiez, P. Knochel, *Synlett* **2015**, *26*, 1515.
[184] a) G. Cahiez, A. Masuda, D. Bernard, J. F. Normant, *Tetrahedront Lett.* **1976**, *36* ,3155; b) G. Friour, A. Alexakis, G. Cahiez, J. F. Normant, *Tetrahedron* **1984**, *40*, 683; c) T. Kauffmann, M. Bisling, *Tetrahedron Lett.* **1984**, *25*, 293; d) G. Cahiez, M. Alami, *Tetrahedron Lett.* **1986**, *27*, 569; e) G. Cahiez, M. Alami, *Tetrahedron Lett.* **1989**, *30*, 3541; f) G. Cahiez, M. Alami, *J. Organomet. Chem.* **1990**, *397*, 291.
[185] G. Cahiez, O. Gager, F. Lecomte, *Org. Lett.* **2008**, *10*, 5255.

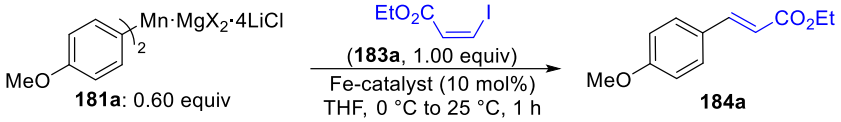


Scheme 55: One-pot preparation of *bis*-(aryl)manganese reagents by *in situ* transmetalation followed by iron-catalyzed cross-couplings with alkenyl iodides and bromides.

6.2 Optimization and Scope of the Iron-Catalyzed Cross-Coupling of Functionalized *Bis*-(aryl)manganese Nucleophiles with Alkenyl Halides

In preliminary experiments, the *bis*-(aryl)manganese reagent **181a** was conveniently prepared by treating 4-bromoanisole (**182a**, 1.00 equiv) in THF at –5 °C with magnesium turnings and LiCl (2.40 equiv) in the presence of $MnCl_2$ (0.60 equiv) within 1 h. Titration[178] with iodine led to a yield for **181a** of 87%.

Table 12: Catalyst screening of the reaction between the *bis*-(aryl)manganese reagent **181a** and (*Z*)-ethyl 3-iodoacrylate (**183a**).



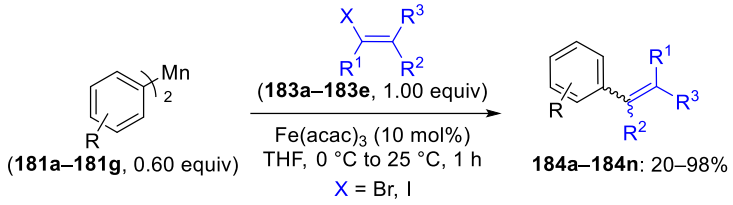
Entry	Catalyst (10 mol%)	Yield [%][a]
1	none	60[b]
2	$FeBr_2$	42
3	$FeCl_3$	54
4	$FeBr_3$	57
5	$FeCl_2$	64
6	$Fe(acac)_2$	67
7	$Fe(acac)_3$ (>99% purity)	79

[a] Yield of analytically pure product. [b] A *Z*/*E* = 50:50 mixture of **184a** was obtained.

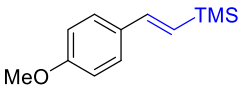
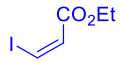
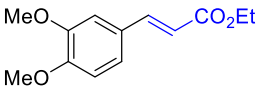
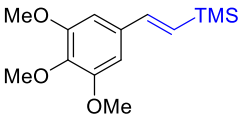
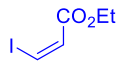
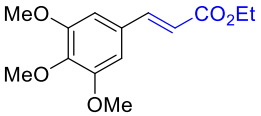
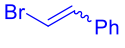
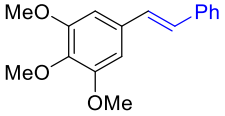
In the absence of any iron catalyst, the cross-coupling of **181a** with (*Z*)-ethyl 3-iodoacrylate (**183a**; 25 °C, 1 h) produced a *Z*/*E* = 50:50 mixture of the desired cross-coupling product **184a** in 60% yield (Table

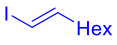
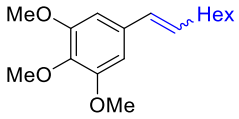
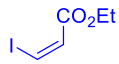
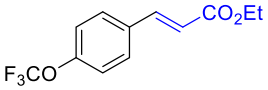
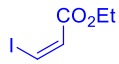
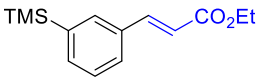
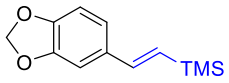
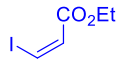
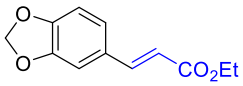
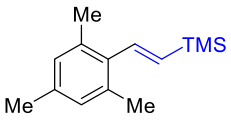
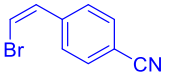
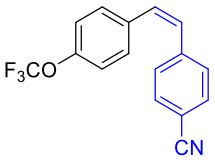
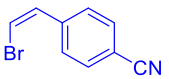
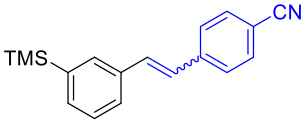
12, entry 1). Although the cross-coupling performed with $FeBr_2$ gave a moderate yield of 42%, the use of $FeCl_3$, $FeBr_3$, or $FeCl_2$ afforded the *E* isomer of **184a** in 54–64% yield (entries 2–5). Using $Fe(acac)_2$ proved to be more effective since the yield increased to 67% (entry 6). Our best result was obtained with $Fe(acac)_3$ (>99% purity) as a catalyst, producing the *E* isomer of **184a** in a 79% yield (entry 7).

Table 13: Iron-catalyzed couplings of *bis*-(aryl)manganese (**181a–181g**)[a] with alkenyl electrophiles (**183a–183e**).



R = 3-TMS; 4-OMe; 4-OCF_3; 3,4-$(OMe)_2$; 3,4,5-$(OMe)_3$; 3,4-dioxole; 2,4,6-Me_3

Entry	Ar_2Mn	Electrophile	Product, yield [%][b]
1	**181a**	 **183b**: *Z*/*E* = 10:90	 **184b**: 98, *Z*/*E* = 1:99 (24, *Z*/*E* = 20:80)[c]
2	**181b**	 **183a**: *Z*/*E* = 99:1	 **184c**: 69, *Z*/*E* = 1:99 (58, *Z*/*E* = 69:31)[c]
3	**181c**	 **183b**: *Z*/*E* = 10:90	 **184d**: 80, *Z*/*E* = 1:99 (8, *Z*/*E* = 1:99)[c]
4	**181c**	 **183a**: *Z*/*E* = 99:1	 **184e**: 57, *Z*/*E* = 1:99 (66, *Z*/*E* = 72:28)[c]
5	**181c**	 **183c**: *Z*/*E* = 18:82	 **184f**: 82, *Z*/*E* = 1:99 (80, *Z*/*E* = 53:47)[c]

6	**181c**	 **183d**: *Z*/*E* = 1:99	 **184g**: 87, *Z*/*E* = 9:91 (77, *Z*/*E* = 4:96)[c]
7	**181d**	 **183a**: *Z*/*E* = 99:1	 **184h**: 77, *Z*/*E* = 1:99 (74, *Z*/*E* = 81:19)[c]
8	**181e**	 **183a**: *Z*/*E* = 99:1	 **184i**: 64, *Z*/*E* = 1:99 (51, *Z*/*E* = 57:43)[c]
9	**181f**	 **183b**: *Z*/*E* = 10:90	 **184j**: 78, *Z*/*E* = 1:99 (39, *Z*/*E* = 20:80)[c]
10	**181f**	 **183a**: *Z*/*E* = 99:1	 **184k**: 84, *Z*/*E* = 1:99 (48, *Z*/*E* = 99:1)[c]
11	**181g**	 **183b**: *Z*/*E* = 10:90	 **184l**:[d] 20, *Z*/*E* = 21:79 91, *Z*/*E* = 5:95[e] (traces, *Z*/*E* = 50:50)[c]
12	**181d**	 **183e**: *Z*/*E* = 98:2	 **184m**: 74, *Z*/*E* = 98:2 (19, *Z*/*E* = 73:27)[c]
13	**181e**	 **183e**: *Z*/*E* = 98:2	 **184n**: 66, *Z*/*E* = 70:30 (41, *Z*/*E* = 72:28)[c]

[a] For clarity reasons, the magnesium salt has been omitted. [b] Yield of analytically pure product. [c] In parentheses, yield and *Z*/*E* ratio obtained without catalysis. [d] Yields determined by GC and ^{1}H-NMR. [e] After 18 h.

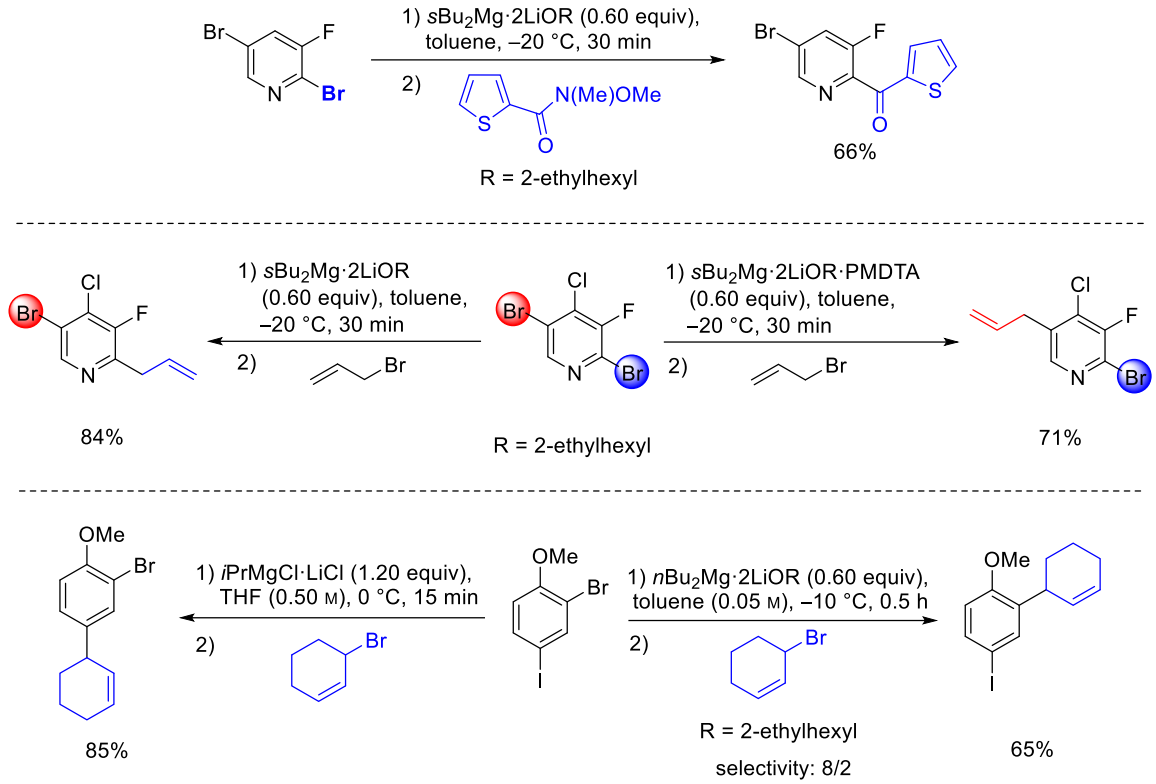
Furthermore, the cross-coupling of **181a** with (2-bromovinyl)trimethylsilane (**183b**; *Z/E* = 10:90) gave the olefin **184b** in 98% yield with complete *E*-selectivity (*Z/E* = 1:99) whereas the yield without iron salt was 24% (*Z/E* = 20:80, Table 13, entry 1). When the electron-rich *bis*-(3,4-dimethoxyphenyl)manganese (**181b**) was mixed with **183a**, the *E*-acrylate **184c** was generated in 69% yield and a *Z/E* = 69:31 mixture of products was obtained in 58% yield without an iron catalyst (entry 2). The tri-substituted *bis*-(3,4,5-trimethoxyphenyl)manganese (**181c**) underwent smooth cross-coupling with **183b** to afford the *E*-alkene **184d** in 80% (8% were obtained without a catalyst, entry 3). Additionally, **181c** reacted with **183a** and 2-bromostyrene (**183c**; *Z/E* = 18:82) to give the acrylate **184e** and **184f** (*Z/E* = 1:99) in 57% and 82% yield whereas 66% (*Z/E* = 72:28) and 80% (*Z/E* = 53:47) were respectively obtained without a catalyst (entries 4–5). In the last experiment, **181c** reacted with (*E*)-1-iodooctene (**183d**) to provide the alkene **184g** in 87% yield (*Z/E* = 9:91) when 77% yield (*Z/E* = 4:96) was obtained without a catalyst (entry 6). Furthermore, *bis*-(4-(trifluoromethoxy)phenyl)manganese (**181d**) reacted with **183a** to provide the acrylate **184h** (*Z/E* = 1:99) in 77% yield (entry 7). The reaction without $Fe(acac)_3$ gave a similar yield but a mix of the two isomers (74%, *Z/E* = 81:19, entry 7). The silicon-containing *bis*-(aryl)manganese reagent **181e** could also react with **183a**, which produces **184i** (*Z/E* = 1:99) in 64% yield (51%, *Z/E* = 57:43 were obtained without $Fe(acac)_3$, entry 8). Some good yields could be achieved in the absence of the iron catalyst (entries 2, 4–8), which could be attributed to the catalytic activity of the manganese(II) itself. For example, manganese salts proved to efficiently catalyze several couplings of organomagnesium reagents with alkenyl electrophiles in the past.[185] The *bis*-benzo[d][1,3]dioxol-5-ylmanganese (**181f**) also reacted with **183a** and **183b** to yield the *E*-alkenes **184j** and **184k** in 78–84% yield (entries 9–10). The bulkier *bis*-mesitylmanganese **181g** reacted with **183b** to afford **184l** with a small 20% yield (91% after 18 h, entry 11). This method also proved to tolerate nitriles, since 4-(2-bromovinyl)benzonitrile **183e** (*Z*/*E* = 98:2) could be used as a coupling partner with **181d** and **181e** in good yields (entries 12–13).

7 Summary

In this thesis, several challenges in the field of organometallic chemistry have been dealt with. First, the use of the highly reactive exchange reagents of type *s*Bu_2Mg·2LiOR (R = 2-ethylhexyl) to perform regioselective Br/Mg exchanges on a plethora of polyhalogenated (hetero)arenes offered a versatile method for the generation of highly functionalized halogenated building blocks. The fact that this type of reagents was utilized in apolar solvants such as toluene avoided any solvent coordination and displayed interesting regioselectivities by proximity effect. Moreover, it triggered a total regioselectivity switch on dibromo-pyridines and -quinoline when the substrate was prevented from coordinating to the exchange reagent by adding PMDTA. Although never being observed in any case before, a preference for a Br/Mg over an I/Mg exchange on 2-bromo-4-iodoanisole derivatives was discovered using *n*Bu_2Mg·2LiOR. Next, reagents of the type R_2Mg (R = *s*Bu, Mes) were successfully used to generate di(hetero)aryl magnesium species bearing sensitive functional groups such as a triazene, an ester or a nitro group *via* I/Mg- and Br/Mg- exchange reactions in apolar solvents. The methodology was extended to alkenyl iodides to provide the first dialkenyl magnesium reagents in apolar solvents. Furthermore, a lithium alkoxide complexed dialkylzinc reagent was developed for a solvent independent halogen/zinc exchange. These reagents of type ^1R_2Zn·2LiOR allowed not only the exchange of aryl iodides in solvents such as THF or toluene, but also the first bromine/zinc exchange using dialkylzinc reagents. Additionally, highly sensitive functional groups such as ketones, aldehydes or nitro groups were tolerated by these new reagents. Also, a regioselective version of those I/Zn exchanges was developed on polyiodinated (hetero)arenes, furnishing iodinated (hetero)aryl zincs. Many iodinated building blocks bearing sensitive functional groups were obtained. Next, an iron-catalyzed cross-coupling of functionalized benzylic manganese chlorides – which were prepared in a one-pot manner – with alkenyl iodides, bromides and triflates provided a greener alternative to usual transition-metal-catalyzed carbon-carbon bond-forming coupling methodologies for accessing various di-, tri- and tetra-substituted alkenes with total retention of stereochemistry. Sensitive functional groups such as nitriles or esters were tolerated, which resulted in the acquisition of highly functionalized alkenes. Finally, owing to the development of a new one-pot reaction, an extension of the last method to *bis*-(aryl)manganese species allowed the preparation of alkenes through an iron-catalyzed cross-coupling with alkenyl halides.

7.1 Regioselective Bromine/Magnesium Exchange for the Selective Functionalization of Polyhalogenated Arenes and Heterocycles

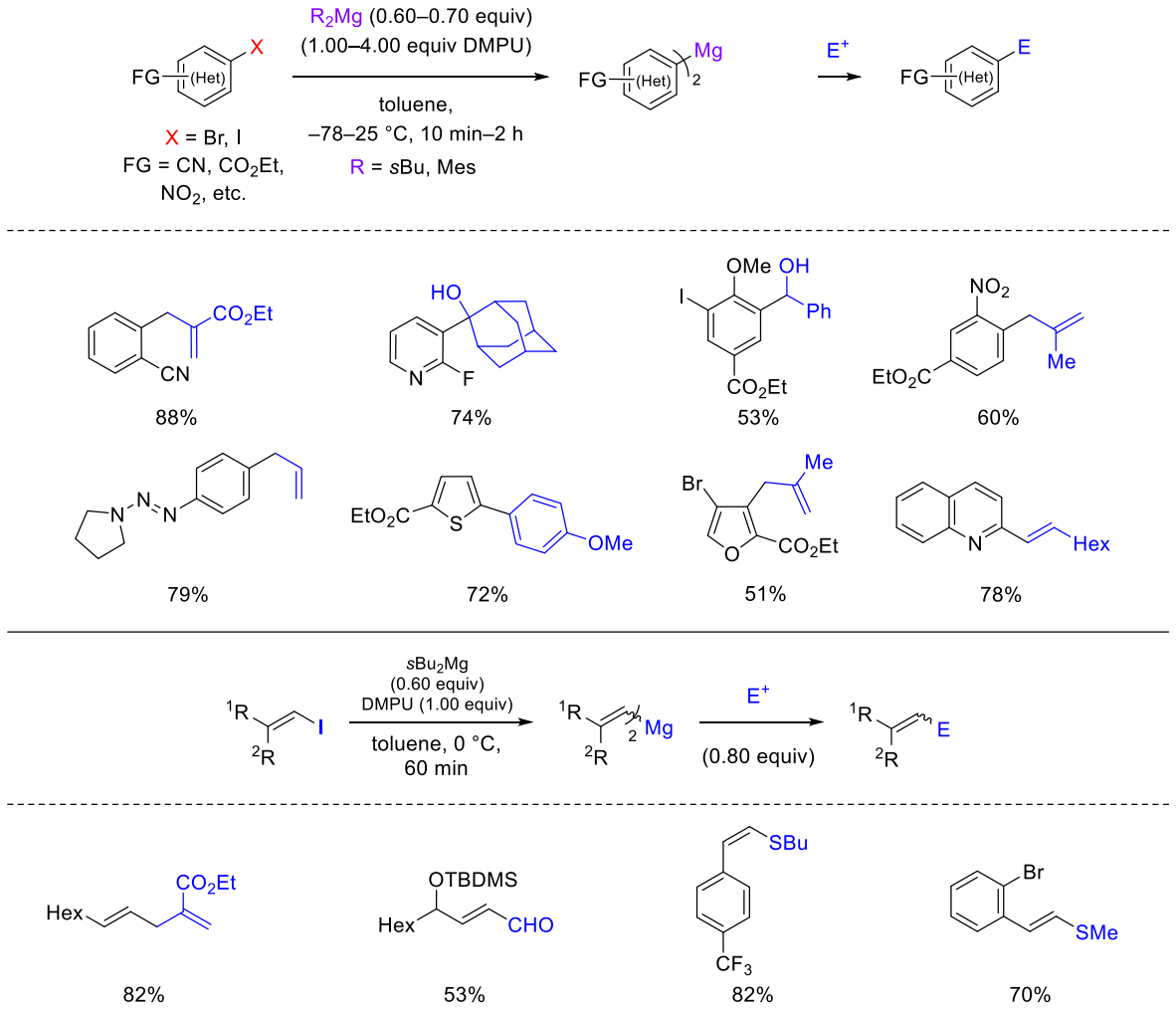
Regioselective Br/Mg exchanges of polybromo(hetero)arenes using reagents of the type $R_2Mg{\cdot}2LiOR^1$ (R = *s*Bu, *n*Bu; R^1 = 2-ethylhexyl) in toluene have been reported. In some cases, a regioselectivity switch of the exchange could be achieved by adding a chelating ligand like PMDTA. These interesting selectivites which cannot be reached using *turbo*-Grignard reagents allowed for the first time a preference for a Br/Mg over an I/Mg exchange on some 2-bromo-4-iodoanisole derivatives (Scheme 56).



Scheme 56: Examples of selective Br/Mg exchanges and regioselectivitiy switch using reagents of the type $R_2Mg{\cdot}2LiOR^1$.

7.2 Preparation of Functionalized Diorganomagnesium Reagents in Toluene *via* Bromine or Iodine/Magnesium Exchange Reactions

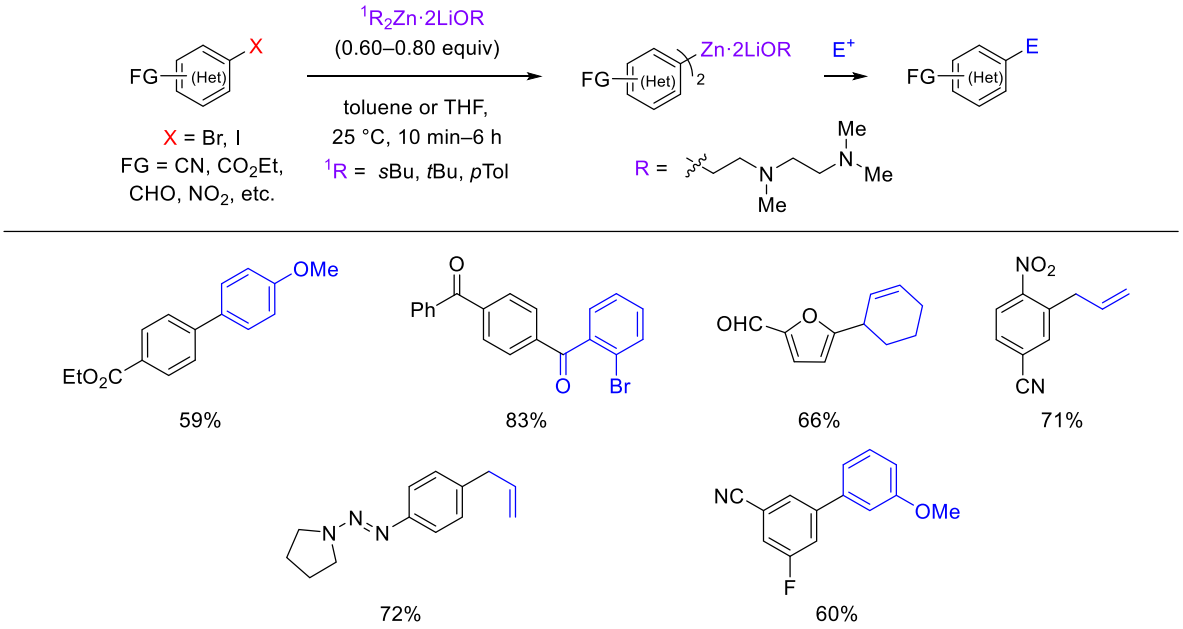
Various polyfunctionalized iodo- and bromo(hetero)arenes underwent efficient halogen/magnesium exchange upon addition of R_2Mg (R = *s*Bu, Mes) in toluene under mild reaction conditions. The resulting di(hetero)arylmagnesium reagents, which tolerated functions like a nitro or triazene group, reacted smoothly with electrophiles *via* cross-couplings, allylations, acylations, and addition to aldehydes or ketones. The method was successfully extended to a retentive I/Mg exchange on alkenyl iodides to provide reactive alkenylmagnesium species in toluene (Scheme 57).



Scheme 57: Examples of Halogen/Magnesium exchanges on sensitive (hetero)aryl halides using R_2Mg (R = *s*Bu, Mes).

7.3 Preparation of Polyfunctional Arylzinc Organometallics in Toluene *via* Halogen/Zinc Exchange Reactions

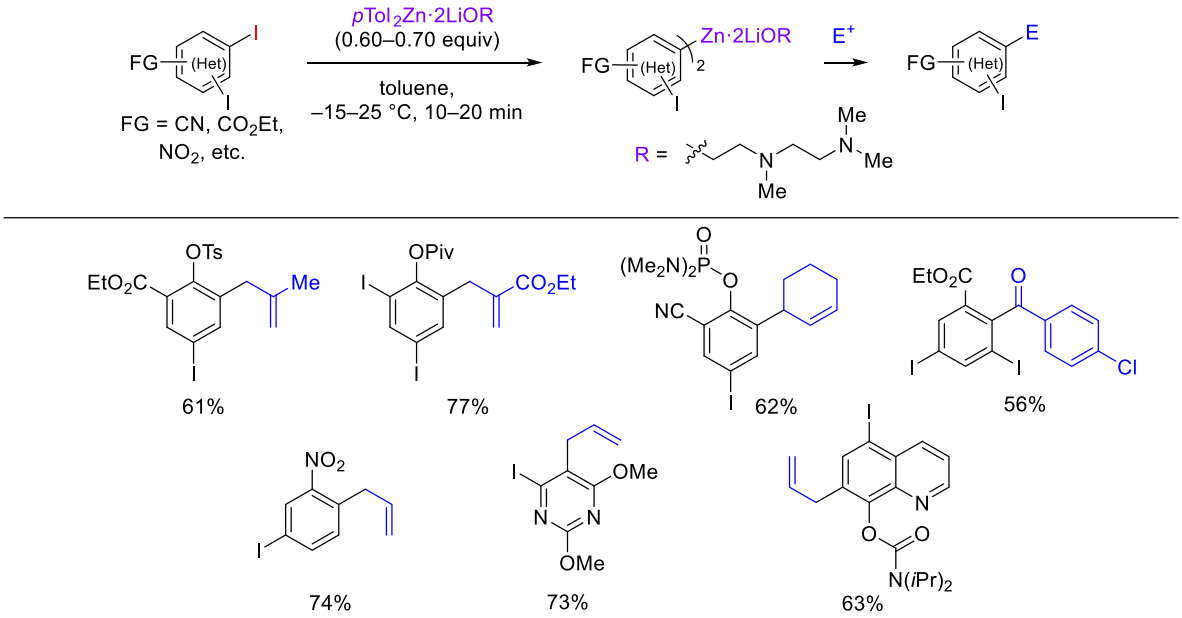
New bimetallic reagents of type $^{1}R_2Zn{\cdot}2LiOR$ for the I/Zn and Br/Zn exchange reactions have been developed. Thanks to the mild nature of organozinc compounds, several highly sensitive functional groups including triazines, ketones, aldehydes or nitro groups could be tolerated. Thus, quenching of the formed diarylzinc species with various electrophiles allowed the preparation of a plethora of functionalized (hetero)arenes. Additionally, the exchange could not only be performed in hydrocarbons such as toluene or hexane, but also in ethereal solvents including THF, 2-methyl-THF or MTBE (Scheme 58).



Scheme 58: The halogen/zinc exchange using dialkylzinc reagents complexed with lithium alkoxides of type $^{1}R_2Zn{\cdot}2LiOR$.

7.4 Regioselective Iodine/Zinc Exchange for the Selective Functionalization of Polyiodinated Arenes and Heterocycles in Toluene

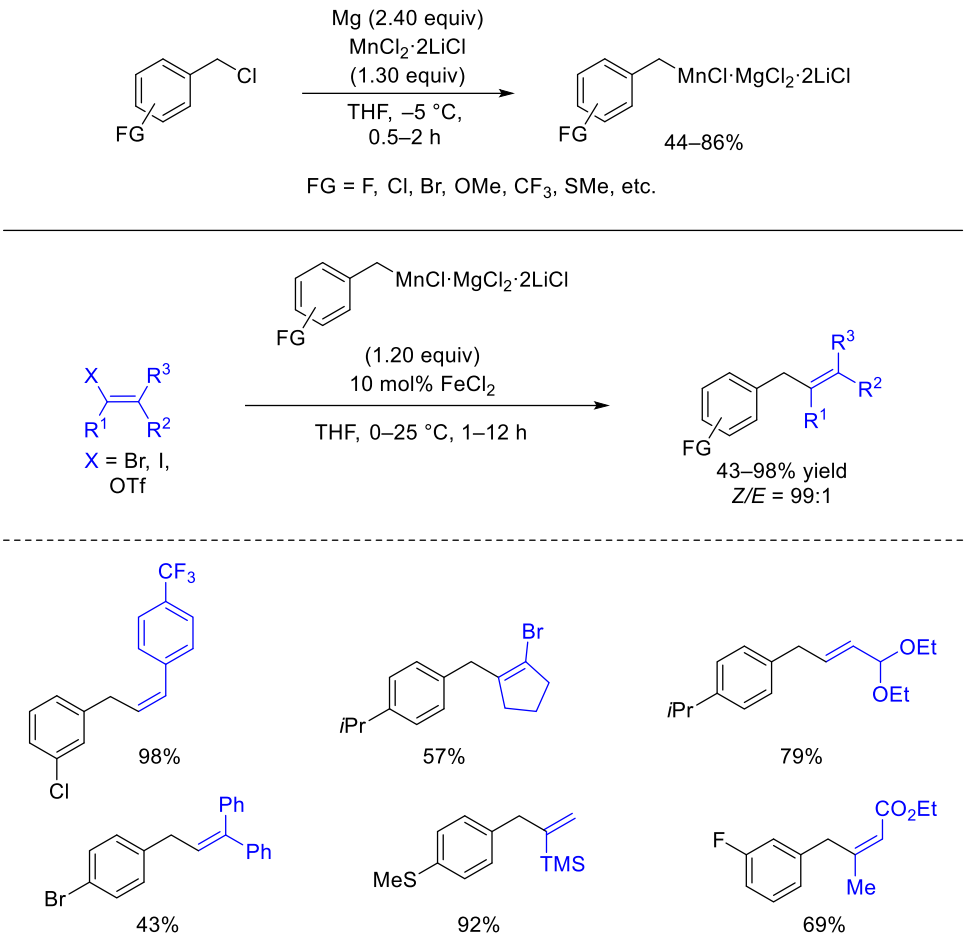
Various polyiodo-arenes and –heteroarenes underwent efficient and regioselective I/Zn exchanges upon addition of the bimetallic combination *p*Tol$_2$Zn·2LiOR (R = (CH$_2$)$_2$N(Me)(CH$_2$)$_2$NMe$_2$) in toluene under mild reaction conditions. The resulting iodo-substituted diorganozinc reagents reacted effectively with electrophiles such as allyl bromides and acyl chlorides (Scheme 59).



Scheme 59: Regioselective iodine/zinc exchange on polyiodo(hetero)arenes using *p*Tol$_2$Zn·2LiOR.

7.5 Iron-Catalyzed Cross-Coupling of Functionalized Benzylmanganese Halides with Alkenyl Iodides, Bromides and Triflates

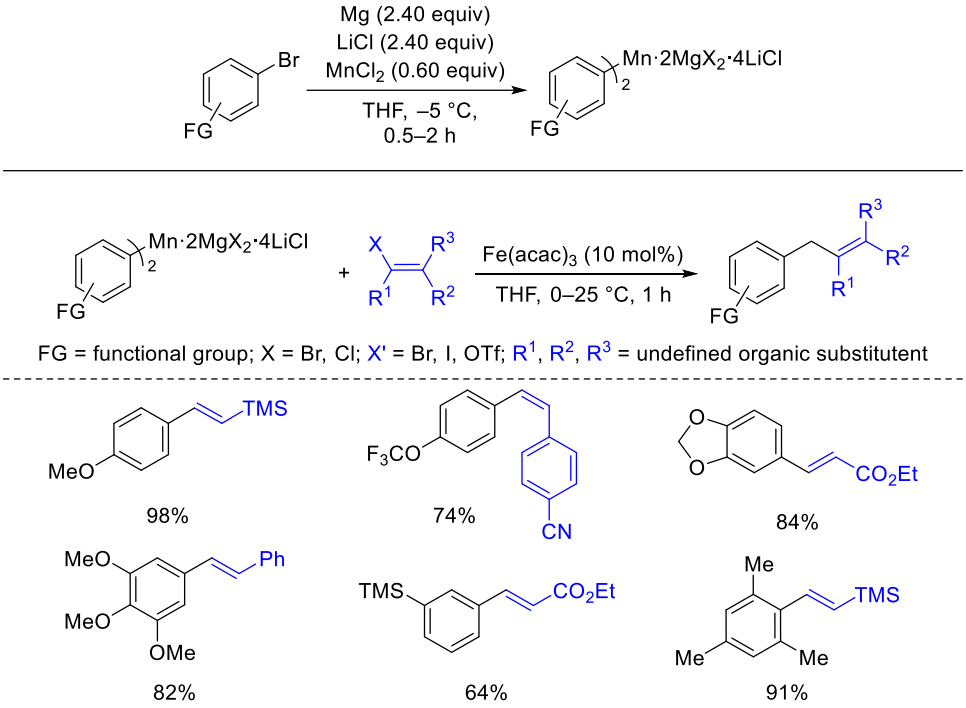
Starting from benzylic chlorides, various functionalized benzylic manganese species have been readily prepared by insertion of magnesium in the presence of $MnCl_2 \cdot 2LiCl$ in THF under convenient conditions. These benzylic manganese reagents smoothly reacted with various functionalized alkenyl iodides, bromides, triflates and iodoacrylates in the presence of a catalytic amount of $FeCl_2$ at room temperature. Di-, tri- or tetra-substituted alkenes were formed with a good functional group tolerance. Aryl halides were for instance tolerated and can serve as a handle for further functionalization (Scheme 60).



Scheme 60: Generation of benzylic manganese reagents *via* Mg insertion and *in situ* transmetalation in the presence of $MnCl_2 \cdot 2LiCl$, followed by Fe-catalyzed cross-couplings with alkenyl iodides, bromides, triflates and iodoacrylates with retention of stereochemistry.

7.6 Iron-Catalyzed Cross-Coupling of Functionalized *Bis*-(aryl)manganese Nucleophiles with Alkenyl Halides

Various substituted *bis*-(aryl)manganese species were prepared from aryl bromides by a new one-pot insertion of magnesium turnings in the presence of LiCl and *in situ* transmetalation with $MnCl_2$ in THF at −5 °C within 2 h. These *bis*-(aryl)manganese reagents underwent smooth iron-catalyzed cross-couplings using 10 mol% $Fe(acac)_3$ with various functionalized alkenyl iodides and bromides in 1 h at 25 °C.Various alkenes were formed with a good functional group tolerance (Scheme 61).



Scheme 61: Generation of *bis*-(aryl)manganese reagents *via* Mg insertion and *in situ* transmetalation in the presence of $MnCl_2$ and LiCl, followed by Fe-catalyzed cross-couplings with alkenyl halides.

C. EXPERIMENTAL PART

1 General Considerations

All reactions were carried out under argon or nitrogen atmosphere in glassware dried with a heat gun (650 °C) under high vacuum (<1 mbar). Syringes which were used to transfer anhydrous solvents or reagents were purged thrice with argon or nitrogen prior to use. Indicated yields are isolated yields of compounds estimated to be >95% pure as determined by ^{1}H-NMR (25 °C) and capillary GC. Unless otherwise indicated, all reagents were obtained from commercial sources.

1.1 Solvents

Solvents were dried according to standard procedures by distillation over drying agents as stated below and stored under argon. Otherwise, they were obtained from commercial sources and used without further purification.

THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen and then stored over molecular sieves.
Toluene was continuously refluxed and freshly distilled from sodium under nitrogen and stored over molecular sieves.
CH_2Cl_2 (DCM), ***N*,*N*′-Dimethylpropyleneurea (DMPU)**, **MeCN**, **Me_2NCHO (DMF), MTBE** and **NMP** were distilled from CaH_2 and stored over molecular sieves.
Et_2O was predried over calcium hydride and dried with the solvent purification system SPS-400-2 from Innovative Technologies Inc.
TMEDA and **PMDTA** were freshly distilled from calcium hydride under nitrogen.

Solvents for column chromatography were distilled on a rotary evaporator prior to use.

1.2 Reagents

All reagents were obtained from commercial sources and used without further purification unless otherwise stated. Liquid aldehydes and acyl chlorides were distilled prior to use.

***n*BuLi**, ***s*BuLi**, ***t*BuLi** solutions in hexane were purchased from Albemarle and the concentrations were titrated with *N*-benzylbenzamide in THF at –20 °C (–40 °C for *s*BuLi).[186]

***p*Tolyllithium (*p*TolLi)**: According to a literature procedure,[159] lithium granulas (306 mg, 44 mmol) were placed in a dry and argon-flushed *Schlenk*-flask and cooled to 0 °C. Then, a solution of 4-

[186] A. F. Burchat, J. M. Chong, N. Nielsen, *J. Organomet. Chem.* **1997**, *542*, 281.

chlorotoluene (2.37 mL, 20 mmol) in dry Et_2O (20 mL) was added dropwise over 40 min and stirred for 2 hours at the same temperature. A concentration of 0.80-1.00 M was obtained. The solution was filtered twice prior to use and was titrated with *N*-benzylbenzamide in THF at 0 °C.[186]

MesLi solution in ether: MesBr (20.00 mmol) was diluted in ether (40 mL) and *t*Buli (44.0 mmol) in hexane was added dropwise at −60 °C. After 1 h, the solution was titrated with *N*-benzylbenzamide at 0 °C.[186]

***s*BuMgCl** and **MesMgCl** solution in diethyl ether were purchased from Sigma Aldrich and were titrated with I_2 in a 0.50 M LiCl solution in THF at 25 °C.[178]

***i*PrMgCl·LiCl** solution in THF was obtained from Albemarle and the concentration was determind by iodometric titration.[178]

***n*Bu$_2$Mg** solution in hexane was purchased from Albemarle and titrated with I_2 in a 0.50 M LiCl solution in THF at 0 °C.[178]

Magnesium-2-ethylhexanolate was purchased from Albemarle and the concentration was determined by acidimetric titration with 4-(phenylazo)-diphenylamine and CF_3CO_2H (TFA) in toluene at 0 °C.

Et$_2$Zn: **Either** a Commerially available Et_2Zn (purchased from Sigma Aldrich, 15 wt.% (= 1.11 M) in toluene) was used **or** Et_2Zn (100 mmol) was dissolved in dry toluene (100 mL) and titrated against I_2 in a 0.50 M LiCl solution in THF at 0 °C. Both Et_2Zn reagents were suitable for the performed reactions.

1.00 M CuCN·2LiCl solution in THF: CuCN (80.0 mmol, 7.17 g) and LiCl (160 mmol, 6.77 g) were dried in a *Schlenk*-flask under vacuum at 140 °C for 12 h. After cooling, dry THF (80 mL) was added and stirring continued until the salts were dissolved.[130]

1.00 M ZnCl$_2$ solution in THF: $ZnCl_2$ (100 mmol, 13.6 g) was dried in a *Schlenk*-flask under vacuum at 140 °C for 5 h. After cooling, 100 mL dry THF were added and stirring was continued until the salt was dissolved.

1.00 M MnCl$_2$·2LiCl solution in THF: A dry and argon-flushed 250 mL *Schlenk*-flask, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (8.48 g, 200 mmol), heated to 450 °C under high vacuum and after cooling to room temperature under vacuum furthermore vigorously stirred at 160 °C for 3 h. Subsequently, $MnCl_2$ (12.6 g, 100 mmol) was added under argon at room temperature and the reaction mixture as heated to 160 °C for 3 h under high vacuum. After cooling to room temperature, the flask as charged with freshly distilled THF (100 mL) and the mixture was stirred for 48 h at 25 °C. The resulting $MnCl_2·2LiCl$ (1.00 M in THF) solution appeared as a light brown liquid.

0.50 M LiCl solution in THF: LiCl (5.00 mmol) was dried in vacuo using a heatgun (400 °C) for 10 min. After cooling to room tempetature, dry THF (10 mL) was added and the mixture stirred until the salt was dissolved completely.

2-((2-(Dimethylamino)ethyl)(methyl)amino)ethane-1-ol: The alcohol was distilled in vacuo from CaH_2 (29 mbar, 95 °C) and stored under argon in a *Schlenk*-flask.

1.3 Chromatography

Flash column chromatography was performed using silica gel 60 (0.040–0.063 mm, 230–400 mesh ASTM) from Merck.
Thin layer chromatography was performed using aluminum plates covered with SiO_2 (Merck 60, F-254). The chromatograms were examined under 254 nm UV irradiation. When necessary, a staining of the TLC plate was performed with a PMA solution (10 g of PMA dissolved in 100 mL absolute ethanol) followed by heating with a heat gun.

1.4 Analytical Data

NMR spectra were recorded on VARIAN Mercury 200, BRUKER AXR 300, VARIAN VXR 400 S and BRUKER AMX 600 instruments in $CDCl_3$ unless otherwise stated. Chemical shifts are reported as δ-values in parts per million (ppm) relative to the residual solvent peak $CDCl_3$ (δH: 7.26; δC: 77.16), $(CD_3)_2SO$ (δH: 2.50; δC: 39.52). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. If not otherwise noted, the coupling constants given are H-H-coupling constants for proton signals and C-F-coupling constants for carbon signals.

High Resolution Mass Spectroscopy (HRMS) electron impact ionization (EI) and low resolution (MS) spectra were recorded on a FINNIGAN MAT 95Q instrument. EI was conducted with an electron energy of 70 eV. Electrospray ionization (ESI) spectra were recorded on a FINNIGAN LTQ FTICR instrument.

Gas chromatography (GC) was performed on machines of the types Hewlett-Packard 6890 or 5890 Series II (Hewlett Packard, 5% phenylmethylpolysiloxane; length: 10 m, diameter: 0.25 mm; film thickness: 0.25 μm). The detection was accomplished using a flame ionization detector.

Infrared spectra (IR) were recorded from 4500 cm^{-1} to 650 cm^{-1} on a PERKIN ELMER Spectrum BX-59343 instrument. For detection a SMITHS DETECTION DuraSamplIR II Diamond ATR sensor was used. Samples were measured neat. The absorption bands are reported in wavenumbers (cm^{-1}).

Melting points (M.p.) were determined on a BÜCHI B-540 apparatus and are uncorrected.

2 Regioselective Bromine/Magnesium Exchange for the Selective Functionalization of Polyhalogenated Arenes and Heterocycles

2.1 Preparation and Titration of Reagents of Type ^{1}RMgOR·LiOR and^{1}R$_2$Mg·2LiOR

Preparation of *s*BuMgOCH$_2$CH(Et)Bu·LiOCH$_2$CH(Et)Bu (134a):[71]

Method A:

A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with *n*Bu$_2$Mg (0.66 M in hexane, 15.0 mL, 9.90 mmol) and the reaction mixture was cooled to 0 °C. Then, 2-ethylhexanol (3.10 mL, 19.8 mmol) was added dropwise. After 12 h a gelatinous solution was obtained. To the reaction mixture *s*BuLi (1.21 M in hexane, 8.18 mL, 9.9 mmol) was added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature for 2 h. The solvents were removed under vaccum affording a lightly yellow foam. Freshly distilled toluene (9 mL) was added under vigourous stirring at 0 °C. The freshly prepared *s*BuMgOCH$_2$CH(Et)Bu·LiOCH$_2$CH(Et)Bu was titrated prior to use at 0 °C by iodometric titration.[178] The *s*BuMgOCH$_2$CH(Et)Bu·LiOCH$_2$CH(Et)Bu concentration of the resulting clear solution was 1.00–1.50 M.

Method B:

A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with Mg[OCH$_2$CH(Et)Bu]$_2$ (0.85 M in heptane, 15.0 mL, 12.8 mmol)[187] and was cooled to 0 °C. Then, *s*BuLi (1.21 M in hexane, 10.6 mL, 12.8 mmol) was added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature for 2 h. The solvents were removed under vaccum affording a lightly yellow foam. Freshly distilled toluene (9 mL) was added under vigourous stirring at 0 °C. The prepared *s*BuMgOCH$_2$CH(Et)Bu·LiOCH$_2$CH(Et)Bu was titrated prior to use at 0 °C by iodometric titration.[178] The *s*BuMgOCH$_2$CH(Et)Bu·LiOCH$_2$CH(Et)Bu concentration of the resulting clear solution was 1.00–1.50 M.

Preparation of *s*Bu$_2$Mg·2LiOCH$_2$CH(Et)Bu (134b):[71]

Method A:

A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with *n*Bu$_2$Mg (0.66 M in hexane, 15.0 mL, 9.90 mmol) and the reaction mixture was cooled to 0 °C.

[187] This magnesium alkoxide solution (0.94 M in *n*heptane) is commercially available from Albemarle, Frankfurt: U. Wietelmann, U. Emmel, J. Roeder, M. Steinbild, K. Papstein (Albemarle), WO-2010146122, **2010**.

Then, 2-ethylhexanol (3.10 mL, 19.8 mmol) was added dropwise. After 12 h a gelatinous solution was obtained. To the reaction mixture *s*BuLi (1.21 M in hexane, 16.36 mL, 19.8 mmol) was added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature for 2 h. The solvents were removed under vaccum affording a lightly yellow foam. Freshly distilled toluene (9 mL) was added under vigourous stirring at 0 °C. The prepared *s*Bu_2Mg·2LiOCH_2CH(Et)Bu was titrated prior to use at 0 °C by iodometric titration.[178] The *s*Bu_2Mg·2LiOCH_2CH(Et)Bu concentration of the resulting clear solution was 0.60–0.85 M.

Method B:

A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with Mg[OCH_2CH(Et)Bu]$_2$ (0.85 M in heptane, 15.0 mL, 12.8 mmol)[187] and was cooled to 0 °C. Then, *s*BuLi (1.21 M in hexane, 21.2 mL, 25.6 mmol) was added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature for 2 h. The solvents were removed under vaccum affording a lightly yellow foam. Freshly distilled toluene (9 mL) was added under vigourous stirring at 0 °C. The freshly prepared *s*Bu_2Mg·2LiOCH_2CH(Et)Bu was titrated prior to use at 0 °C by iodometric titration.[178] The *s*Bu_2Mg·2LiOCH_2CH(Et)Bu concentration of the resulting clear solution was 0.60–0.85 M.

Note 1: Analogous reagents *t*Bu_2Mg·2LiOR and *n*Bu_2Mg·2LiOR (**134c**) were prepared following the same procedures using *t*BuLi or *n*BuLi instead of *s*BuLi and gave similar concentrations.
Note 2: All reagents should be storred at –20 °C and used within 2 weeks.

Titration Using Iodine[178]

A dry-*flask* was charged with accurately weighed I_2 (128 mg, 0.504 mmol), fitted with a rubber septum, and flushed with argon. THF (2 mL) was added and stirring was started. After the iodine was completely dissolved, the resulting brown solution was cooled to 0 °C in an ice bath and the organomagnesium reagent was added dropwise *via* a 1.00-mL syringe (0.01-mL graduations) until the brown color disappeared. The amount consumed contains 1.00 equiv of the organometallic reagent relative to iodine in the case of monoorganometallic reagents and 0.50 equiv for diorganometallic reagents.

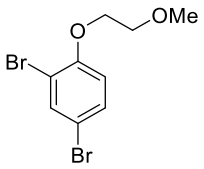
2.2 Typical Procedure

Typical Procedure 1: Preparation of Di(hetero)arylmagnesium Alkoxides *via* a Bromine/Magnesium-Exchange Followed by Electrophilic Functionalization

A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding (hetero)aryl bromide (1.00 equiv) and dissolved in dry toluene (0.50 M or 0.05 M, specified for every single procedure). When needed, *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDTA, 0.60 equiv, specified for every single procedure) was added. Then, the exchange reagent $^{1}R_2Mg \cdot 2LiOR$ (R = 2-ethylhexyl, ^{1}R = *s*Bu for **134b** or *n*Bu for **134c**, 0.60 equiv) was added dropwise at the specified temperature and the reaction stirred for the indicated time. The completion of the bromine/magnesium exchange was checked by GC-analysis of reaction aliquots quenched with a sat. aq. NH_4Cl solution, using undecane as internal standard. Subsequent reactions with electrophiles were carried out under the indicated conditions. After complete conversion, the mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel using the appropriate eluent.

2.3 Starting Materials

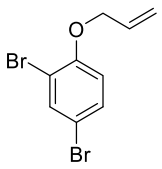
Synthesis of 2,4-dibromo-1-(2-methoxyethoxy)benzene (135b)



A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with 2,4-dibromophenol (1.00 g, 3.97 mmol) and DMF (10 mL) and was cooled to 0 °C. NaH (60%, 191 mg, 4.76 mmol) was slowly added at 0 °C and the reaction mixture was stirred for 30 min. 1-Chloro-2-methoxyethane (451 mg, 4.76 mmol) was then added at 0 °C and the reaction mixture was stirred at 100 °C overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.43) to give the product **135b** (1.22 g, 3.94 mmol, 99% yield) as a brown oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.66 (d, *J* = 2.4 Hz, 1H), 7.35 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 4.31 – 3.99 (m, 2H), 3.86 – 3.74 (m, 2H), 3.47 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 154.8, 135.7, 131.3, 114.9, 113.4, 70.9, 69.4, 59.7.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2926, 2879, 1579, 1474, 1449, 1382, 1369, 1283, 1264, 1246, 1197, 1150, 1127, 1097, 1083, 1057, 1041, 926, 866, 798, 696, 677.
MS (EI, 70 eV, %) m/z = 312 (48), 310 (97), 308 (50), 254 (47), 252 (100), 251 (12), 250 (53), 225 (16), 223 (33), 221 (17), 156 (13), 154 (13), 145 (10), 143 (10), 75 (11), 63 (12), 59 (64).
HRMS (EI, 70 eV) m/z: calc. for **$C_9H_{10}Br_2O_2$**: 307.9048; found: 307.9041.

Synthesis of 1-(allyloxy)-2,4-dibromobenzene (135c)



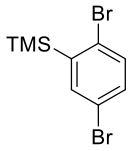
A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with 2,4-dibromophenol (5.04 g, 20.0 mmol), DMF (10 mL) and K_2CO_3 (3.32 g, 24.0 mmol) and stirred for 5 min. Allyl bromide (2.42 g, 20.0 mmol) was slowly added and the reaction mixture was stirred

overnight. The mixture was diluted with water (100 mL) and extracted with hexanes (3 x 100 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified *via* silica plug (*iso*hexane) to give the product **135c** (4.87 g, 16.7 mmol, 84% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.67 (d, *J* = 2.4 Hz, 1H), 7.35 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 6.04 (ddt, *J* = 17.3, 10.2, 5.0 Hz, 1H), 5.47 (dq, *J* = 17.3, 1.7 Hz, 1H), 5.32 (dq, *J* = 10.6, 1.5 Hz, 1H), 4.59 (dt, *J* = 5.0, 1.6 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 154.4, 135.7, 132.3, 131.3, 118.2, 114.8, 113.3 (2C), 70.0.

The spectra matched those of the literature.[188]

Synthesis of (2,5-dibromophenyl)trimethylsilane (139c)



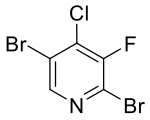
A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with *i*PrMgCl·LiCl (7.9 mL, 8.70 mmol) and was cooled to −50 °C. 1,2,4-Tribromobenzene (2.50 g, 7.90 mmol) was added at −50 °C and the reaction mixture was stirred for 2 h. The completion of the bromine/magnesium exchange was checked by GC-analysis of reaction aliquots quenched with water, using undecane as internal standard. Trimethylsilyl chloride (2.0 mL, 15.8 mmol) was then added at −20 °C and the reaction mixture was allowed to warm to room temperature overnight. After complete conversion, the mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.90) to give the product **139c** (2.08 g, 6.75 mmol, 85% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.40 (d, *J* = 2.5 Hz, 1H), 7.28 (s, 1H), 7.19 (dd, *J* = 8.4, 2.5 Hz, 1H), 0.30 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 144.2, 138.7, 134.5, 133.7, 128.9, 121.6, −0.6.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2954, 2899, 1560, 1541, 1535, 1438, 1407, 1355, 1260, 1249, 1136, 1102, 1084, 1045, 1024, 1013, 886, 837, 810, 761, 751, 703, 690, 661.

[188] W. Lasek, M. Makosza, *Synthesis* **1993**, 780.

MS (EI, 70 eV, %) m/z = 308 (12), 295 (50), 293 (100), 291 (52), 213 (23), 211 (28), 171 (13), 169 (13), 149 (27), 131 (50), 105 (22).
HRMS (EI, 70 eV) m/z: calc. for **$C_9H_{12}Br_2Si$**: 305.9075; found: 305.9066.

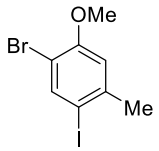
Synthesis of 2,5-dibromo-4-chloro-3-fluoropyridine (143e)



A dry and argon flushed round-bottomed-flask, equipped with a magnetic stirring bar, was charged with diisopropylamine (2.18 mL, 15.5 mmol) and freshly distilled THF (45 mL). The mixture was cooled to −78 °C and *n*BuLi (6.62 mL, 14.1 mmol) was slowly added. The reaction mixture was stirred for 10 min then cooled to 0 °C for 5 min. Then, 2,5-dibromo-3-fluoropyridine (**135g**, 3.6 g, 14.1 mmol, dissolved in 10 mL THF) was slowly added at −78 °C and the mixture was stirred for 1 h. After completion of the deprotonation, 1,1,2-trichloro-1,2,2-trifluoroethane (2.51 mL, 21.2 mmol) was slowly added at −78 °C. The reaction mixture was allowed to warm to room temperature overnight. The mixture was then quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.28) to give the product **143e** (2.67 g, 9.23 mmol, 65% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.38 (s, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 153.1 (d, *J* = 265.7 Hz), 147.0 (d, *J* = 6.6 Hz), 132.8 (d, *J* = 17.9 Hz), 129.0 (d, *J* = 23.8 Hz), 121.4 (d, *J* = 4.5 Hz).
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = −107.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1540, 1418, 1394, 1280, 1212, 1190, 1121, 1102, 907, 891, 807, 784.
MS (EI, 70 eV, %) m/z = 293 (12), 291 (70), 289 (100), 287 (42), 212 (16), 210 (64), 208 (49), 131 (21), 129 (62), 94 (11).
HRMS (EI, 70 eV) m/z: calc. for **C_5HBr_2ClFN**: 288.8128; found: 288.8124.

Synthesis of 1-bromo-5-iodo-2-methoxy-4-methylbenzene (148b)[189]



Under air, 1-bromo-2-methoxy-4-methylbenzene (3.00 g, 14.9 mmol), (diacetoxy)iodobenzene (2.64 g, 8.21 mmol) and finely crushed iodine (2.08 g, 8.21 mmol) were suspended in a mixture of acetic acid (30 mL) and acetic anhydride (15 mL). Then, H_2SO_4 (96% aq., 0.762 mL, 14.9 mmol) was added dropwise to start the reaction (exothermic addition), and then more slowly to avoid going over 40 °C. After coming back to room temperature, the mixture was diluted with DCM and the phases were separated. The organic phase was washed with water and then stirred vigorously with a 1.00 M NaOH solution in an Erlenmeyer-*flask* in order to quench the remaining $AcOH/Ac_2O$. Only then a 0.10 M $Na_2S_2O_3$ solution was added to quench the remaining iodine. The organic phase was dried and the solvent removed under reduced pressure. Then, the iodobenzene by-product was removed under vacuum. Recrystallization from MeOH (reflux to −18 °C) afforded the product **148b** (3.90 g, 11.9 mmol, 80% yield) as white crystals.

M.p. (°C): 108-110.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.89 (s, 1H), 6.79 (s, 1H), 3.87 (s, 3H), 2.39 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 156.1, 141.9 (d, *J* = 18.7 Hz), 113.4, 109.4, 89.5, 56.4, 28.2.

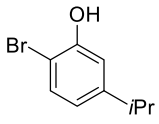
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2934, 1577, 1557, 1484, 1471, 1457, 1438, 1357, 1282, 1248, 1189, 1172, 1049, 878, 842.

MS (EI, 70 eV, %) m/z = 328 (99), 326 (100), 313 (30), 311 (31), 283 (10), 204 (17), 158 (12), 156 (11), 77 (15).

HRMS (EI, 70 eV) m/z: calc. for **C_8H_8BrIO**: 325.8803; found: 325.8799.

[189] Procedure from: Q. Dherbassy, J.-P. Djukic, J. Wencel-Delord, F. Colobert, *Angew. Chem. Int. Ed.* **2018**, *57*, 4668.

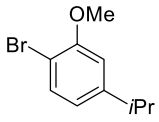
Synthesis of 2-bromo-5-isopropylphenol[190]



A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with 3-isopropylphenol (2.74 mL, 20.0 mmol) and DCM (35 mL) and was cooled down to 0 °C. Br_2 (1.05 mL, 20.4 mmol, in 17 mL DCM) was slowly added at 0 °C and the reaction mixture was allowed to warm to room temperature overnight. The mixture was quenched with a 0.10 M $Na_2S_2O_3$ solution and extracted with DCM (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.15) to give the product (1.70 g, 7.90 mmol, 40% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.35 (d, *J* = 8.2 Hz, 1H), 6.90 (d, *J* = 2.1 Hz, 1H), 6.69 (dd, *J* = 8.3, 2.1 Hz, 1H), 5.44 (s, 1H), 2.84 (p, *J* = 6.9 Hz, 1H), 1.22 (d, *J* = 6.9 Hz, 6H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 152.1, 150.9, 131.7, 120.3, 114.2, 107.2, 33.9, 23.9.
IR (ATR, cm^{-1}) ṽ = 3508, 2962, 1595, 1573, 1482, 1461, 1439, 1420, 1346, 1306, 1289, 1254, 1202, 1178, 1142, 1024, 941, 870, 806.
MS (EI, 70 eV, %) m/z = 216 (39), 214 (39), 201 (90), 199 (91), 120 (100), 91 (17).
HRMS (EI, 70 eV) m/z: calc. for **$C_9H_{11}BrO$**: 213.9993; found: 213.9987.

Synthesis of 1-bromo-2-methoxy-4-isopropylbenzene



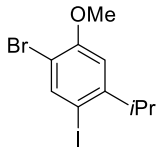
A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with 2-bromo-5-isopropylphenol (1.70 g, 7.90 mmol) and DMF (20 mL) and was cooled down to 0 °C. NaH (60%, 382 mg, 9.50 mmol) was slowly added at 0 °C and the reaction solution was stirred for 30 min. Methyl iodide (0.76 mL, 11.9 mmol) was then added at 0 °C and the reaction was allowed to warm to room temperature overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts

[190] Adapted procedure from: L. Shu, P. Wang, W. Liu, C. Gu, *Org. Process Res. Dev.* **2012**, *16*, 1866.

were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified *via* column chromatography (*iso*hexane, $R_f = 0.33$) to give the product (1.52 g, 6.63 mmol, 84% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.43 (d, *J* = 8.1 Hz, 1H), 6.76 (d, *J* = 1.9 Hz, 1H), 6.72 (dd, *J* = 8.1, 2.0 Hz, 1H), 3.90 (s, 3H), 2.88 (p, *J* = 6.9 Hz, 1H), 1.24 (d, *J* = 6.9 Hz, 6H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 155.8, 150.1, 133.1, 119.9, 110.6, 108.6, 56.2, 34.3, 24.1.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2961, 2938, 1590, 1577, 1482, 1464, 1410, 1286, 1259, 1197, 1059, 1045, 1025, 852, 812.
MS (EI, 70 eV, %) m/z = 230 (33), 228 (34), 215 (79), 213 (80), 149 (17), 134 (100), 119 (19), 91 (18).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{13}BrO$**: 228.0150; found: 228.0143.

Synthesis of 1-bromo-5-iodo-4-isopropyl-2-methoxybenzene (148c)[168]

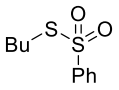


Under air, 1-bromo-2-methoxy-4-isopropylbenzene (1.51 g, 6.60 mmol), (diacetoxy)iodobenzene (1.20 g, 3.73 mmol) and finely crushed iodine (936 mg, 3.73 mmol) were suspended in a mixture of acetic acid (13 mL) and acetic anhydride (6 mL). Then, H_2SO_4 (96% aq., 0.330 mL, 6.71 mmol) was added dropwise to start the reaction (exothermic addition), and then more slowly to avoid going over 40 °C. After coming back to room temperature, the mixture was diluted with DCM and the phases were separated. The organic phase was washed with water and then stirred vigorously with a 1.00 M NaOH solution in an Erlenmeyer-*flask* in order to quench the remaining AcOH/Ac_2O. Only then a 0.10 M $Na_2S_2O_3$ solution was added to quench the remaining iodine. The organic phase was dried and the solvent removed under reduced pressure. Then, the iodobenzene by-product was removed under vacuum. Recrystallization from MeOH (reflux to −18 °C) afforded the product **148c** (1.06 g, 2.99 mmol, 45% yield) as yellow crystals.

M.p. (°C): 46-48.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.92 (s, 1H), 6.77 (s, 1H), 3.89 (s, 3H), 3.13 (p, *J* = 6.8 Hz, 1H), 1.22 (d, *J* = 6.8 Hz, 6H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 156.6, 151.2, 142.2, 109.9, 109.5, 89.3, 56.3, 38.2, 23.2.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2962, 1576, 1469, 1440, 1386, 1361, 1338, 1244, 1083, 1047.

MS (EI, 70 eV, %) m/z = 356 (48), 354 (49), 341 (40), 339 (41), 245 (11), 215 (10), 214 (96), 213 (10), 212 (100), 171 (17), 169 (17), 148 (12), 147 (10), 133 (18), 127 (29), 118 (11), 117 (15), 115 (21), 105 (23), 103 (22), 102 (12), 91 (12), 90 (19), 89 (36), 77 (21), 63 (10).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{12}BrIO$**: 353.9116; found: 353.9110.

Synthesis of *S*-butyl benzenesulfonothioate[191]



A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with butane-1-thiol (4.28 mL, 40.0 mmol), DCM (50 mL), water (25 mL) and iodine (5.58 g, 22 mmol) and stirred at room temperature for 30 min. The mixture was extracted with DCM (3 x 30 mL). The combined organic extracts were washed with water and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting solution of dibutyl disulfide was mixed with sodium benzenesulfinate (10.5 g, 64.0 mmol), iodine (10.1 g, 40 mmol) and DCM (50 mL) and stirred for 22 h at room temperature. Then, a 0.10 M $Na_2S_2O_3$ solution was added to quench the excess of iodine. The organic phase was washed and dried and the solvent removed under reduced pressure to afford *S*-butyl benzenesulfonothioate (8.77 g, 38.1 mmol, 95% yield) as a yellow oil.

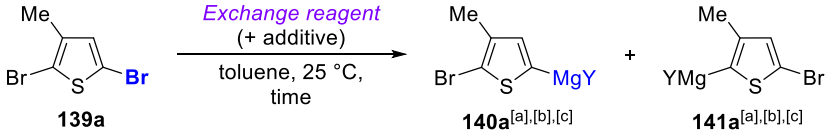
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.10 – 7.81 (m, 2H), 7.69 – 7.60 (m, 1H), 7.60 – 7.50 (m, 2H), 3.00 (t, *J* = 7.4 Hz, 2H), 1.57 (tt, *J* = 8.8, 6.9 Hz, 2H), 1.32 (dq, *J* = 14.6, 7.3 Hz, 2H), 0.84 (t, *J* = 7.4 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 145.0, 133.7, 129.4, 127.1, 35.9, 30.7, 21.8, 13.5.
IR (ATR, cm^{-1}) ṽ = 2960, 2874, 1465, 1458, 1447, 1322, 1307, 1292, 1139, 1099, 1077, 1023, 999, 754, 714, 685, 670.
MS (EI, 70 eV, %) m/z = 141 (19), 125 (18), 97 (13), 89 (56), 77 (100), 55 (39).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{14}O_2S_2$**: 230.0435; found: 230.0507.

[191] Adapted procedure from: K. Fujiki, N. Tanifuji, Y. Sasaki, T. Yokoyama, *Synthesis* **2002**, 343.

2.4 Additional Results and Screening Tables

Complete table of optimization for Scheme 37

Table 14: Screening of the regioselective Br/Mg exchange on 2,5-dibromo-3-methylthiophene (**139a**).

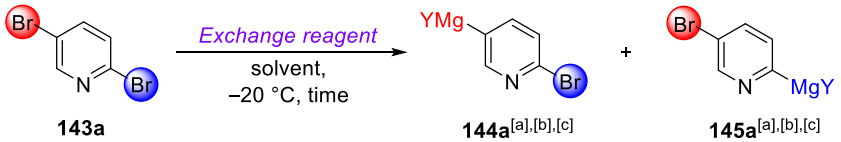


Entry	Exchange reagent[d]	Time (min)	Ratio **140a**:**141a**	Conv. [%][e]
1	*i*PrMgCl·LiCl[f]	60	80:20	99[a]
2	*s*BuMgOR·LiOR (**134a**)	30	76:24	40[b]
3	**134a·TMEDA**	30	99:1	66[b]
4	*s*Bu_2Mg·2LiOR (**134b**)	5	90:10	99[c]
5	*t*Bu_2Mg·2LiOR	5	70:30	99[c]
6	*n*Bu_2Mg·2LiOR (**134c**)	5	84:16	99[c]
7	**134b·TMEDA**	5	96:4	99[c]
8[g]	**134b·PMDTA**	5	99:1	99[c]

[a] Y = Cl·LiCl. [b] Y = OR·LiOR. [c] Y = thienyl·2LiOR(·ligand). [d] R = 2-ethylhexyl, these reactions were carried out at 0.50 M using 1.20 equiv of alkylmagnesium species. Reagents are displayed accordingly to their stoichiometry and not their actual structure. [e] Conversion determined by GC-analysis of reaction aliquots after aqueous quench. [f] Reaction performed in THF at −20 °C. [g] When performed in THF, a ratio **140a**:**141a** = 71:29 and a conversion of 53% were obtained.

Complete table of optimization for Table 2

Table 15: Br/Mg exchange on 2,5-dibromopyridine (**143a**) using various exchange reagents.



143a **144a**[a],[b],[c] **145a**[a],[b],[c]

Entry	Exchange reagent[d]	Solvent	Time (min)	Ratio **144a**:**145a**	Conv. [%][e]
1	*i*PrMgCl·LiCl	THF	120	99:1	94[a]
2	*s*BuMgOR·LiOR (**134a**)	toluene	60	1:99	20[b]
3	*s*Bu$_2$Mg·2LiOR (**134b**)	toluene	30	1:99	99[c]
4	**134a·TMEDA**	toluene	60	99:1	81[b]
5	**134b·PMDTA**	toluene	30	99:1	99[c]

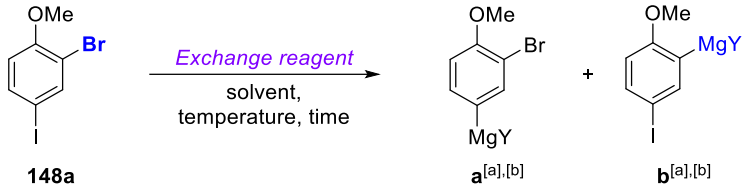
[a] Y = Cl·LiCl. [b] Y = OR·LiOR(·TMEDA). [c] Y = pyridyl·2LiOR(·PMDTA). [d] R = 2-ethylhexyl, these reactions were carried out at 0.50 M using 1.20 equiv of alkylmagnesium species. Reagents are displayed accordingly to their stoichiometry and not their actual structure. [e] Conversion determined by GC-analysis of reaction aliquots after aqueous quench.

Note: The addition of 12-crown-4 (2.40 equiv)[192] had the same effect as a chelating ligand, producing a majority of **144a** (**144a**:**145a** = 90:10) with 57% of conversion.

[192] For literature about 12-crown-4, a specific lithium cation ionophore, see: a) C. J. Pedersen, *J. Am. Chem. Soc.* **1967**, *89*, 2495; b) C. J. Pedersen, *J. Am. Chem. Soc.* **1967**, *89*, 7017; c) F. A. L. Anet, J. Krane, J. Dale, K. Daasvatn, P. O. Kristiansen, *Acta Chem. Scand.* **1973**, *27*, 3395; d) A. Pullman, C. Giessner-Prettre, Y. V. Kruglyak, *Chem. Phys. Lett.* **1975**, *35*, 156.

Optimization Br/Mg vs. I/Mg exchanges

Table 16: Br/Mg exchange in the presence of an iodine on 2-bromo-4-iodoanisole (**148a**).

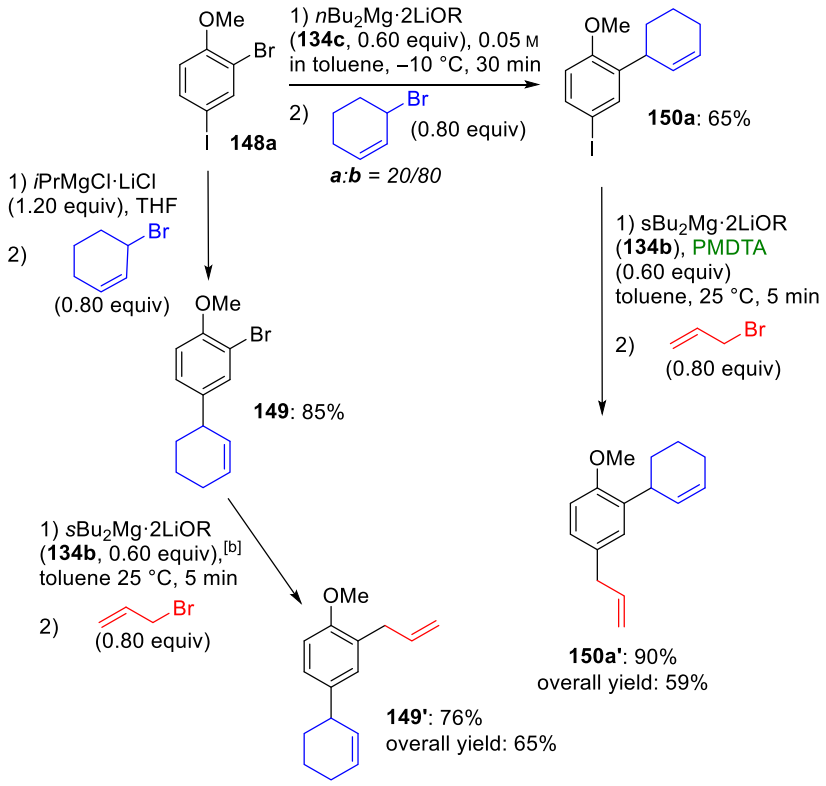


148a **a**[a],[b] **b**[a],[b]

Entry	Exchange reagent[c]	Time (min)	Ratio **a**:**b**[d]	Conv. [%][e]
1	*i*PrMgCl·LiCl	60	99:1	81[a]
2	*s*Bu$_2$Mg·2LiOR (**134b**)	30	24:76	99[b]
3[f]	*n*Bu$_2$Mg·2LiOR (**134c**)	30	20:80	99[b] (71)
4	**134c·PMDTA**	30	99:1	99[b]

[a] Y = Cl·LiCl. [b] Y = anisyl·2LiOR(·ligand). [c] R = 2-ethylhexyl, reactions were carried out at 0.05 M and −10 °C using 1.20 equiv of alkylmagnesium species. Reagents are displayed accordingly to their stoichiometry and not their actual structure. [d] A mixture of 2-bromoanisole and 4-bromoanisole was obtained by halogen dance when the reactions were done at 25 °C. An increase in concentration (0.5 M in toluene) hampered the selectivity. [e] Conversion determined by GC-analysis of reaction aliquots after aqueous quench. Isolated yield in parenthesis. [f] A regioselectivity of **a**:**b** = 80:20 was observed using 2.40 equiv of 12-crown-4 as an additive.

Additional results Br/Mg vs. I/Mg exchanges

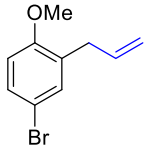


[a] CuCN·2LiCl (10 mol%) was used. [b] After 33 h of reaction at 25 °C, 67% of **149** remained when the exchange was carried out with *i*PrMgCl·LiCl (1.20 equiv) and **134b** had to be employed.

Scheme 62: Selective Br/Mg exchange with 2-bromo-4-iodoanisole (**148a**) followed by allylation[a] reaction: comparison with *i*PrMgCl·LiCl.

2.5 Preparation of Compounds 138 to 150

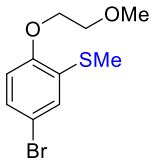
Synthesis of 2-allyl-4-bromo-1-methoxybenzene (138a)



Compound **138a** was prepared *via* **TP1** using 2,4-dibromoanisole (**135a**, 133 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and allyl bromide (34 µL, 0.40 mmol) were added at 0 °C and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.43) to give the product **138a** (65 mg, 286 µmol, 72% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.29 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.26 – 7.21 (m, 1H), 6.72 (d, *J* = 8.6 Hz, 1H), 5.95 (ddt, *J* = 15.7, 11.2, 6.6 Hz, 1H), 5.09 (s, 1H), 5.06 (dt, *J* = 5.6, 1.8 Hz, 1H), 3.81 (s, 3H), 3.34 (dt, *J* = 6.6, 1.6 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 156.5, 136.1, 132.5, 131.1, 130.0, 116.3, 112.8, 112.0, 55.7, 34.0.
IR (ATR, cm^{-1}) ṽ = 2938, 2836, 1638, 1592, 1488, 1463, 1440, 1432, 1401, 1322, 1304, 1278, 1243, 1172, 1135, 1127, 1032, 996, 917, 861, 804.
MS (EI, 70 eV, %) m/z = 228 (45), 226 (46), 199 (24), 197 (26), 148 (11), 147 (100), 132 (84), 131 (70), 119 (17), 118 (91), 117 (12), 115 (36), 104 (11), 103 (18), 91 (73), 90 (12), 89 (13), 77 (12).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{11}BrO$**: 225.9993; found: 225.9978.

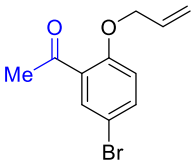
Synthesis of (5-bromo-2-(2-methoxyethoxy)phenyl)(methyl)sulfane (138b)



Compound **138b** was prepared *via* **TP1** using 2,4-dibromo-1-(2-methoxyethoxy)benzene (**135b**, 155 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, *S*-methyl methanesulfonothioate (51 mg, 0.40 mmol) was added and the reaction mixture was allowed to stir at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.44) to give the product **138b** (86 mg, 310 µmol, 78% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.23 – 7.11 (m, 2H), 6.70 (d, *J* = 8.2 Hz, 1H), 4.18 – 4.11 (m, 2H), 3.90 – 3.68 (m, 2H), 3.46 (s, 3H), 2.41 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 154.6, 130.6, 128.2, 128.0, 114.0, 113.1, 71.0, 68.8, 59.6, 14.6.
IR (ATR, cm^{-1}) ṽ = 2923, 2879, 1573, 1472, 1450, 1438, 1382, 1368, 1300, 1266, 1238, 1198, 1128, 1087, 1074, 1050, 1033, 924, 854, 799, 733, 713.
MS (EI, 70 eV, %) m/z = 278 (20), 276 (20), 220 (100), 218 (99), 205 (16), 203 (16), 138 (14).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{13}BrO_2S$**: 275.9820; found: 275.9813.

Synthesis of 1-(2-(allyloxy)-5-bromophenyl)ethan-1-one (138c)



Compound **138c** was prepared *via* **TP1** using 1-(allyloxy)-2,4-dibromobenzene (**135c**, 146 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, *N*-methoxy-*N*-methylacetamide (41 mg, 0.40 mmol) was added and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.27) to give the product **138c** (65 mg, 255 µmol, 64% yield) as a white solid.

M.p. (°C): 56-58.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.83 (d, *J* = 2.6 Hz, 1H), 7.51 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.06 (ddt, *J* = 17.3, 10.6, 5.4 Hz, 1H), 5.42 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.34 (dq, *J* = 10.5, 1.3 Hz, 1H), 4.62 (dt, *J* = 5.3, 1.5 Hz, 2H), 2.62 (s, 3H).

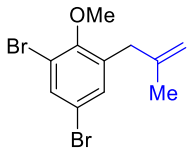
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 198.5, 157.0, 136.1, 133.2, 132.3, 130.2, 118.8, 114.9, 113.5, 69.9, 32.0.

IR (ATR, cm^{-1}) ṽ = 3093, 2931, 1660, 1628, 1588, 1566, 1481, 1460, 1423, 1409, 1398, 1369, 1352, 1296, 1280, 1233, 1223, 1153, 1064, 1021, 1002, 992, 976, 931, 906, 816, 655.

MS (EI, 70 eV, %) m/z = 241 (38), 239 (41), 213 (20), 211 (21), 201 (96), 199 (100), 160 (16), 132 (32), 131 (17), 129 (15), 78 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{11}BrO_2$**: 253.9942; found: 253.9937.

Synthesis of 1,5-dibromo-2-methoxy-3-(2-methylallyl)benzene (138d)



Compound **138d** was prepared *via* **TP1** using 2,4,6-tribromoanisole (**135d**, 172 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromo-2-methylprop-1-ene (40 µL, 0.40 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.39) to give the product **138d** (111 mg, 347 µmol, 87% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.56 (d, *J* = 2.4 Hz, 1H), 7.31 – 7.14 (m, 1H), 4.89 (s, 1H), 4.67 (s, 1H), 3.79 (s, 3H), 3.35 (s, 2H), 1.72 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 154.9, 143.7, 136.8, 133.9, 132.8, 118.4, 117.2, 113.2, 61.2, 38.2, 22.6.

IR (ATR, cm^{-1}) ṽ = 2938, 1652, 1576, 1553, 1461, 1438, 1417, 1393, 1375, 1276, 1251, 1220, 1147, 1001, 895, 859, 810, 805, 753, 667.

MS (EI, 70 eV, %) m/z = 322 (15), 320 (32), 318 (17), 241 (12), 239 (13), 226 (34), 225 (13), 224 (31), 212 (11), 211 (21), 210 (12), 209 (22), 198 (10), 196 (12), 161 (10), 160 (69), 159 (19), 155 (14), 146 (12), 145 (100), 144 (11), 129 (21), 128 (31), 117 (28), 116 (11), 115 (69), 102 (14), 91 (18), 89 (26), 76 (10), 75 (16).

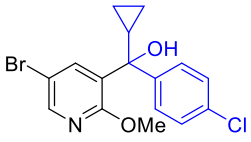
HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{12}Br_2O$**: 317.9255; found: 317.9243.

Synthesis of 5-bromo-2-methoxy-3-(2-methylallyl)pyridine (138ea)

Compound **138ea** was prepared *via* **TP1** using 3,5-dibromo-2-methoxypyridine (**135e**, 133 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromo-2-methylprop-1-ene (40 µL, 0.40 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 96:4, R_f = 0.50) to give the product **138ea** (78 mg, 322 µmol, 81% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.06 (d, *J* = 2.5 Hz, 1H), 7.47 (dt, *J* = 2.6, 0.7 Hz, 1H), 4.95 – 4.79 (m, 1H), 4.67 (dd, *J* = 2.1, 1.0 Hz, 1H), 3.91 (s, 3H), 3.24 (s, 2H), 1.71 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 161.3, 145.1, 142.9, 140.5, 124.7, 113.0, 111.8, 53.9, 37.4, 22.5.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2976, 2950, 1653, 1578, 1569, 1560, 1465, 1414, 1390, 1376, 1308, 1247, 1154, 1138, 1020, 893, 752.
MS (EI, 70 eV, %) m/z = 243 (99), 242 (59), 241 (100), 240 (61), 228 (78), 226 (79), 214 (50), 212 (71), 210 (74), 200 (65), 198 (96), 196 (30), 188 (72), 186 (74), 172 (28), 170 (27), 147 (54), 146 (86), 130 (42), 129 (32), 119 (72), 118 (70), 117 (28), 91 (27).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{12}BrNO$**: 241.0102; found: 241.0097.

Synthesis of (5-bromo-2-methoxypyridin-3-yl)(4-chlorophenyl)(cyclopropyl)methanol (138eb)



Compound **138eb** was prepared *via* **TP1** using 3,5-dibromo-2-methoxypyridine (**135e**, 133 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, (4-chlorophenyl)(cyclopropyl)methanone (72 mg, 0.40 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.28) to give the product **138eb** (100 mg, 271 µmol, 68% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.16 (q, *J* = 2.4 Hz, 2H), 7.44 – 6.93 (m, 4H), 3.87 (d, *J* = 1.0 Hz, 1H), 3.73 (s, 3H), 1.45 (ddtd, *J* = 8.2, 6.5, 5.5, 1.1 Hz, 1H), 0.66 – 0.50 (m, 3H), 0.46 (ddt, *J* = 7.9, 5.4, 2.9 Hz, 1H).

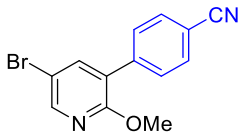
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.7, 146.4, 144.6, 138.8, 133.0, 131.0, 128.1, 127.2, 112.4, 75.3, 54.0, 20.3, 1.9, 1.6.

IR (ATR, cm^{-1}) ṽ = 3546, 3011, 2952, 1578, 1564, 1489, 1461, 1409, 1381, 1331, 1294, 1242, 1202, 1175, 1154, 1146, 1120, 1105, 1092, 1014, 985, 970, 942, 927, 899, 882, 871, 833, 806, 758, 734, 720, 681.

MS (EI, 70 eV, %) m/z = 343 (10), 341 (42), 339 (33), 216 (98), 214 (100), 139 (21).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{15}BrClNO_2$**: 366.9975; found: 366.9971.

Synthesis of 4-(5-bromo-2-methoxypyridin-3-yl)benzonitrile (138ec)



Compound **138ec** was prepared *via* **TP1** using 3,5-dibromo-2-methoxypyridine (**135e**, 133 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, $ZnCl_2$ (1.00 M in THF, 0.65 mL, 0.65 mmol), $Pd(OAc)_2$ (5 mg, 4 mol%), SPhos (17 mg, 8 mol%) and 4-iodobenzonitrile (92 mg, 0.40 mmol) were added and the reaction mixture was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.74) to give the product **138ec** (61 mg, 211 µmol, 53% yield) as a white solid.

M.p. (°C): 155-157.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.25 (d, *J* = 2.4 Hz, 1H), 7.75 – 7.70 (m, 3H), 7.68 – 7.62 (m, 2H), 3.96 (s, 3H).

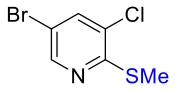
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.6, 147.6, 140.9, 140.2, 132.3, 130.0, 124.4, 118.8, 112.2, 111.9, 54.3.

IR (ATR, cm^{-1}) ṽ = 2955, 2226, 1742, 1608, 1566, 1463, 1415, 1395, 1299, 1245, 1220, 1032, 1017, 1006, 843, 772.

MS (EI, 70 eV, %) m/z = 290 (30), 289 (100), 288 (32), 287 (99), 273 (14), 271 (30), 269 (15), 259 (12), 208 (15), 207 (13), 194 (22), 180 (50), 179 (54), 178 (13), 166 (30), 165 (29), 152 (20), 151 (20), 140 (16), 139 (58), 138 (34), 125 (14), 88 (13), 86 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_9BrN_2O$**: 287.9898; found: 287.9901.

Synthesis of 5-bromo-3-chloro-2-(methylthio)pyridine (138f)



Compound **138f** was prepared *via* **TP1** using 2,5-dibromo-3-chloropyridine (**135f**, 136 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 30 min, *S*-methyl methanesulfonothioate (51 mg, 0.40 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.31) to give the product **138f** (57 mg, 239 µmol, 60% yield) as a white solid.

M.p. (°C): 65-67.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.41 (d, *J* = 2.1 Hz, 1H), 7.68 (d, *J* = 2.0 Hz, 1H), 2.53 (s, 3H).

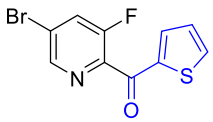
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 157.1, 148.0, 137.7, 129.4, 114.8, 13.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3037, 2924, 1548, 1415, 1351, 1220, 1210, 1150, 1105, 1036, 900, 894, 812, 718.

MS (EI, 70 eV, %) m/z = 241 (18), 239 (72), 238 (30), 237 (56), 236 (24), 208 (13), 206 (54), 204 (100), 202 (98), 194 (12), 193 (18), 191 (14), 125 (14), 112 (26).

HRMS (EI, 70 eV) m/z: calc. for **$C_6H_5BrClNS$**: 236.9015; found: 236.9010.

Synthesis of (5-bromo-3-fluoropyridin-2-yl)(thiophen-2-yl)methanone (138g)



Compound **138g** was prepared *via* **TP1** using 2,5-dibromo-3-fluoropyridine (**135g**, 128 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 30 min, *N*-methoxy-*N*-methylthiophene-2-carboxamide (69 mg, 0.40 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 97:3, R_f = 0.20) to give the product **138g** (75 mg, 262 µmol, 66% yield) as a yellow solid.

M.p. (°C): 134-136.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.60 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.98 (dd, *J* = 3.9, 1.2 Hz, 1H), 7.88 – 7.70 (m, 2H), 7.17 (dd, *J* = 4.9, 3.9 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 181.3 (d, *J* = 4.6 Hz), 158.0 (d, *J* = 277.1 Hz), 145.6 (d, *J* = 5.3 Hz), 141.5 (d, *J* = 8.4 Hz), 141.2, 136.7, 136.5, 128.6 (d, *J* = 21.4 Hz), 128.2, 123.7 (d, *J* = 3.4 Hz).

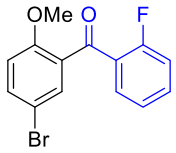
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –117.6.

IR (ATR, cm^{-1}) ṽ = 3109, 3097, 3068, 2924, 1656, 1634, 1572, 1514, 1442, 1436, 1408, 1396, 1353, 1307, 1234, 1218, 1199, 1134, 1082, 1050, 909, 882, 868, 862, 826, 782, 729, 716, 679, 660.

MS (EI, 70 eV, %) m/z = 259 (62), 257 (60), 111 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_5BrFNOS$**: 284.9259; found: 284.9250.

Synthesis of (5-bromo-2-methoxyphenyl)(2-fluorophenyl)methanone (138aa)



Compound **138aa** was prepared *via* **TP1** using 2,4-dibromoanisole (**135a**, 266 mg, 1.00 mmol) and dry toluene (2.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.76 mL, 0.60 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, CuCN·2LiCl (1.00 M in THF, 100 µL, 100 µmol) and 2-fluorobenzoyl chloride (0.36 mL, 3.00 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.18) to give the product **138aa** (233 mg, 754 µmol, 75% yield) as a white solid.

M.p. (°C): 57-59.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.71 (td, *J* = 7.5, 1.9 Hz, 1H), 7.64 (d, *J* = 2.6 Hz, 1H), 7.57 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.51 (dddd, *J* = 8.3, 7.2, 5.0, 1.9 Hz, 1H), 7.23 (td, *J* = 7.5, 1.1 Hz, 1H), 7.06 (ddd, *J* = 10.7, 8.3, 1.1 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 3.66 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 191.1, 161.3 (d, *J* = 255.5 Hz), 157.5 (d, *J* = 1.7 Hz), 135.7, 134.1 (d, *J* = 8.8 Hz), 132.8 (d, *J* = 0.7 Hz), 131.4 (d, *J* = 1.2 Hz), 131.0 (d, *J* = 2.1 Hz), 127.8 (d, *J* = 11.8 Hz), 124.3 (d, *J* = 3.6 Hz), 116.1 (d, *J* = 22.3 Hz), 113.5, 113.1, 56.0.

^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –112.3.

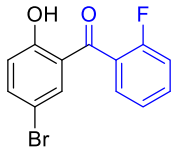
IR (ATR, cm^{-1}) ṽ = 2939, 1655, 1610, 1591, 1576, 1482, 1454, 1396, 1301, 1271, 1255, 1238, 1215, 1181, 1162, 1152, 1126, 1101, 1023, 954, 832, 813, 790, 758.

MS (EI, 70 eV, %) m/z = 310 (37), 308 (39), 293 (40), 291 (29), 215 (72), 213 (92), 212 (91), 201 (71), 199 (76), 123 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{10}BrFO_2$**: 307.9848; found: 307.9843.

Synthesis of 2-bromo-9*H*-xanthen-9-one (138ab)

Step 1: Synthesis of (5-bromo-2-hydroxyphenyl)(2-fluorophenyl)methanone[193]



A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with (5-bromo-2-methoxyphenyl)(2-fluorophenyl)methanone (**138aa,** 106 mg, 0.34 mmol) and dissolved in dry DCM (1.0 mL). Then, BBr_3 (1.00 M in DCM, 0.68 mL, 0.68 mmol) was added dropwise at −78 °C and the reaction solution was allowed to warm to room temperature overnight. The mixture was quenched with water (10 mL) and extracted with ether (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.44) to give the product (5-bromo-2-hydroxyphenyl)(2-fluorophenyl)methanone (98 mg, 332 µmol, 98% yield) as a yellow solid.

M.p. (°C): 88-90.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 11.89 (s, 1H), 7.63 – 7.54 (m, 2H), 7.51 (t, *J* = 2.7 Hz, 1H), 7.47 (ddd, *J* = 8.5, 6.6, 1.8 Hz, 1H), 7.32 (td, *J* = 7.5, 1.0 Hz, 1H), 7.23 (ddd, *J* = 9.5, 8.4, 1.0 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 197.8, 162.1, 159.3 (d, *J* = 252.2 Hz), 139.8, 135.3 (d, *J* = 2.6 Hz), 133.6 (d, *J* = 8.3 Hz), 130.0 (d, *J* = 2.7 Hz), 125.8 (d, *J* = 15.5 Hz), 124.7 (d, *J* = 3.6 Hz), 121.1, 120.6, 116.7 (d, *J* = 21.3 Hz), 110.8.

^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = −111.9.

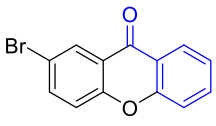
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3072, 1629, 1613, 1583, 1485, 1464, 1452, 1400, 1330, 1293, 1268, 1238, 1212, 1159, 1149, 1122, 1100, 1084, 951, 944, 838, 829, 816, 792, 759, 720.

MS (EI, 70 eV, %) m/z = 296 (37), 295 (96), 294 (39), 293 (100), 277 (37), 276 (31), 275 (32), 274 (32), 201 (34), 200 (47), 199 (35), 198 (42), 172 (28), 170 (29), 145 (17), 143 (18), 123 (72).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_8BrFO_2$**: 293.9692; found: 293.9693.

[193] Adapted procedure from: J. F. W. McOmie, D. E. West, *Org. Synth.* **1969**, *49*, 50.

Step 2: Synthesis of 2-bromo-9*H*-xanthen-9-one (**138ab**)[134]



A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with (5-bromo-2-hydroxyphenyl)(2-fluorophenyl)methanone (88 mg, 0.30 mmol), K_2CO_3 (83 mg, 0.60 mmol) and dry acetone (3.0 mL). Then, the tube was sealed and stirred at 50 °C for 4 h. The mixture was quenched with water (10 mL) and extracted with ether (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo* to give the product **138ab** (81 mg, 294 µmol, 98% yield) as an off-white solid.

M.p. (°C): 146-148.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.45 (d, *J* = 2.4 Hz, 1H), 8.33 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.80 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.75 (ddd, *J* = 8.7, 7.1, 1.8 Hz, 1H), 7.50 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.44 – 7.36 (m, 2H).

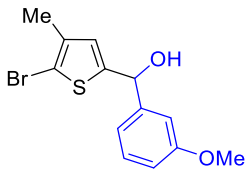
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 176.2, 156.2, 155.1, 137.8, 135.4, 129.4, 127.0, 124.4, 123.3, 121.7, 120.2, 118.2, 117.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3077, 2925, 1663, 1616, 1606, 1472, 1458, 1439, 1424, 1337, 1315, 1266, 1216, 1170, 1153, 1132, 1108, 882, 843, 824, 756, 718, 680, 672.

MS (EI, 70 eV, %) m/z = 277 (14), 276 (98), 275 (17), 274 (100), 248 (19), 246 (20), 195 (27), 139 (78).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_7BrO_2$**: 273.9629; found: 273.9625.

Synthesis of (5-bromo-4-methylthiophen-2-yl)(3-methoxyphenyl)methanol (142a)

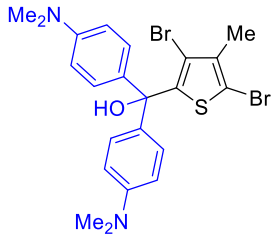


Compound **142a** was prepared *via* **TP1** using 2,5-dibromo-3-methylthiophene (**139a**, 128 mg, 0.50 mmol), dry toluene (1.0 mL) and PMDTA (63 µL, 0.30 mmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, 3-methoxybenzaldehyde (55 mg, 0.40 mmol) was added and the reaction solution was allowed to stir at room temperature

overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.25) to give the product **142a** (100 mg, 319 µmol, 80% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.36 – 7.19 (m, 1H), 7.05 – 6.94 (m, 2H), 6.85 (ddd, *J* = 8.3, 2.5, 1.1 Hz, 1H), 6.61 – 6.47 (m, 1H), 5.86 (d, *J* = 3.7 Hz, 1H), 3.81 (s, 3H), 2.39 (dd, *J* = 3.9, 0.9 Hz, 1H), 2.10 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.9, 147.1, 144.2, 136.9, 129.9, 126.9, 118.7, 113.8, 111.8, 109.5, 72.6, 55.4, 15.4.
IR (ATR, cm^{-1}) ṽ = 2975, 1608, 1600, 1587, 1489, 1464, 1455, 1436, 1316, 1281, 1263, 1256, 1156, 1131, 1094, 1082, 1050, 1020, 765.
MS (EI, 70 eV, %) m/z = 314 (18), 312 (18), 234 (13), 233 (100), 207 (14), 205 (37), 203 (23), 201 (14), 190 (11), 178 (14), 176 (14), 173 (11), 172 (83), 157 (15), 135 (83), 129 (16), 128 (17), 125 (17), 115 (11), 109 (16), 98 (24), 97 (35), 94 (11), 92 (12), 77 (20).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{13}BrO_2S$**: 311.9820; found: 311.9813.

Synthesis of (3,5-dibromo-4-methylthiophen-2-yl)bis(4-(dimethylamino)phenyl)metha nol (142b)



Compound **142b** was prepared *via* **TP1** using 2,4,5-tribromo-3-methylthiophene (**139b**, 167 mg, 0.50 mmol), dry toluene (1.0 mL) and PMDTA (63 µL, 0.30 mmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, bis(4-(dimethylamino)phenyl)methanone (107 mg, 0.40 mmol) was added and the reaction solution was allowed to stir at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.41) to give the product **142b** (128 mg, 244 µmol, 61% yield) as a blue oil.

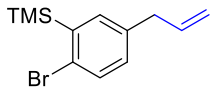
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.22 – 7.10 (m, 4H), 6.73 – 6.52 (m, 4H), 3.73 (s, 1H), 2.95 (s, 12H), 2.18 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 150.0, 147.4, 137.8, 133.0, 128.7, 111.5, 110.0, 108.3, 79.7, 40.6, 16.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2918, 1610, 1585, 1543, 1518, 1481, 1443, 1369, 1321, 1286, 1269, 1228, 1188, 1171, 1129, 1115, 1063, 1022, 945, 819, 754.

MS (EI, 70 eV, %) m/z = 526 (39), 525 (17), 524 (63), 523 (11), 522 (35), 510 (21), 509 (49), 508 (43), 507 (84), 506 (23), 505 (44), 444 (23), 442 (17), 430 (16), 429 (21), 428 (16), 427 (18), 404 (14), 364 (11), 349 (10), 348 (12), 347 (20), 331 (11), 308 (16), 306 (12), 283 (16), 270 (18), 269 (74), 268 (26), 253 (16), 241 (10), 149 (10), 148 (100), 121 (18), 120 (16), 44 (30).

HRMS (EI, 70 eV) m/z: calc. for **$C_{22}H_{24}Br_2N_2OS$**: 521.9976; found: 521.9969.

Synthesis of (5-allyl-2-bromophenyl)trimethylsilane (142c)



Compound **142c** was prepared *via* **TP1** using (2,5-dibromophenyl)trimethylsilane (**139c**, 154 mg, 0.50 mmol), dry toluene (1.0 mL) and PMDTA (63 µL, 0.30 mmol). Then, *s*Bu$_2$Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and allyl bromide (34 µL, 0.40 mmol) were added and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.80) to give the product **142c** (89 mg, 331 µmol, 83% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.45 (d, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 2.4 Hz, 1H), 7.03 (dd, *J* = 8.1, 2.4 Hz, 1H), 6.03 – 5.84 (m, 1H), 5.17 – 5.02 (m, 2H), 3.34 (dt, *J* = 6.8, 1.5 Hz, 2H), 0.39 (s, 9H).

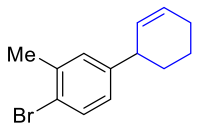
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 141.1, 138.3, 137.1, 136.5, 132.8, 131.2, 128.1, 116.3, 39.8, –0.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2954, 2899, 1456, 1447, 1436, 1380, 1262, 1250, 1140, 1109, 1016, 992, 914, 871, 839, 814, 761, 690.

MS (EI, 70 eV, %) m/z = 273 (12), 271 (12), 268 (10), 256 (10), 255 (100), 254 (10), 253 (99), 191 (11), 173 (44), 171 (13), 163 (29), 145 (86), 139 (10), 137 (11), 133 (10), 131 (27), 129 (34), 128 (10), 115 (13), 91 (12), 75 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{17}BrSi$**: 268.0283; found: 268.0277.

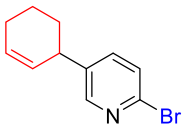
Synthesis of 4'-bromo-3'-methyl-1,2,3,4-tetrahydro-1,1'-biphenyl (142d)



Compound **142d** was prepared *via* **TP1** using 1,4-dibromo-2-methylbenzene (**139d**, 125 mg, 0.50 mmol), dry toluene (1.0 mL) and PMDTA (63 µL, 0.30 mmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 5 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromocyclohexene (46 µL, 0.40 mmol) were added at 0 °C and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.71) to give the product **142d** (66 mg, 263 µmol, 66% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.44 (d, *J* = 8.2 Hz, 1H), 7.08 (d, *J* = 2.2 Hz, 1H), 6.90 (dd, *J* = 8.2, 2.3 Hz, 1H), 5.90 (dtd, *J* = 9.8, 3.7, 2.3 Hz, 1H), 5.71 – 5.58 (m, 1H), 3.33 (ddt, *J* = 8.3, 5.5, 2.8 Hz, 1H), 2.38 (s, 3H), 2.08 (ddq, *J* = 6.8, 3.6, 2.0, 1.5 Hz, 2H), 2.03 – 1.95 (m, 1H), 1.79 – 1.68 (m, 1H), 1.67 – 1.56 (m, 1H), 1.53 – 1.46 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 146.1, 137.7, 132.2, 130.4, 129.8, 128.8, 127.0, 122.3, 41.4, 32.7, 25.1, 23.1, 21.2.
IR (ATR, cm^{-1}) ṽ = 2929, 2860, 1653, 1477, 1446, 1436, 1027, 892, 878, 814, 756.
MS (EI, 70 eV, %) m/z = 252 (41), 250 (42), 171 (51), 156 (23), 144 (10), 143 (100), 142 (11), 141 (26), 129 (28), 128 (76), 115 (32), 105 (24), 79 (12).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{15}Br$**: 250.0357; found: 250.0350.

Synthesis of 2-bromo-5-(cyclohex-2-en-1-yl)pyridine (146a)

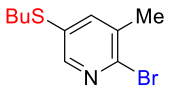


Compound **146a** was prepared *via* **TP1** using 2,5-dibromopyridine (**143a**, 119 mg, 0.50 mmol), dry toluene (1.0 mL) and PMDTA (63 µL, 0.30 mmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromocyclohexene (46 µL, 0.40 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column

chromatography (*iso*hexane:diethyl ether = 10:0.05, R_f = 0.15) to give the product **146a** (69 mg, 290 µmol, 72% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.23 (t, *J* = 1.7 Hz, 1H), 7.40 (d, *J* = 1.6 Hz, 2H), 5.96 (dtd, *J* = 9.9, 3.7, 2.3 Hz, 1H), 5.68 – 5.48 (m, 1H), 3.40 (ddt, *J* = 8.2, 5.5, 2.8 Hz, 1H), 2.09 (dddd, *J* = 8.9, 5.4, 4.2, 2.6 Hz, 2H), 2.06 – 1.94 (m, 1H), 1.77 – 1.67 (m, 1H), 1.67 – 1.57 (m, 1H), 1.50 (dddd, *J* = 13.1, 10.1, 8.1, 3.1 Hz, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 149.9, 141.3, 139.6, 138.2, 130.1, 128.2, 127.9, 38.8, 32.4, 24.9, 20.8.
IR (ATR, cm^{-1}) ṽ = 2927, 2868, 2857, 1670, 1606, 1574, 1560, 1453, 1430, 1377, 1355, 1346, 1260, 1190, 1088, 1022, 830.
MS (EI, 70 eV, %) m/z = 240 (12), 239 (93), 238 (29), 237 (100), 236 (17), 224 (31), 222 (32), 211 (27), 210 (39), 209 (31), 208 (33), 183 (10), 158 (24), 143 (17), 130 (70), 129 (12), 128 (15), 117 (23), 116 (15), 104 (14), 103 (19), 89 (11), 79 (10), 77 (26), 51 (13), 41 (10).
HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{12}BrN$**: 237.0153; found: 237.0148.

Synthesis of 2-bromo-5-(butylthio)-3-methylpyridine (146b)

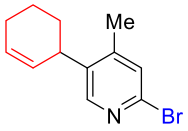


Compound **146b** was prepared *via* **TP1** using 2,5-dibromo-3-methylpyridine (**143b**, 251 mg, 1.00 mmol), dry toluene (2.0 mL) and PMDTA (0.13 mL, 0.60 mmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.71 mL, 0.60 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, *S*-butyl benzenesulfonothioate (184 mg, 0.80 mmol) was added and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:diethyl ether = 98:2, R_f = 0.20) to give the product **146b** (181 mg, 696 µmol, 87% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.11 (d, *J* = 2.4 Hz, 1H), 7.67 – 7.40 (m, 1H), 3.04 – 2.72 (m, 2H), 2.35 (s, 3H), 1.66 – 1.55 (m, 2H), 1.49 – 1.38 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 147.2, 142.0, 139.4, 135.2, 133.6, 33.6, 31.2, 22.0, 21.9, 13.7.
IR (ATR, cm^{-1}) ṽ = 2957, 2929, 2872, 1534, 1453, 1436, 1397, 1383, 1376, 1124, 1047, 718, 685.
MS (EI, 70 eV, %) m/z = 261 (11), 259 (10), 232 (34), 230 (35), 228 (13), 226 (16), 219 (99), 218 (17), 217 (100), 216 (18), 214 (15), 212 (15), 205 (83), 204 (25), 203 (82), 202 (24), 201 (14), 199 (14), 186 (32), 184 (32), 173 (10), 172 (13), 171 (10), 170 (13), 161 (20), 159 (19).

HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{14}BrNS$**: 259.0030; found: 259.0023.

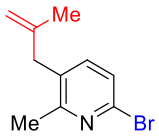
Synthesis of 2-bromo-5-(cyclohex-2-en-1-yl)-4-methylpyridine (146c)



Compound **146c** was prepared *via* **TP1** using 2,5-dibromo-4-methylpyridine (**143c**, 126 mg, 0.50 mmol), dry toluene (1.0 mL) and PMDTA (63 µL, 0.30 mmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromocyclohexene (46 µL, 0.40 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:diethyl ether = 99:1, R_f = 0.11) to give the product **146c** (99 mg, 393 µmol, 98% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.10 (s, 1H), 7.24 (s, 1H), 5.96 (dtd, *J* = 10.0, 3.7, 2.4 Hz, 1H), 5.60 (dq, *J* = 9.9, 2.3 Hz, 1H), 3.53 (ddt, *J* = 8.2, 5.6, 2.8 Hz, 1H), 2.31 (s, 3H), 2.13 – 2.05 (m, 2H), 2.00 – 1.90 (m, 1H), 1.76 – 1.65 (m, 1H), 1.64 – 1.55 (m, 1H), 1.45 (dddd, *J* = 12.9, 9.8, 7.7, 3.1 Hz, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 149.7, 148.1, 139.7, 139.2, 129.9, 129.0, 128.2, 35.7, 30.2, 24.9, 20.7, 18.7.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2926, 2857, 2836, 1579, 1545, 1465, 1446, 1349, 1341, 1293, 1154, 1142, 1086, 983, 893, 883, 864, 784, 723.
MS (EI, 70 eV, %) m/z = 253 (72), 252 (13), 251 (74), 250 (14), 238 (36), 225 (32), 224 (96), 223 (30), 222 (100), 210 (20), 209 (11), 208 (20), 187 (12), 185 (12), 172 (36), 157 (22), 156 (14), 144 (84), 143 (17), 142 (16), 131 (16), 130 (16), 128 (16), 115 (23), 77 (11).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{14}BrN$**: 251.0310; found: 251.0305.

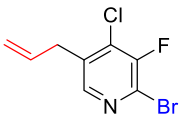
Synthesis of 6-bromo-2-methyl-3-(2-methylallyl)pyridine (146d)



Compound **146d** was prepared *via* **TP1** using 2,5-dibromo-6-methylpyridine (**143d**, 126 mg, 0.50 mmol), dry toluene (1.0 mL) and PMDTA (63 µL, 0.30 mmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromo-2-methylprop-1-ene (40 µL, 0.40 mmol) were added and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:diethyl ether = 99:1, R_f = 0.11) to give the product **146d** (84 mg, 371 µmol, 93% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, CD_3CN, ppm) δ = 7.36 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 4.84 (s, 1H), 4.49 (s, 1H), 3.29 (s, 2H), 2.41 (s, 3H), 1.71 (s, 3H).
^{13}C-NMR (101 MHz, CD_3CN, ppm) δ = 159.8, 144.3, 141.3, 139.0, 133.7, 126.2, 112.5, 40.5, 22.6, 22.0.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2954, 2926, 1651, 1576, 1558, 1435, 1168, 1126, 893, 881, 811.
MS (EI, 70 eV, %) m/z = 226 (99), 224 (100), 212 (52), 211 (11), 210 (54), 209 (11), 187 (35), 185 (35), 145 (22), 144 (16), 131 (19), 130 (15).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{12}NBr$**: 225.0153; found: 225.0067.

Synthesis of 5-allyl-2-bromo-4-chloro-3-fluoropyridine (146e)



Compound **146e** was prepared *via* **TP1** using 2,5-dibromo-4-chloro-3-fluoropyridine (**143e**, 116 mg, 0.40 mmol), dry toluene (0.8 mL) and PMDTA (52 µL, 0.24 mmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.29 mL, 0.24 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 40 µL, 40 µmol) and allyl bromide (28 µL, 0.32 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.15) to give the product **146e** (58 mg, 232 µmol, 72% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.06 (s, 1H), 5.91 (ddt, *J* = 16.7, 10.1, 6.4 Hz, 1H), 5.39 – 4.92 (m, 2H), 3.49 (dt, *J* = 6.4, 1.6 Hz, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 152.6 (d, *J* = 260.8 Hz), 145.7 (d, *J* = 6.5 Hz), 135.6 (d, *J* = 2.8 Hz), 133.0, 131.7, 128.0 (d, *J* = 23.8 Hz), 118.4, 34.3 (d, *J* = 1.5 Hz).

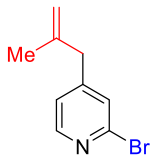
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –113.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1640, 1570, 1443, 1400, 1207, 992, 923, 789.

MS (EI, 70 eV, %) m/z = 253 (13), 252 (24), 251 (56), 250 (100), 249 (42), 248 (76), 216 (12), 215 (15), 214 (13), 213 (15), 169 (10), 168 (13), 135 (41), 134 (23), 107 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_8H_6BrClFN$:** 248.9356; found: 248.9353.

Synthesis of 2-bromo-4-(2-methylallyl)pyridine (146f)



Compound **146f** was prepared *via* **TP1** using 2,4-dibromopyridine (**143f**, 119 mg, 0.50 mmol), dry toluene (1.0 mL) and PMDTA (63 µL, 0.30 mmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromo-2-methylprop-1-ene (40 µL, 0.40 mmol) were added and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 97:3, R_f = 0.18) to give the product **146f** (54 mg, 255 µmol, 64% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.26 (d, *J* = 5.0 Hz, 1H), 7.33 (s, 1H), 7.09 (d, *J* = 5.0 Hz, 1H), 4.90 (s, 1H), 4.76 (s, 1H), 3.27 (s, 2H), 1.66 (s, 3H).

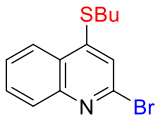
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 152.1, 150.0, 142.5, 142.4, 128.5, 123.6, 114.2, 43.6, 22.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2974, 2937, 2912, 1650, 1587, 1541, 1463, 1446, 1436, 1378, 1207, 1117, 1079, 987, 897, 874, 850, 806, 734, 706, 693.

MS (EI, 70 eV, %) m/z = 133 (10), 132 (100), 117 (29), 57 (13), 55 (10), 43 (13), 41 (14), 38 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_9H_{10}BrN$**: 210.9997; found: 210.9983.

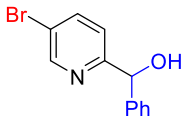
Synthesis of 2-bromo-4-(butylthio)quinoline (146g)



Compound **146g** was prepared *via* **TP1** using 2,4-dibromoquinoline (**143g**, 144 mg, 0.50 mmol), dry toluene (1.0 mL) and PMDTA (63 µL, 0.30 mmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 30 min, *S*-butyl benzenesulfonothioate (92 mg, 0.40 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.15) to give the product **146g** (68 mg, 230 µmol, 57% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.02 (ddd, *J* = 32.3, 8.5, 1.0 Hz, 2H), 7.71 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.55 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.22 (s, 1H), 3.09 (t, *J* = 7.3 Hz, 2H), 1.89 – 1.75 (m, 2H), 1.56 (dq, *J* = 14.6, 7.4 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 151.2, 147.6, 141.6, 130.9, 129.3, 126.8, 125.4, 123.7, 119.1, 31.0, 30.0, 22.3, 13.8.
IR (ATR, cm^{-1}) ṽ = 2965, 2955, 2925, 1560, 1545, 1492, 1464, 1455, 1394, 1382, 1261, 1253, 1147, 1101, 829, 763, 701.
MS (EI, 70 eV, %) m/z = 268 (43), 266 (44), 255 (91), 254 (40), 253 (91), 252 (29), 250 (34), 248 (37), 241 (99), 239 (100), 236 (10), 234 (11), 208 (44), 207 (11), 206 (37), 160 (22), 159 (38), 128 (28), 127 (64), 116 (10).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{14}BrNS$**: 295.0030; found: 295.0022.

Synthesis of (5-bromopyridin-2-yl)(phenyl)methanol (147a)



Compound **147a** was prepared *via* **TP1** using 2,5-dibromopyridine (**143a**, 119 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 30 min, benzaldehyde (42 µL, 0.40 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 8:2, R_f = 0.28) to give the product **147a** (78 mg, 295 µmol, 74% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.64 (d, *J* = 2.0 Hz, 1H), 7.78 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.41 – 7.27 (m, 5H), 7.13 (dt, *J* = 8.5, 0.7 Hz, 1H), 5.78 (s, 1H), 4.70 (s, 1H).

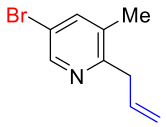
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.8, 148.8, 142.5, 140.1, 128.9, 128.3, 127.1, 122.9, 119.5, 74.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3313, 3286, 1466, 1453, 1366, 1091, 1055, 1026, 1009, 764, 700.

MS (EI, 70 eV, %) m/z = 265 (55), 264 (25), 263 (56), 262 (22), 188 (22), 186 (25), 166 (15), 160 (16), 159 (33), 158 (32), 157 (34), 156 (17), 154 (10), 107 (18), 105 (29), 91 (16), 79 (62), 78 (40), 77 (100), 76 (22), 52 (11), 51 (54), 50 (24).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{10}BrNO$:** 262.9946; found: 262.9943.

Synthesis of 2-allyl-5-bromo-3-methylpyridine (147b)



Compound **147b** was prepared *via* **TP1** using 2,5-dibromo-3-methylpyridine (**143b**, 126 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and allyl bromide (34 µL, 0.40 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.19) to give the product **147b** (63 mg, 297 µmol, 74% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.43 (d, *J* = 2.3 Hz, 1H), 7.57 (d, *J* = 1.9 Hz, 1H), 5.99 (ddt, *J* = 16.7, 10.1, 6.4 Hz, 1H), 5.19 – 4.88 (m, 2H), 3.52 (dt, *J* = 6.4, 1.6 Hz, 2H), 2.28 (s, 3H).

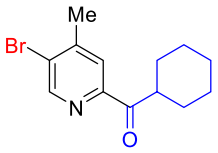
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 156.9, 147.8, 140.1, 134.5, 133.6, 118.3, 116.7, 39.9, 18.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2978, 2925, 1637, 1558, 1458, 1438, 1420, 1393, 1237, 1152, 1136, 1129, 1110, 995, 908, 890, 882, 728, 667.

MS (EI, 70 eV, %) m/z = 212 (98), 210 (100), 131 (35), 130 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_9H_{10}BrN$:** 210.9997; found: 210.9990.

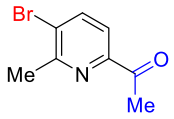
Synthesis of (5-bromo-4-methylpyridin-2-yl)(cyclohexyl)methanone (147c)



Compound **147c** was prepared *via* **TP1** using 2,5-dibromo-4-methylpyridine (**143c**, 126 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, *N*-methoxy-*N*-methylcyclohexanecarboxamide (69 mg, 0.40 mmol) was added and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.28) to give the product **147c** (59 mg, 209 µmol, 52% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.67 (s, 1H), 7.87 (s, 1H), 3.79 (ddt, *J* = 11.2, 7.7, 3.3 Hz, 1H), 2.44 (s, 3H), 1.93 – 1.77 (m, 4H), 1.52 – 1.32 (m, 4H), 1.30 – 1.07 (m, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 204.7, 151.6, 150.6, 148.1, 127.6, 124.7, 44.1, 29.0, 26.1, 25.8, 22.5.
IR (ATR, cm^{-1}) ṽ = 2926, 2853, 1692, 1583, 1449, 1385, 1309, 1256, 1240, 1165, 1058, 1046, 1031, 1006, 987, 898, 779.
MS (EI, 70 eV, %) m/z = 283 (17), 281 (19), 255 (16), 253 (17), 240 (14), 238 (14), 226 (14), 224 (15), 200 (22), 198 (22), 187 (41), 186 (11), 185 (44), 173 (99), 172 (22), 171 (100), 170 (23), 92 (15), 91 (10), 90 (11).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{16}BrNO$**: 281.0415; found: 281.0409.

Synthesis of 1-(5-bromo-6-methylpyridin-2-yl)ethan-1-one (147d)



Compound **147d** was prepared *via* **TP1** using 2,5-dibromo-6-methylpyridine (**143d**, 126 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, *N*-methoxy-*N*-methylacetamide (41 mg, 0.40 mmol) was added and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.39) to give the product **147d** (69 mg, 322 µmol, 81% yield) as a white solid.

M.p. (°C): 95-97.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.90 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 1H), 2.70 (s, 3H), 2.67 (s, 3H).

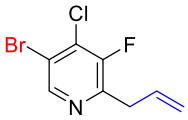
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 199.8, 157.0, 151.7, 140.6, 126.0, 120.5, 25.8, 25.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3066, 2919, 1692, 1656, 1567, 1554, 1430, 1392, 1385, 1357, 1297, 1248, 1209, 1129, 1110, 1032, 984, 957, 835, 755, 695, 668.

MS (EI, 70 eV, %) m/z = 215 (50), 213 (53), 190 (11), 188 (12), 187 (96), 185 (100), 173 (71), 171 (72), 170 (52), 145 (15), 143 (15), 92 (40), 91 (23), 90 (19), 65 (12), 63 (12), 43 (12).

HRMS (EI, 70 eV) m/z: calc. for **C_8H_8BrNO**: 212.9789; found: 212.9785.

Synthesis of 2-allyl-5-bromo-4-chloro-3-fluoropyridine (147e)



Compound **147e** was prepared *via* **TP1** using 2,5-dibromo-4-chloro-3-fluoropyridine (**143e**, 116 mg, 0.40 mmol) and dry toluene (0.8 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.29 mL, 0.24 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 40 µL, 40 µmol) and allyl bromide (28 µL, 0.32 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.15) to give the product **147e** (67 mg, 267 µmol, 84% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.50 (s, 1H), 6.00 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.33 – 5.05 (m, 2H), 3.61 (ddt, *J* = 6.6, 2.8, 1.5 Hz, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 153.9 (d, *J* = 263.7 Hz), 148.0 (d, *J* = 16.1 Hz), 147.0 (d, *J* = 6.6 Hz), 133.1 (d, *J* = 1.4 Hz), 131.5 (d, *J* = 17.4 Hz), 119.4 (d, *J* = 4.3 Hz), 118.0, 36.3 (d, *J* = 2.3 Hz).

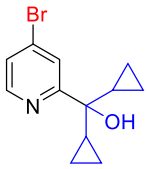
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –122.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1641, 1572, 1540, 1440, 1401, 1188, 993, 946, 919, 900, 855, 768, 704.

MS (EI, 70 eV, %) m/z = 253 (13), 252 (24), 251 (56), 250 (100), 249 (42), 248 (76), 216 (12), 215 (15), 214 (13), 213 (15), 169 (10), 168 (13), 135 (41), 134 (23), 107 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_8H_6BrClFN$**: 248.9356; found: 248.9353.

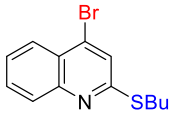
Synthesis of (4-bromopyridin-2-yl)dicyclopropylmethanol (147f)



Compound **147f** was prepared *via* **TP1** using 2,4-dibromopyridine (**143f**, 119 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, dicyclopropyl ketone (44 mg, 0.40 mmol) was added and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.32) to give the product **147f** (74 mg, 276 µmol, 69% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.27 (d, *J* = 5.3 Hz, 1H), 7.71 (d, *J* = 1.4 Hz, 1H), 7.37 (dd, *J* = 5.4, 1.8 Hz, 1H), 4.70 (s, 1H), 1.13 (tt, *J* = 8.3, 5.3 Hz, 2H), 0.67 (dtd, *J* = 9.6, 5.6, 4.2 Hz, 2H), 0.48 (dddd, *J* = 9.2, 8.3, 5.9, 4.2 Hz, 2H), 0.32 (dtd, *J* = 9.7, 5.6, 4.3 Hz, 2H), 0.26 – 0.16 (m, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 167.3, 147.7, 133.7, 125.6, 123.6, 71.8, 20.1, 1.6, –0.6.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3400, 3008, 1573, 1551, 1459, 1400, 1377, 1343, 1283, 1234, 1201, 1183, 1133, 1104, 1091, 1037, 1024, 1014, 926, 913, 874, 850, 820, 787, 739, 681.
MS (EI, 70 eV, %) m/z = 245 (11), 233 (79), 232 (13), 231 (100), 228 (18), 214 (11), 212 (14), 199 (16), 197 (11), 186 (12), 184 (15), 173 (15), 171 (12), 160 (14), 159 (13), 158 (35), 157 (14), 156 (31), 111 (44), 78 (17), 77 (10), 71 (10), 69 (13), 57 (23), 55 (15), 44 (13), 43 (44), 41 (37).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{14}BrNO$:** 267.0259; found: 267.0253.

Synthesis of 4-bromo-2-(butylthio)quinoline (147g)



Compound **147g** was prepared *via* **TP1** using 2,4-dibromoquinoline (**143g**, 144 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.36 mL, 0.30 mmol) was added at –20 °C. After stirring at –20 °C for 30 min, *S*-butyl benzenesulfonothioate (92 mg, 0.40 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.15) to give the product **147g** (92 mg, 311 µmol, 78% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.12 – 8.02 (m, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.67 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.52 (s, 1H), 7.49 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 3.40 – 3.16 (m, 2H), 1.76 (tt, *J* = 8.6, 6.8 Hz, 2H), 1.52 (h, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H).

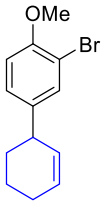
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.9, 148.8, 133.0, 130.6, 128.5, 126.9, 126.3, 125.5, 124.5, 31.5, 29.8, 22.2, 13.9.

IR (ATR, cm^{-1}) ṽ = 2956, 2928, 2871, 1612, 1574, 1542, 1485, 1464, 1455, 1385, 1365, 1270, 1250, 1203, 1144, 1091, 863, 853, 814, 755, 690.

MS (EI, 70 eV, %) m/z = 268 (43), 266 (44), 255 (91), 254 (40), 253 (91), 252 (29), 250 (34), 248 (37), 241 (99), 239 (100), 236 (10), 234 (11), 208 (44), 207 (11), 206 (37), 160 (22), 159 (38), 128 (28), 127 (64), 116 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{14}BrNS$**: 295.0030; found: 295.0022.

Synthesis of 3'-bromo-4'-methoxy-1,2,3,4-tetrahydro-1,1'-biphenyl (149)



A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with 4-bromo-2-iodoanisole (**148a**, 313 mg, 1.00 mmol) and dissolved in dry THF (2.0 mL). Then, *i*PrMgCl·LiCl (1.0 mL, 1.20 mmol) was added dropwise at room temperature and the reaction was stirred for 15 min. The completion of the iodine/magnesium exchange was checked by GC-analysis of reaction aliquots quenched with water, using undecane as internal standard. CuCN·2LiCl (1.00 M in THF, 100 µL, 100 µmol) and 3-bromocyclohexene (0.09 mL, 0.80 mmol) were then added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.20) to give the product **149** (181 mg, 677 µmol, 85% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.39 (d, *J* = 2.2 Hz, 1H), 7.11 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 5.89 (dtd, *J* = 9.9, 3.7, 2.3 Hz, 1H), 5.74 – 5.54 (m, 1H), 3.87 (s, 3H), 3.33 (ddp, *J* = 8.2, 5.5, 2.8 Hz, 1H), 2.08 (dddd, *J* = 9.0, 7.7, 4.3, 2.1 Hz, 2H), 2.02 – 1.92 (m, 1H), 1.76 – 1.67 (m, 1H), 1.67 – 1.42 (m, 2H).

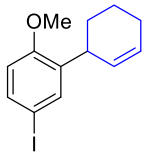
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 154.2, 140.5, 132.6, 129.8, 128.9, 127.8, 111.9, 111.5, 56.4, 40.8, 32.8, 25.1, 21.1.

IR (ATR, cm^{-1}) ṽ = 2921, 2854, 1589, 1480, 1451, 1438, 1201, 1023, 767.

MS (EI, 70 eV, %) m/z = 268 (64), 266 (67), 188 (12), 187 (84), 172 (28), 160 (12), 159 (100), 158 (21), 146 (11), 145 (22), 144 (73), 141 (10), 131 (16), 129 (15), 128 (36), 121 (41), 116 (15), 115 (36).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{15}BrO$**: 266.0306; found: 266.0301.

Synthesis of 5'-iodo-2'-methoxy-1,2,3,4-tetrahydro-1,1'-biphenyl (150a)



Compound **150a** was prepared *via* **TP1** using 2-bromo-4-iodoanisole (**148a**, 125 mg, 0.40 mmol) and dry toluene (8.0 mL). Then, *n*Bu_2Mg·2LiOR (**134c**, 0.32 mL, 0.28 mmol) was added at −10 °C. After stirring at −10 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 40 µL, 40 µmol) as well as 3-bromocyclohexene (37 µL, 0.32 mmol) were added at −10 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.45) to give the product **150a** (65 mg, 207 µmol, 65% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.46 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.42 (d, *J* = 2.3 Hz, 1H), 6.62 (d, *J* = 8.5 Hz, 1H), 5.93 (dtd, *J* = 9.9, 3.7, 2.3 Hz, 1H), 5.74 – 5.48 (m, 1H), 3.80 (s, 3H), 3.76 (ddt, *J* = 8.4, 5.6, 2.8 Hz, 1H), 2.07 (dtt, *J* = 9.4, 3.7, 2.2 Hz, 2H), 1.97 (dddd, *J* = 12.8, 7.3, 5.6, 3.1 Hz, 1H), 1.71 – 1.57 (m, 2H), 1.45 (dddd, *J* = 12.7, 9.4, 7.4, 3.5 Hz, 1H).

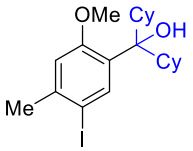
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 156.9, 137.5, 137.3, 135.8, 129.5, 129.3, 112.7, 83.2, 55.6, 34.2, 30.1, 25.2, 20.9.

IR (ATR, cm^{-1}) ṽ = 2934, 2831, 1639, 1592, 1485, 1468, 1447, 1431, 1406, 1326, 1304, 1279, 1241, 1174, 1138, 1124, 1038, 991, 912, 869, 801.

MS (EI, 70 eV, %) m/z = 315 (13), 314 (100), 299 (12), 281 (21), 260 (27), 258 (12), 225 (25), 207 (61), 191 (12), 187 (25), 172 (20), 159 (32), 158 (11), 157 (12), 153 (11), 144 (75), 131 (17), 129 (14), 128 (36), 127 (16), 121 (19), 118 (14), 116 (12), 115 (56), 91 (12), 89 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{15}IO$**: 314.0168; found: 314.0162.

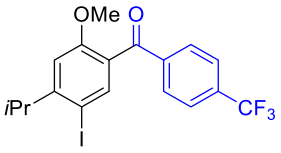
Synthesis of dicyclohexyl(5-iodo-2-methoxy-4-methylphenyl)methanol (150b)



Compound **150b** was prepared *via* **TP1** using 1-bromo-5-iodo-4-methyl-2-methoxybenzene (**148b**, 164 mg, 0.50 mmol) and dry toluene (10 mL). Then, *n*Bu$_2$Mg·2LiOR (**134c**, 0.38 mL, 0.30 mmol) was added at −10 °C. After stirring at −10 °C for 30 min, dicyclohexyl ketone (78 mg, 0.40 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.22) to give the product **150b** (140 mg, 316 µmol, 79%) as a colorless oil.

^{1}H-NMR (400 MHz, DMSO-d$_6$, ppm) δ = 7.50 (s, 1H), 6.55 (s, 1H), 3.82 (s, 1H), 2.14 (p, *J* = 1.9 Hz, 6H), 1.95 (s, 2H), 1.77 (t, *J* = 11.3 Hz, 2H), 1.28 (ddd, *J* = 50.8, 27.4, 12.5 Hz, 7H), 1.05 – 0.90 (m, 2H), 0.89 – 0.66 (m, 4H), 0.66 – 0.47 (m, 3H), 0.46 – 0.26 (m, 2H).
^{13}C-NMR (101 MHz, DMSO-d$_6$, ppm) δ = 156.7, 139.5, 132.2, 113.8, 90.0, 80.1, 55.3, 43.2, 27.9, 27.0, 26.8, 26.4, 26.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3481, 3437, 2251, 2123, 1053, 1024, 1005, 821, 758.
MS (EI, 70 eV, %) m/z = 360 (15), 359 (100), 214 (36), 83 (10).
HRMS (EI, 70 eV) m/z: calc. for **$C_{21}H_{31}IO_2$**: 442.1369; found: 442.1363.

Synthesis of (5-iodo-4-isopropyl-2-methoxyphenyl)(4-(trifluoromethyl)phenyl)metha none (150c)



Compound **150c** was prepared *via* **TP1** using 1-bromo-5-iodo-4-isopropyl-2-methoxybenzene (**148c**, 178 mg, 0.50 mmol) and dry toluene (10 mL). Then, *n*Bu$_2$Mg·2LiOR (**134c**, 0.38 mL, 0.30 mmol) was added at −10 °C. After stirring at −10 °C for 30 min, *N*-methoxy-*N*-methyl-4-(trifluoromethyl)benzamide (93 mg, 0.40 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.27) to give the product **150c** (147 mg, 328 µmol, 82% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.88 (dt, *J* = 7.9, 0.8 Hz, 2H), 7.82 (s, 1H), 7.75 – 7.66 (m, 2H), 6.87 (s, 1H), 3.70 (s, 3H), 3.22 (h, *J* = 6.8 Hz, 1H), 1.28 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 193.7, 158.4, 155.6, 140.7, 140.2, 134.2 (q, *J* = 32.5 Hz), 130.0, 127.8, 125.4 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 272.7 Hz), 109.5, 89.6, 55.7, 38.7, 23.0.

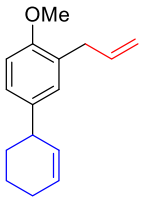
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –63.0.

IR (ATR, cm^{-1}) ṽ = 2964, 1667, 1594, 1463, 1410, 1390, 1373, 1340, 1324, 1311, 1277, 1252, 1233, 1168, 1129, 1108, 1066, 1034, 1017, 955, 857, 778.

MS (EI, 70 eV, %) m/z = 449 (18), 448 (97), 431 (40), 430 (11), 379 (21), 306 (12), 304 (58), 303 (100), 290 (10), 289 (40), 245 (12), 176 (10), 173 (88), 165 (12), 161 (63), 147 (15), 145 (68).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{16}F_3IO_2$**: 448.0147; found: 448.0144.

Synthesis of 3'-allyl-4'-methoxy-1,2,3,4-tetrahydro-1,1'-biphenyl (149')



Compound **149'** was prepared *via* **TP1** using 3'-bromo-4'-methoxy-1,2,3,4-tetrahydro-1,1'-biphenyl (**149**, 50 mg, 187 µmol) and dry toluene (0.4 mL). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.13 mL, 0.11 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuCN·2LiCl (1.00 M in THF, 19 µL, 19 µmol) and allyl bromide (13 µL, 150 µmol) were added at 0 °C and the reaction mixture was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.15) to give the product **149'** (26 mg, 114 µmol, 76% yield) as a colorless oil.

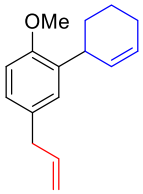
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.05 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.00 (d, *J* = 2.3 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.02 (ddt, *J* = 16.8, 10.0, 6.6 Hz, 1H), 5.92 – 5.81 (m, 1H), 5.77 – 5.60 (m, 1H), 5.12 – 5.00 (m, 2H), 3.82 (s, 3H), 3.39 (dd, *J* = 6.6, 1.6 Hz, 2H), 3.35 (ddt, *J* = 8.2, 5.5, 2.8 Hz, 1H), 2.16 – 2.05 (m, 2H), 2.00 (dddd, *J* = 15.1, 7.8, 3.9, 2.0 Hz, 1H), 1.75 (dtq, *J* = 11.7, 4.6, 2.2, 1.6 Hz, 1H), 1.70 – 1.47 (m, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 155.7, 138.7, 137.3, 130.8, 129.4, 128.4, 128.2, 126.3, 115.4, 110.3, 55.6, 41.2, 34.5, 32.9, 25.3, 21.5.

IR (ATR, cm^{-1}) ṽ = 2930, 2835, 1638, 1608, 1499, 1464, 1443, 1421, 1295, 1248, 1182, 1130, 1034, 996, 911, 811.

MS (EI, 70 eV, %) m/z = 228 (44), 188 (14), 187 (100), 172 (10), 159 (48), 145 (14), 144 (39), 141 (13), 129 (11), 128 (17), 121 (32), 115 (17), 79 (10).
HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{20}O$**: 228.1514; found: 228.1508.

Synthesis of 5'-allyl-2'-methoxy-1,2,3,4-tetrahydro-1,1'-biphenyl (150a')



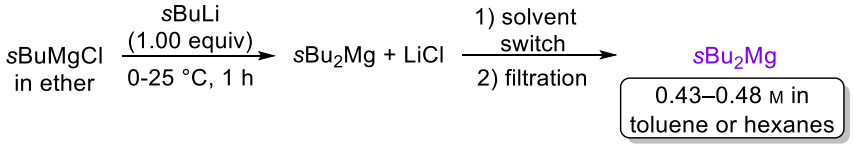
Compound **150a'** was prepared *via* **TP1** using 5'-iodo-2'-methoxy-1,2,3,4-tetrahydro-1,1'-biphenyl (**150a**, 30 mg, 97 µmol), dry toluene (0.3 mL) and PMDTA (10 µL, 45 µmol). Then, *s*Bu_2Mg·2LiOR (**134b**, 0.06 mL, 58 µmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuCN·2LiCl (1.00 M in THF, 10 µL, 10 µmol) and allyl bromide (7 µL, 78 µmol) were added at 0 °C and the reaction was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.20) to give the product **150a'** (16 mg, 70.1 µmol, 90% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.00 (dq, *J* = 5.2, 2.3 Hz, 2H), 6.87 – 6.72 (m, 1H), 6.08 – 5.83 (m, 2H), 5.66 (dq, *J* = 10.2, 2.4 Hz, 1H), 5.13 – 4.89 (m, 2H), 3.82 (s, 4H), 3.32 (dt, *J* = 6.7, 1.5 Hz, 2H), 2.17 – 2.03 (m, 2H), 2.02 – 1.93 (m, 1H), 1.78 – 1.58 (m, 2H), 1.55 – 1.40 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 155.4, 138.2, 134.6, 131.8, 130.5, 128.9, 128.5, 126.8, 115.4, 110.4, 55.6, 39.7, 34.4, 30.4, 25.3, 21.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2930, 2858, 2835, 2359, 1684, 1654, 1497, 1464, 1458, 1446, 1437, 1244, 1117, 1033, 810.
MS (EI, 70 eV, %) m/z = 229 (17), 228 (100), 213 (14), 187 (70), 185 (14), 174 (20), 172 (28), 171 (31), 159 (87), 158 (16), 157 (16), 155 (14), 153 (23), 152 (19), 147 (27), 145 (17), 144 (76), 141 (37), 131 (30), 129 (32), 128 (58), 121 (30), 115 (75), 91 (36), 79 (16), 77 (19).
HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{20}O$**: 228.1514; found: 228.1508.

3 Preparation of Functionalized Diorganomagnesium Reagents in Toluene *via* Bromine or Iodine/Magnesium Exchange Reactions

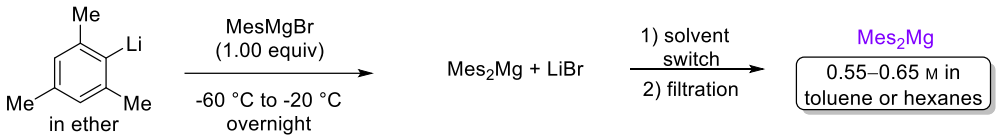
3.1 Preparation and Titration of Reagents of Type R_2Mg

Preparation of *s*Bu_2Mg



A dry and argon-flushed *Schlenk*-flask equipped with a stirring bar and a septum, was charged with *s*BuMgCl (10.2 mL, 20 mmol, 1.95 M in Et_2O, 1.00 equiv). Then *s*BuLi (12.8 mL, 20 mmol, 1.56 M in cyclohexane, 1.00 equiv) was added at room temperature under vigorous stirring. The resulting suspension was stirred for 2 h at room temperature. The solvents were removed under vacuum followed by addition of dry toluene (40 mL). The resulting suspension was vigorously stirred and allowed to settle overnight. The colourless solution was carefully transferred by cannula using a syringe filter to obtain *s*Bu_2Mg (0.43-0.48 M, 96% yield) in toluene.

Preparation of Mes_2Mg



A dry and argon-flushed *Schlenk*-flask equipped with a stirring bar and a septum, was charged with MesMgCl (23.5 mL, 20 mmol, 0.85 M in Et_2O, 1.00 equiv). Then MesLi (13.3 mL, 20 mmol, 1.50 M in Et_2O, 1.00 equiv) was added at −60 °C under vigorous stirring. The resulting suspension was stirred at −20 °C overnight. The solvents were removed under vacuum followed by addition of dry toluene (30 mL). The resulting suspension was vigorously stirred and allowed to settle overnight. The solution was carefully transferred by cannula using a syringe filter to obtain Mes_2Mg (0.55-0.65 M, 80% yield) in toluene.

Both reagents were titrated against I_2 in a 0.50 M LiCl solution in THF.

Note: All reagents should be storred at −20 °C and used within 2 weeks.

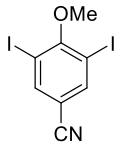
3.2 Typical Procedure

Typical Procedure 2: Preparation of Diorganomagnesium Species by Halide/Magnesium Exchange Followed by Electrophilic Functionalization

A dry and argon-flushed *Schlenk*-flask equipped with a magnetic stirring bar and a septum was charged with the corresponding (hetero)aryl or alkenyl halide (1.00 equiv) and dissolved in dry toluene at the indicated concentration. When necessary, DMPU was added (detailed for each compound thereafter). Then, the exchange reagent R_2Mg (R = *s*Bu, **151a**; R = Mes, **151b** 0.60-0.70 equiv) was added dropwise at the indicated temperature and the reaction stirred for the indicated time. Subsequent reactions with electrophiles were carried out under the indicated conditions. The mixture was then quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel using the appropriate eluent.

3.3 Preparation of Compounds 152 to 160

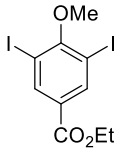
Synthesis of 3,5-diiodo-4-methoxybenzonitrile (152h)



A dry and argon-flushed 25 mL *Schlenk*-flask equipped with a magnetic stirring bar and a septum was charged with 4-hydroxy-3,5-diiodobenzonitrile (740 mg, 2.00 mmol) and DMF (5 mL) and was cooled down to 0 °C. NaH (60%, 88 mg, 2.20 mmol) was slowly added at 0 °C and the reaction solution was stirred for 30 min. Methyl iodide (0.15 mL, 2.40 mmol) was then added at 0 °C and the reaction was allowed to warm to room temperature overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified via column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.51) to give **152h** (756 mg, 1.96 mmol, 98% yield) as a white solid.

M.p. (°C): 140-142.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.05 (s, 2H), 3.91 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 163.2, 143.2, 115.5, 111.8, 90.9, 61.1.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2922, 2231, 1408, 978, 717.
MS (EI, 70 eV, %) m/z = 386 (9), 385 (100), 371 (3), 370 (43), 342 (6), 244 (4), 243 (64), 228 (6), 164 (4), 127 (14), 101 (5), 100 (4), 88 (20).
HRMS (EI, 70 eV) m/z: calc. **$C_8H_5I_2NO$**: 384.8460; found: 384.8456.

Synthesis of ethyl 3,5-diiodo-4-methoxybenzoate (152i)



A dry and argon-flushed 25 mL *Schlenk*-flask equipped with a magnetic stirring bar and a septum was charged with ethyl 4-hydroxy-3,5-diiodobenzoate (834 mg, 2.00 mmol) and DMF (5 mL) and was cooled down to 0 °C. K_2CO_3 (304 mg, 2.20 mmol) was added at 0 °C and the reaction solution was stirred for 30 min. Methyl iodide (0.15 mL, 2.40 mmol) was then added at 0 °C and the reaction was

allowed to warm to room temperature overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified via column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.65) to give the product **152i** (858 mg, 1.98 mmol, 98% yield) as a white solid.

M.p. (°C): 97-99.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.42 (s, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H).

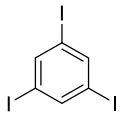
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 163.5, 162.6, 141.3, 129.8, 90.2, 61.8, 60.9, 14.4.

IR (ATR, cm^{-1}) ṽ = 2978, 1711, 1271, 1259, 995.

MS (EI, 70 eV, %) m/z = 433 (11), 432 (100), 404 (88), 389 (11), 387 (77), 344 (10), 305 (13), 290 (10), 287 (9), 262 (19), 245 (31), 231 (9), 229 (9), 218 (9), 217 (11), 189 (16), 178 (9).

HRMS (EI, 70 eV) m/z: calc. **$C_{10}H_{10}I_2O_3$**: 431.8719; found: 431.8713.

Synthesis of 1,3,5-triiodobenzene (152q)[194]



A dry and argon-flushed two-neck 250 mL *Schlenk*-flask equipped with a magnetic stirring bar, a septum and a reflux condenser was charged with 1,3,5-tribromobenzene (4.40 g, 14.0 mmol), KI (24.0 g, 145 mmol), Ni powder (3.20 g, 54.5 mmol), I_2 (30.0 g, 118 mmol) and anhydrous DMF (75 mL). The mixture was refluxed under argon at 187 °C for 8 h. After cooling, the solution was washed with 3% aqueous HCl (150 mL) and extracted with DCM (3 x 75 mL). The combined DCM phase was washed with brine (3 x 100 mL) and dried over $MgSO_4$. The solvent was evaporated and the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.69) to give a white solid (5.15 g) which was subjected to a second cycle under the same conditions to yield after recrystallization from *iso*hexane **152q** (5.04 g, 11.1 mmol, 79% yield) as a white solid.

M.p. (°C): 168-170.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.00 (s, 3H).

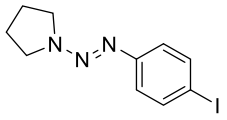
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 144.5, 95.4.

IR (ATR, cm^{-1}) ṽ = 1531, 1393, 846, 733, 699, 657.

[194] Adapted procedure from: S. Deng, J. Zhi, X. Zhang, Q. Wu, Y. Ding, A. Hu, *Angew. Chem. Int. Ed.* **2014**, *53*, 14144; *Angew. Chem.* **2014**, *127*, 14368.

MS (EI, 70 eV, %) m/z = 456 (100), 329 (24), 202 (17), 75 (59), 74 (39).
HRMS (EI, 70 eV) m/z: calc. for **$C_6H_3I_3$**: 455.7369; found 455.7369.

Synthesis of 1-((4-iodophenyl)diazenyl)pyrrolidine (152r)[195]

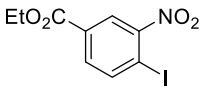


A dry and argon-flushed 100 mL *Schlenk*-flask was charged with 4-iodoaniline (1.00 g, 4.60 mmol), water (16 mL), conc. HCl (1.6 mL) and MeCN (38 mL). The mixture was cooled to 0 °C. A solution of $NaNO_2$ (347 mg, 5.00 mmol) in water (2 mL) was added drop by drop and the mixture was stirred for 45 min at 0 °C. Then, the mixture was transferred to a flask containing K_2CO_3 (2.15 g, 15.5 mmol) and pyrrolidine (0.76 mL, 9.20 mmol) in 25 mL H_2O at 0 °C. The reaction was allowed to warm to room temperature and stirred for another 2 h before being extracted with EtOAc (3 x 100 mL). After extraction, the organic phase was dried over $MgSO_4$. The solvent was evaporated and the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.32) to give **152r** (1.04 g, 3.50 mmol, 76% yield) as a yellow solid.

M.p. (°C): 104-106.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.69 – 7.52 (m, 2H), 7.23 – 7.09 (m, 2H), 3.77 (s, 4H), 2.20 – 1.90 (m, 4H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 151.2, 137.9, 122.5, 89.2, 23.9 (2C).
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2966, 2872, 1420, 1391, 1316, 826.
MS (EI, 70 eV, %) m/z = 231 (100), 203 (62), 76 (18).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{12}IN_3$**: 301.0076; found 301.0070.

[195] Adapted procedure from: K. Erden, İ. Savaş, C. Dengiz, *Tetrahedron Letters* **2019**, *60*, 1982.

Synthesis of ethyl 4-iodo-3-nitrobenzoate (152t)[51b]



A cold mixture of conc. HNO_3 (1.9 mL) and conc. H_2SO_4 (2.7 mL) was added slowly to a solution of ethyl 4-iodobenzoate (2.75 g, 10.0 mmol) dissolved in conc. H_2SO_4 (5 mL) within 30 min under vigorous stirring. Upon completion of the addition, the solution was allowed to warm to ambient temperature and stirring was continued overnight. The reaction mixture was then poured onto ice (100 g). The solid was filtrated, taken up in ethyl acetate (100 mL) and washed with sat. aq. $NaHCO_3$ (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified via column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.39) to give the product **152t** (2.40 g, 7.40 mmol, 75% yield) as a yellow solid.

M.p. (°C): 88-90.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.44 (d, *J* = 2.0 Hz, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.89 (dd, *J* = 8.2, 2.0 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

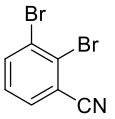
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 164.2, 153.3, 142.5, 133.6, 132.1, 126.2, 92.2, 62.3, 14.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2981, 1713, 1533, 1284, 1237.

MS (EI, 70 eV, %) m/z = 321 (22), 293 (100), 277 (10), 276 (58), 247 (15), 230 (28), 229 (8), 201 (11), 191 (12), 136 (21), 103 (22), 75 (14), 92 (9), 75 (14).

HRMS (EI, 70 eV) m/z: calc. **$C_9H_8INO_4$**: 320.9498; found: 320.9492.

Synthesis of 2,3-dibromobenzonitrile (155e)[196]



*n*BuLi in hexanes (4.33 mL, 1.50 m, 6.50 mmol) was added to a solution of 2,2,6,6-tetramethylpiperidine (1.10 mL, 6.50 mmol) in THF (10 mL) inside a dry and argon-flushed 100 mL *Schlenk*-flask at −20 °C. After stirring for 30 min, the solution was cooled to −78 °C and a solution of 3-bromobenzonitrile (980 mg, 5.44 mmol) in THF (6 mL) was added dropwise while maintaining the temperature below −70 °C. After 2 h, a 1.00 M solution of $ZnCl_2$ in THF (1.20 mL, 6.50 mmol) was added dropwise and the reaction solution was allowed to stir for an additional 30 min. Bromine (0.42

[196] Adapted procedure from: K. Menzel, E. L. Fisher, L. DiMichele, D. E. Frantz, T. D. Nelson, M. H. Kress, *J. Org. Chem.* **2006**, *71*, 2188.

mL, 8.10 mmol) was added dropwise while keeping the temperature below −50 °C. The reaction was monitored by GC and the completed reaction was allowed to warm to 25 °C and quenched with H_2O after 1 h. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified via column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.38) to give the product **155e** (970 mg, 3.74 mmol, 69% yield) as a white solid.

M.p. (°C): 115-117.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.85 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.62 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.30 (t, *J* = 7.9 Hz, 1H).

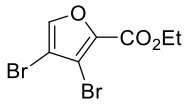
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 137.9, 133.2, 128.8, 128.2, 126.9, 118.1, 117.0.

IR (ATR, cm^{-1}) ṽ = 3071, 2230, 1441, 1406, 783.

MS (EI, 70 eV, %) m/z = 264 (4), 263 (49), 262 (7), 261 (100), 260 (4), 259 (52), 210 (22), 208 (23), 101 (5), 100 (16), 99 (5), 75 (7), 74 (4), 50 (4).

HRMS (EI, 70 eV) m/z: calc. **$C_7H_3Br_2N$**: 258.8632; found: 258.8627.

Synthesis of ethyl 3,4-dibromofuran-2-carboxylate (155f)



A two-neck 250 mL *Schlenk*-flask equipped with a magnetic stirring bar, a septum and a reflux condenser was charged with 3,4-dibromofuran-2-carboxylic acid (2.50 g, 9.40 mmol) and ethanol (50 mL). Conc. H_2SO_4 (2 mL) was added and the mixture was heated under reflux overnight. The reaction mixture was quenched with a saturated aqueous sodium bicarbonate solution until neutral pH and extracted with ethyl acetate (3 x 60 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified via column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.58) to give **155f** (689 mg, 2.32 mmol, 25% yield) as a white solid.

M.p. (°C): 62-64.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.17 (s, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 157.1, 146.3, 128.4, 121.9, 103.9, 61.8, 14.4.

IR (ATR, cm^{-1}) ṽ = 2983, 1723, 1479, 1292, 1179, 982, 730.

MS (EI, 70 eV, %) m/z = 299 (12), 298 (26), 296 (13), 272 (47), 270 (100), 268 (52), 255 (32), 254 (18), 253 (64), 251 (34), 228 (17), 226 (34), 224 (17), 199 (24), 197 (53), 195 (25), 175 (12), 119 (15), 118 (37), 117 (14), 116 (37).
HRMS (EI, 70 eV) m/z: calc. **$C_7H_6Br_2O_3$**: 295.8684; found: 295.8676.

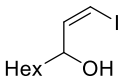
Synthesis of (*Z*)-1-iodohept-1-ene (158b)[197]

A dry and argon-flushed 50 mL *Schlenk*-flask was charged with $BH_3 \cdot SMe_2$ (5.00 M in ether, 2.12 mL, 10.6 mmol). Cyclohexene (2.14 mL, 21.1 mmol) was added drop by drop over 10 min at 0 °C. After stirring at this temperature for 5 min, the reaction was allowed to warm to room temperature and was further stirred for 1 h. The reaction was cooled to 0 °C, and 1-iodo-hept-1-yne (2.22 g, 10.0 mmol) was added drop by drop over a 10 min period. The reaction was further stirred for 30 min and the ice bath was then removed. The reaction was stirred 1 h at room temperature and cooled again to 0 °C. Glacial acetic acid (4 mL) was added slowly and the mixture was extracted with diethyl ether (3 x 100 mL). After extraction, the organic phase was dried over $MgSO_4$. The solvent was evaporated and the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.85) to give **158b** (1.20 g, 5.40 mmol, 54% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.34 – 6.01 (m, 2H), 2.13 (dtd, *J* = 7.5, 5.3, 1.5 Hz, 2H), 1.51 – 1.38 (m, 2H), 1.38 – 1.26 (m, 4H), 0.98 – 0.78 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 141.7, 82.3, 34.8, 31.5, 27.8, 22.7, 14.2.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3011, 1713, 1466, 1071, 728, 665.
MS (EI, 70 eV, %) m/z = 224 (19), 167 (45), 154 (100), 97 (74), 69 (31), 55 (69).
HRMS (EI, 70 eV) m/z: calc. for **$C_7H_{13}I$**: 224.0062; found 224.0056.

[197] Adapted procedure from: S. E., Denmark, W. Wang, M. Campbell, D. P. Curran, *Organic Syntheses* **2005**, *81*, 42.

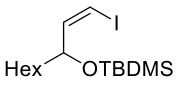
Synthesis of (*Z*)-1-iodonon-1-en-3-ol[198]



A dry and argon-flushed 100 mL *Schlenk*-flask equipped with a thermometer charged with ethyl *cis*-3-iodoacrylate (3.39 g, 15.0 mmol) and DCM (30 mL) was cooled to −78 °C. DIBAL-H (1.00 M in DCM, 15 mL, 15.0 mmol) was slowly added so that the temperature of the reaction mixture did not exceed −75 °C. After stirring at −78 °C for 30 min, hexylmagnesium bromide (16.5 mmol) was added dropwise at −70 °C. The reaction was allowed to warm to room temperature and stirred overnight. 1.00 M HCl (30 mL) was added dropwise at −5 °C and the mixture was warmed to room temperature. After extraction with diethyl ether (3 x 30 mL), the organic phase was dried over $MgSO_4$. The solvent was evaporated and the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.30) to give the product (3.48 g, 13.0 mmol, 87% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.33 (dd, *J* = 7.6, 0.9 Hz, 1H), 6.24 (t, *J* = 7.6 Hz, 1H), 4.40 (tdd, *J* = 7.3, 5.9, 0.9 Hz, 1H), 1.76 – 1.60 (m, 2H), 1.61 – 1.50 (m, 1H), 1.48 – 1.17 (m, 8H), 0.96 – 0.74 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 143.6, 82.5, 74.6, 36.1, 31.9, 29.4, 25.1, 22.7, 14.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2924, 2854, 1456, 1377, 1171.
MS (EI, 70 eV, %) m/z = 183 (100), 81 (11).
HRMS (EI, 70 eV) m/z: calc. for **C_3H_4OI**: 182.9307; found 182.9301.

Synthesis of (*Z*)-tert-butyl((1-iodonon-1-en-3-yl)oxy)dimethylsilane (158c)



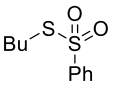
A dry and argon-flushed 25 mL *Schlenk*-flask charged with (*Z*)-1-iodonon-1-en-3-ol (402 mg, 1.50 mmol), imidazole (255 mg, 3.80 mmol) and DMF (5 mL) was cooled to 0 °C. TBDMSCl (271 mg, 1.80 mmol) was slowly added and the reaction was allowed to warm to room temperature and stirred overnight. A saturated aqueous solution of NH_4Cl (30 mL) was added and the mixture was extracted with EtOAc (3 x 30 mL). The organic phase was washed with Brine (3 x 100 mL) and dried over $MgSO_4$. The solvent was evaporated and the crude product was purified *via* column chromatography

[198] Adapted procedure from: I. Marek, C. Meyer, J.-F. Normant, *Organic Syntheses* **1997**, *74*, 194.

(*iso*hexane:ethyl acetate = 99:1, R_f = 0.78) to give **158c** (540 mg, 1.47 mmol, 98% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.26 – 6.06 (m, 2H), 4.33 (dtd, *J* = 7.6, 5.1, 1.3 Hz, 1H), 1.53 – 1.36 (m, 3H), 1.32 – 1.20 (m, 7H), 0.99 – 0.82 (m, 12H), 0.09 (s, 3H), 0.05 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 145.0, 79.7, 75.6, 37.0, 32.0, 29.4, 26.0, 25.1, 22.8, 18.3, 14.3, –4.1, –4.6.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2928, 1251, 1087, 836, 776.
MS (EI, 70 eV, %) m/z = 325 (100), 241 (34), 185 (44), 113 (33), 85 (31), 75 (60).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{28}OISi$**: 367.0954; found 367.0947.

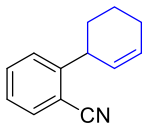
Synthesis of *S*-butyl benzenesulfonothioate



A dry and argon-flushed *Schlenk*-flask equipped with a magnetic stirring bar and a septum was charged with butane-1-thiol (4.28 mL, 40.0 mmol), DCM (50 mL), water (25 mL) and iodine (5.58 g, 22.0 mmol) and stirred at room temperature for 30 min. The mixture was extracted with DCM (3 x 30 mL). The combined organic extracts were washed with water and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting solution of dibutyl-disulfide was mixed with sodium benzenesulfinate (10.5 g, 64.0 mmol), iodine (10.1 g, 40.0 mmol) and DCM (50 mL) and stirred for 22 h at room temperature. Then, a 0.10 M $Na_2S_2O_3$ solution was added to quench the remaining iodine. The organic phase was washed and dried and the solvent removed under reduced pressure to afford *S*-butyl benzenesulfonothioate (8.77 g, 38.1 mmol, 95% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.10 – 7.81 (m, 2H), 7.69 – 7.60 (m, 1H), 7.60 – 7.50 (m, 2H), 3.00 (t, *J* = 7.4 Hz, 2H), 1.57 (tt, *J* = 8.8, 6.9 Hz, 2H), 1.32 (dq, *J* = 14.6, 7.3 Hz, 2H), 0.84 (t, *J* = 7.4 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 145.0, 133.7, 129.4, 127.1, 35.9, 30.7, 21.8, 13.5.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2960, 1458, 1292, 1139, 1077, 999, 670.
MS (EI, 70 eV, %) m/z = 141 (19), 125 (18), 97 (13), 89 (56), 77 (100), 55 (39).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{14}O_2S_2$**: 230.0435; found: 230.0507.

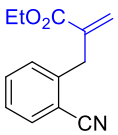
Synthesis of 1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-carbonitrile (154aa)



Allylated benzonitrile **154aa** was prepared *via* **TP2** using 2-iodobenzonitrile (115 mg, 0.50 mmol) and dry toluene (5.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 10 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromocyclohexene (47 µL, 0.40 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 60:40, R_f = 0.29) to give the product **154aa** (90 mg, 491 µmol, 98% yield) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.61 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.52 (td, *J* = 7.7, 1.5 Hz, 1H), 7.36 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.28 (td, *J* = 7.6, 1.2 Hz, 1H), 6.04 – 5.94 (m, 1H), 5.63 (dd, *J* = 10.1, 2.5 Hz, 1H), 3.86 (ddt, *J* = 8.3, 5.6, 2.8 Hz, 1H), 2.19 – 2.05 (m, 3H), 1.75 – 1.61 (m, 2H), 1.57 – 1.47 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 150.4, 133.0, 132.9, 130.1, 128.4, 128.1, 126.7, 118.2, 112.1, 40.2, 31.7, 24.9, 21.0.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2931, 1633, 1570, 1445, 1046.
MS (EI, 70 eV, %) m/z = 183 (18), 182 (100), 168 (24), 167 (27), 166 (15), 165 (45), 154 (31), 140 (15), 115 (23).
HRMS (EI, 70 eV) m/z: calc. **$C_{13}H_{13}N$**: 183.1048; found: 183.1040.

Synthesis of ethyl 2-(2-cyanobenzyl)acrylate (154ab)



Ester **154ab** was prepared *via* **TP2** using 2-iodobenzonitrile (115 mg, 0.50 mmol) and dry toluene (5.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 10 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and ethyl 2-(bromomethyl)acrylate (83 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 80:20, R_f = 0.35) to give the product **154ab** (88 mg, 409 µmol, 88% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.63 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.51 (td, *J* = 7.7, 1.5 Hz, 1H), 7.40 – 7.35 (m, 1H), 7.31 (td, *J* = 7.6, 1.2 Hz, 1H), 6.32 (d, *J* = 1.0 Hz, 1H), 5.57 (d, *J* = 1.3 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 2H), 1.25 (t, *J* = 7.1 Hz, 3H).

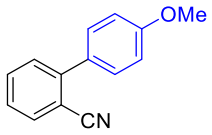
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.3, 142.7, 138.2, 133.0, 132.8, 130.3, 127.7, 127.1, 118.0, 113.1, 61.1, 36.6, 14.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2981, 2224, 1712, 1137, 761.

MS (EI, 70 eV, %) m/z = 187 (20), 170 (9), 169 (14), 143 (10), 142 (28), 141 (100), 140 (32), 115 (30), 114 (19).

HRMS (EI, 70 eV) m/z: calc. **$C_{13}H_{13}NO_2$**: 215.0946; found: 215.0941.

Synthesis of 4'-methoxy-[1,1'-biphenyl]-2-carbonitrile (154ac)



Biaryl **154ac** was prepared *via* **TP2** using 2-iodobenzonitrile (115 mg, 0.50 mmol) and dry toluene (5.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −78 °C. After stirring at –78 °C for 10 min, $ZnCl_2$ (1.00 M in THF, 0.65 mL, 0.65 mmol), $Pd(OAc)_2$ (5 mg, 4 mol%), SPhos (17 mg, 8 mol%) and 4-iodoanisole (93 mg, 0.40 mmol) were added and the reaction mixture was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.30) to give the product **154ac** (61 mg, 291 µmol, 73% yield) as a white solid.

M.p. (°C): 84-86.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.74 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.62 (td, *J* = 7.7, 1.4 Hz, 1H), 7.55 – 7.47 (m, 3H), 7.40 (td, *J* = 7.6, 1.2 Hz, 1H), 7.04 – 6.99 (m, 2H), 3.87 (s, 3H).

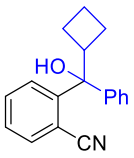
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.2, 145.3, 133.9, 132.9, 130.6, 130.1, 130.0, 127.2, 119.2, 114.3, 111.2, 55.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2922, 2222, 1608, 1478, 1246, 763.

MS (EI, 70 eV, %) m/z = 210 (15), 209 (100), 194 (12), 167 (7), 166 (47), 140 (27), 139 (13), 113 (7), 63 (8), 42 (6).

HRMS (EI, 70 eV) m/z: calc. **$C_{14}H_{11}NO$**: 209.0841; found: 209.0831.

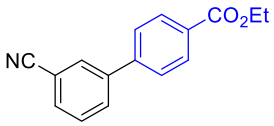
Synthesis of 2-(cyclobutyl(hydroxy)(phenyl)methyl)benzonitrile (154ad)



Tertiary alcohol **154ad** was prepared *via* **TP2** using 2-iodobenzonitrile (115 mg, 0.50 mmol) and dry toluene (5.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 10 min, cyclobutyl(phenyl)methanone (91 µL, 0.60 mmol) were added and the reaction solution was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 80:20, R_f = 0.34) to give the product **154ad** (72 mg, 273 µmol, 55% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.60 – 7.52 (m, 2H), 7.51 – 7.43 (m, 2H), 7.38 – 7.20 (m, 5H), 3.39 (dt, *J* = 16.6, 8.5 Hz, 1H), 2.26 (s, 1H), 2.08 – 1.96 (m, 3H), 1.94 – 1.84 (m, 1H), 1.83 – 1.73 (m, 1H), 1.72 – 1.64 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 151.4, 145.2, 132.0, 128.6, 128.5, 127.7, 127.1, 126.5, 126.3, 119.1, 110.6, 78.5, 43.8, 23.3, 22.3, 17.2.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2938, 2168, 1724, 906, 730.
MS (EI, 70 eV, %) m/z = 209 (15), 208 (100), 190 (2), 130 (80), 105 (5), 102 (2), 77 (3).
HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{17}NO$**: 263.1310; found: 263.1308.

Synthesis of ethyl 3'-cyano-[1,1'-biphenyl]-4-carboxylate (154b)



Biaryl **154b** was prepared *via* **TP2** using 3-iodobenzonitrile (115 mg, 0.50 mmol) and dry toluene (2.0 mL). Then, *s*Bu_2Mg (**151a**, 0.38 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 10 min, $ZnCl_2$ (1.00 M in THF, 0.65 mL, 0.65 mmol), $Pd(OAc)_2$ (5 mg, 4 mol%), SPhos (17 mg, 8 mol%) and ethyl 4-iodobenzoate (67 µL, 0.40 mmol) were added and the reaction mixture was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.30) to give the product **154b** (72 mg, 286 µmol, 72% yield) as a white solid.

M.p. (°C): 89-91.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.19 – 8.11 (m, 2H), 7.90 (t, *J* = 1.7 Hz, 1H), 7.84 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.68 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.65 – 7.61 (m, 2H), 7.58 (t, *J* = 7.8 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

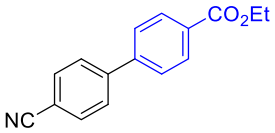
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.3, 143.1, 141.5, 131.7, 131.6, 131.0, 130.5, 129.9, 127.2, 118.7, 113.3, 61.3, 14.5.

IR (ATR, cm^{-1}) ṽ = 2981, 1710, 1273, 1103, 767.

MS (EI, 70 eV, %) m/z = 252 (5), 251 (28), 224 (5), 223 (30), 207 (15), 206 (100), 179 (5), 178 (23), 177 (28), 176 (5), 152 (9), 151 (26), 150 (9), 75 (6), 51 (5).

HRMS (EI, 70 eV) m/z: calc. **$C_{16}H_{13}NO_2$**: 251.0946; found: 251.0934.

Synthesis of ethyl 4'-cyano-[1,1'-biphenyl]-4-carboxylate (154c)



Biaryl **154c** was prepared *via* **TP2** using 4-iodobenzonitrile (115 mg, 0.50 mmol) and dry toluene (2.0 mL). Then, *s*Bu_2Mg (**151a**, 0.38 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 10 min, $ZnCl_2$ (1.00 M in THF, 0.65 mL, 0.65 mmol), $Pd(OAc)_2$ (5 mg, 4 mol%), SPhos (17 mg, 8 mol%) and ethyl 4-iodobenzoate (67 µL, 0.40 mmol) were added and the reaction mixture was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.23) to give the product **154c** (70 mg, 278 µmol, 70% yield) as a white solid.

M.p. (°C): 118-120.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.18 – 8.12 (m, 2H), 7.78 – 7.70 (m, 4H), 7.67 – 7.63 (m, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

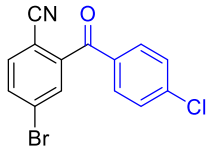
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.3, 144.6, 143.4, 132.9, 130.7, 130.5, 128.1, 127.3, 118.8, 111.9, 61.4, 14.5.

IR (ATR, cm^{-1}) ṽ = 2987, 2223, 1707, 1098, 771.

MS (EI, 70 eV, %) m/z = 251 (88), 223 (83), 207 (42), 206 (100), 178 (58), 177 (71), 152 (16), 151 (64), 150 (18).

HRMS (EI, 70 eV) m/z: calc. **$C_{16}H_{13}NO_2$**: 251.0946; found: 251.0944.

Synthesis of 4-bromo-2-(4-chlorobenzoyl)benzonitrile (154d)



Diaryl ketone **154d** was prepared *via* **TP2** using 4-bromo-2-iodobenzonitrile (154 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.38 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 10 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 4-chlorobenzoyl chloride (77 µL, 0.60 mmol) were added and the reaction solution was allowed to warm at −20 °C and was stirred at this temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.23) to give the product **154d** (121 mg, 380 µmol, 76% yield) as a white solid.

M.p. (°C): 171-173.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.82 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.78 – 7.73 (m, 3H), 7.70 (d, *J* = 8.3 Hz, 1H), 7.54 – 7.49 (m, 2H).

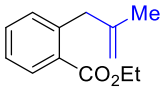
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 191.2, 142.7, 141.2, 135.3, 134.9, 133.8, 133.0, 131.8, 129.5, 127.7, 116.4, 110.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2922, 1665, 1580, 1286, 941.

MS (EI, 70 eV, %) m/z = 287 (7), 286 (47), 285 (8), 284 (49), 242 (7), 240 (22), 141 (33), 140 (7), 139 (100), 111 (14), 100 (7), 75 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_7BrClNO$**: 318.9400; found: 318.9393.

Synthesis of ethyl 2-(2-methylallyl)benzoate (154e)



Ester **154e** was prepared *via* **TP2** using ethyl 2-iodobenzoate (138 mg, 0.50 mmol) and dry toluene (0.8 mL). Then, *s*Bu_2Mg (**151a**, 0.38 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 15 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and methallyl bromide (60 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.15) to give the product **154e** (94 mg, 459 µmol, 92% yield) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.86 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.43 (td, *J* = 7.5, 1.5 Hz, 1H), 7.35 – 7.18 (m, 2H), 4.78 (dq, *J* = 2.4, 1.3 Hz, 1H), 4.45 (tt, *J* = 1.6, 0.8 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.71 (s, 2H), 1.74 (dd, *J* = 1.4, 0.8 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H).

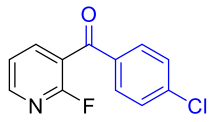
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 168.0, 145.5, 140.9, 131.7, 131.5, 130.9, 130.5, 126.3, 111.6, 61.0, 41.9, 23.0, 14.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2925, 1717, 1253, 1076, 740.

MS (EI, 70 eV, %) m/z = 189 (100), 161 (85), 159 (56), 158 (57), 157 (25), 143 (20), 131 (51), 130 (25), 129 (74), 128 (26), 115 (51), 91 (29).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{16}O_2$**: 204.1150; found 204.1144.

Synthesis of (4-chlorophenyl)(2-fluoropyridin-3-yl)methanone (154fa)



Ketone **154fa** was prepared *via* **TP2** using 2-fluoro-3-iodopyridine (112 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 15 min, CuCN·2LiCl (1.00 M in THF, 0.30 mL, 0.30 mmol) and 4-chlorobenzoyl chloride (77 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperqture overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.15) to give the product **154fa** (86 mg, 365 µmol, 73% yield) as a white solid.

M.p. (°C): 93-95.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.44 (d, *J* = 4.3 Hz, 1H), 8.05 (ddd, *J* = 9.2, 7.4, 2.0 Hz, 1H), 7.82 – 7.72 (m, 2H), 7.54 – 7.44 (m, 2H), 7.38 (ddd, *J* = 7.0, 4.8, 1.9 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 190.7 (d, *J* = 4.8 Hz), 161.3, 158.9, 150.9 (d, *J* = 14.9 Hz), 142.0 (d, *J* = 3.3 Hz), 135.0, 131.1 (d, *J* = 1.3 Hz), 129.2, 122.0 (d, *J* = 4.7 Hz), 121.3 (d, *J* = 30.1 Hz).

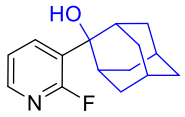
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –62.4.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2921, 1656, 1090, 848, 772.

MS (EI, 70 eV, %) m/z = 237 (5), 235 (16), 141 (33), 140 (8), 139 (100), 124 (7), 111 (9), 96 (5), 75 (6).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_7ClFNO$**: 235.0200; found: 235.0194.

Synthesis of (1R,3R,5R,7R)-2-(2-fluoropyridin-3-yl)adamantan-2-ol (154fb)



Tertiary alcohol **154fb** was prepared *via* **TP2** using 2-fluoro-3-iodopyridine (112 mg, 0.50 mmol), dry THF (48 µL, 0.60 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 15 min, adamantone previously dissolved in 0.2 mL of toluene (150 mg, 1.00 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 60:40, R_f = 0.32) to give the product **154fb** (91 mg, 368 µmol, 74% yield) as a white solid.

M.p. (°C): 110-113.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.17 – 8.05 (m, 1H), 7.89 (ddd, *J* = 10.4, 7.6, 1.9 Hz, 1H), 7.19 (ddd, *J* = 7.7, 4.8, 2.1 Hz, 1H), 2.65 (s, 2H), 2.42 (d, *J* = 12.5 Hz, 2H), 2.13 (d, *J* = 2.8 Hz, 1H), 1.93 – 1.78 (m, 4H), 1.76 – 1.63 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 161.8 (d, *J* = 241.3 Hz), 146.2 (d, *J* = 16.1 Hz), 139.4 (d, *J* = 5.5 Hz), 127.8 (d, *J* = 24.2 Hz), 121.4 (d, *J* = 4.2 Hz), 75.8 (d, *J* = 5.1 Hz), 37.6, 35.6, 35.5, 35.1, 32.9, 27.2, 26.7.

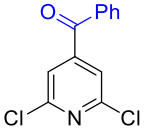
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –62.0.

IR (ATR, cm^{-1}) ṽ = 2915, 1596, 1242, 1103, 968, 808.

MS (EI, 70 eV, %) m/z = 230 (16), 229 (100), 204 (11), 187 (40), 186 (11), 175 (12), 152 (15), 151 (19), 151 (15), 150 (16), 140 (20), 136 (20), 127 (11), 124 (11), 124 (25), 93 (15), 91 (14), 81 (12), 79 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{18}FNO$**: 247.1372; found: 247.1369.

Synthesis of (2,6-dichloropyridin-4-yl)(phenyl)methanone (154g)



Ketone **154g** was prepared *via* **TP2** using 2,6-dichloro-4-iodopyridine (137 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 15 min, CuCN·2LiCl (1.00 M in THF, 0.30 mL, 0.30 mmol) and benzoyl chloride (70 µL,

0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.46) to give the product **154g** (95 mg, 377 µmol, 75% yield) as a white solid.

M.p. (°C): 85-87.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.85 – 7.77 (m, 2H), 7.73 – 7.66 (m, 1H), 7.59 – 7.49 (m, 4H).

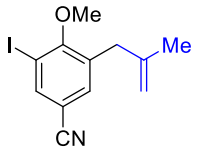
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 192.3, 151.4, 149.9, 135.1, 134.4, 130.2, 129.1, 122.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3079, 1657, 1280, 1165, 661.

MS (EI, 70 eV, %) m/z = 251 (12), 216 (3), 146 (3), 110 (4), 106 (8), 105 (100), 77 (25).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_7Cl_2NO$**: 250.9905; found: 250.9894.

Synthesis of 3-iodo-4-methoxy-5-(2-methylallyl)benzonitrile (154h)



Iodoanisole **154h** was prepared *via* **TP2** using 3,5-diiodo-4-methoxybenzonitrile (**152h**, 192 mg, 0.50 mmol) and dry toluene (1.0 mL). Then *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 15 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and methallyl bromide (60 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to −20 °C and stirred at this temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.54) to give the product **154h** (80 mg, 255 µmol, 51% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.95 (d, *J* = 2.0 Hz, 1H), 7.56 – 7.37 (m, 1H), 4.93 (tt, *J* = 1.7, 0.9 Hz, 1H), 4.66 (tq, *J* = 1.4, 0.7 Hz, 1H), 3.81 (s, 3H), 3.40 (s, 2H), 1.72 (t, *J* = 1.0 Hz, 3H).

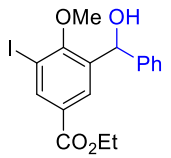
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 162.2, 143.2, 141.3, 135.5, 135.0, 117.3, 113.9, 110.0, 92.5, 61.5, 38.4, 22.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2940, 2359, 1464, 1265, 994.

MS (EI, 70 eV, %) m/z = 313 (86), 284 (35), 186 (45), 171 (100), 170 (64), 157 (65), 156 (93), 144 (26), 143 (35), 140 (26), 115 (60).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{12}INO$**: 312.9964; found: 312.9964.

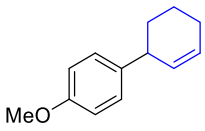
Synthesis of ethyl 3-(hydroxy(phenyl)methyl)-5-iodo-4-methoxybenzoate (154i)



Alcohol **154i** was prepared *via* **TP2** using ethyl 3,5-diiodo-4-methoxybenzoate (**152i**, 215 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −78 °C. After stirring at −78 °C for 15 min, benzaldehyde (0.69 µL, 0.60 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 80:20, R_f = 0.12) to give the product **154i** (109 mg, 265 µmol, 53% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.41 (d, *J* = 2.1 Hz, 1H), 8.18 (d, *J* = 2.1 Hz, 1H), 7.39 – 7.32 (m, 4H), 7.30 – 7.27 (m, 1H), 6.09 (d, *J* = 4.8 Hz, 1H), 4.36 (qd, *J* = 7.1, 1.2 Hz, 2H), 3.62 (s, 3H), 2.57 (d, *J* = 5.1 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 164.9, 160.9, 143.0, 140.7, 138.5, 129.9, 128.8, 128.5, 128.1, 126.8, 91.4, 72.1, 61.6, 61.5, 14.5.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3439, 1715, 1275, 1144, 700.
MS (EI, 70 eV, %) m/z = 412 (31), 398 (17), 397 (100), 394 (11), 367 (12), 349 (14), 347 (27), 333 (11), 319 (35), 291 (15), 194 (20), 165 (12), 152 (13).
HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{17}IO_4$**: 412.0172; found: 412.0167.

Synthesis of 4'-methoxy-1,2,3,4-tetrahydro-1,1'-biphenyl (154ja)



Allylated anisole **154ja** was prepared *via* **TP2** using 4-iodoanisole (94 mg, 0.40 mmol), dry THF (39 µL, 0.48 mmol) and dry toluene (0.8 mL). Then, *s*Bu_2Mg (**151a**, 0.58 mL, 0.28 mmol) was added at 25 °C. After stirring at 25 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 40 µL, 40 µmol) and 3-bromocyclohexene (55 µL, 0.48 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.29) to give the product **154ja** (59 mg, 312 µmol, 78% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.16 – 7.12 (m, 2H), 7.00 – 6.64 (m, 2H), 5.87 (dtd, *J* = 9.9, 3.6, 2.3 Hz, 1H), 5.69 (dq, *J* = 10.2, 2.5 Hz, 1H), 3.79 (s, 3H), 3.36 (ddt, *J* = 8.2, 5.6, 2.8 Hz, 1H), 2.11 – 2.04 (m, 2H), 2.02 – 1.94 (m, 1H), 1.72 (dddd, *J* = 11.7, 6.6, 4.8, 2.2 Hz, 1H), 1.61 (dddd, *J* = 12.2, 6.9, 3.6, 1.5 Hz, 1H), 1.52 (dddd, *J* = 13.1, 10.6, 8.0, 2.6 Hz, 1H).

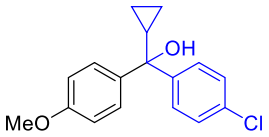
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 158.0, 138.9, 130.6, 128.8, 128.3, 113.8, 55.4, 41.1, 32.9, 25.2, 21.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2931, 1510, 1245, 1035, 827.

MS (EI, 70 eV, %) m/z = 188 (52), 160 (25), 111 (33), 109 (25), 97 (72), 95 (34), 85 (36), 83 (54), 81 (32), 71 (54), 69 (52), 57 (100), 56 (30), 55 (52), 43 (63), 41 (34).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{16}O$**: 188.1201; found: 188.1199.

Synthesis of (4-chlorophenyl)(cyclopropyl)(4-methoxyphenyl)methanol (154jb)



Alcohol **154jb** was prepared *via* **TP2** using 4-iodoanisole (94 mg, 0.40 mmol), dry THF (39 µL, 0.48 mmol) and dry toluene (0.8 mL). Then, *s*Bu_2Mg (**151a**, 0.58 mL, 0.28 mmol) was added at 25 °C. After stirring at 25 °C for 30 min, (4-chlorophenyl)(cyclopropyl)methanone (87 mg, 0.48 mmol) was added and the reaction solution was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.29) to give the product **154jb** (73 mg, 253 µmol, 63% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.38 – 7.29 (m, 4H), 7.29 – 7.21 (m, 2H), 6.88 – 6.79 (m, 2H), 3.78 (s, 3H), 1.81 (s, 1H), 1.54 (tt, *J* = 8.2, 5.4 Hz, 1H), 0.73 – 0.56 (m, 1H), 0.56 – 0.47 (m, 1H), 0.43 (dddd, *J* = 9.1, 6.6, 5.2, 3.7 Hz, 2H).

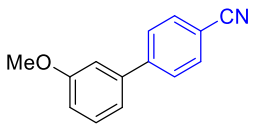
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 158.9, 146.1, 139.1, 132.8, 128.3 (2C), 128.1, 113.5, 55.4, 21.8, 2.3, 1.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3490, 3004, 1509, 1248, 825.

MS (EI, 70 eV, %) m/z = 262 (20), 260 (60), 247 (15), 141 (25), 139 (76), 135 (38), 121 (100), 77 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{17}ClO_2$**: 288.0917; found: 288.0911.

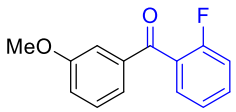
Synthesis of 3'-methoxy-[1,1'-biphenyl]-4-carbonitrile (154ka)



Biaryl **154ka** was prepared *via* **TP2** using 3-iodoanisole (94 mg, 0.40 mmol), dry THF (39 µL, 0.48 mmol) and dry toluene (0.8 mL). Then, *s*Bu_2Mg (**151a**, 0.58 mL, 0.28 mmol) was added at 25 °C. After stirring at 25 °C for 30 min, $ZnCl_2$ (1.00 M in THF, 0.52 mL, 0.52 mmol), $Pd(OAc)_2$ (4 mg, 4 mol%), SPhos (13 mg, 8 mol%) and 4-iodobenzonitrile (73 mg, 0.32 mmol) were added and the reaction solution was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.21) to give the product **154ka** (59 mg, 282 µmol, 88% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.83 – 7.61 (m, 4H), 7.40 (t, *J* = 7.9 Hz, 1H), 7.17 (ddd, *J* = 7.6, 1.8, 0.9 Hz, 1H), 7.10 (t, *J* = 2.1 Hz, 1H), 6.97 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 3.87 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.2, 145.6, 140.7, 132.7, 130.3, 127.9, 119.8, 119.1, 114.0, 113.2, 111.1, 55.5.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2226, 1603, 1480, 1296, 1215, 836.
MS (EI, 70 eV, %) m/z = 210 (15), 209 (100), 180 (38), 179 (82), 178 (28), 166 (25), 151 (10), 140 (36), 139 (14).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}NO$**: 209.0841; found: 209.0832.

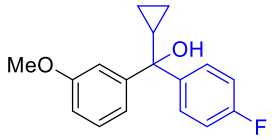
Synthesis of (2-fluorophenyl)(3-methoxyphenyl)methanone (154kb)



Ketone **154kb** was prepared *via* **TP2** using 3-iodoanisole (94 mg, 0.40 mmol), dry THF (39 µL, 0.48 mmol) and dry toluene (0.8 mL). Then, *s*Bu_2Mg (**151a**, 0.58 mL, 0.28 mmol) was added at 25 °C. After stirring at 25 °C for 30 min, CuCN·2LiCl (1.00 M in THF, 0.24 mL, 0.24 mmol) and 2-fluorobenzoyl chloride (76 mg, 0.48 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.24) to give the product **154kb** (55 mg, 239 µmol, 60% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.56 – 7.47 (m, 2H), 7.44 – 7.42 (m, 1H), 7.39 – 7.32 (m, 2H), 7.26 (td, *J* = 7.6, 1.1 Hz, 1H), 7.19 – 7.11 (m, 2H), 3.86 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 193.4, 160.2 (d, *J* = 252.4 Hz), 159.8, 138.8, 133.2 (d, *J* = 8.4 Hz), 130.8 (d, *J* = 2.9 Hz), 129.6, 127.2 (d, *J* = 14.8 Hz), 124.3 (d, *J* = 3.6 Hz), 123.1 (d, *J* = 1.5 Hz), 120.2, 116.4 (d, *J* = 21.7 Hz), 113.7, 55.6.
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –111.4.
IR (ATR, cm^{-1}) ṽ = 1664, 1482, 1450, 1295, 753.
MS (EI, 70 eV, %) m/z = 230 (59), 210 (14), 199 (19), 135 (100), 123 (67), 107 (32), 95 (11), 77 (22).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}FO_2$**: 230.0743; found: 230.0736.

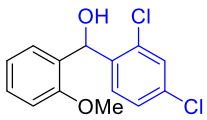
Synthesis of cyclopropyl(4-fluorophenyl)(3-methoxyphenyl)methanol (154kc)



Alcohol **154kc** was prepared *via* **TP2** using 3-iodoanisole (94 mg, 0.40 mmol), dry THF (39 µL, 0.48 mmol) and dry toluene (0.8 mL). Then, *s*Bu_2Mg (**151a**, 0.58 mL, 0.28 mmol) was added at 25 °C. After stirring at 25 °C for 30 min, (4-fluorophenyl)(cyclopropyl)methanone (79 mg, 0.48 mmol) was added and the reaction solution was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.18) to give the product **154kc** (102 mg, 375 µmol, 94% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, DMSO-d_6, ppm) δ = 7.57 – 7.33 (m, 2H), 7.20 (t, *J* = 7.9 Hz, 1H), 7.13 – 7.06 (m, 2H), 6.99 – 6.90 (m, 2H), 6.77 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 5.26 (s, 1H), 3.71 (s, 3H), 1.96 – 1.45 (m, 1H), 0.43 (dddd, *J* = 15.2, 6.8, 3.8, 1.8 Hz, 4H).
^{13}C-NMR (101 MHz, DMSO-d_6, ppm) δ = 160.8 (d, *J* = 242.3 Hz), 158.7, 150.2, 144.8 (d, *J* = 3.0 Hz), 128.7, 128.4 (d, *J* = 8.0 Hz), 119.0, 114.2 (d, *J* = 21.0 Hz), 112.7, 111.2, 74.7, 54.9, 21.3, 1.4 (2C).
^{19}F-NMR (377 MHz, DMSO-d_6, ppm) δ = –117.0.
IR (ATR, cm^{-1}) ṽ = 3490, 3004, 1506, 1221, 777.
MS (EI, 70 eV, %) m/z = 245 (11), 244 (64), 183 (10), 136 (36), 135 (14), 123 (100), 108 (11), 95 (10).
HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{17}FO_2$**: 272.1213; found: 272.1209.

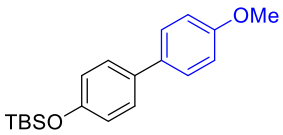
Synthesis of (2,4-dichlorophenyl)(2-methoxyphenyl)methanol (154l)



Secondary alcohol **154l** was prepared *via* **TP2** using 2-iodoanisole (234 mg, 1.00 mmol), dry THF (100 µL, 1.20 mmol) and dry toluene (2.0 mL). Then, *s*Bu_2Mg (**151a**, 1.46 mL, 0.70 mmol) was added at 25 °C. After stirring at 25 °C for 30 min, 2,4-dichlorobenzaldehyde (263 mg, 1.50 mmol) was added and the reaction solution was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.28) to give the product **154l** (211 mg, 745 µmol, 75% yield) as a white solid.

M.p. (°C): 92-94.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.53 (d, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 2.1 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.09 – 6.77 (m, 3H), 6.38 (s, 1H), 3.88 (s, 3H), 3.03 (s, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 157.1, 138.7, 133.7, 133.6, 130.0, 129.6, 129.4, 129.2, 127.7, 127.3, 120.9, 110.7, 68.4, 55.6.
IR (ATR, cm^{-1}) ṽ = 3368, 1463, 1241, 1022, 749.
MS (EI, 70 eV, %) m/z = 284 (28), 282 (51), 229 (31), 173 (34), 137 (37), 135 (52), 109 (100), 107 (29), 77 (36).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{12}Cl_2O_2$**: 282.0214; found: 282.0206.

Synthesis of *tert*-butyl((4'-methoxy-[1,1'-biphenyl]-4-yl)oxy)dimethylsilane (154m)



Diaryl **154m** was prepared *via* **TP2** using *tert*-butyl(4-iodophenoxy)dimethylsilane (134 mg, 0.40 mmol), dry THF (39 µL, 0.48 mmol) and dry toluene (0.8 mL). Then, *s*Bu_2Mg (**151a**, 0.58 mL, 0.28 mmol) was added at 25 °C. After stirring at 25 °C for 30 min, $ZnCl_2$ (1.00 M in THF, 0.52 mL, 0.52 mmol), $Pd(OAc)_2$ (4 mg, 4 mol%), SPhos (13 mg, 8 mol%) and 4-iodoanisole (75 mg, 0.32 mmol) were added and the reaction solution was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:toluene = 70:30, R_f = 0.49) to give the product **154m** (65 mg, 207 µmol, 65% yield) as a white solid.

M.p. (°C): 84-86.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.68 – 7.35 (m, 4H), 7.02 – 6.76 (m, 4H), 3.84 (s, 3H), 1.00 (s, 9H), 0.22 (s, 6H).

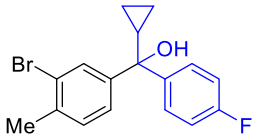
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 158.8, 154.9, 134.1, 133.7, 127.9, 127.8, 120.4, 114.2, 55.5, 25.9, 18.4, –4.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2926, 2364, 1502, 1251, 822.

MS (EI, 70 eV, %) m/z = 314 (66), 258 (34), 257 (100), 71 (19), 57 (29), 43 (35).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{26}SiO_2$**: 314.1702; found: 314.1701.

Synthesis of (3-bromo-4-methylphenyl)(cyclopropyl)(4-fluorophenyl)methanol (154n)



Alcohol **154n** was prepared *via* **TP2**using 2-bromo-4-iodo-1-methylbenzene (119 mg, 0.40 mmol), dry THF (39 µL, 0.48 mmol) and dry toluene (0.8 mL). Then, *s*Bu_2Mg (**151a**, 0.58 mL, 0.28 mmol) was added at 25 °C. After stirring at 25 °C for 30 min, (4-fluorophenyl)(cyclopropyl)methanone (79 mg, 0.48 mmol) was added and the reaction solution was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.46) to give the product **154n** (71 mg, 212 µmol, 53% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.63 (d, *J* = 1.8 Hz, 1H), 7.47 – 7.34 (m, 2H), 7.24 – 7.11 (m, 2H), 7.05 – 6.93 (m, 2H), 2.37 (s, 3H), 1.83 (s, 1H), 1.56 (tt, *J* = 8.3, 5.4 Hz, 1H), 0.72 – 0.55 (m, 2H), 0.45 (dd, *J* = 5.4, 1.8 Hz, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 162.1 (d, *J* = 246.1 Hz), 146.8, 142.7 (d, *J* = 3.3 Hz), 136.8, 130.7, 130.5, 128.7 (d, *J* = 8.0 Hz), 125.9, 124.8, 115.0 (d, *J* = 21.2 Hz), 76.4, 22.7, 21.8, 2.1, 1.9.

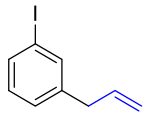
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –115.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3467, 1506, 1225, 1159, 836.

MS (EI, 70 eV, %) m/z = 308 (49), 306 (50), 295 (11), 293 (11), 199 (37), 197 (20), 184 (10), 183 (17), 136 (26), 123 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{16}BrFO$**: 334.0369; found: 334.0363.

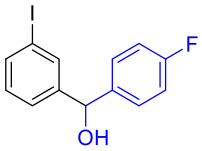
Synthesis of 1-allyl-3-iodobenzene (154oa)



Iodobenzene **154oa** was prepared *via* **TP2** using 1,3-diiodobenzene (165 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (0.50 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 60 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and allyl bromide (52 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.60) to give the product **154oa** (79 mg, 324 µmol, 65% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.84 – 7.50 (m, 2H), 7.27 – 7.15 (m, 1H), 7.11 – 6.87 (m, 1H), 5.92 (ddt, *J* = 15.8, 11.0, 6.7 Hz, 1H), 5.11 (t, *J* = 1.5 Hz, 1H), 5.08 (dq, *J* = 7.6, 1.6 Hz, 1H), 3.33 (dt, *J* = 6.7, 1.5 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 142.6, 137.7, 136.7, 135.3, 130.3, 128.0, 116.7, 94.7, 39.8.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2923, 1710, 1456, 1259, 1024.
MS (EI, 70 eV, %) m/z = 244 (33), 118 (10), 117 (100), 115 (82), 91 (14).
HRMS (EI, 70 eV) m/z: calc. for **C_9H_9I**: 243.9749; found 243.9744.

Synthesis of (4-fluorophenyl)(3-iodophenyl)methanol (154ob)



Secondary alcohol **154ob** was prepared *via* **TP2** using 1,3-diiodobenzene (165 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (0.50 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 60 min, 4-fluorobenzaldehyde (0.69 µL, 0.60 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.17) to give the product **154ob** (120 mg, 366 µmol, 73% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.74 (t, *J* = 1.8 Hz, 1H), 7.61 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.36 – 7.27 (m, 3H), 7.10 – 6.99 (m, 3H), 5.76 (d, *J* = 3.0 Hz, 1H), 2.23 (d, *J* = 3.4 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 162.4 (d, *J* = 246.4 Hz), 146.0, 139.1 (d, *J* = 3.2 Hz), 136.9, 135.4, 130.4, 128.4 (d, *J* = 8.2 Hz), 125.8, 115.7 (d, *J* = 21.6 Hz), 94.7, 75.0.

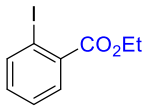
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –114.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3341, 1506, 1221, 905, 727.

MS (EI, 70 eV, %) m/z = 328 (15), 231 (92), 204 (19), 203 (11), 201 (11), 183 (22), 125 (14), 123 (100), 97 (19), 78 (11), 77 (15), 76 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{10}FIO$**: 327.9760; found: 327.9755.

Synthesis of ethyl 2-iodobenzoate (154pa)



Ester **154pa** was prepared *via* **TP2** using 1,2-diiodobenzene (165 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (0.50 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 60 min, ethyl cyanoformate (59 µL, 0.60 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.31) to give the product **154pa** (62 mg, 225 µmol, 45% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.97 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.78 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.39 (td, *J* = 7.6, 1.2 Hz, 1H), 7.13 (td, *J* = 7.7, 1.7 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H).

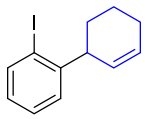
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.7, 141.3, 135.5, 132.6, 130.9, 128.0, 94.1, 61.8, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2979, 1725, 1288, 1250, 741.

MS (EI, 70 eV, %) m/z = 276 (24), 248 (33), 231 (100), 203 (30), 127 (11), 76 (37), 50 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_9H_9O_2I$**: 275.9647; found 275.9645.

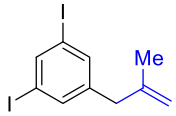
Synthesis of 2'-iodo-1,2,3,4-tetrahydro-1,1'-biphenyl (154pb)



Iodobenzene **154pb** was prepared *via* **TP2** using 1,2-diiodobenzene (165 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (0.50 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 60 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromocyclohexene (69 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.79) to give the product **154pb** (91 mg, 320 µmol, 64% yield) as a red oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.83 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.36 – 7.13 (m, 2H), 6.89 (td, *J* = 7.5, 1.9 Hz, 1H), 5.96 (dtd, *J* = 9.9, 3.7, 2.3 Hz, 1H), 5.65 (dq, *J* = 10.2, 2.5 Hz, 1H), 3.69 (ddp, *J* = 8.3, 5.5, 2.8 Hz, 1H), 2.08 (tqd, *J* = 8.7, 6.1, 3.4 Hz, 3H), 1.79 – 1.60 (m, 2H), 1.41 (dddd, *J* = 13.1, 9.9, 7.8, 3.4 Hz, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 148.3, 139.6, 129.7, 129.2, 128.7, 128.4, 128.0, 101.3, 45.9, 30.6, 25.2, 20.9.
IR (ATR, cm^{-1}) ṽ = 2928, 1460, 1432, 1009, 750.
MS (EI, 70 eV, %) m/z = 284 (100), 230 (27), 142 (20), 141 (23), 129 (92), 128 (70), 116 (23), 115 (37).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{13}I$**: 284.0062; found 284.0057.

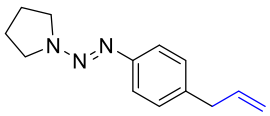
Synthesis of 1,3-diiodo-5-(2-methylallyl)benzene (154q)



Diiodobenzene **154q** was prepared *via* **TP2** using 1,3,5-triiodobenzene (**152q**, 228 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (0.50 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 60 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and methallyl bromide (60 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.75) to give the product **154q** (126 mg, 328 µmol, 66% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.07 – 7.81 (m, 1H), 7.50 (d, *J* = 1.5 Hz, 2H), 4.86 (t, *J* = 1.7 Hz, 1H), 4.74 (dd, *J* = 2.1, 1.1 Hz, 1H), 3.19 (s, 2H), 1.66 (t, *J* = 1.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 144.1, 143.6, 143.0, 137.3, 113.4, 94.9, 43.8, 22.1.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2907, 1572, 1539, 1416, 895, 707.
MS (EI, 70 eV, %) m/z = 384 (12), 257 (18), 226 (19), 196 (14), 194 (18), 165 (12), 130 (26), 129 (15), 115 (21), 57 (26), 55 (10), 45 (100), 44 (40), 43 (17), 41 (15).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{10}I_2$**: 383.8872; found 383.8875.

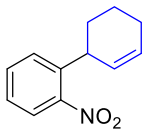
Synthesis of 1-((4-allylphenyl)diazenyl)pyrrolidine (154r)



Triazene **154r** was prepared *via* **TP2** using 1-((4-iodophenyl)diazenyl)pyrrolidine (**152r**, 90 mg, 0.30 mmol), DMPU (36 µL, 0.30 mmol) and dry toluene (0.60 mL). Then, Mes_2Mg (**151b**, 0.28 mL, 0.18 mmol) was added at −20 °C. After stirring at −20 °C for 1 h, CuCN·2LiCl (1.00 M in THF, 30 µL, 30 µmol) and allyl bromide (31 µL, 0.36 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 97:3, R_f = 0.25) to give the product **154r** (51 mg, 237 µmol, 79% yield) as a yellowish solid.

M.p. (°C): 50-52.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.56 – 7.31 (m, 2H), 7.20 – 6.98 (m, 2H), 5.98 (ddt, *J* = 16.8, 10.1, 6.6 Hz, 1H), 5.21 – 4.89 (m, 2H), 3.78 (s, 4H), 3.37 (dd, *J* = 6.7, 1.6 Hz, 2H), 2.39 – 1.49 (m, 4H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 149.9, 137.9, 137.0, 129.2, 120.5, 115.6, 39.9, 24.0 (2C).
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2973, 2870, 1430, 1404, 1319.
MS (EI, 70 eV, %) m/z = 207 (20), 145 (74), 117 (16), 115 (100), 91 (33).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{17}N_3$**: 215.1422; found 215.1417.

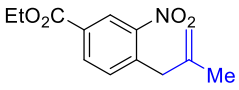
Synthesis of 2'-nitro-1,2,3,4-tetrahydro-1,1'-biphenyl (154s)



Nitrobenzene **154s** was prepared *via* **TP2** using 1-iodo-2-nitrobenzene (125 mg, 0.50 mmol), DMPU (0.25 mL, 2.00 mmol) and dry toluene (0.50 mL). Then, Mes_2Mg (**151b**, 0.46 mL, 0.30 mmol) was added at −50 °C. After stirring at −50 °C for 1 h, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromocyclohexene (46 µL, 0.40 mmol) were added and the reaction solution was allowed to warm to −20 °C and stirred at this temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 97:3, R_f = 0.25) to give the product **154s** (58 mg, 284 µmol, 71% yield) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.78 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.53 (td, *J* = 7.6, 1.4 Hz, 1H), 7.45 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.33 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H), 6.04 – 5.92 (m, 1H), 5.65 – 5.53 (m, 1H), 3.95 (ddt, *J* = 8.4, 5.6, 2.8 Hz, 1H), 2.26 – 2.16 (m, 1H), 2.11 (ddq, *J* = 6.9, 3.8, 2.0, 1.4 Hz, 2H), 1.81 – 1.60 (m, 2H), 1.58 – 1.47 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 149.9, 140.7, 132.6, 130.4, 129.8, 129.0, 127.0, 124.2, 36.9, 31.8, 25.0, 21.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2928, 1672, 1564, 1233, 758.
MS (EI, 70 eV, %) m/z = 186 (60), 169 (12), 168 (93), 167 (58), 158 (66), 156 (21), 153 (17), 152 (16), 147 (13), 146 (63), 143 (39), 141 (20), 132 (18), 130 (100), 129 (14), 128 (54), 117 (20), 115 (55), 105 (13), 91 (17), 77 (20).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{13}NO_2$**: 203.0946; found: 203.0894.

Synthesis of ethyl 4-(2-methylallyl)-3-nitrobenzoate (154t)

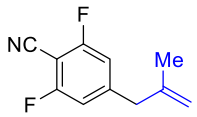


Nitrobenzene **154t** was prepared *via* **TP2** using ethyl 4-iodo-3-nitrobenzoate (**152t**, 160 mg, 0.50 mmol), DMPU (0.25 mL, 2.0 mmol) and dry toluene (1.0 mL). Then, Mes_2Mg (**151b**, 0.46 mL, 0.30 mmol) was added at −70 °C. After stirring at −70 °C for 1 h, CuI (13 mg, 10 mol%) and methallyl bromide (40 µL, 0.40 mmol) were added and the reaction solution was allowed to warm to −20 °C and stirred at this temperature overnight. After work-up, the crude product was purified *via* column

chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.46) to give the product **154t** (60 mg, 240 µmol, 60% yield) as a red oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.54 (d, *J* = 1.8 Hz, 1H), 8.18 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 4.89 – 4.85 (s, 1H), 4.54 – 4.49 (s, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 3.69 (s, 2H),1.75 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 164.6, 142.6, 139.2, 133.4, 132.7, 130.3, 125.9, 113.4, 100.1, 61.9, 40.7, 23.0, 14.4.
IR (ATR, cm^{-1}) ṽ = 2980, 1720, 1532, 1261, 727.
MS (EI, 70 eV, %) m/z = 219 (54), 204 (31), 203 (60), 191 (35), 188 (16), 176 (16), 175 (29), 174 (53), 172 (17), 163 (21), 162 (17), 158 (100), 146 (23), 144 (28), 130 (52), 128 (16), 118 (40), 117 (18), 115 (18).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{15}NO_4$**: 249.1001; found: 249.0998.

Synthesis of 2,6-difluoro-4-(2-methylallyl)benzonitrile (157a)

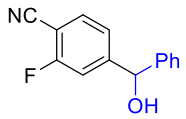


Benzonitrile **157a** was prepared *via* **TP2** using 4-bromo-2,6-difluorobenzonitrile (108 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 2 h, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and methallyl bromide (60 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.54) to give the product **157a** (95 mg, 492 µmol, 98% yield) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.91 (s, 1H), 6.89 (s, 1H), 4.96 – 4.92 (s, 1H), 4.80 – 4.76 (s, 1H), 3.36 (s, 2H), 1.67 (s, 3H).
^{13}C-NMR (101 MHz, CDCl3, ppm) δ = 164.5 (d, *J* = 4.9 Hz), 161.9 (d, *J* = 4.9 Hz), 150.2 (t, *J* = 9.2 Hz), 142.1, 114.7, 112.7 (d, *J* = 3.4 Hz), 112.5 (d, *J* = 3.3 Hz), 109.5, 90.2 (t, *J* = 19.4 Hz), 44.8 (t, *J* = 1.8 Hz), 22.1.
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –104.5.
IR (ATR, cm^{-1}) ṽ = 2924, 1632, 1442, 1044, 904.
MS (EI, 70 eV, %) m/z = 194 (13), 193 (85), 192 (17), 179 (12), 178 (100), 176 (13), 165 (13), 153 (14), 152 (41), 125 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_9F_2N$**: 193.0703; found: 193.0690.

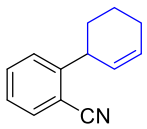
Synthesis of 2-fluoro-4-(hydroxy(phenyl)methyl)benzonitrile (157b)



Benzonitrile **157b** was prepared *via* **TP2** using 4-bromo-2-fluorobenzonitrile (99 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (0.50 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 2 h, benzaldehyde (0.61 µL, 0.60 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 60:40, R_f = 0.46) to give the product **157b** (70 mg, 308 µmol, 62% yield) as pale yellow solid.

M.p. (°C): 54-56.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.56 (dd, *J* = 8.1, 6.5 Hz, 1H), 7.40 – 7.30 (m, 6H), 7.28 – 7.24 (m, 1H), 5.84 (d, *J* = 2.8 Hz, 1H), 2.44 (d, *J* = 3.0 Hz, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 163.40 (d, *J* = 259.3 Hz), 152.3 (d, *J* = 7.2 Hz), 142.4, 133.5, 129.2, 128.8, 126.9, 122.7 (d, *J* = 3.3 Hz), 114.4, 114.2 (d, *J* = 5.2 Hz), 100.1 (d, *J* = 15.7 Hz), 75.4 (d, *J* = 1.7 Hz).
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –105.9.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3438, 2237, 1620, 1427, 906, 726.
MS (EI, 70 eV, %) m/z = 227 (13), 226 (8), 208 (18), 207 (8), 190 (8), 148 (77), 122 (42), 121 (18), 107 (12), 106 (8), 105 (100), 100 (12), 79 (66), 78 (17), 77 (46).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{10}FNO$**: 227.0746; found: 227.0741.

Synthesis of 1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-carbonitrile (157c)

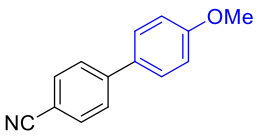


Benzonitrile **157c** was prepared *via* **TP2** using 2-bromobenzonitrile (91 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (0.50 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 2 h, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromocyclohexene (47 µL, 0.40 mmol) were added and the reaction solution was allowed to warm to

room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.36) to give the product **157c** (58 mg, 317 µmol, 79% yield) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.61 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.52 (td, *J* = 7.7, 1.5 Hz, 1H), 7.36 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.28 (td, *J* = 7.6, 1.2 Hz, 1H), 6.04 – 5.94 (m, 1H), 5.63 (dd, *J* = 10.1, 2.5 Hz, 1H), 3.86 (ddt, *J* = 8.3, 5.6, 2.8 Hz, 1H), 2.19 – 2.05 (m, 3H), 1.75 – 1.61 (m, 2H), 1.57 – 1.47 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 150.4, 133.0, 132.9, 130.1, 128.4, 128.1, 126.7, 118.2, 112.1, 40.2, 31.7, 24.9, 21.0.
IR (ATR, cm^{-1}) ṽ = 2931, 1633, 1570, 1445, 1046.
MS (EI, 70 eV, %) m/z = 183 (40), 182 (100), 168 (22), 167 (26), 166 (19), 165 (43), 154 (27), 140 (13), 128 (12), 115 (19).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{13}N$**: 183.1048; found 183.1040.

Synthesis of 4'-methoxy-[1,1'-biphenyl]-4-carbonitrile (157d)

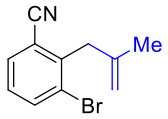


Diaryl **157d** was prepared *via* **TP2** using 4-bromobenzonitrile (91 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 2 h, $ZnCl_2$ (1.00 M in THF, 0.65 mL, 0.65 mmol), $Pd(OAc)_2$ (5 mg, 4 mol%), SPhos (17 mg, 8 mol%) and 4-iodoanisole (94 mg, 0.40 mmol) were added and the reaction mixture was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 96:4, R_f = 0.25) to give the product **157d** (47 mg, 220 µmol, 55% yield) as a white solid.

M.p. (°C): 107-109.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.79 – 7.59 (m, 4H), 7.57 – 7.43 (m, 2H), 7.09 – 6.84 (m, 2H), 3.87 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.3, 145.4, 132.7, 131.6, 128.5, 127.2, 119.2, 114.7, 110.2, 55.5.
IR (ATR, cm^{-1}) ṽ = 2224, 1605, 1494, 1036, 822, 753.
MS (EI, 70 eV, %) m/z = 210 (15), 209 (100), 194 (59), 166 (62), 140 (31), 139 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}ON$**: 209.0841; found 209.0835.

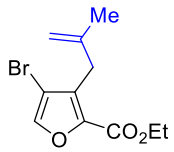
Synthesis of 3-bromo-2-(2-methylallyl)benzonitrile (157e)



Benzonitrile **157e** was prepared *via* **TP2** using 2,3-dibromobenzonitrile (**155e**, 131 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 2 h, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and methallyl bromide (60 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to −20 °C and was stirred at this temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.52) to give the product **157e** (100 mg, 425 µmol, 85% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.80 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.62 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 4.87 (s, 1H), 4.34 (s, 1H), 3.70 (s, 2H), 1.86 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 143.1, 141.4, 137.6, 132.2, 128.3, 126.4, 117.5, 115.4, 112.5, 42.5, 23.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2225, 1439, 1116, 891, 784, 723.
MS (EI, 70 eV, %) m/z = 237 (31), 236 (28), 235 (31), 234 (29), 156 (100), 155 (17), 154 (18), 129 (88), 128 (46), 116 (25), 115 (19).
HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{10}BrN$**: 234.9997; found: 234.9992.

Synthesis of ethyl 4-bromo-3-(2-methylallyl)furan-2-carboxylate (157f)

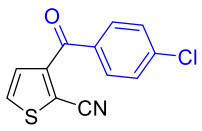


Furan **157f** was prepared *via* **TP2** using ethyl 3,4-dibromofuran-2-carboxylate (**155f**, 148 mg, 0.50 mmol), DMPU (60 µL, 0.50 mmol) and dry toluene (0.50 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 90 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and methallyl bromide (40 µL, 0.40 mmol) were added and the reaction solution was allowed to warm to −20 °C and was stirred at this temperature overnight. After work-up, the crude

product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.51) to give the product **157f** (55 mg, 202 µmol, 51% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.13 (s, 1H), 4.86 (s, 1H), 4.74 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.42 (s, 2H), 1.75 (t, *J* = 1.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 158.2, 155.3, 143.5, 140.1, 121.1, 113.4, 99.3, 61.3, 35.0, 22.4, 14.5.
IR (ATR, cm^{-1}) ṽ = 1720, 1303, 1181, 906, 729.
MS (EI, 70 eV, %) m/z = 275 (100), 272 (99), 259 (25), 257 (26), 246 (18), 244 (18), 229 (33), 227 (34), 205 (39), 203 (40), 201 (46), 199 (43), 173 (29), 171 (20), 150 (19), 120 (77), 119 (31), 92 (28), 91 (61).
HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{13}BrO_3$**: 272.0048; found: 272.0041.

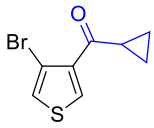
Synthesis of 3-(4-chlorobenzoyl)thiophene-2-carbonitrile (157g)



Thiophene **157g** was prepared *via* **TP2** using 3-bromothiophene-2-carbonitrile (94 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 45 min, CuCN·2LiCl (1.00 M in THF, 0.30 mL, 0.30 mmol) and 4-chlorobenzoyl chloride (77 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 60:40, R_f = 0.49) to give the product **157g** (113 mg, 456 µmol, 91% yield) as a light yellow solid.

M.p. (°C): 71-73.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.83 – 7.77 (m, 2H), 7.67 (d, *J* = 5.1 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.39 (d, *J* = 5.1 Hz, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 187.5, 147.9, 141.0, 135.3, 132.4, 131.6, 129.8, 129.6, 114.0, 113.0.
IR (ATR, cm^{-1}) ṽ = 2220, 1656, 1264, 1089, 863, 725.
MS (EI, 70 eV, %) m/z = 247 (9), 219 (7), 213 (12), 212 (100), 184 (6), 141 (23), 139 (77), 136 (33), 110 (11), 75 (9).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_6ClNOS$**: 246.9859; found: 246.9853.

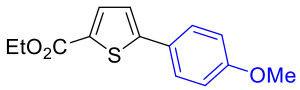
Synthesis of (4-bromothiophen-3-yl)(cyclopropyl)methanone (157h)



Ketone **157h** was prepared *via* **TP2** using 3,4-dibromothiophene (121 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −20 °C. After stirring at −20 °C for 45 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and cyclopropanecarbonyl chloride (92 µL, 1.00 mmol) were added and the reaction solution was stirred at this temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 60:40, R_f = 0.74) to give the product **157h** (72 mg, 313 µmol, 63% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.04 (d, *J* = 3.5 Hz, 1H), 7.33 (d, *J* = 3.5 Hz, 1H), 2.62 – 2.53 (m, 1H), 1.25 (dt, *J* = 6.9, 3.4 Hz, 2H), 1.07 – 1.01 (m, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 195.1, 140.3, 132.6, 125.6, 109.7, 19.8, 12.2.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3105, 1664, 1416, 1052, 931, 727.
MS (EI, 70 eV, %) m/z = 232 (4), 230 (4), 193 (4), 192 (5), 191 (100), 190 (5), 189 (98), 150 (6), 82 (13).
HRMS (EI, 70 eV) m/z: calc. for **C_8H_7BrOS**: 229.9401; found: 229.9396.

Synthesis of ethyl 5-(4-methoxyphenyl)thiophene-2-carboxylate (157i)

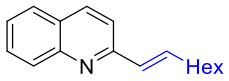


Thiophene **157i** was prepared *via* **TP2** using ethyl 5-bromothiophene-2-carboxylate (118 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at −40 °C. After stirring at −40 °C for 45 min, $ZnCl_2$ (1.00 M in THF, 0.65 mL, 0.65 mmol), $Pd(OAc)_2$ (5 mg, 4 mol%), SPhos (17 mg, 8 mol%) and 4-iodoanisole (93 mg, 0.40 mmol) were added and the reaction mixture was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.32) to give the product **157i** (75 mg, 282 µmol, 72% yield) as a white solid.

M.p. (°C): 71-73.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.73 (d, *J* = 3.9 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.18 (d, *J* = 3.9 Hz, 1H), 6.97 – 6.90 (m, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 162.5, 160.3, 151.3, 134.4, 131.6, 127.6, 126.4, 122.7, 114.6, 61.2, 55.5, 14.5.
IR (ATR, cm^{-1}) ṽ = 2930, 1697, 1446, 1252, 1091, 749.
MS (EI, 70 eV, %) m/z = 263 (15), 262 (100), 235 (12), 234 (94), 220 (10), 219 (84), 217 (50), 191 (42), 190 (36), 189 (13), 175 (16), 163 (11), 145 (57), 102 (14).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{14}O_3S$**: 262.0664; found: 262.0659.

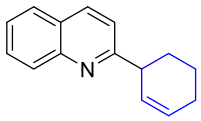
Synthesis of (*E*)-2-(Oct-1-en-1-yl)quinoline (157ja)



Quinoline **157ja** was prepared *via* **TP2** using 2-bromoquinoline (105 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 60 min, $ZnCl_2$ (1.00 M in THF, 0.65 mL, 0.65 mmol), $Pd(OAc)_2$ (5 mg, 4 mol%), SPhos (17 mg, 8 mol%) and trans-1-Iodo-1-octene (95 mg, 0.40 mmol) were added and the reaction mixture was stirred at room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 90:10, R_f = 0.51) to give the product **157ja** (75 mg, 313 µmol, 78% yield) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.07 (d, *J* = 8.6 Hz, 1H), 8.02 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.67 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H), 7.53 (d, *J* = 8.6 Hz, 1H), 7.51 – 7.40 (m, 1H), 6.83 (dt, *J* = 16.0, 6.7 Hz, 1H), 6.71 (d, *J* = 15.9 Hz, 1H), 2.39 – 2.28 (m, 2H), 1.60 – 1.51 (m, 2H), 1.41 – 1.29 (m, 6H), 0.90 (t, *J* = 6.7 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 156.7, 148.2, 138.2, 136.3, 131.1, 129.6, 129.2, 127.6, 127.3, 125.9, 118.8, 33.2, 31.9, 29.1, 29.0, 22.8, 14.3.
IR (ATR, cm^{-1}) ṽ = 2923, 1596, 1502, 966, 749.
MS (EI, 70 eV, %) m/z = 238 (15), 210 (43), 196 (20), 183 (12), 182 (84), 180 (18), 168 (77), 167 (100), 166 (12), 156 (26), 143 (20).
HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{21}N$**: 239.1674; found: 239.1670.

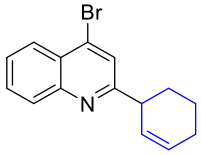
Synthesis of 2-(cyclohex-2-en-1-yl)quinoline (157jb)



Quinoline **157jb** was prepared *via* **TP2** using 2-bromoquinoline (105 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 60 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromocyclohexene (47 µL, 0.40 mmol) were added at 0 °C and the reaction solution was cooled down to −20 °C and was stirred at this temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 80:20, R_f = 0.62) to give the product **157jb** (59 mg, 280 µmol, 70% yield) as a brown oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.09 (d, *J* = 8.7 Hz, 1H), 8.06 (d, *J* = 8.3 Hz, 1H), 7.78 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.68 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H), 7.49 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 6.03 – 5.94 (m, 1H), 5.92 – 5.84 (m, 1H), 3.84 – 3.75 (m, 1H), 2.22 – 2.13 (m, 3H), 1.88 – 1.81 (m, 1H), 1.78 – 1.69 (m, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.0, 147.9, 136.6, 129.5, 129.3, 129.1, 128.7, 127.6, 127.1, 125.9, 120.3, 45.4, 30.9, 25.2, 21.6.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2931, 1661, 1595, 1502, 819, 754.
MS (EI, 70 eV, %) m/z = 210 (11), 209 (82), 208 (100), 206 (11), 194 (61), 193 (16), 192 (10), 180 (52), 167 (24), 143 (14), 128 (11).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{15}N$**: 209.1204; found: 209.1200.

Synthesis of 2-bromo-4-(cyclohex-2-en-1-yl)quinoline (157k)

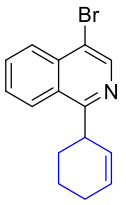


Bromoquinoline **157k** was prepared *via* **TP2** using 2,4-dibromoquinoline (143 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 60 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromocyclohexene (69 µL, 0.50 mmol) were added at 0 °C and the reaction solution was cooled down to −20 °C and was stirred at this temperature overnight. After work-up, the crude product was purified *via* column chromatography

(*iso*hexane:ethyl acetate = 80:20, R_f = 0.68) to give the product **157k** (97:3, 102 mg, 355 µmol, 71% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.14 (dd, *J* = 8.4, 1.4 Hz, 1H), 8.05 (d, *J* = 8.5 Hz, 1H), 7.73 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.65 (s, 1H), 7.58 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 6.05 – 5.98 (m, 1H), 5.89 – 5.83 (m, 1H), 3.82 – 3.72 (m, 1H), 2.22 – 2.13 (m, 3H), 1.88 – 1.80 (m, 1H), 1.80 – 1.69 (m, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.0, 148.6, 134.5, 130.4, 130.0, 129.5, 128.0, 127.2, 126.7, 126.6, 124.2, 45.0, 30.8, 25.1, 21.5.
IR (ATR, cm^{-1}) ṽ = 2930, 1663, 1575, 1491, 762.
MS (EI, 70 eV, %) m/z = 289 (44), 288 (55), 287 (45), 286 (79), 274 (40), 272 (41), 260 (97), 258 (100), 223 (41), 221 (42), 208 (43), 204 (35), 179 (30), 178 (32), 167 (31).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{14}BrN$**: 287.0310; found: 287.0307.

Synthesis of 4-bromo-1-(cyclohex-2-en-1-yl)isoquinoline (157l)

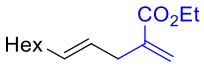


Isoquinoline **157l** was prepared *via* **TP2** using 1,4-dibromoisoquinoline (143 mg, 0.50 mmol) and dry toluene (1.0 mL). Then, *s*Bu_2Mg (**151a**, 0.63 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 60 min, CuCN·2LiCl (1.00 M in THF, 50 µL, 50 µmol) and 3-bromocyclohexene (69 µL, 0.50 mmol) were added at 0 °C and the reaction solution was cooled down to −20 °C and was stirred at this temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 80:20, R_f = 0.70) to give the product **157l** (114 mg, 397 µmol, 79% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.68 (s, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.77 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.65 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 6.05 – 5.99 (m, 1H), 5.93 – 5.87 (m, 1H), 4.44 – 4.37 (m, 1H), 2.27 – 2.10 (m, 3H), 1.94 – 1.74 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 164.4, 143.9, 135.2, 131.1, 128.8, 128.7, 128.0, 127.9, 127.0, 125.4, 118.1, 40.2, 30.4, 25.0, 22.1.
IR (ATR, cm^{-1}) ṽ = 2928, 1671, 1233, 903, 760, 722.

MS (EI, 70 eV, %) m/z = 288 (17), 286 (18), 261 (11), 260 (98), 258 (100), 223 (18), 221 (18), 179 (18), 166 (15).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{14}BrN$**: 287.0310; found: 287.0308.

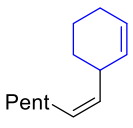
Synthesis of ethyl (*E*)-2-methyleneundec-4-enoate (160a)



Alkene **160a** was prepared *via* **TP2** using (*E*)-1-iodooct-1-ene (95 mg, 0.40 mmol), DMPU (48 µL, 0.40 mmol) and dry toluene (0.40 mL). Then, *s*Bu_2Mg (**151a**, 0.50 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 1 h, CuCN·2LiCl (1.00 M in THF, 40 µL, 40 µmol) and ethyl 2-(bromomethyl)acrylate (44 µL, 0.32 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.16) to give the product **160a** (59 mg, 263 µmol, 82% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.15 (q, *J* = 1.1 Hz, 1H), 5.53 (d, *J* = 1.6 Hz, 1H), 5.50 – 5.38 (m, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.12 – 2.72 (m, 2H), 2.01 (q, *J* = 6.7 Hz, 2H), 1.48 – 1.15 (m, 11H), 1.01 – 0.72 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 167.3, 140.3, 133.5, 126.4, 124.8, 60.8, 34.9, 32.7, 31.9, 29.5, 29.0, 22.8, 14.4, 14.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2926, 1720, 1465, 1190, 1025.
MS (EI, 70 eV, %) m/z = 149 (20), 139 (57), 121 (19), 111 (100), 107 (18), 95 (34), 94 (18), 93 (50), 91 (19), 81 (43), 79 (60), 77 (19), 67 (48).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{24}O_2$**: 224.1776; found 224.1767.

Synthesis of (*Z*)-3-(hept-1-en-1-yl)cyclohex-1-ene (160b)

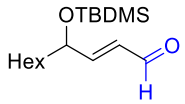


Alkene **160b** was prepared *via* **TP2** using (*Z*)-1-iodohept-1-ene (**158b**, 90 mg, 0.40 mmol), DMPU (48 µL, 0.40 mmol) and dry toluene (0.40 mL). Then, *s*Bu_2Mg (**151a**, 0.50 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 1 h, CuCN·2LiCl (1.00 M in THF, 40 µL, 40 µmol) and 3-bromocyclohexene (37 µL, 0.32 mmol) were added and the reaction solution was allowed to warm to

room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.72) to give the product **160b** (38 mg, 213 µmol, 66% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 5.70 (dtd, *J* = 9.9, 3.7, 2.3 Hz, 1H), 5.45 (dq, *J* = 10.0, 2.4 Hz, 1H), 5.39 – 5.30 (m, 1H), 5.23 (ddt, *J* = 10.9, 9.5, 1.6 Hz, 1H), 3.06 (ddq, *J* = 11.1, 5.4, 2.6 Hz, 1H), 2.06 (qd, *J* = 7.2, 1.5 Hz, 2H), 1.98 (dtt, *J* = 9.5, 5.0, 2.7 Hz, 2H), 1.74 (dtd, *J* = 9.7, 5.7, 5.1, 2.1 Hz, 2H), 1.56 (tdd, *J* = 12.5, 7.3, 3.6 Hz, 2H), 1.40 – 1.19 (m, 6H), 0.91 – 0.86 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 134.1, 130.9, 129.5, 127.3, 34.0, 31.7, 29.8, 29.7, 27.5, 25.0, 22.7, 21.3, 14.2.
IR (ATR, cm^{-1}) ṽ = 3017, 3010, 3003, 1684, 1456, 668.
MS (EI, 70 eV, %) m/z = 135 (21), 107 (20), 94 (26), 93 (21), 91 (20), 81 (25), 80 (23), 79 (100), 77 (13).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{22}$**: 178.1722; found 178.1714.

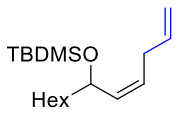
Synthesis of (*E*)-4-((tert-butyldimethylsilyl)oxy)dec-2-enal (160ca)



Michael acceptor **160ca** was prepared *via* **TP2** using (*Z*)-tert-butyl((1-iodonon-1-en-3-yl)oxy)dimethylsilane (**158c**, 147 mg, 0.40 mmol), DMPU (48 µL, 0.40 mmol) and dry toluene (0.40 mL). Then, *s*Bu_2Mg (**151a**, 0.50 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 1 h, DMF (25 µL, 0.32 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.35) to give the product **160ca** (48 mg, 169 µmol, 53% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 9.57 (d, *J* = 8.0 Hz, 1H), 6.80 (dd, *J* = 15.5, 4.6 Hz, 1H), 6.26 (ddd, *J* = 15.5, 8.0, 1.6 Hz, 1H), 4.40 (tdd, *J* = 6.1, 4.5, 1.6 Hz, 1H), 1.71 – 1.46 (m, 2H), 1.40 – 1.17 (m, 8H), 0.91 (s, 9H), 0.89 – 0.86 (m, 3H), 0.06 (s, 3H), 0.03 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 193.9, 160.5, 130.8, 71.8, 37.3, 31.9, 29.4, 25.9, 24.9, 22.7, 18.3, 14.2, –4.5, –4.8.
IR (ATR, cm^{-1}) ṽ = 2929, 2857, 1699, 1095, 836.
MS (EI, 70 eV, %) m/z = 227 (54), 199 (26), 143 (37), 131 (13), 129 (100), 75 (100), 73 (35).
HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{32}O_2Si$**: 284.2172; found 284.2534.

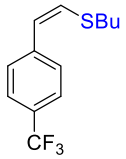
Synthesis of (*Z*)-tert-butyl(dodeca-1,4-dien-6-yloxy)dimethylsilane (160cb)



Alkene **160cb** was prepared *via* **TP2** using (*Z*)-tert-butyl((1-iodonon-1-en-3-yl)oxy)dimethylsilane (**158c**, 147 mg, 0.40 mmol), DMPU (48 µL, 0.40 mmol) and dry toluene (0.40 mL). Then, *s*Bu_2Mg (**151a**, 0.50 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 1 h, CuCN·2LiCl (1.00 M in THF, 40 µL, 40 µmol) and allyl bromide (28 µL, 0.32 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.48) to give the product **160cb** (69 mg, 233 µmol, 73% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 5.80 (ddt, *J* = 16.6, 10.1, 6.2 Hz, 1H), 5.42 (ddt, *J* = 11.3, 8.4, 1.5 Hz, 1H), 5.34 (dtd, *J* = 11.0, 7.3, 1.0 Hz, 1H), 5.05 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.00 (dq, *J* = 10.1, 1.6 Hz, 1H), 4.47 – 4.33 (m, 1H), 2.86 – 2.75 (m, 2H), 1.52 (ddd, *J* = 12.8, 6.0, 3.3 Hz, 1H), 1.40 – 1.32 (m, 2H), 1.28 (dq, *J* = 13.9, 5.3, 4.5 Hz, 7H), 0.91 – 0.86 (m, 12H), 0.04 (s, 3H), 0.03 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 136.7, 135.5, 125.8, 115.2, 68.8, 38.6, 32.3, 32.1, 29.4, 26.0, 25.5, 22.8, 18.4, 14.3, –4.1, –4.6.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2927, 1251, 1071, 833, 773.
MS (EI, 70 eV, %) m/z = 240 (3), 239 (23), 221 (3), 211 (25), 75 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{33}OSi$**: 281.2301; found 281.2291.

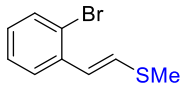
Synthesis of (*Z*)-butyl(4-(trifluoromethyl)styryl)sulfane (160d)



Alkene **160d** was prepared *via* **TP2** using (*Z*)-1-(2-iodovinyl)-4-(trifluoromethyl)benzene (119 mg, 0.40 mmol), DMPU (48 µL, 0.40 mmol) and dry toluene (0.40 mL). Then, *s*Bu_2Mg (**151a**, 0.50 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 1 h, *S*-butyl benzenesulfonothioate (74 mg, 0.32 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.41) to give the product **160d** (68 mg, 261 µmol, 82% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.68 – 7.50 (m, 4H), 6.43 (dd, *J* = 11.0, 2.6 Hz, 2H), 2.82 (t, *J* = 7.4 Hz, 2H), 1.82 – 1.61 (m, 2H), 1.46 (dq, *J* = 14.6, 7.4 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 140.6 (q, *J* = 1.3 Hz), 131.1, 128.7, 128.2 (q, *J* = 32.4 Hz), 125.3 (q, *J* = 3.9 Hz), 124.4 (q, *J* = 271.8 Hz), 123.8, 35.9, 32.4, 21.8, 13.8.
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –62.5.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2959, 1319, 1112, 1066, 838.
MS (EI, 70 eV, %) m/z = 260 (74), 204 (47), 183 (36), 135 (100), 134 (18).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{15}F_3S$**: 260.0847; found 260.0841.

Synthesis of (*E*)-(2-bromostyryl)(methyl)sulfane (160e)



Alkene **160e** was prepared *via* **TP2** using (*E*)-1-bromo-2-(2-iodovinyl)benzene (124 mg, 0.40 mmol), DMPU (48 µL, 0.40 mmol) and dry toluene (0.40 mL). Then, *s*Bu_2Mg (**151a**, 0.50 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 1 h, *S*-methyl methanethiosulfonate (33 µL, 0.32 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.45) to give the product **160e** (51 mg, 223 µmol, 70% yield) as a pale-yellow oil.

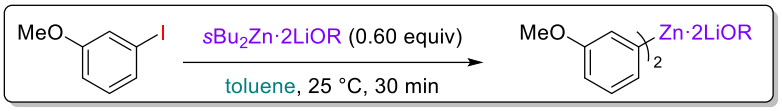
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.53 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.43 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.23 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.04 (td, *J* = 7.7, 1.7 Hz, 1H), 6.80 (d, *J* = 15.3 Hz, 1H), 6.61 (d, *J* = 15.4 Hz, 1H), 2.43 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 136.9, 133.1, 129.2, 128.0, 127.7, 126.2, 123.0, 122.7, 14.8.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2916, 1588, 1432, 1020, 927, 740.
MS (EI, 70 eV, %) m/z = 149 (92), 134 (100).
HRMS (EI, 70 eV) m/z: calc. for **C_9H_9BrS**: 227.9608; found 227.9601.

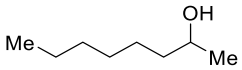
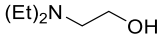
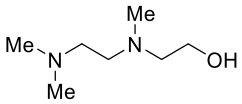
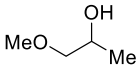
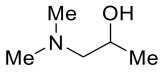
4 Preparation of Polyfunctional Arylzinc Organometallics in Toluene via Halogen/Zinc Exchange Reactions

4.1 Screening Tables

Variation of the alkoxide residue

Table 17: I/Zn exchange on 3-iodoanisole with *s*Bu_2Zn·2LiOR in function of the nature of R.

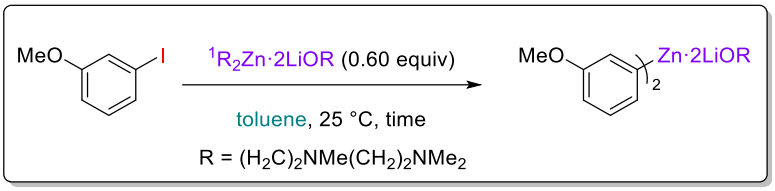


Entry	ROH	Exchange reagent	GC Conv. [%][a]
1		**161a**	23
2		**161b**	95
3		**161c**	99
4			97
5			91

[a] Yield determined by GC-analysis of water quenched reaction aliquots.

Reaction time screening

Table 18: Reaction time of the I/Zn exchange on 3-iodoanisole with *s*Bu_2Zn·2LiOR.

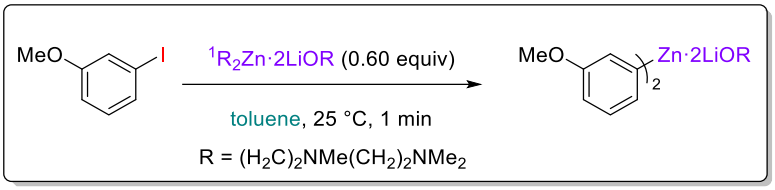


Entry	time (min)	GC Conv. [%][a]
1	0.5	93
2	1	99
3	60	99

[a] Yield determined by GC-analysis of water quenched reaction aliquots.

Variation of the alkyl residue

Table 19: I/Zn exchange on 3-iodoanisole with $^{1}R_2Zn{\cdot}2LiOR$ in function of the nature of ^{1}R.

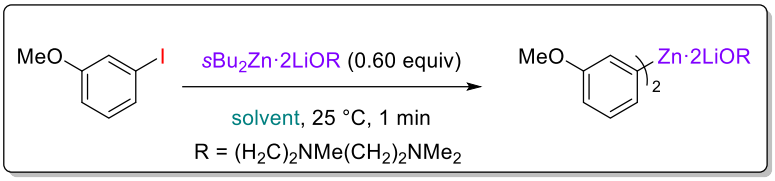


Entry	^{1}R	GC Conv. [%][a]
1	*n*Bu	80
2	*s*Bu	99
3	*t*Bu	89

[a] Yield determined by GC-analysis of water quenched reaction aliquots.

Solvent screening

Table 20: I/Zn exchange on 3-iodoanisole with $sBu_2Zn{\cdot}2LiOR$ in function of the solvent.

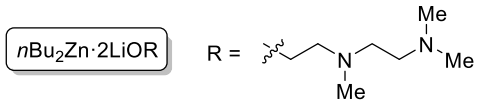


Entry	Solvent	GC Yield [%][a]	
		hydrolysis	iodolysis
1	Et_2O	99	91
2	THF	99	87
3	2-MeTHF	99	85
4	Dioxane	99	86
5	MTBE	99	89
6	Acetone	9	0
7	MeCN	99	36
8	DMF	99	31
9	Ethyl acetate	99	19
10	1,2-Dichloroethane	99	80
11	Chlorobenzene	99	60
12	Toluene	99	86
13	Hexane	99	90

[a] Yield determined by GC-analysis of water quenched reaction aliquots.

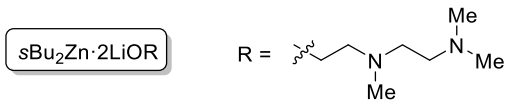
4.2 Preparation and Titration of Reagents of Type $^{1}R_2Zn \cdot 2LiOR$

Preparation of *n*$Bu_2Zn \cdot 2LiOR$:



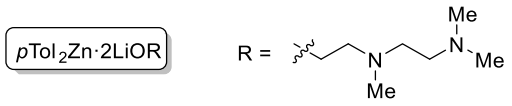
A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with Et_2Zn (1.11 M in toluene, 9.01 mL, 10.0 mmol) and the reaction mixture was cooled to –40 °C. Then, 2-((2-(dimethylamino)ethyl)(methyl)amino)ethane-1-ol (2.925 g, 20.0 mmol) was added dropwise and the reaction stirred for 2 h. Then, the reaction mixture was cooled to –40 °C and *n*BuLi (2.40 M in hexane, 8.33 mL, 20.0 mmol) added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature and stir for 2 h. The solvents were removed *in vacuo* affording a light yellow oil. Freshly distilled toluene was added under vigorous stirring until the residue was dissolved (6-8 mL). The prepared *n*$Bu_2Zn \cdot 2LiO(CH_2)_2N(Me)(CH_2)_2N(Me)_2$ was titrated prior to use at 0 °C by iodometric titration. The *n*$Bu_2Zn \cdot 2LiO(CH_2)_2N(Me)(CH_2)_2N(Me)_2$ concentration of the resulting clear solution was 0.80–1.20 M.

Preparation of *s*$Bu_2Zn \cdot 2LiOR$ (161c):



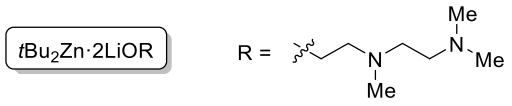
A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with Et_2Zn (1.11 M in toluene, 9.01 mL, 10.0 mmol) and the reaction mixture was cooled to –40 °C. Then, 2-((2-(dimethylamino)ethyl)(methyl)amino)ethane-1-ol (2.925 g, 20.0 mmol) was added dropwise and the reaction stirred for 2 h. Then, the reaction mixture was cooled to –0 °C and *s*BuLi (1.32 M in cyclohexane, 15.15 mL, 20.0 mmol) added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature and stir for 2 h. The solvents were removed *in vacuo* affording a light-yellow oil. Freshly distilled toluene was added under vigorous stirring until the residue was dissolved (6-8 mL). The prepared *s*$Bu_2Zn \cdot 2LiO(CH_2)_2N(Me)(CH_2)_2N(Me)_2$ was titrated prior to use at 0 °C by iodometric titration. The *s*$Bu_2Zn \cdot 2LiO(CH_2)_2N(Me)(CH_2)_2N(Me)_2$ concentration of the resulting clear solution was 0.80–1.20 M.

Preparation of *p*Tol$_2$Zn·2LiOR (*p*Tol = *p*-tolyl-, 167)



A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with Et_2Zn (1.11 M in toluene, 9.01 mL, 10.0 mmol) and the reaction mixture was cooled to –40 °C. Then, 2-((2-(dimethylamino)ethyl)(methyl)amino)ethane-1-ol (2.925 g, 20.0 mmol) was added dropwise and the reaction stirred for 2 h. Then, the reaction mixture was cooled to –40 °C and *p*TolLi (0.98 M in Et_2O, 20.4 mL, 20.0 mmol) added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature and stir for 2 h. The solvents were removed *in vacuo* affording a light-yellow oil. Freshly distilled toluene was added under vigorous stirring until the residue was dissolved (6-8 mL). The prepared *p*Tol$_2$Zn·2LiO(CH$_2$)$_2$N(Me)(CH$_2$)$_2$N(Me)$_2$ was titrated prior to use at 0 °C by iodometric titration. The *p*Tol$_2$Zn·2LiO(CH$_2$)$_2$N(Me)(CH$_2$)$_2$N(Me)$_2$ concentration of the resulting clear solution was 0.80–1.20 M.

Preparation of *t*Bu$_2$Zn·2LiOR (168):



A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with Et_2Zn (1.11 M in toluene, 9.01 mL, 10.0 mmol) and the reaction mixture was cooled to –40 °C. Then, 2-((2-(dimethylamino)ethyl)(methyl)amino)ethane-1-ol (2.925 g, 20.0 mmol) was added dropwise and the reaction stirred for 2 h. Then, the reaction mixture was cooled to –40 °C and *t*BuLi (1.93 M in pentane, 10.36 mL, 20.0 mmol) added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature and stir for 2 h. The solvents were removed *in vacuo* affording a light-yellow oil. Freshly distilled toluene was added under vigorous stirring until the residue was dissolved (6-8 mL). The prepared *t*Bu$_2$Zn·2LiO(CH$_2$)$_2$N(Me)(CH$_2$)$_2$N(Me)$_2$ was titrated prior to use at 0 °C by iodometric titration. The *t*Bu$_2$Zn·2LiO(CH$_2$)$_2$N(Me)(CH$_2$)$_2$N(Me)$_2$ concentration of the resulting clear solution was 0.60–1.00 M.

Titration Using Iodine[178]

A dry flask was charged with accurately weighed I_2 (128 mg, 0.504 mmol), fitted with a rubber septum, and flushed with argon. THF (2 mL) was added and stirring was started. After the iodine was completely dissolved, the resulting brown solution was cooled to 0 °C in an ice bath and the organozinc reagent was added dropwise via a 1.00-mL syringe (0.01-mL graduations) until the brown color disappeared. The obtained concentration needs to be divided by 2 to obtain the concentration of the dialkyl zinc species.

4.3 Typical Procedures

Typical Procedure 3: Preparation of Diarylzinc Alkoxides via an Iodine/Zinc Exchange Followed by Electrophilic Functionalization

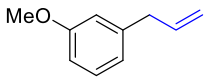
A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding aryl halide (1.00 equiv) and dissolved in dry toluene (0.50 M): Then, the exchange reagent $R_2Zn{\cdot}2LiO(CH_2)_2N(Me)(CH_2)_2N(Me)_2$ (**161c**, **167** or **168**) (0.60–0.80 equiv) was added dropwise and the reaction stirred for 10 minutes unless otherwise stated. The completion of the halogen-zinc exchange was checked by GC-analysis of reaction aliquots quenched with water, using undecane as internal standard. Subsequent reactions with electrophiles were carried out under the indicated conditions. After complete conversion, the mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. If the crude product needed purification, it was purified by flash chromatography on silica gel using the appropriate eluent.

Typical Procedure 4: Preparation of Diarylzinc Alkoxides via a Bromine/Zinc Exchange Followed by Electrophilic Functionalization

A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding aryl halide (1.00 equiv) and dissolved in dry toluene (1.00 M): Then, $s Bu_2Zn{\cdot}2LiO(CH_2)_2N(Me)(CH_2)_2N(Me)_2$ (**161c**, 0.80 equiv) was added dropwise and the reaction stirred for 5 hours. The completion of the halogen-zinc exchange was checked by GC-analysis of reaction aliquots quenched with water, using undecane as internal standard. Subsequent reactions with electrophiles were carried out under the indicated conditions. After complete conversion, the mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. If the crude product needed purification, it was purified by flash chromatography on silica gel using the appropriate eluent.

4.4 Preparation of Compounds 166 to 170

Synthesis of 1-allyl-3-methoxybenzene (166a)

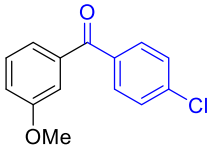


Anisole **166a** was prepared *via* **TP3** using 3-iodoanisole (59 mg, 0.25 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.20 mL, 0.15 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (10 mg, 0.05 mmol) was added. After stirring at 0 °C for 30 min, allyl bromide (0.03 mL, 0.38 mmol) was added and the reaction stirred for 2 h at the same temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 10:0.2) to give **166a** (29 mg, 196 µmol, 78%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.25 – 7.20 (m, 1H), 6.83 – 6.74 (m, 3H), 5.98 (m, 1H), 5.14 – 5.06 (m, 2H), 3.81 (s, 3H), 3.38 (dt, *J* = 6.6, 1.5 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.8, 141.8, 137.4, 129.5, 121.1, 116.1, 114.4, 111.5, 55.3, 40.4.

The spectra matched those of the literature.[199]

Synthesis of (4-chlorophenyl)(3-methoxyphenyl)methanone (166b)



Arene **166b** was prepared *via* **TP3** using 1-iodo-3-methoxybenzene (59 mg, 0.25 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.20 mL, 0.15 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (29 mg, 0.15 mmol) was added. After stirring at 0 °C for 30 min, 4-chlorobenzoyl chloride (131 mg, 0.75 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 100:2) to give **166b** (53 mg, 215 µmol, 86%) as a colorless oil.

[199] X. Cheng, M. Prehm, M. K. Das, J. Kain, U. Baumeister, S. Diele, D. Leine, A. Blume, C. Tschierske, *J. Am. Chem. Soc.* **2003**, *125*, 10977.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.79 – 7.73 (m, 2H), 7.50 – 7.43 (m, 2H), 7.39 (m, 1H), 7.31 (m, 2H), 7.14 (m, 1H), 3.86 (s, 3H).

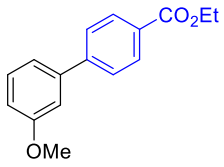
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 195.5, 159.8, 139.1, 138.6, 136.0, 131.6, 129.5, 128.8, 122.8, 119.2, 114.3, 55.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3016, 1658, 1595, 1584, 1569, 1485, 1464, 1449, 1426, 1399, 1301, 1287, 1273, 1215, 1175, 1138, 1090, 1049, 1040, 1015, 981, 968, 948, 845, 745, 703, 682, 667.

MS (EI, 70 eV, %) m/z = 246 (18), 211 (15), 141 (44), 139 (100), 135 (76), 92 (22), 77 (13), 75 (23), 63 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}ClO_2$**: 246.0448; found: 246.0443.

Synthesis of ethyl 3'-methoxy-[1,1'-biphenyl]-4-carboxylate (166c)



Biaryl **166c** was prepared *via* **TP3** using 1-iodo-3-methoxybenzene (59 mg, 0.25 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.20 mL, 0.15 mmol). After the exchange was complete, $Pd(OAc)_2$ (3 mg, 10 µmol), SPhos (8 mg, 20 µmol) and ethyl 4-iodobenzoate (55 mg, 0.20 mmol) were added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2) to give **166c** (39 mg, 152 µmol, 76%) as a light yellow oil.

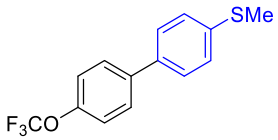
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.14 – 8.08 (m, 2H), 7.68 – 7.62 (m, 2H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.21 (ddd, *J* = 7.7, 1.7, 1.0 Hz, 1H), 7.15 (t, *J* = 2.1 Hz, 1H), 6.94 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.6, 160.1, 145.5, 141.7, 130.2, 130.1, 129.5, 127.2, 119.9, 113.6, 113.2, 61.1, 55.5, 14.5.

The spectra matched those of the literature.[200]

[200] M. Amatore, C. Gosmini, *Angew. Chem. Int. Ed.* **2008**, *47*, 2089.

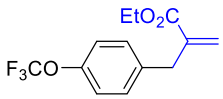
Synthesis of methyl(4'-(trifluoromethoxy)-[1,1'-biphenyl]-4-yl)sulfane (166d)



Biaryl **166d** was prepared *via* **TP3** using 1-iodo-4-(trifluoromethoxy)benzene (139 mg, 0.48 mmol) and *s*Bu$_2$Zn·2LiOR (**161c**, 0.30 mL, 0.29 mmol). After the exchange was complete, Pd(OAc)$_2$ (3 mg, 14 µmol), SPhos (12 mg, 29 µmol) and 4-iodothioanisole (100 mg, 0.40 mmol) were added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 10:0.04) to give **166d** (55 mg, 193 µmol, 48%) as a colorless solid.

M.p. (°C): 103-105.
^{1}H-NMR (400 MHz, CDCl$_3$, ppm) δ = 7.60 – 7.55 (m, 2H), 7.51 – 7.47 (m, 2H), 7.36 – 7.31 (m, 2H), 7.30 – 7.26 (m, 2H), 2.53 (s, 3H).
^{13}C-NMR (101 MHz, CDCl$_3$, ppm) δ = 148.7 (q, *J* = 2 Hz), 139.4, 138.4, 136.6, 128.2, 127.5, 127.0, 121.4, 120.6 (q, *J* = 257 Hz), 15.9.
IR (ATR, cm^{-1}) ṽ = 2623, 1594, 1523, 1484, 1205, 1155, 1100, 805.
MS (EI, 70 eV, %) m/z = 284 (100), 269 (42), 236 (10), 184 (9), 139 (14).
HRMS (EI, 70 eV) m/z: calc. for **C$_{14}$H$_{11}$F$_3$OS**: 284.0483; found: 284.0475.

Synthesis of 2',4'-dichloro-1,2,3,4-tetrahydro-1,1'-biphenyl (166e)



Arene **166e** was prepared *via* **TP3** using 1-iodo-4-(trifluoromethoxy)benzene (139 mg, 0.48 mmol) and *s*Bu$_2$Zn·2LiOR (**161c**, 0.30 mL, 0.29 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (19 mg, 0.1 mmol) was added. After stirring at 0 °C for 30 min, ethyl 2-(bromomethyl)acrylate (139 mg, 0.72 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 1000:1 to 9:1) to give **166e** (88 mg, 321 µmol, 67%) as a colorless oil. The product was detected by GC-analysis.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.25 – 7.19 (m, 2H), 7.16 – 7.11 (m, 2H), 6.25 (q, *J* = 0.9 Hz, 1H), 5.49 (q, *J* = 1.4 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.63 (d, *J* = 1.2 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

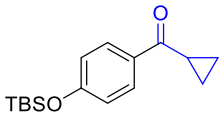
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.8, 147.9, 140.0, 137.7, 130.4, 126.5, 121.1, 61.0, 37.6, 14.3.

IR (ATR, cm^{-1}) ṽ = 2984, 2932, 1716, 1634, 1508, 1257, 1222, 1196, 1161, 1021, 950, 813.

MS (EI, 70 eV, %) m/z = 274 (25), 229 (12), 201 (24), 200 (100), 199 (17), 161 (11), 131 (15), 115 (47), 103 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{13}F_3O_3$**: 274.0817; found: 274.0811.

Synthesis of (4-((*tert*-butyldimethylsilyl)oxy)phenyl)(cyclopropyl)methanone (166f)



Arene **166f** was prepared *via* **TP3** using *tert*-butyl(4-iodophenoxy)dimethylsilane (154 mg, 0.46 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.29 mL, 0.28 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (53 mg, 0.28 mmol) was added. After stirring at 0 °C for 30 min, cyclopropanecarbonyl chloride (0.13 mL, 1.38 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 10:0.5) to give **166f** (77 mg, 279 µmol, 61%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.98 – 7.92 (m, 2H), 6.92 – 6.86 (m, 2H), 2.63 (tt, *J* = 7.8, 4.5 Hz, 1H), 1.20 (dt, *J* = 4.5, 3.4 Hz, 2H), 0.99 (s, 11H), 0.23 (s, 6H).

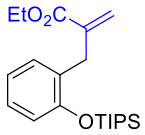
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 199.4, 160.2, 131.7, 130.3, 120.0, 25.7, 18.4, 16.8, 11.4, –4.2.

IR (ATR, cm^{-1}) ṽ = 3008, 2955, 2930, 2858, 1664, 1599, 1508, 1415, 1272, 1257, 1225, 1164, 994, 910, 840, 782.

MS (EI, 70 eV, %) m/z = 277 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{25}O_2Si$**: 277.1624; found: 277,1620.

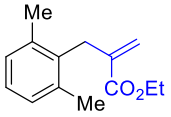
Synthesis of ethyl 2-(2-((triisopropylsilyl)oxy)benzyl)acrylate (166g)



Arene **166g** was prepared *via* **TP3** using (2-iodophenoxy)triisopropylsilane (376 mg, 1.00 mmol) and *s*Bu$_2$Zn·2LiOR (**161c**, 0.62 mL, 0.60 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (38 mg, 0.2 mmol) was added. After stirring at 0 °C for 30 min, ethyl 2-(bromomethyl)acrylate (289 mg, 1.50 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 10:0.5) to give **166g** (300 mg, 827 µmol, 83%) as a colorless oil.

^{1}H-NMR (400 MHz, CDCl$_3$, ppm) δ = 7.09 (dd, *J* = 8.2, 6.5 Hz, 2H), 6.87 (td, *J* = 7.4, 1.2 Hz, 1H), 6.80 (dt, *J* = 7.3, 1.1 Hz, 1H), 6.20 (q, *J* = 1.4 Hz, 1H), 5.22 (q, *J* = 1.7 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.64 (t, *J* = 1.6 Hz, 2H), 1.34 – 1.23 (m, 6H), 1.08 (d, *J* = 7.3 Hz, 18H).
^{13}C-NMR (101 MHz, CDCl$_3$, ppm) δ = 167.4, 154.2, 139.7, 131.0, 128.9, 127.6, 125.5, 120.8, 118.1, 60.7, 32.6, 18.2, 14.4, 13.2.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2945, 2867, 1718, 1491, 1453, 1265, 1132, 1108, 910, 755, 683.
MS (EI, 70 eV, %) m/z = 319 (100), 291 (33), 175 (23), 161 (24), 159 (17), 149 (18), 131 (35), 115 (18), 103 (46), 89 (14), 75 (55), 61 (11).
HRMS (EI, 70 eV) m/z: calc. for **C$_{18}$H$_{27}$O$_3$Si**: 319.1729; found: 319.1725.

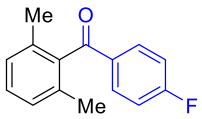
Synthesis of ethyl 2-(2,6-dimethylbenzyl)acrylate (166h)



Arene **166h** was prepared *via* **TP3** using 2-iodo-1,3-dimethylbenzene (116 mg, 0.50 mmol) and *s*Bu$_2$Zn·2LiOR (**161c**, 0.28 mL, 0.30 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (19 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, ethyl 2-(bromomethyl)acrylate (145 mg, 0.75 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1) to give **166h** (73 mg, 0.33 mmol, 67%) as a light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.05 (q, *J* = 5.5 Hz, 3H), 6.12 (q, *J* = 1.8 Hz, 1H), 4.91 (q, *J* = 2.0 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.63 (t, *J* = 2.1 Hz, 2H), 2.22 (s, 6H), 1.36 (t, *J* = 7.2 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 167.5, 138.2, 137.2, 135.2, 128.2, 126.6, 124.1, 61.0, 31.3, 19.9, 14.4.
IR (ATR, cm^{-1}) ṽ = 2978, 2962, 2934, 2872, 1712, 1632, 1469, 1445, 1402, 1389, 1378, 1367, 1339, 1299, 1274, 1249, 1171, 1128, 1095, 1026, 960, 941, 868, 817, 767.
MS (EI, 70 eV, %) m/z = 157 (12), 145 (27), 144 (68), 143 (33), 130 (32), 129 (100), 128 (53), 127 (11), 117 (13), 115 (35), 105 (41), 91 (16), 77 (10).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{18}O_2$**: 218.1307; found: 218.1300.

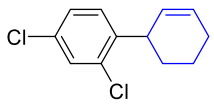
Synthesis of (2,6-dimethylphenyl)(4-fluorophenyl)methanone (166i)



Arene **166i** was prepared *via* **TP3** using 2-iodo-1,3-dimethylbenzene (162 mg, 0.70 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.51 mL, 0.42 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (80 mg, 0.42 mmol) was added. After stirring at 0 °C for 30 min, 4-fluorobenzoyl chloride (333 mg, 2.10 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1) to give **166i** (128 mg, 0.56 mmol, 80%) as a light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.86 (dd, *J* = 8.4, 5.5 Hz, 2H), 7.29 (d, *J* = 6.4 Hz, 1H), 7.19 – 7.09 (m, 4H), 2.15 (s, 6H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 199.0, 166.3 (d, *J* = 256.0 Hz), 139.4, 134.2, 133.6 (d, *J* = 2.9 Hz), 132.2 (d, *J* = 9.5 Hz), 129.0, 127.8, 116.2 (d, *J* = 22.0 Hz), 19.5.
IR (ATR, cm^{-1}) ṽ = 2955, 2924, 2870, 2855, 1734, 1717, 1700, 1670, 1635, 1592, 1558, 1550, 1539, 1520, 1502, 1461, 1423, 1408, 1380, 1319, 1303, 1293, 1268, 1237, 1225, 1157, 1143, 1093, 1034, 1012, 970, 926, 876, 848, 816, 769, 760, 731, 700, 687, 668, 664, 657.
MS (EI, 70 eV, %) m/z = 228 (29), 227 (100), 213 (62), 212 (35), 211 (17), 210 (42), 207 (10), 196 (14), 193 (12), 183 (19), 133 (26), 123 (45), 105 (20), 95 (13), 79 (10), 77 (13).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}FO$**: 228.0950; found: 228.0944.

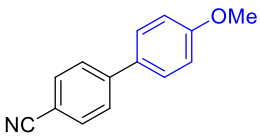
Synthesis of 2',4'-dichloro-1,2,3,4-tetrahydro-1,1'-biphenyl (166j)



Arene **166j** was prepared *via* **TP3** using 2,4-dichloro-1-iodobenzene (273 mg, 1.00 mmol) and *s*Bu$_2$Zn·2LiOR (**161c**, 0.85 mL, 0.60 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (38 mg, 0.20 mmol) was added. After stirring at 0 °C for 30 min, 3-bromocyclohexene (0.17 mL, 1.50 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 1000:1) to give **166j** (202 mg, 889 µmol, 89%) as a colorless oil.

^{1}H-NMR (400 MHz, CDCl$_3$, ppm) δ = 7.36 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.22 – 7.17 (m, 2H), 5.98 (m, 1H), 5.66 – 5.56 (m, 1H), 3.84 (m, 1H), 2.15 – 2.01 (m, 3H), 1.65 (m, 2H), 1.52 – 1.41 (m, 1H).
^{13}C-NMR (101 MHz, CDCl$_3$, ppm) δ = 142.1, 134.4, 132.3, 130.2, 129.8, 129.2, 128.8, 127.0, 37.7, 30.0, 25.1, 20.7.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3020, 2928, 2858, 2834, 2360, 1587, 1557, 1468, 1378, 1101, 1052, 881, 865, 819, 804, 728, 681, 670.
MS (EI, 70 eV, %) m/z = 226 (57), 211 (23), 192 (41), 165 (32), 163 (100), 155 (20), 128 (55), 127 (20).
HRMS (EI, 70 eV) m/z: calc. for **C$_{12}$H$_{12}$Cl$_2$**: 226.0316; found: 226.0311.

Synthesis of 4'-methoxy-[1,1'-biphenyl]-4-carbonitrile (166k)



Biaryl **166k** was prepared *via* **TP3** using 4-iodobenzonitrile (57 mg, 0.25 mmol) and *s*Bu$_2$Zn·2LiOR (**161c**, 0.22 mL, 0.15 mmol). After the exchange was complete, Pd(OAc)$_2$ (3 mg, 10 µmol), SPhos (8 mg, 20 µmol) and 1-iodo-4-methoxybenzene (47 mg, 0.20 mmol) were added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 9.5:0.5) to give **166k** (37 mg, 177 µmol, 89%) as a colorless solid.

M.p. (°C): 101-103.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.70 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.57 – 7.52 (m, 2H), 7.04 – 6.98 (m, 2H), 3.87 (s, 3H).

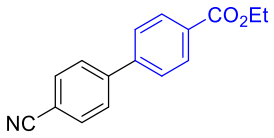
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.3, 145.4, 132.7, 131.6, 128.5, 127.3, 119.3, 114.7, 110.2, 55.6.

IR (ATR, cm^{-1}) ṽ = 2958, 2923, 2225, 1604, 1509, 1494, 1464, 1457, 1293, 1249, 1180, 1037, 822, 730, 668.

MS (EI, 70 eV, %) m/z = 209 (100), 194 (44), 166 (53), 140 (35), 139 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}NO$**: 209.0841; found: 209.0836.

Synthesis of ethyl 4'-cyano-[1,1'-biphenyl]-4-carboxylate (166l)



Biaryl **166l** was prepared *via* **TP3** using 4-iodobenzonitrile (57 mg, 0.25 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.22 mL, 0.15 mmol). After the exchange was complete, $Pd(OAc)_2$ (3 mg, 10 µmol), SPhos (8 mg, 20 µmol) and ethyl 4-iodobenzoate (55 mg, 0.20 mmol) were added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 9.5:0.5) to give **166l** (35 mg, 140 µmol, 70%) as a colorless solid.

M.p. (°C): 114-116.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.18 – 8.12 (m, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.68 – 7.63 (m, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

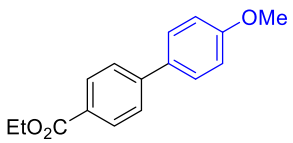
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.3, 144.6, 143.4, 132.9, 130.7, 130.5, 128.1, 127.3, 118.8, 111.9, 61.4, 14.5.

IR (ATR, cm^{-1}) ṽ = 2924, 2852, 2221, 1701, 1675, 1605, 1494, 1464, 1395, 1365, 1311, 1290, 1275, 1208, 1180, 1116, 1101, 1020, 1005, 984, 972, 961, 906, 870, 847, 835, 794, 771, 728, 698, 668.

MS (EI, 70 eV, %) m/z = 251 (16), 223 (50), 207 (14), 206 (100), 179 (17), 178 (26), 177 (36), 151 (34), 150 (23).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{13}NO_2$**: 251.0946; found: 251.0943.

Synthesis of ethyl 4'-methoxy-[1,1'-biphenyl]-4-carboxylate (166m)



Biaryl **166m** was prepared *via* **TP3** using ethyl 4-iodobenzoate (67 mg, 0.25 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.22 mL, 0.15 mmol). After the exchange was complete, $Pd(OAc)_2$ (3 mg, 10 µmol), SPhos (8 mg, 20 µmol) and 1-iodo-4-methoxybenzene (47 mg, 0.20 mmol) were added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 9.8:0.2) to give **166m** (30 mg, 117 µmol, 59%) as a light yellow solid.

M.p. (°C): 101-103.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.11 – 8.06 (m, 2H), 7.65 – 7.55 (m, 4H), 7.03 – 6.97 (m, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H).

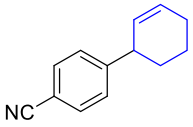
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.7, 159.9, 145.2, 132.6, 130.2, 128.7, 128.5, 126.6, 114.5, 61.1, 55.5, 14.5.

IR (ATR, cm^{-1}) ṽ = 2981, 2929, 1705, 1604, 1581, 1562, 1526, 1497, 1464, 1442, 1425, 1400, 1367, 1310, 1275, 1248, 1181, 1109, 1103, 1038, 1024, 1015, 1001, 905, 862, 853, 828, 773, 761, 726, 702, 668.

MS (EI, 70 eV, %) m/z = 256 (80), 228 (52), 213 (22), 212 (14), 211 (100), 185 (20), 183 (22), 168 (41), 157 (11), 152 (29), 140 (50), 139 (95).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{16}O_3$**: 256.1099; found: 256.1095.

Synthesis of 1',2',3',4'-tetrahydro-[1,1'-biphenyl]-4-carbonitrile (166n)



Arene **166n** was prepared *via* **TP3** using 4-iodobenzonitrile (57 mg, 0.25 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.20 mL, 0.15 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (10 mg, 0.15 mmol) was added. After stirring at 0 °C for 30 min, 3-bromocyclohexene (60 mg, 0.38 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 10:0.1) to give **166n** (45 mg, 246 µmol, 98%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.58 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 6.00 – 5.91 (m, 1H), 5.70 – 5.61 (m, 1H), 3.51 – 3.40 (m, 1H), 2.13 – 2.06 (m, 2H), 2.06 – 1.98 (m, 1H), 1.77 – 1.57 (m, 2H), 1.56 – 1.45 (m, 1H).

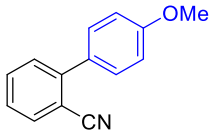
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 152.4, 132.3, 129.8, 128.7, 128.6, 119.3, 109.9, 42.1, 32.4, 25.0, 21.0.

IR (ATR, cm^{-1}) ṽ = 2924, 2884, 2854, 2226, 1606, 1502, 1445, 899, 882, 831, 795, 733, 720, 668.

MS (EI, 70 eV, %) m/z = 183 (22), 182 (41), 179 (59), 178 (19), 169 (11), 168 (100), 167 (10), 155 (52), 154 (74), 153 (21), 142 (18), 141 (12), 140 (43), 129 (25), 128 (26), 116 (17), 115 (47) 42 (37).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{13}N$**: 183.1048; found: 183.1042.

Synthesis of 4'-methoxy-[1,1'-biphenyl]-2-carbonitrile (166o)



Biaryl **166o** was prepared *via* **TP3** using 2-iodobenzonitrile (57 mg, 0.25 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.22 mL, 0.15 mmol). After the exchange was complete, $Pd(OAc)_2$ (3 mg, 10 µmol), SPhos (8 mg, 20 µmol) and 1-iodo-4-methoxybenzene (47 mg, 0.20 mmol) were added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 9.5:0.5) to give **166o** (32 mg, 153 µmol, 76%) as a light yellow solid.

M.p. (°C): 83-85.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.74 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.62 (td, *J* = 7.7, 1.4 Hz, 1H), 7.50 (td, *J* = 8.3, 7.6, 1.7 Hz, 3H), 7.40 (td, *J* = 7.6, 1.3 Hz, 1H), 7.06 – 6.98 (m, 2H), 3.87 (s, 3H).

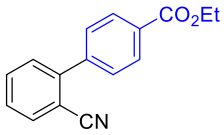
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.2, 145.3, 133.9, 132.9, 130.6, 130.1, 130.0, 127.2, 119.2, 114.3, 111.2, 55.5.

IR (ATR, cm^{-1}) ṽ = 2955, 2933, 2837, 2222, 1608, 1597, 1578, 1516, 1478, 1464, 1441, 1413, 1306, 1293, 1269, 1246, 1179, 1115, 1108, 1047, 1033, 1016, 1000, 957, 833, 810, 762, 750, 733, 729, 720, 680, 668.

MS (EI, 70 eV, %) m/z = 209 (100), 194 (28), 167 (11), 166 (84), 140 (47), 139 (25), 113 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}NO$**: 209.0841; found: 209.0835.

Synthesis of ethyl 2'-cyano-[1,1'-biphenyl]-4-carboxylate (166p)



Biaryl **166p** was prepared *via* **TP3** using 2-iodobenzonitrile (57 mg, 0.25 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.22 mL, 0.15 mmol). After the exchange was complete, $Pd(OAc)_2$ (3 mg, 10 µmol), SPhos (8 mg, 20 µmol) and ethyl 4-iodobenzoate (55 mg, 0.20 mmol) were added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 9.8:0.2) to give **166p** (44 mg, 175 µmol, 88%) as a light yellow solid.

M.p. (°C): 119-121.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.2 – 8.1 (m, 2H), 7.8 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.7 – 7.6 (m, 3H), 7.5 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.5 (td, *J* = 7.6, 1.3 Hz, 1H), 4.4 (q, *J* = 7.1 Hz, 2H), 1.4 (t, *J* = 7.1 Hz, 3H).

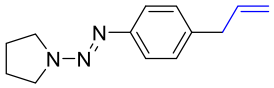
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.3, 144.5, 142.5, 134.0, 133.1, 130.8, 130.1, 130.1, 128.9, 128.4, 118.5, 111.4, 61.3, 14.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2960, 2920, 2909, 2224, 1709, 1608, 1594, 1479, 1464, 1443, 1406, 1392, 1367, 1315, 1271, 1185, 1126, 1120, 1111, 1098, 1030, 1006, 962, 891, 860, 778, 763, 741, 722, 705.

MS (EI, 70 eV, %) m/z = 223 (27), 207 (15), 206 (100), 179 (80), 178 (53), 177 (68), 169 (18), 151 (70), 150 (60), 75 (13).

HRMS (EI, 70 eV) m/z: calc. for $C_{16}H_{13}NO_2$: 251.0946; found: 251.0941.

Synthesis of 1-((4-allylphenyl)diazenyl)pyrrolidine (166q)



Arene **166q** was prepared *via* **TP3** using 1-((4-iodophenyl)diazenyl)pyrrolidine (301 mg, 1.00 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.58 mL, 0.60 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (38 mg, 0.20 mmol) was added. After stirring at 0 °C for 30 min, allyl bromide (0.13 mL, 1.50 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 10:0.2) to give **166q** (166 mg, 771 µmol, 77%) as a light yellow solid.

M.p. (°C): 50-52.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.38 – 7.33 (m, 2H), 7.18 – 7.13 (m, 2H), 5.99 (m, 1H), 5.13 – 5.02 (m, 2H), 3.79 (s, 4H), 3.38 (dt, *J* = 6.6, 1.6 Hz, 2H), 2.06 – 1.96 (m, 4H).

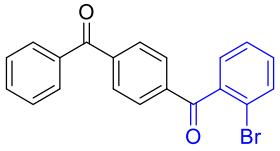
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 149.9, 137.9, 136.9, 129.1, 120.4, 115.6, 48.8, 39.9, 23.9.

IR (ATR, cm^{-1}) ṽ = 3025, 2986, 2972, 2921, 2874, 1500, 1427, 1404, 1347, 1319, 1261, 1154, 886, 923, 849, 810, 689.

MS (EI, 70 eV, %) m/z = 215 (9), 145 (92), 117 (7), 115 (100), 91 (29).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{17}N_3$**: 215.1422; found: 215.1416.

Synthesis of (4-benzoylphenyl)(2-bromophenyl)methanone (166r)



Arene **166r** was prepared *via* **TP3** using (4-iodophenyl)(phenyl)methanone (77 mg, 0.25 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.18 mL, 0.15 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (29 mg, 0.15 mmol) was added. After stirring at 0 °C for 30 min, 2-bromobenzoyl chloride (165 mg, 0.75 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give **166r** (76 mg, 208 µmol, 83%) as a light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.94 – 7.89 (m, 2H), 7.88 – 7.84 (m, 2H), 7.84 – 7.80 (m, 2H), 7.70 – 7.66 (m, 1H), 7.65 – 7.59 (m, 1H), 7.54 – 7.47 (m, 2H), 7.47 – 7.43 (m, 1H), 7.43 – 7.37 (m, 2H).

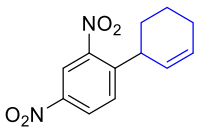
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 196.0, 195.5, 141.9, 140.3, 138.9, 137.0, 133.5, 133.2, 131.7, 130.3, 130.1, 130.1, 129.3, 128.6, 127.5, 119.7.

IR (ATR, cm^{-1}) ṽ = 1798, 1736, 1657, 1596, 1588, 1447, 1430, 1403, 1307, 1273, 1246, 1204, 1178, 1159, 1072, 1060, 1047, 1027, 1016, 1000, 984, 939, 920, 864, 759, 748, 731, 711, 698, 660.

MS (EI, 70 eV, %) m/z = 209 (50), 185 (74), 184 (98), 181 (19), 180 (24), 157 (13), 153 (15), 152 (57), 151 (23), 150 (16), 105 (100), 77 (88), 76 (37), 75 (21).

HRMS (EI, 70 eV) m/z: calc. for **$C_{20}H_{13}BrO_2$**: 364.0099; found: 364.0094.

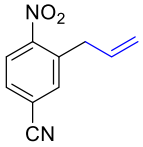
Synthesis of 2',4'-dinitro-1,2,3,4-tetrahydro-1,1'-biphenyl (166s)



Arene **166s** was prepared *via* **TP3** using 1-iodo-2,4-dinitrobenzene (294 mg, 1.00 mmol) and *p*Tol$_2$Zn·2LiOR (**167**, 0.76 mL, 0.60 mmol) at –15 °C for 15 min. After the exchange was complete, CuI (38 mg, 0.20 mmol) and 3-bromocyclohexene (0.17 mL, 1.50 mmol) were added and the reaction stirred for 2 h at the same temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.8:0.2) to give **166s** (196 mg, 0.79 mmol, 79%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.62 (d, *J* = 2.4 Hz, 1H), 8.38 – 8.31 (m, 1H), 7.69 (d, *J* = 8.7 Hz, 1H), 6.10 – 6.01 (m, 1H), 5.57 (m, 1H), 4.02 (m, 1H), 2.27 – 2.18 (m, 1H), 2.17 – 2.10 (m, 2H), 1.80 – 1.61 (m, 2H), 1.51 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 149.6, 147.9, 146.2, 131.9, 131.2, 127.3, 126.7, 119.8, 37.3, 31.6, 24.8, 20.9.
IR (ATR, cm^{-1}) ṽ = 3105, 3025, 2930, 1603, 1526, 1447, 1341, 1065, 901, 834, 788, 743, 724, 661.
MS (EI, 70 eV, %) m/z = 231 (56), 214 (32), 203 (32), 191 (94), 185 (61), 184 (51), 175 (35), 168 (43), 167 (100), 166 (28), 157 (64), 156 (61), 155 (21), 154 (26), 153 (41), 152 (58), 145 (39), 139 (34), 130 (31), 129 (24), 129 (38), 128 (77), 127 (30), 126 (23), 117 (27), 115 (96), 102 (28), 89 (36), 77 (39).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{12}N_2O_4$**: 248.0797; found: 248.0746.

Synthesis of 3-allyl-4-nitrobenzonitrile (166t)

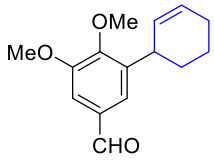


Arene **166t** was prepared *via* **TP3** using 3-iodo-4-nitrobenzonitrile (132 mg, 0.48 mmol) and *p*Tol$_2$Zn·2LiOR (**167**, 0.42 mL, 0.29 mmol) at –15 °C for 15 min. After the exchange was complete, the reaction was cooled to –40 °C and CuI (19 mg, 0.10 mmol) and allyl bromide (0.06 mL, 0.72 mmol) were added and the reaction stirred for 30 min at the same temperature. After work-up, the crude product

was purified *via* column chromatography (pentane:ethyl acetate = 9:1) to give **166t** (64 mg, 340 µmol, 71%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.21 (d, *J* = 1.8 Hz, 1H), 7.82 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.62 – 7.53 (m, 1H), 5.93 (m, 1H), 5.29 – 5.08 (m, 2H), 3.75 (dt, *J* = 6.5, 1.5 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 149.5, 140.4, 135.9, 133.5, 133.3, 128.5, 118.9, 116.7, 111.9, 37.1.
IR (ATR, cm^{-1}) ṽ = 3058, 2983, 2236, 1616, 1531, 1412, 1352, 1195, 1074, 995, 922, 902, 845, 812, 678.
MS (EI, 70 eV, %) m/z = 187 (24), 171 (98), 154 (40), 143 (49), 142 (57), 141 (40), 140 (100), 129 (55), 116 (82), 114 (32), 113 (36), 89 (40).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_7N_2O_2$**: 187.0508; found: 187.0498.

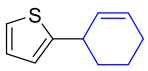
Synthesis of 5,6-dimethoxy-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carbaldehyde (166u)



Arene **166u** was prepared *via* **TP3** using 3-iodo-4,5-dimethoxybenzaldehyde (115 mg, 0.394 mmol) and *t*Bu_2Zn·2LiOR (**168**, 0.35 mL, 0.24 mmol) at 0 °C for 10 min. After the exchange was complete, CuI (15 mg, 0.08 mmol) and 3-bromocyclohexene (0.07 mL, 0.59 mmol) were added and the reaction stirred for 30 min at the same temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 9:1) to give **166u** (47 mg, 191 µmol, 48%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 9.87 (s, 1H), 7.34 (dd, *J* = 13.0, 1.9 Hz, 2H), 5.96 (dtd, *J* = 9.9, 3.7, 2.4 Hz, 1H), 5.65 – 5.57 (m, 1H), 3.97 – 3.78 (m, 7H), 2.18 – 1.95 (m, 3H), 1.78 – 1.59 (m, 2H), 1.50 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 191.8, 153.3, 152.4, 140.7, 132.3, 129.6, 129.4, 125.7, 108.6, 61.2, 56.0, 34.9, 31.2, 25.1, 21.3.
IR (ATR, cm^{-1}) ṽ = 3018, 2932, 2858, 2835, 2736, 1689, 1583, 1482, 1455, 1426, 1386, 1296, 1134, 1086, 1002, 977, 859, 723, 670.
MS (EI, 70 eV, %) m/z = 246 (100), 231 (42), 217 (31), 192 (28), 165 (22), 137 (17), 115 (15).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{18}O_3$**: 246.1256; found: 246.1249.

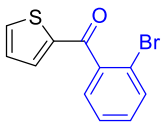
Synthesis of 2-(cyclohex-2-en-1-yl)thiophene (169a)



Thiophene **169a** was prepared *via* **TP3** using 2-iodothiophene (106 mg, 0.50 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.30 mL, 0.30 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (19 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, 3-bromocyclohexene (121 mg, 0.75 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane) to give **169a** (58 mg, 353 µmol, 71%) as a light-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.15 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.95 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.85 (dt, *J* = 3.5, 1.1 Hz, 1H), 5.92 – 5.77 (m, 2H), 3.77 – 3.66 (m, 1H), 2.19 – 2.02 (m, 3H), 1.84 – 1.59 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 150.6, 129.8, 128.5, 126.7, 123.5, 123.1, 36.8, 32.6, 25.0, 20.8.
IR (ATR, cm^{-1}) ṽ = 3022, 2930, 2857, 2835, 1446, 1276, 1232, 1223, 896, 884, 876, 850, 821, 758, 722, 690.
MS (EI, 70 eV, %) m/z = 164 (100), 163 (16), 149 (40), 136 (32), 135 (92), 115 (10), 91 (12).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{12}S$**: 164.0660; found: 164.0654.

Synthesis of (2-bromophenyl)(thiophen-2-yl)methanone (169b)

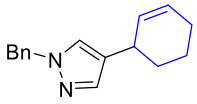


Arene **169b** was prepared *via* **TP3** using 2-iodothiophene (106 mg, 0.50 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.30 mL, 0.30 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (57 mg, 0.30 mmol) was added. After stirring at 0 °C for 30 min, 2-bromobenzoyl chloride (329 mg, 1.50 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give **169b** (82 mg, 307 µmol, 61%) as a light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.77 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.68 – 7.63 (m, 1H), 7.45 – 7.38 (m, 3H), 7.35 (ddd, *J* = 7.8, 6.1, 3.1 Hz, 1H), 7.12 (dd, *J* = 4.9, 3.8 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 188.0, 143.6, 140.6, 136.2, 135.8, 133.5, 131.4, 128.9, 128.5, 127.2, 119.6.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1644, 1588, 1514, 1467, 1431, 1409, 1354, 1294, 1275, 1256, 1232, 1054, 1040, 1030, 885, 844, 770, 741, 727, 685, 668.
MS (EI, 70 eV, %) m/z = 187 (22), 185 (18), 183 (19), 115 (14), 111 (100), 76 (11), 75 (12).
HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_7BrOS$**: 265.9401; found: 265.9393.

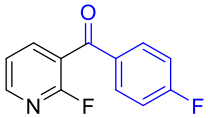
Synthesis of 1-benzyl-4-(cyclohex-2-en-1-yl)-1*H*-pyrazole (169c)



Pyrazole **169c** was prepared *via* **TP3** using 1-benzyl-4-iodopyrazole (142 mg, 0.50 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.38 mL, 0.30 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (19 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, 3-bromocyclohexene (0.09 mL, 0.75 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate:triethylamine = 9:1:0.1) to give **169c** (95 mg, 0.40 mmol, 80%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.32 (s, 1H), 7.28 – 7.17 (m, 3H), 7.14 – 7.10 (m, 2H), 7.09 (s, 1H), 5.71 – 5.59 (m, 2H), 5.17 (s, 2H), 3.27 – 3.23 (m, 1H), 1.97 – 1.84 (m, 3H), 1.67 – 1.41 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 138.3, 137.0, 130.3, 128.8, 128.0, 127.7, 127.6, 127.1, 127.1, 56.1, 31.7, 31.6, 25.0, 20.8.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2933, 1709, 1649, 1455, 1431, 1358, 1221, 1177, 1072, 996, 848, 714.
MS (EI, 70 eV, %) m/z = 238 (48), 147 (17), 119 (29), 91 (100), 65 (16).
HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{18}N_2$**: 238.1470; found: 238.1465.

Synthesis of (4-fluorophenyl)(2-fluoropyridin-3-yl)methanone (169d)



Pyridine **169d** was prepared *via* **TP3** using 2-fluoro-3-iodopyridine (118 mg, 0.53 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.38 mL, 0.32 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (61 mg, 0.32 mmol) was added. After stirring at 0 °C for 30 min,

4-fluorobenzoyl chloride (0.19 mL, 1.59 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 8:2) to give **169d** (111 mg, 506 µmol, 96%) as a colorless solid.

M.p. (°C): 77-78.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.41 (ddd, *J* = 4.9, 2.1, 1.1 Hz, 1H), 8.03 (ddd, *J* = 9.2, 7.4, 2.0 Hz, 1H), 7.88 – 7.81 (m, 2H), 7.37 (ddd, *J* = 7.3, 4.9, 1.9 Hz, 1H), 7.20 – 7.12 (m, 2H).

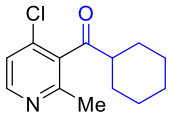
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 190.2 (d, *J* = 5 Hz), 166.2 (d, *J* = 257 Hz), 156.0 (d, *J* = 243 Hz), 150.6 (d, p*J* = 15 Hz), 141.8 (d, *J* = 3 Hz), 132.9 (t, *J* = 3, 1 Hz), 132.4 (dd, *J* = 10, 1 Hz), 121.8 (d, *J* = 5 Hz), 121.3 (d, *J* = 30 Hz), 116.0 (d, *J* = 22 Hz).

IR (ATR, cm^{-1}) ṽ = 3071, 2360, 2343, 1664, 1596, 1573, 1412, 1430, 1229, 1150, 930, 855, 772.

MS (EI, 70 eV, %) m/z = 219 (28), 123 (12), 123 (100), 96 (5), 75 (6).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_7F_2NO$**: 219.0496; found: 219.0490.

Synthesis of (4-chloro-2-methylpyridin-3-yl)(cyclohexyl)methanone (169e)



Pyridine **169e** was prepared *via* **TP3** using 4-chloro-3-iodo-2-methylpyridine (106 mg, 0.50 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.30 mL, 0.30 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (57 mg, 0.30 mmol) was added. After stirring at 0 °C for 30 min, cyclohexanecarbonyl chloride (220 mg, 1.50 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.6:0.4) to give **169e** (85 mg, 0.36 mmol, 72%) as a light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.34 (dd, *J* = 5.2, 0.7 Hz, 1H), 7.39 (d, *J* = 5.1 Hz, 1H), 3.61 – 3.50 (m, 1H), 2.45 (s, 3H), 1.90 – 1.82 (m, 2H), 1.79 (ddd, *J* = 10.2, 4.2, 2.1 Hz, 2H), 1.74 – 1.66 (m, 1H), 1.42 – 1.32 (m, 4H), 1.30 – 1.19 (m, 1H).

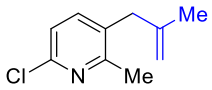
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 206.9, 156.0, 146.5, 146.2, 131.7, 126.0, 47.0, 28.3, 26.1, 25.7, 15.5.

IR (ATR, cm^{-1}) ṽ = 2930, 2854, 1700, 1552, 1449, 1397, 1383, 1364, 1310, 1264, 1234, 1206, 1170, 973, 833, 713.

MS (EI, 70 eV, %) m/z = 194 (10), 154 (19), 141 (29), 129 (33), 128 (19), 127 (100), 126 (19), 92 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{16}ClNO$**: 237.0920; found: 237.0912.

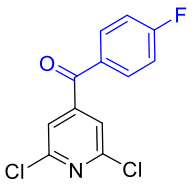
Synthesis of 6-chloro-2-methyl-3-(2-methylallyl)pyridine (169f)



Pyridine **169f** was prepared *via* **TP3** using 6-chloro-3-iodo-2-methylpyridine (127 mg, 0.50 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.30 mL, 0.30 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (19 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, 3-bromo-2-methylprop-1-ene (102 mg, 0.75 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.6:0.4) to give **169f** (87 mg, 0.48 mmol, 96%) as a light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.35 (d, *J* = 7.9 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 4.83 (p, *J* = 1.3 Hz, 1H), 4.50 (tt, *J* = 1.6, 0.8 Hz, 1H), 3.25 (s, 2H), 2.45 (s, 3H), 1.70 (dd, *J* = 1.5, 0.8 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 158.3, 148.2, 142.7, 140.2, 131.9, 121.5, 112.7, 40.4, 22.7, 22.1.
IR (ATR, cm^{-1}) ṽ = 2972, 2920, 2851, 1651, 1581, 1564, 1433, 1392, 1376, 1365, 1194, 1169, 1139, 1109, 1033, 1018, 979, 921, 892, 838, 813, 785, 777, 670.
MS (EI, 70 eV, %) m/z = 180 (21), 168 (32), 167 (10), 166 (100), 131 (29), 130 (16).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{12}ClN$**: 181.0658; found: 181.0650.

Synthesis of (2,6-dichloropyridin-4-yl)(4-fluorophenyl)methanone (169g)



Pyridine **169g** was prepared *via* **TP3** using 2,6-dichloro-4-iodopyridine (120 mg, 0.50 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.36 mL, 0.30 mmol) in THF (1 mL). After the exchange was complete, the reaction was cooled to 0 °C and CuI (57 mg, 0.30 mmol) was added. After stirring at 0 °C for 30 min, 4-fluorobenzoyl chloride (238 mg, 1.50 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.9:0.1) to give **169g** (85 mg, 444 µmol, 89%) as a light yellow solid.

M.p. (°C): 117-119.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.89 – 7.83 (m, 2H), 7.51 (s, 2H), 7.27 – 7.22 (m, 2H).

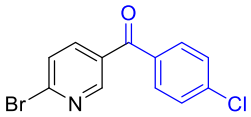
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 190.8, 166.5 (d, *J* = 258.0 Hz), 151.5, 149.7, 133.0 (d, *J* = 9.7 Hz), 131.4 (d, *J* = 3.0 Hz), 122.3, 116.5 (d, *J* = 22.2 Hz).

IR (ATR, cm^{-1}) ṽ = 3079, 2926, 1668, 1594, 1578, 1533, 1504, 1467, 1412, 1360, 1303, 1274, 1230, 1184, 1158, 1101, 1012, 993, 973, 964, 886, 847, 837, 814, 759, 718, 692.

MS (EI, 70 eV, %) m/z = 269 (11), 123 (100), 95 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_6Cl_2FNO$**: 268.9810; found: 268.9806.

Synthesis of (6-bromopyridin-3-yl)(4-chlorophenyl)methanone (169h)



Pyridine **169h** was prepared *via* **TP3** using 2-bromo-5-iodopyridine (142 mg, 0.50 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.30 mL, 0.30 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (57 mg, 0.30 mmol) was added. After stirring at 0 °C for 30 min, 4-chlorobenzoyl chloride (263 mg, 1.50 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give **169h** (126 mg, 425 µmol, 85%) as a colorless solid.

M.p. (°C): 129-131.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.7 (dd, *J* = 2.5, 0.8 Hz, 1H), 8.0 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.8 – 7.7 (m, 2H), 7.7 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.5 – 7.5 (m, 2H).

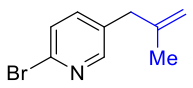
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 192.7, 151.3, 146.5, 140.2, 139.4, 134.8, 132.1, 131.4, 129.3, 128.4.

IR (ATR, cm^{-1}) ṽ = 1665, 1588, 1574, 1357, 1304, 1291, 1276, 1215, 1087, 924, 850, 744, 681, 667.

MS (EI, 70 eV, %) m/z = 262 (97), 260 (100), 186 (13), 184 (14), 158 (12), 156 (12), 141 (21), 139 (74), 111 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_7BrClNO$**: 294.9400; found: 294.9395.

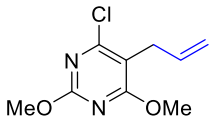
Synthesis of 2-bromo-5-(2-methylallyl)pyridine (169i)



Pyrazole **169i** was prepared *via* **TP3** using 2-bromo-5-iodopyridine (142 mg, 0.50 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.30 mL, 0.30 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (19 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, 3-bromo-2-methylprop-1-ene (102 mg, 0.75 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give **169i** (98 mg, 0.46 mmol, 92%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.2 – 8.2 (m, 1H), 7.4 – 7.3 (m, 2H), 4.9 (t, *J* = 1.7 Hz, 1H), 4.7 (dt, *J* = 2.2, 1.1 Hz, 1H), 3.3 (d, *J* = 1.2 Hz, 2H), 1.7 (t, *J* = 1.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 150.7, 143.5, 139.9, 139.2, 134.5, 127.8, 113.3, 40.9, 22.1.
IR (ATR, cm^{-1}) ṽ = 2965, 2928, 2360, 2342, 2336, 1578, 1560, 1454, 1378, 1087, 1024, 896, 802.
MS (EI, 70 eV, %) m/z = 211 (43), 210 (92), 198 (91), 196 (94), 132 (34), 131 (13), 130 (21), 117 (100), 116 (26), 91 (14).
HRMS (EI, 70 eV) m/z: calc. for **$C_9H_{10}BrN$**: 210.9997; found: 210.9991.

Synthesis of 5-allyl-4-chloro-2,6-dimethoxypyrimidine (169j)

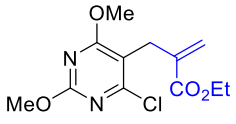


Pyrimidine **169j** was prepared *via* **TP3** using 4-chloro-5-iodo-2,6-dimethoxypyrimidine (150 mg, 0.50 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.36 mL, 0.30 mmol) in THF (1 mL). After the exchange was complete, the reaction was cooled to 0 °C and CuI (19 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, allyl bromide (91 mg, 0.75 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give **169j** (101 mg, 0.47 mmol, 94%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 5.8 (ddt, *J* = 17.5, 9.7, 6.2 Hz, 1H), 5.1 – 5.0 (m, 2H), 4.0 (d, *J* = 5.6 Hz, 6H), 3.3 (dt, *J* = 6.2, 1.6 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 170.2, 162.8, 160.1, 133.5, 116.1, 110.8, 55.3, 55.0, 29.7.

IR (ATR, cm^{-1}) ṽ = 2958, 1639, 1589, 1546, 1482, 1463, 1375, 1348, 1330, 1303, 1290, 1246, 1225, 1202, 1181, 1082, 1031, 993, 946, 930, 915, 855, 813, 781.
MS (EI, 70 eV, %) m/z = 214 (100), 213 (39), 201 (14), 199 (44), 187 (24), 185 (42), 184 (17), 179 (46), 173 (16), 169 (11), 149 (10), 130 (16), 122 (13).
HRMS (EI, 70 eV) m/z: calc. for **$C_9H_{11}ClN_2O_2$**: 214.0509; found: 214.0501.

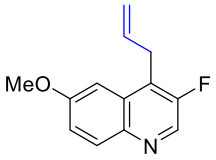
Synthesis of ethyl 2-((4-chloro-2,6-dimethoxypyrimidin-5-yl)methyl)acrylate (169k)



Pyrimidine **169k** was prepared *via* **TP3** using 4-chloro-5-iodo-2,6-dimethoxypyrimidine (150 mg, 0.50 mmol) and *s*Bu$_2$Zn·2LiOR (**161c**, 0.36 mL, 0.30 mmol) in THF (1 mL). After the exchange was complete, the reaction was cooled to 0 °C and CuI (19 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, ethyl 2-(bromomethyl)acrylate (145 mg, 0.75 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give **169k** (137 mg, 0.48 mmol, 96%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.2 (q, *J* = 1.6 Hz, 1H), 5.1 (td, *J* = 2.0, 0.9 Hz, 1H), 4.2 (q, *J* = 7.1 Hz, 2H), 4.0 (d, *J* = 13.5 Hz, 6H), 3.6 (t, *J* = 1.8 Hz, 2H), 1.3 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 170.6, 166.8, 163.2, 161.1, 136.7, 124.5, 109.6, 61.1, 55.4, 55.0, 27.7, 14.4.
IR (ATR, cm^{-1}) ṽ = 2985, 1717, 1637, 1593, 1548, 1484, 1465, 1426, 1382, 1348, 1282, 1256, 1225, 1199, 1174, 1135, 1083, 1033, 945, 782.
MS (EI, 70 eV, %) m/z = 251 (56), 241 (13), 240 (16), 224 (11), 223 (100), 214 (28), 212 (87), 211 (23), 203 (28), 197 (15), 187 (15), 183 (21), 177 (91).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{15}ClN_2O_4$**: 286.0720; found: 286.0713.

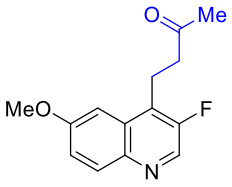
Synthesis of 4-allyl-3-fluoro-6-methoxyquinoline (169l)



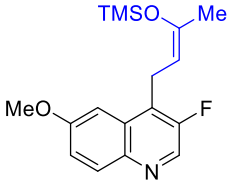
Quinoline **169l** was prepared *via* **TP3** using 3-fluoro-4-iodo-6-methoxyquinoline (155 mg, 0.51 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.37 mL, 0.31 mmol) at 0 °C for 10 min. After the exchange was complete, CuI (19 mg, 0.09 mmol) was added. After stirring at 0 °C for 30 min, allyl bromide (0.07 mL, 0.77 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 9:1) to give **169l** (102 mg, 0.47 mmol, 92%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.61 (d, *J* = 1.2 Hz, 1H), 7.98 (d, *J* = 9.2 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.14 (d, *J* = 2.8 Hz, 1H), 5.97 (ddt, *J* = 17.2, 10.1, 6.0 Hz, 1H), 5.11 (dq, *J* = 10.1, 1.6 Hz, 1H), 5.05 (dq, *J* = 17.0, 1.7 Hz, 1H), 3.90 (s, 3H), 3.77 (dq, *J* = 6.1, 1.7 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 158.6, 154.9 (d, *J* = 252.6 Hz), 141.6 (d, *J* = 2.5 Hz), 138.4 (d, *J* = 29.3 Hz), 133.7, 131.7, 129.3 (d, *J* = 3.6 Hz), 127.1 (d, *J* = 12.8 Hz), 120.5 (d, *J* = 2.7 Hz), 117.1, 102.1 (d, *J* = 5.5 Hz), 55.6, 28.4 (d, *J* = 4.0 Hz).
IR (ATR, cm^{-1}) ṽ = 3081, 3007, 2938, 2831, 2360, 1620, 1506, 1468, 1360, 1320, 1263, 1216, 1136, 1029, 908, 827, 784, 699, 674.
MS (EI, 70 eV, %) m/z = 218 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{13}FNO$:** 218.0981; found: 218.0974.

Synthesis of 4-(3-fluoro-6-methoxyquinolin-4-yl)butan-2-one (169m)



Step 1:



Enol intermediate was prepared *via* **TP3** using 3-fluoro-4-iodo-6-methoxyquinoline (155 mg, 0.51 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.44 mL, 0.31 mmol) at 0 °C for 10 min. After the exchange was complete, CuI (19 mg, 0.09 mmol) was added. After stirring at 0 °C for 30 min, a solution of methyl vinyl ketone (0.13 mL, 0.53 mL) and TMSCl (0.28 mL, 2.15 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was obtained as a yellow oil and used as is in the next step.

Step 2: Synthesis of **169m**

The enol product from step 1 was dissolved in THF (2.5 mL) and TBAF (1.00 M in THF, 0.6 mL, 0.6 mmol) added dropwise. The reaction was stirred at room temperature for 1 h. Then, a sat. aq. NH_4Cl solution (10 mL) was added and the reaction mixture extracted with ethyl acetate (3 x 30 mL). After purification *via* column chromatography (pentane:ethyl acetate = 7:3) **169m** (71 mg, 287 µmol, 56%) was obtained as a colorless solid over two steps.

M.p. (°C): 61-63.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.56 (d, *J* = 1.3 Hz, 1H), 7.96 (d, *J* = 9.2 Hz, 1H), 7.29 (dd, *J* = 9.2, 2.7 Hz, 1H), 7.16 (d, *J* = 2.7 Hz, 1H), 3.92 (s, 3H), 3.28 (td, *J* = 8.3, 7.9, 1.8 Hz, 2H), 2.83 – 2.77 (m, 2H), 2.17 (s, 3H).

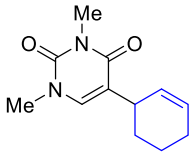
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 206.9, 158.9, 155.1 (d, *J* = 252.2 Hz), 141.6 (d, *J* = 2.4 Hz), 138.2 (d, *J* = 29.0 Hz), 131.9, 129.0 (d, *J* = 3.7 Hz), 128.8 (d, *J* = 12.7 Hz), 120.6 (d, *J* = 2.8 Hz), 101.6 (d, *J* = 5.4 Hz), 55.7, 42.5 (d, *J* = 1.3 Hz), 30.0, 18.2 (d, *J* = 3.5 Hz).

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3003, 2958, 2835, 1712, 1620, 1508, 1469, 1359, 1229, 1207, 1027, 907, 829, 788, 731.

MS (EI, 70 eV, %) m/z = 247 (100), 205 (11), 204 (91), 190 (60), 173 (19), 172 (20), 161 (11), 160 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{14}FNO_2$**: 247.1009; found: 247.1003.

Synthesis of 5-(cyclohex-2-en-1-yl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (169n)



Uracil **169n** was prepared *via* **TP3** using 5-iodo-1,3-dimethyluracil (137 mg, 0.515 mmol) and *s*Bu$_2$Zn·2LiOR (**161c**, 0.37 mL, 0.31 mmol) in THF (1 mL) at 0 °C for 10 min. After the exchange was complete, CuI (19 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, 3-bromocyclohexene (0.09 mL, 0.77 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate:triethylamine = 6:4:0.1) to give **169n** (91 mg, 413 µmol, 80%) as a colorless solid.

M.p. (°C): 79-82.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.87 (d, *J* = 0.8 Hz, 1H), 5.93 (dtd, *J* = 9.8, 3.7, 2.1 Hz, 1H), 5.49 (ddt, *J* = 10.1, 4.0, 2.2 Hz, 1H), 3.54 – 3.47 (m, 1H), 3.38 (s, 3H), 3.35 (s, 3H), 2.06 – 1.99 (m, 2H), 1.97 – 1.87 (m, 1H), 1.59 (m, 1H), 1.55 – 1.42 (m, 2H).

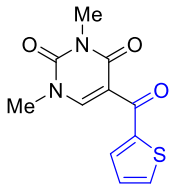
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 163.4, 151.8, 139.9, 130.6, 127.6, 117.2, 37.1, 32.4, 28.3, 28.1, 25.2, 19.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3062, 3019, 2927, 2860, 2836, 1696, 1656, 1632, 1449, 1338, 1238, 1089, 784, 756.

MS (EI, 70 eV, %) m/z = 220 (90), 205 (43), 192 (13), 191 (41), 179 (19), 166 (100), 165 (23), 153 (20), 148 (12), 134 (14), 107 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{16}N_2O_2$**: 220.1212; found: 220.1205.

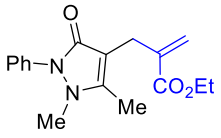
Synthesis of 1,3-dimethyl-5-(thiophene-2-carbonyl)pyrimidine-2,4(1*H*,3*H*)-dione (169o)



Uracil **169o** was prepared *via* **TP3** using 5-iodo-1,3-dimethyluracil (136 mg, 0.51 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.44 mL, 0.31 mmol) in THF (1 mL) at 0 °C for 10 min. After the exchange was complete, CuI (58 mg, 0.31 mmol) was added. After stirring at 0 °C for 30 min, 2-thiophenecarbonyl chloride (0.17 mL, 1.53 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 4:6) to give **169o** (99 mg, 396 µmol, 77%) as a colorless solid.

M.p. (°C): 193-196.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.88 (s, 1H), 7.78 (dd, *J* = 3.9, 1.1 Hz, 1H), 7.68 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.13 (dd, *J* = 4.9, 3.9 Hz, 1H), 3.51 (s, 3H), 3.41 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 181.8, 160.4, 151.2, 148.2, 143.5, 135.0, 134.8, 128.1, 113.5, 37.9, 28.5.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3105, 301, 2953, 1706, 1648, 1635, 1599, 1410, 1335, 1220, 1056, 794, 748, 670.
MS (EI, 70 eV, %) m/z = 250 (61), 222 (21), 221 (100), 207 (15), 167 (27), 124 (11), 111 (58).
HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{10}N_2O_3S$**: 250.0412; found: 250.0409.

Synthesis of ethyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)methyl)acrylate (169p)



Antipyrine **169p** was prepared *via* **TP3** using iodoantipyrine (145 mg, 0.46 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.33 mL, 0.28 mmol) in THF (1 mL) at 0 °C for 10 min. After the exchange was complete, CuI (19 mg, 0.09 mmol) was added. After stirring at 0 °C for 30 min, ethyl 2-(bromomethyl)acrylate (134 mg, 0.69 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 4:6) to give **169p** (103 mg, 343 µmol, 74%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.44 – 7.37 (m, 4H), 7.22 (ddt, *J* = 6.6, 5.7, 2.6 Hz, 1H), 6.22 (q, *J* = 1.0 Hz, 1H), 5.71 (q, *J* = 1.5 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.30 (t, *J* = 1.2 Hz, 2H), 3.01 (s, 3H), 2.21 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

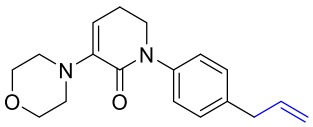
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 167.1, 166.0, 154.4, 137.3, 135.5, 129.1, 126.3, 126.1, 123.4, 107.6, 60.8, 36.4, 24.8, 14.3, 11.4.

IR (ATR, cm^{-1}) ṽ = 2982, 2906, 1713, 1667, 1595, 1496, 1292, 1254, 1025, 946, 757, 696.

MS (EI, 70 eV, %) m/z = 300 (31), 299 (31), 271 (89), 255 (19), 254 (20), 227 (100), 226 (19), 208 (18), 207 (29), 201 (19), 196 (18), 152 (22), 124 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{20}N_2O_3$**: 300.1474; found: 300.1471.

Synthesis of 1-(4-allylphenyl)-3-(piperidin-1-yl)-5,6-dihydropyridin-2(1*H*)-one (169q)



Morpholine **169q** was prepared *via* **TP3** using 1-(4-iodophenyl)-3-(piperidin-1-yl)-5,6-dihydropyridin-2(1*H*)-one (76 mg, 0.20 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.17 mL, 0.12 mmol) at 0 °C for 10 min. After the exchange was complete, CuI (8 mg, 0.04 mmol) was added. After stirring at 0 °C for 30 min, allyl bromide (0.03 mL, 0.30 mmol) was added and the reaction stirred for 2 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 6:4) to give **169q** (50 mg, 168 µmol, 85%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.37 – 7.26 (m, 4H), 6.09 – 5.97 (m, 1H), 5.71 (t, *J* = 4.7 Hz, 1H), 5.21 – 5.11 (m, 2H), 3.93 – 3.88 (m, 4H), 3.85 (t, *J* = 6.7 Hz, 2H), 3.48 – 3.43 (m, 2H), 3.01 – 2.96 (m, 4H), 2.60 – 2.52 (m, 2H).

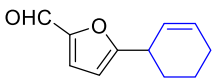
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 161.5, 143.9, 141.0, 138.0, 137.3, 129.0, 125.1, 116.0, 114.2, 66.9, 50.6, 48.7, 39.9, 23.5.

IR (ATR, cm^{-1}) ṽ = 2957, 2924, 2892, 2854, 2818, 1659, 1620, 1511, 1219, 1118, 924, 811, 782.

MS (EI, 70 eV, %) m/z = 298 (5), 280 (100), 279 (29), 239 (34), 212 (55), 146 (39), 117 (18), 115 (27).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{24}N_2O$**: 298.1681; found: 298.1681.

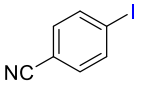
Synthesis of 5-(cyclohex-2-en-1-yl)furan-2-carbaldehyde (169r)



Furane **169r** was prepared *via* **TP3** using 5-iodofuran-2-carbaldehyde (56 mg, 0.25 mmol) and *t*Bu$_2$Zn·2LiOR (**168**, 0.30 mL, 0.20 mmol) at 0 °C for 10 min. After the exchange was complete, CuI (10 mg, 0.05 mmol) and 3-bromocyclohexene (61 mg, 0.38 mmol) was added and the reaction stirred for 30 min at the same temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 9.9:0.1) to give **169r** (29 mg, 164 µmol, 66%) as a colorless oil.

^{1}H-NMR (400 MHz, CDCl$_3$, ppm) δ = 9.5 (s, 1H), 7.2 (d, *J* = 3.5 Hz, 1H), 6.2 (dd, *J* = 3.5, 0.8 Hz, 1H), 6.0 – 5.9 (m, 1H), 5.8 – 5.7 (m, 1H), 3.6 – 3.5 (m, 1H), 2.1 – 2.0 (m, 3H), 1.9 – 1.8 (m, 1H), 1.7 – 1.6 (m, 2H).
^{13}C-NMR (101 MHz, CDCl$_3$, ppm) δ = 177.3, 166.5, 152.0, 130.3, 125.4, 108.5, 35.4, 27.9, 24.9, 20.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2933, 2863, 2836, 1673, 1511, 1449, 1400, 1300, 1281, 1198, 1023, 966, 873, 803, 764, 726.
MS (EI, 70 eV, %) m/z = 176 (53), 161 (10), 148 (14), 147 (100), 119 (45), 91 (50).
HRMS (EI, 70 eV) m/z: calc. for **C$_{11}$H$_{12}$O$_2$**: 176.0837; found: 176.0830.

Synthesis of 4-iodobenzonitrile (170a)

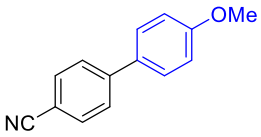


Benzonitrile **170a** was prepared *via* **TP4** using 4-bromobenzonitrile (94 mg, 516 µmol) and *s*Bu$_2$Zn·2LiOR (**161c**, 0.55 mL, 413 µmol). After the exchange was complete, a solution of I$_2$ (262 mg, 1.03 mmol) in THF (2 mL) was added and the reaction stirred for 30 min. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1) to give **170a** (91 mg, 397 µmol, 77%) as a colorless solid.

^{1}H-NMR (400 MHz, CDCl$_3$, ppm) δ = 7.88 – 7.81 (m, 2H), 7.40 – 7.32 (m, 2H).
^{13}C-NMR (101 MHz, CDCl$_3$, ppm) δ = 138.6, 133.3, 118.3, 111.8, 100.5.
The spectra matched those of the literature.[201]

[201] Y.-H. Chen, M. Sun, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 2236.

Synthesis of 4'-methoxy-[1,1'-biphenyl]-4-carbonitrile (170b)

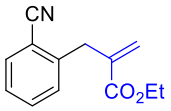


Biaryl **170b** was prepared *via* **TP4** using 4-bromobenzonitrile (52 mg, 286 µmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.305 mL, 229 µmol). After the exchange was complete, $Pd(OAc)_2$ (2 mg, 9 µmol), SPhos (7 mg, 17 µmol) and 4-iodoanisole (53 mg, 0.23 mmol) were added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1) to give **170b** (31 mg, 148 µmol, 64%) as a colorless solid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.72 – 7.61 (m, 4H), 7.57 – 7.50 (m, 2H), 7.04 – 6.97 (m, 2H), 3.87 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.3, 145.3, 132.7, 131.6, 128.5, 127.2, 119.3, 114.7, 110.2, 55.5.

The spectra matched those of the literature.[202]

Synthesis of ethyl 2-(2-cyanobenzyl)acrylate (170c)



Benzonitrile **170c** was prepared *via* **TP4** using 2-bromobenzonitrile (89 mg, 0.49 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.47 mL, 0.39 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (19 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, ethyl 2-(bromomethyl)acrylate (171 mg, 0.74 mmol) was added and the reaction stirred for 2 h at the same temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 7:3) to give **170c** (66 mg, 0.31 mmol, 63%) as a colorless oil.

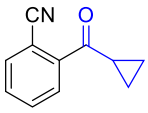
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.63 (ddd, *J* = 7.8, 1.5, 0.6 Hz, 1H), 7.51 (td, *J* = 7.7, 1.4 Hz, 1H), 7.37 (ddd, *J* = 7.9, 1.2, 0.6 Hz, 1H), 7.32 (td, *J* = 7.6, 1.2 Hz, 1H), 6.33 (q, *J* = 0.9 Hz, 1H), 5.57 (q, *J* = 1.3 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 2H), 1.25 (t, *J* = 7.1 Hz, 3H).

[202] S. Bernhardt, G. Manolikakes, T. Kunz, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9205.

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.3, 142.8, 138.3, 133.0, 132.9, 130.3, 127.6, 127.2, 118.0, 113.1, 61.1, 36.7, 14.2.

The spectra matched those of the literature.[203]

Synthesis of 2-(cyclopropanecarbonyl)benzonitrile (170d)

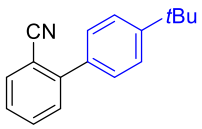


Benzonitrile **170d** was prepared *via* **TP4** using 2-bromobenzonitrile (85 mg, 0.47 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.48 mL, 0.38 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (71 mg, 0.38 mmol) was added. After stirring at 0 °C for 30 min, cyclopropanecarbonyl chloride (147 mg, 1.41 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 7:3) to give **170d** (54 mg, 315 µmol, 67%) as a colorless solid.

M.p. (°C): 66-67.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.99 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.79 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.71 (td, *J* = 7.7, 1.4 Hz, 1H), 7.62 (td, *J* = 7.6, 1.3 Hz, 1H), 2.59 (tt, *J* = 7.7, 4.5 Hz, 1H), 1.35 (p, *J* = 3.8 Hz, 2H), 1.16 (dq, *J* = 7.4, 3.7 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 199.6, 141.5, 134.8, 132.7, 132.0, 129.3, 118.1, 110.8, 19.4, 13.3.
IR (ATR, cm^{-1}) ṽ = 3076, 3006, 2220, 1673, 1590, 1571, 1486, 1383, 1223, 989, 871, 756.
MS (EI, 70 eV, %) m/z = 170 (10), 143 (13), 130 (100), 115 (8), 75 (6).
HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_9NO$**: 171.0684; found: 171.0678.

[203] M. Ketels, M. A. Ganiek, N. Weidmann, P. Knochel, *Angew. Chem. Int. Ed.* **2017**, *56*, 12770.

Synthesis of 4'-(tert-butyl)-[1,1'-biphenyl]-2-carbonitrile (170e)

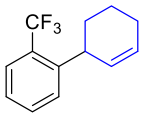


Biaryl **170e** was prepared *via* **TP4** using 2-bromobenzonitrile (93 mg, 0.51 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.49 mL, 0.41 mmol). After the exchange was complete, the reaction was cooled to 0 °C and TMSCl (0.05 mL, 0.41 mmol) added at 0 °C and stirred for 10 min. Then, $Pd(OAc)_2$ (4 mg, 15 µmol), SPhos (13 mg, 31 µmol) and 4-*tert*butyliodobenzene (107 mg, 0.41 mmol) were added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 10:0.2) to give **170e** (62 mg, 263 µmol, 64%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.76 (ddd, *J* = 7.7, 1.4, 0.6 Hz, 1H), 7.63 (ddd, *J* = 7.5, 1.4 Hz, 1H), 7.54 – 7.50 (m, 5H), 7.42 (td, *J* = 7.6, 1.3 Hz, 1H), 1.38 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 151.9, 145.6, 135.3, 133.9, 132.9, 130.2, 128.6, 127.4, 125.8, 119.1, 111.2, 34.8, 31.4.

The spectra matched those of the literature.[204]

Synthesis of 2'-(trifluoromethyl)-1,2,3,4-tetrahydro-1,1'-biphenyl (170f)



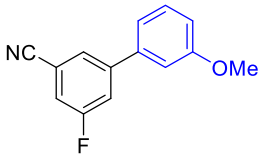
Arene **170f** was prepared *via* **TP4** using 1-bromo-2-(trifluoromethyl)benzene (238 mg, 1.06 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 1.05 mL, 0.85 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuCN·2LiCl (1.00 M in THF, 0.21 mL, 0.21 mmol) was added. After stirring at 0 °C for 10 min, 3-bromocyclohexene (0.18 mL, 1.59 mmol) was added and the reaction stirred for 2 h at the same temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:diethyl ether = 1000:1) to give **170f** (185 mg, 818 µmol, 77%) as a colorless oil.

[204] S. Sarkar, M. Jana, T. Narender, *Eur. J. Org. Chem.* **2013**, 6491.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.61 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.52 – 7.40 (m, 2H), 7.29 (t, *J* = 7.6 Hz, 1H), 5.97 – 5.87 (m, 1H), 5.64 – 5.55 (m, 1H), 3.86 – 3.77 (m, 1H), 2.17 – 2.03 (m, 3H), 1.86 – 1.76 (m, 1H), 1.74 – 1.61 (m, 1H), 1.53 – 1.41 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 145.8 (d, *J* = 1.5 Hz), 131.9, 130.0 (d, *J* = 29.3 Hz), 128.7, 128.0 (q, *J* = 29.2 Hz), 126.2, 126.0, 125.7 (q, *J* = 5.9 Hz), 123.5, 37.9 (d, *J* = 2.0 Hz), 32.8, 25.0, 21.8.

The spectra matched those of the literature.[205]

Synthesis of 5-fluoro-3'-methoxy-[1,1'-biphenyl]-3-carbonitrile (170g)

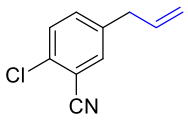


Biaryl **170g** was prepared *via* **TP4** using 3-bromo-5-fluorobenzonitrile (193 mg, 0.97 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.96 mL, 0.78 mmol). After the exchange was complete, $Pd(OAc)_2$ (7 mg, 29 µmol), SPhos (24 mg, 58 µmol) and 3-iodoanisole (159 mg, 0.68 mmol) were added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 10:0.5) to give **170g** (93 mg, 409 µmol, 60%) as a colorless solid.

M.p. (°C): 109-110.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.7 (t, *J* = 1.5 Hz, 1H), 7.5 (ddd, *J* = 9.6, 2.5, 1.6 Hz, 1H), 7.4 (t, *J* = 8.0 Hz, 1H), 7.3 (ddd, *J* = 7.7, 2.5, 1.4 Hz, 1H), 7.1 (ddd, *J* = 7.6, 1.8, 0.9 Hz, 1H), 7.1 (t, *J* = 2.1 Hz, 1H), 7.0 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 3.9 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 162.6 (d, *J* = 250.1 Hz), 160.3, 145.0 (d, *J* = 8.1 Hz), 139.2 (d, *J* = 2.1 Hz), 130.5, 126.9 (d, *J* = 3.2 Hz), 119.5, 119.1 (d, *J* = 21.8 Hz), 117.8 (d, *J* = 3.5 Hz), 117.7 (d, *J* = 24.8 Hz), 114.4, 114.2 (d, *J* = 10.0 Hz), 112.9, 55.5.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3081, 2928, 2234, 1580, 1460, 1440, 1403, 1332, 1287, 1240, 1046, 966, 865, 776, 685.
MS (EI, 70 eV, %) m/z = 228 (15), 227 (100), 198 (49), 184 (26), 158 (29).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{10}FNO$**: 227.0746; found: 227.0740.

[205] L. Baker, T. Minehan, *J. Org. Chem.* **2004**, *69*, 3957.

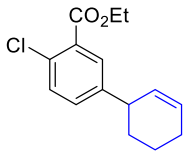
Synthesis of 5-allyl-2-chlorobenzonitrile (170h)



Benzonitrile **170h** was prepared *via* **TP4** using 3-bromo-5-fluorobenzonitrile (222 mg, 1.03 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 1.01 mL, 0.82 mmol) at 25 °C for 1 h. After the exchange was complete, the reaction was cooled to 0 °C and CuCN·2LiCl (1.00 M in THF, 0.21 mL, 0.21 mmol) and allyl bromide (0.13 mL, 1.53 mmol) was added and the reaction stirred for 1 h at the same temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 10:0.2) to give **170h** (144 mg, 811 µmol, 79%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.5 (d, *J* = 2.1 Hz, 1H), 7.4 (d, *J* = 8.4 Hz, 1H), 7.4 (dd, *J* = 8.4, 2.1 Hz, 1H), 5.9 (ddt, *J* = 16.8, 10.1, 6.7 Hz, 1H), 5.2 – 5.0 (m, 2H), 3.4 – 3.4 (m, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 139.8, 135.4, 134.6, 134.4, 134.0, 130.0, 117.8, 116.2, 113.3, 39.0.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3082, 2982, 2902, 2837, 1711, 1640, 1472, 1432, 1359, 1220, 1055, 994, 919, 829
MS (EI, 70 eV, %) m/z = 179 (17), 177 (54), 150 (10), 143 (10), 142 (100), 141 (11), 140 (33), 115 (70).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_8ClN$**: 177.0345; found: 177.0338.

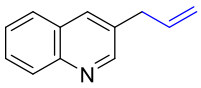
Synthesis of ethyl 4-chloro-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxylate (170i)



Arene **170i** was prepared *via* **TP4** using ethyl 5-bromo-2-chlorobenzoate (130 mg, 0.49 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.46 mL, 0.39 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (18 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, 3-bromocyclohexene (0.09 mL, 0.74 mmol) was added and the reaction stirred for 12 h at the same temperature. After work-up, the crude product was purified *via* column chromatography (pentane:ethyl acetate = 10:0.05) to give **170i** (95 mg, 359 µmol, 73%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.55 (d, *J* = 2.3 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 1H), 7.20 – 7.17 (m, 1H), 5.90 – 5.82 (m, 1H), 5.61 – 5.55 (m, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 3.39 – 3.30 (m, 1H), 2.06 – 1.98 (m, 2H), 1.98 – 1.90 (m, 1H), 1.69 – 1.59 (m, 1H), 1.59 – 1.49 (m, 1H), 1.49 – 1.39 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.3, 145.6, 131.9, 131.0, 130.9, 130.6, 130.5, 129.5, 129.1, 61.7, 41.2, 32.5, 25.0, 21.0, 14.4.
IR (ATR, cm^{-1}) ṽ = 3020, 2981, 2930, 2858, 1731, 1472, 1294, 1251, 1189, 1118, 1045, 827.
MS (EI, 70 eV, %) m/z = 264 (100), 219 (48), 191 (46), 183 (52), 163 (67), 129 (55), 128 (98), 115 (50).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{17}ClO_2$**: 264.0917; found: 264.0912.

Synthesis of 3-allylquinoline (170j)



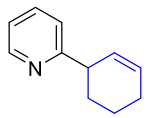
Quinoline **170j** was prepared *via* **TP4** using 3-bromoquinoline (100 mg, 0.48 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.45 mL, 0.38 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (18 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, allyl bromide (0.07 mL, 0.72 mmol) was added and the reaction stirred for 2 h at the same temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1) to give **170j** (57 mg, 337 µmol, 70%) as a light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.77 (d, *J* = 2.2 Hz, 1H), 8.09 (dq, *J* = 8.4, 0.9 Hz, 1H), 7.92 (dd, *J* = 2.2, 1.0 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.66 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.51 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 6.11 – 5.95 (m, 1H), 5.21 – 5.09 (m, 2H), 3.62 – 3.53 (m, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 152.1, 147.1, 136.2, 134.7, 132.7, 129.3, 128.9, 128.3, 127.5, 126.8, 117.2, 37.5.

The spectra matched those of the literature.[206]

[206] D. Seomoon, P. H. Lee, *J. Org. Chem.* **2008**, *73*, 1165.

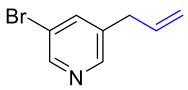
Synthesis of 2-(cyclohex-2-en-1-yl)pyridine (170k)



Pyridine **170k** was prepared *via* **TP4** using 2-bromopyridine (82 mg, 0.52 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.56 mL, 0.42 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (18 mg, 0.10 mmol) was added. After stirring at 0 °C for 30 min, 3-bromocyclohexene (0.09 mL, 0.78 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1) to give **170k** (51 mg, 0.32 mmol, 62%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.53 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.59 (td, *J* = 7.6, 1.9 Hz, 1H), 7.18 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.09 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 5.96 – 5.89 (m, 1H), 5.81 – 5.75 (m, 1H), 3.62 – 3.51 (m, 1H), 2.18 – 1.97 (m, 3H), 1.79 – 1.58 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 165.5, 149.4, 136.5, 129.1, 128.8, 121.9, 121.2, 44.1, 30.8, 25.0, 21.2.
IR (ATR, cm^{-1}) ṽ = 3018, 2928, 2859, 2835, 2360, 1587, 1568, 1469, 1432, 1150, 880, 774, 749, 723, 686.
MS (EI, 70 eV, %) m/z = 159 (2), 158 (20), 144 (16), 131 (10), 130 (100), 117 (14).
HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{13}N$**: 159.1048; found: 159.1041.

Synthesis of 3-allyl-5-bromopyridine (170l)

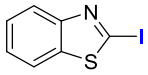


Pyridine **170l** was prepared *via* **TP4** using 3,5-dibromopyridine (235 mg, 1.00 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.76 mL, 0.60 mmol). After the exchange was complete, the reaction was cooled to 0 °C and CuI (38 mg, 0.20 mmol) was added. After stirring at 0 °C for 30 min, allyl bromide (0.13 mL, 1.50 mmol) was added and the reaction stirred for 12 h at room temperature. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give **170l** (120 mg, 0.61 mmol, 61%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.56 (d, *J* = 2.1 Hz, 1H), 8.40 (d, *J* = 1.5 Hz, 1H), 7.69 (t, *J* = 2.0 Hz, 1H), 5.99 – 5.89 (m, 1H), 5.23 – 5.11 (m, 2H), 3.40 (d, *J* = 6.6 Hz, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 148.7, 148.1, 138.8, 137.2, 135.2, 120.7, 117.7, 36.7.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2923, 2356, 1640, 1580, 1555, 1421, 1096, 1022, 993, 921, 884, 851.
MS (EI, 70 eV, %) m/z = 199 (36), 198 (99), 197 (36), 196 (100), 118 (39), 117 (84), 91 (23).
HRMS (EI, 70 eV) m/z: calc. for **C_8H_8BrN**: 196.9840; found: 196.9833.

Synthesis of 2-iodobenzothiazole (170m)



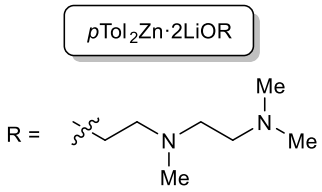
Benzothiazole **170m** was prepared *via* **TP4** using 2-bromobenzothiazole (110 mg, 0.51 mmol) and *s*Bu_2Zn·2LiOR (**161c**, 0.55 mL, 41 mmol). After the exchange was complete, a solution of I_2 (261 mg, 1.02 mmol) in THF (2 mL) was added and the reaction stirred for 30 min. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1) to give **170m** (100 mg, 383 µmol, 75%) as a colorless solid.

M.p. (°C): 79-80.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.06 – 8.00 (m, 1H), 7.87 – 7.81 (m, 1H), 7.48 – 7.34 (m, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 154.3, 139.2, 126.5, 125.7, 122.7, 120.6, 105.9.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3054, 3026, 2965, 2927, 2831, 1451, 1416, 1308, 1228, 951, 940, 750, 722.
MS (EI, 70 eV, %) m/z = 260 (100), 134 (35), 90 (6).
HRMS (EI, 70 eV) m/z: calc. for **C_7H_4INS**: 260.9109; found: 260.9103.

5 Regioselective Iodine/Zinc Exchange for the Selective Functionalization of Polyiodinated Arenes and Heterocycles in Toluene

5.1 Preparation and Titration of *p*Tol$_2$Zn·2LiOR

Preparation of *p*Tol$_2$Zn·2LiOR (*p*Tol = *p*-tolyl-, 167)[142]



A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with Et_2Zn (1.11 M in toluene, 9.01 mL, 10.0 mmol) and the reaction mixture was cooled to –40 °C. Then, 2-((2-(dimethylamino)ethyl)(methyl)amino)ethane-1-ol (2.925 g, 20.0 mmol) was added dropwise and the reaction stirred for 2 h at 25 °C. Then, the reaction mixture was cooled to –40 °C and *p*TolLi (0.98 M in Et_2O, 20.4 mL, 20.0 mmol) added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature and stir for 2 h. The solvents were removed *in vacuo* affording a light yellow oil. Freshly distilled toluene was added under vigorous stirring until the residue was dissolved (6-8 mL). The prepared *p*Tol$_2$Zn·2LiO(CH$_2$)$_2$N(Me)(CH$_2$)$_2$N(Me)$_2$ was titrated prior to use at 0 °C by iodometric titration. The *p*Tol$_2$Zn·2LiO(CH$_2$)$_2$N(Me)(CH$_2$)$_2$N(Me)$_2$ concentration of the resulting clear solution was 0.60-1.00 M.

Titration Using Iodine[178]

A dry flask was charged with accurately weighed I_2 (128 mg, 0.504 mmol), fitted with a rubber septum, and flushed with argon. THF (2 mL) was added and stirring was started. After the iodine was completely dissolved, the resulting brown solution was cooled to 0 °C in an ice bath and the organomagnesium reagent was added dropwise *via* a 1.00-mL syringe (0.01-mL graduations) until the brown color disappeared. The amount consumed contains 0.50 equiv of the organometallic reagent relative to iodine.

5.2 Typical Procedures

Typical Procedure 5: Protection of Polyiodophenol Derivatives

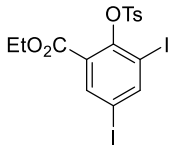
A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding polyiodophenol (1.00 equiv) and dissolved in dry DMF (0.50 M). Then, NaH (60% dispersion in mineral oil, 1.10 equiv) was carefully added at 0 °C. After stirring at 0 °C for 30 min, the corresponding electrophile (1.20 equiv) was added portionwise at 0 °C and the reaction solution was allowed to warm to room temperature overnight. The reaction was then quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel using the appropriate eluent.

Typical Procedure 6: Preparation of Di(hetero)arylzinc Alkoxides *via* an Iodine/Zinc Exchange Followed by Quenching with Allylic Bromides or Acyl Chlorides

A dry and argon-flushed *Schlenk-f*lask, equipped with a magnetic stirring bar and a septum, was charged with the corresponding (hetero)aryl polyiodide (1.0 equiv) and dissolved in dry toluene (0.50 M): Then, the exchange reagent $p\text{Tol}_2\text{Zn}\cdot 2\text{LiO}(\text{CH}_2)_2\text{N}(\text{Me})(\text{CH}_2)_2\text{N}(\text{Me})_2$ (**167**) (0.60 equiv) was added dropwise at the indicated temperature and the reaction stirred for the indicated time. The completion of the iodine/zinc exchange was checked by GC-analysis of reaction aliquots quenched with water, using undecane as internal standard. Subsequent reactions with allylic bromides and acyl chlorides were carried out under the indicated conditions. After complete conversion, the mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. If the crude product needed purification, it was purified by flash chromatography on silica gel using the appropriate eluent.

5.3 Starting Materials

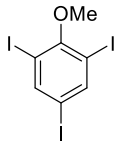
Synthesis of ethyl 3,5-diiodo-2-(tosyloxy)benzoate (171a)



Ethyl 2-hydroxy-3,5-diiodobenzoate (**171a**, 987 mg, 2.36 mmol) was dissolved in dry pyridine (10 mL). Tosyl chloride (541 mg, 2.83 mmol) was then added at 0 °C and the mixture was stirred at room temperature overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (1 0 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 92:8, R_f = 0.21) to give the product **171a** (610 mg, 1.07 mmol, 45%) as a white solid.

M.p. (°C): 107-109.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.16 (dd, *J* = 16.1, 2.2 Hz, 2H), 7.79 – 7.61 (m, 2H), 7.44 – 7.31 (m, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.47 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 163.9, 150.8, 148.0, 146.3, 140.6, 133.5, 130.2, 130.1, 129.1, 93.4, 91.9, 62.6, 22.0, 14.1.
IR (ATR, cm^{-1}) ṽ = 2980, 1721, 1380, 1272, 1174, 740.
MS (EI, 70 eV, %) m/z = 372 (100), 281 (22), 245 (24), 225 (23), 207 (75), 189 (36), 155 (60), 139 (30), 128 (62), 127 (84), 119 (37), 91 (88), 73 (24).
HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{14}I_2O_5S$**: 571.8651; found: 571.8667.

Synthesis of 1,3,5-triiodo-2-methoxybenzene (171b)



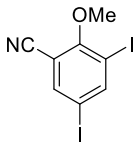
Compound **171b** was prepared *via* **TP5** using 2,4,6-triiodophenol (2.41 g, 5.00 mmol), NaH (60% dispersion in mineral oil, 220 mg, 5.50 mmol) and dry DMF (10 mL). After stirring at 0 °C for 30 min, MeI (852 mg, 6.00 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography

(*iso*hexane:ethyl acetate = 99:1, R_f = 0.47) to give the product **171b** (2.25 g, 4.63 mmol, 95%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.04 (s, 2H), 3.83 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.2, 147.4, 91.8, 89.4, 60.9.

The spectra matched those of the literature.[207]

Synthesis of 3,5-diiodo-2-methoxybenzonitrile (171c)

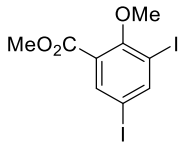


Compound **171c** was prepared *via* **TP5** using 2-hydroxy-3,5-diiodobenzonitrile (1.85 g, 5.00 mmol), NaH (60% dispersion in mineral oil, 220 mg, 5.50 mmol) and dry DMF (10 mL). After stirring at 0 °C for 30 min, MeI (852 mg, 6.00 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.21) to give the product **171c** (1.74 g, 4.52 mmol, 90%) as a yellowish solid.

M.p. (°C): 150-152.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.29 (d, *J* = 2.1 Hz, 1H), 7.84 (d, *J* = 2.1 Hz, 1H), 4.05 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 161.7, 151.9, 142.1, 114.4, 107.9, 93.4, 86.9, 62.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2923, 1465, 1412, 1246, 978, 753.
MS (EI, 70 eV, %) m/z = 385 (100), 370 (39), 342 (14), 243 (54), 127 (34), 88 (28).
HRMS (EI, 70 eV) m/z: calc. for **$C_8H_5I_2NO$**: 384.8460; found: 384.8457.

[207] D. Alberico, A. Rudolph, M. Lautens, *J. Org. Chem.* **2007**, *72*, 775.

Synthesis of methyl 3,5-diiodo-2-methoxybenzoate (171d)



3,5-Diiodosalicylic acid (3.90 g, 10.0 mmol) was dissolved in DMF (20 mL). KOH (1.68 g, 30 mmol) and MeI (1.9 mL) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.57) to give the product **171d** (3.73 g, 8.92 mmol, 89%) as a white solid.

M.p. (°C): 83-85.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.24 (d, *J* = 2.2 Hz, 1H), 8.07 (d, *J* = 2.2 Hz, 1H), 3.92 (s, 3H), 3.87 (s, 3H).

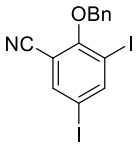
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.6, 156.1, 140.9, 132.2, 129.3, 126.0, 85.5, 62.7, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2944, 1728, 1410, 1273, 1206, 990.

MS (EI, 70 eV, %) m/z = 418 (55), 389 (100), 387 (44), 386 (16), 385 (75), 372 (17), 357 (19), 343 (71), 276 (17), 262 (28), 260 (18), 245 (50), 217 (71), 189 (34), 76 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_9H_8I_2O_3$**: 417.8563; found: 417.8593.

Synthesis of 2-(benzyloxy)-3,5-diiodobenzonitrile (171e)



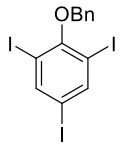
Compound **171e** was prepared *via* **TP5** using 2-hydroxy-3,5-diiodobenzonitrile (2.60 g, 7.00 mmol), NaH (60% dispersion in mineral oil, 308 mg, 7.70 mmol) and dry DMF (20 mL). After stirring at 0 °C for 30 min, BnBr (1.32 g, 7.70 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.32) to give the product **171e** (2.15 g, 4.7 mmol, 67%) as a white solid.

M.p. (°C): 110-112.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.32 (d, *J* = 2.1 Hz, 1H), 7.86 (d, *J* = 2.1 Hz, 1H), 7.66 – 7.49 (m, 2H), 7.48 – 7.32 (m, 3H), 5.20 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.3, 152.0, 142.1, 134.9, 129.2, 128.8, 114.4, 109.1, 94.2, 87.4, 77.1, 29.9.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3059, 2923, 2231, 1433, 1374, 1241.
MS (EI, 70 eV, %) m/z = 91 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_9I_2NO$**: 460.8773; found: 460.8771.

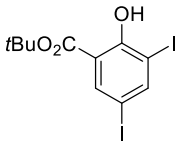
Synthesis of 2-(benzyloxy)-1,3,5-triiodobenzene (171f)



Compound **171f** was prepared *via* **TP5** using 2,4,6-triiodophenol (3.30 g, 7.00 mmol), NaH (60% dispersion in mineral oil, 308 mg, 7.70 mmol) and dry DMF (20 mL). After stirring at 0 °C for 30 min, BnBr (1.44 g, 8.40 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.38) to give the product **171f** (2.68 g, 4.80 mmol, 68%) as a white solid.

M.p. (°C): 120-122.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.10 (s, 2H), 7.73 – 7.54 (m, 2H), 7.48 – 7.36 (m, 3H), 4.98 (s, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 157.7, 147.5, 135.9, 128.7 (3C), 92.4, 89.7, 74.7.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2923, 1424, 1370, 1237, 963, 696.
MS (EI, 70 eV, %) m/z = 435 (7), 343 (5), 189 (12), 91 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_9I_3O$**: 561.7787; found: 561.7791.

Synthesis of tert-butyl 2-hydroxy-3,5-diiodobenzoate[208]



N,*N'*-dicyclohexylcarbodiimide (DCC, 8.00 g, 39 mmol) was dissolved in dry THF (50 mL) and added dropwise over 30 min to a stirred suspension of 3,5-diiodosalicylic acid (14.1 g, 36.1 mmol) and *N*,*N*-

[208] Adapted procedure from: R. Kluger, V. De Stefano, *J. Org. Chem.* **2000**, *65*, 214.

dimethylaminopyridine (DMAP, 170 mg, 1.4 mmol) in tert-butyl alcohol (125 mL). The mixture was stirred at room temperature overnight and then concentrated. The residue was stirred in diethyl ether (50 mL), and oxalic acid (5.3 g, 5.9 mmol) was introduced in portions to decompose excess DCC and precipitate DMAP. The mixture was filtered, and the filtrate was washed with aq. $NaHCO_3$ (0.30 M, 3 x 40 mL) and dried over $MgSO_4$. The solvent was evaporated and the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.70) to give the product (15.2 g, 34.1 mmol, 94%) as a white solid.

M.p. (°C): 137-139.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 11.92 (s, 1H), 8.14 (d, *J* = 2.2 Hz, 1H), 8.01 (d, *J* = 2.2 Hz, 1H), 1.60 (s, 9H).

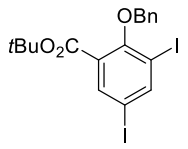
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 168.1, 160.4, 151.6, 138.7, 115.8, 87.0, 84.7, 80.6, 28.2.

IR (ATR, cm^{-1}) ṽ = 2976, 1675, 1430, 1327, 1158, 790.

MS (EI, 70 eV, %) m/z = 390 (100), 373 (22), 372 (98), 57 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{12}I_2O_3$**: 445.8876; found: 445.8862.

Synthesis of tert-butyl 2-(benzyloxy)-3,5-diiodobenzoate (171g)



Compound **171g** was prepared *via* **TP5** using tert-butyl 2-hydroxy-3,5-diiodobenzoate (1.12 g, 2.50 mmol), NaH (60% dispersion in mineral oil, 110 mg, 2.75 mmol) and dry DMF (5 mL). After stirring at 0 °C for 30 min, BnBr (0. 33 mL, 3.00 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.62) to give the product **171g** (1.28 g, 2.38 mmol, 95%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.22 (d, *J* = 2.2 Hz, 1H), 7.94 (d, *J* = 2.2 Hz, 1H), 7.66 – 7.52 (m, 2H), 7.49 – 7.32 (m, 3H), 5.03 (s, 2H), 1.54 (s, 9H).

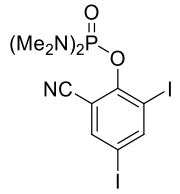
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 163.4, 157.1, 150.0, 139.9, 136.5, 130.2, 128.5, 128.3, 128.3, 95.7, 88.1, 82.9, 76.4, 28.2.

IR (ATR, cm^{-1}) ṽ = 2978, 1722, 1369, 1286, 1158.

MS (EI, 70 eV, %) m/z = 480 (21), 91 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{18}I_2O_3$**: 535.9345; found: 535.9616.

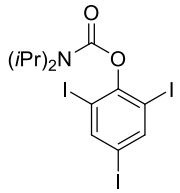
Synthesis of bis-(*N*,*N*-dimethylamido)-*O*-2,4-diiodo-6-cyanophenylphosphate (171h)[93]



2-hydroxy-3,5-diiodobenzonitrile (1.85 g, 5.00 mmol) was dissolved in dry THF (15 mL). Et_3N (0.83 mL, 6.00 mmol), DMAP (61 mg, 0.50 mmol) and tetramethyl-phosphorodiamidic acid chloride (0.74 mL, 5.00 mmol) were then added at 0 °C and the mixture was stirred at room temperature overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified *via* column chromatography (ethyl acetate, $R_f = 0.20$) to give the product **171h** (1.38 g, 2.70 mmol, 55%) as an off-white solid.

M.p. (°C): 194-196.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.33 (dd, *J* = 2.1, 0.7 Hz, 1H), 7.87 (dd, *J* = 2.1, 0.5 Hz, 1H), 2.84 (s, 6H), 2.81 (s, 6H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 153.6 (d, *J* = 6.8 Hz), 152.4 (d, *J* = 1.6 Hz), 142.3 (d, *J* = 1.7 Hz), 114.4, 110.0 (d, *J* = 2.9 Hz), 93.0 (d, *J* = 4.0 Hz), 88.2 (d, *J* = 2.4 Hz), 37.3 (d, *J* = 4.7 Hz).
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2927, 2233, 1430, 1242, 995, 749.
MS (EI, 70 eV, %) m/z = 398 (13), 378 (17), 135 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{14}I_2N_3O_2P$**: 504.8913; found: 504.8904.

Synthesis of 2,4,6-triiodophenyl diisopropylcarbamate (171i)[209]



2,4,6-triiodophenol (2.36 g, 5.00 mmol) was dissolved in dry pyridine (5 mL) in a round bottom flask equipped with an air condenser and a stirring bar. DMAP (61 mg, 0.50 mmol) and diisopropyl carbamoyl chloride (818 mg, 5.00 mmol) were then added at 25 °C and the mixture was heated to reflux

[209] Adapted procedure from: J. Clayden, *J. Chem. Soc., Perkin Trans. 1* **2000**, 3232.

for 2 days. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.28) to give the product **171i** (887 mg, 1.48 mmol, 30%) as a yellow solid.

M.p. (°C): 126-128.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.06 (s, 2H), 4.29 (p, *J* = 6.8 Hz, 1H), 3.87 (p, *J* = 6.8 Hz, 1H), 1.40 (d, *J* = 6.8 Hz, 6H), 1.35 (d, *J* = 6.8 Hz, 6H).

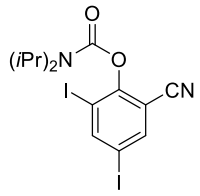
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 152.3, 150.0, 146.9, 93.0, 90.7, 47.7, 46.8, 21.8, 20.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2966, 1724, 1416, 1311, 1231.

MS (EI, 70 eV, %) m/z = 472 (47), 345 (10), 218 (13), 189 (21), 128 (97), 86 (100), 43 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{16}I_3NO_2$**: 598.8315; found: 598.8406.

Synthesis of 2-cyano-4,6-diiodophenyl diisopropylcarbamate (171j)[209]



2-hydroxy-3,5-diiodobenzonitrile (927 mg, 2.50 mmol) was dissolved in dry pyridine (2.5 mL) in a round bottom flask equipped with an air condenser and a stirring bar. DMAP (30 mg, 0.25 mmol) and diisopropyl carbamoyl chloride (409 mg, 2.50 mmol) were then added at 25 °C and the mixture was heated to reflux for 2 days. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 96:4, R_f = 0.18) to give the product **171j** (1.03 g, 2.07 mmol, 83%) as an off-white solid.

M.p. (°C): 96-98.

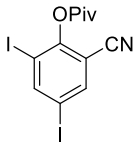
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.32 (d, *J* = 2.0 Hz, 1H), 7.88 (d, *J* = 2.0 Hz, 1H), 4.19 (p, *J* = 6.8 Hz, 1H), 3.96 (p, *J* = 6.8 Hz, 1H), 1.40 (d, *J* = 6.9 Hz, 6H), 1.34 (d, *J* = 6.7 Hz, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 154.1, 151.3, 150.3, 141.2, 113.5, 111.0, 94.5, 89.3, 47.6, 47.5, 21.6, 20.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2971, 1725, 1419, 1311, 1136.

MS (EI, 70 eV, %) m/z = 371 (52), 128 (100), 86 (61), 43 (44).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{16}I_2N_2O_2$**: 497.9301; found: 497.9305.

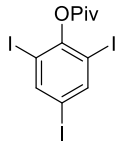
Synthesis of 2-cyano-4,6-diiodophenyl pivalate (171k)[210]



2-hydroxy-3,5-diiodobenzonitrile (927 mg, 2.50 mmol) and Et_3N (0.50 mL) were dissolved in dry THF (5.0 mL) in a round bottom flask. Pivaloyl chloride (0.31 mL, 2.50 mmol) was then added at 0 °C and the mixture was allowed to warm to room temperature overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.24) to give the product **171k** (1.01 g, 2.21 mmol, 89%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.35 (d, *J* = 2.0 Hz, 1H), 7.91 (d, *J* = 2.0 Hz, 1H), 1.46 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 174.9, 153.4, 151.7, 141.4, 113.1, 110.2, 93.5, 90.0, 39.6, 27.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2973, 1771, 1433, 1070, 1025.
MS (EI, 70 eV, %) m/z = 371 (100), 342 (10), 243 (21), 127 (14), 88 (23), 57 (23), 41 (11).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{11}I_2NO_2$**: 454.8879; found: 454.8874.

Synthesis of 2,4,6-triiodophenyl pivalate (171l)[210]



2,4,6-triiodophenol (2.36 g, 5.00 mmol) and Et_3N (1 mL) were dissolved in dry THF (10 mL) in a round bottom flask. Pivaloyl chloride (0.62 mL, 5.00 mmol) was then added at 0 °C and the mixture was allowed to warm to room temperature overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude

[210] Adapted procedure from: M. H. Aukland, M. Šiaučiulis, A. West, G. J. P. Perry, D. J. Procter, *Nat. Cat.* **2020**, *3*, 163.

product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.18) to give the product **171l** (1.49 g, 2.68 mmol, 54%) as an off-white solid.

M.p. (°C): 103-105.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.08 (s, 2H), 1.46 (s, 9H).

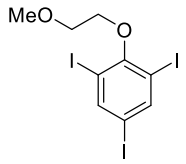
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 174.5, 151.9, 147.3, 91.8, 91.4, 39.7, 27.6.

IR (ATR, cm^{-1}) ṽ = 2971, 1768, 1539, 1421, 1080.

MS (EI, 70 eV, %) m/z = 472 (100), 344 (18), 218 (11), 189 (36), 127 (16), 57 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{11}H_{11}I_3O_2$**: 555.7893; found: 555.7897.

Synthesis of 1,3,5-triiodo-2-(2-methoxyethoxy)benzene (171m)



Compound **171m** was prepared *via* **TP5** using 2,4,6-triiodophenol (4.50 g, 9.50 mmol), NaH (60% dispersion in mineral oil, 456 mg, 11.40 mmol) and dry DMF (19 mL). After stirring at 0 °C for 30 min, 1-chloro-2-methoxyethane (1.05 mL, 11.40 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.31) to give the product **171m** (3.56 g, 6.72 mmol, 71%) as a yellow solid.

M.p. (°C): 92-94.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.05 (s, 2H), 4.13 (dd, *J* = 5.4, 4.3 Hz, 2H), 3.87 (dd, *J* = 5.4, 4.3 Hz, 2H), 3.49 (s, 3H).

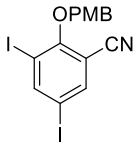
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 158.1, 147.5, 92.1, 89.5, 72.2, 71.6, 59.4.

IR (ATR, cm^{-1}) ṽ = 2924, 1427, 1359, 1245, 1128.

MS (EI, 70 eV, %) m/z = 530 (14), 472 (11), 62 (10), 59 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_9H_9I_3O_2$**: 529.7737; found: 529.7729.

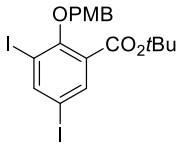
Synthesis of 3,5-diiodo-2-((4-methoxybenzyl)oxy)benzonitrile (171n)



Compound **171n** was prepared *via* **TP5** using 2-hydroxy-3,5-diiodobenzonitrile (464 mg, 1.25 mmol), NaH (60% dispersion in mineral oil, 55 mg, 1.38 mmol) and dry DMF (5 mL). After stirring at 0 °C for 30 min, 4-methoxybenzyl chloride (0.19 mL, 1.38 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.28) to give the product **171n** (300 mg, 0.61 mmol, 49%) as a pink solid.

M.p. (°C): 126-128.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.31 (d, *J* = 2.1 Hz, 1H), 7.84 (d, *J* = 2.1 Hz, 1H), 7.60 – 7.39 (m, 2H), 7.04 – 6.81 (m, 2H), 5.14 (s, 2H), 3.83 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.3 (2C), 151.9, 142.0, 131.1, 127.0, 114.5, 114.1, 109.3, 94.4, 87.3, 76.9, 55.5.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2932, 1611, 1514, 1436, 1239.
MS (EI, 70 eV, %) m/z = 371 (16), 121 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{11}I_2NO_2$**: 490.8879; found: 490.8867.

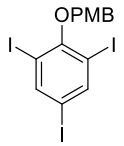
Synthesis of tert-butyl 3,5-diiodo-2-((4-methoxybenzyl)oxy)benzoate (171o)



Compound **171o** was prepared *via* **TP5** using tert-butyl 2-hydroxy-3,5-diiodobenzoate (1.12 g, 2.50 mmol), NaH (60% dispersion in mineral oil, 110 mg, 2.75 mmol) and dry DMF (5 mL). After stirring at 0 °C for 30 min, PMBCl (0. 38 mL, 3.00 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.46) to give the product **171o** (937 mg, 1.65 mmol, 66%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.21 (d, *J* = 2.2 Hz, 1H), 7.93 (d, *J* = 2.2 Hz, 1H), 7.57 – 7.37 (m, 2H), 7.07 – 6.70 (m, 2H), 4.96 (s, 2H), 3.83 (s, 3H), 1.56 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 163.4, 159.8, 157.2, 149.9, 139.9, 130.2, 130.2, 128.7, 113.9, 95.9, 88.0, 82.9, 76.3, 55.4, 28.2.
IR (ATR, cm^{-1}) ṽ = 2974, 1721, 1514, 1244, 1158.
MS (EI, 70 eV, %) m/z = 122 (19), 121 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{20}I_2O_4$**: 565.9451; found: 565.9449.

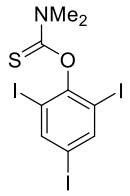
Synthesis of 1,3,5-triiodo-2-((4-methoxybenzyl)oxy)benzene (171p)



Compound **171p** was prepared *via* **TP5** using 2,4,6-triiodophenol (1.18 g, 2.50 mmol), NaH (60% dispersion in mineral oil, 110 mg, 2.75 mmol) and dry DMF (7 mL). After stirring at 0 °C for 30 min, 4-methoxybenzyl chloride (0.37 mL, 2.75 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.42) to give the product **171p** (1.28 g, 2.16 mmol, 86%) as an off-white solid.

M.p. (°C): 143-145.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.09 (s, 2H), 7.62 – 7.49 (m, 2H), 7.04 – 6.75 (m, 2H), 4.91 (s, 2H), 3.84 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.1, 157.7, 147.5, 130.6, 128.0, 114.0, 92.6, 89.6, 74.6, 55.5.
IR (ATR, cm^{-1}) ṽ = 2927, 1514, 1427, 1234, 816.
MS (EI, 70 eV, %) m/z = 472 (5), 122 (8), 121 (100), 78 (3), 77 (3), 62 (3).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}I_3O_2$**: 591.7893; found: 591.7886.

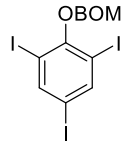
Synthesis of *O*-(2,4,6-triiodophenyl) dimethylcarbamothioate (171q)



Compound **171q** was prepared *via* **TP5** using 2,4,6-triiodophenol (1.42 g, 3.00 mmol), NaH (60% dispersion in mineral oil, 132 mg, 3.30 mmol) and dry DMF (5 mL). After stirring at 0 °C for 30 min, DMAP (18 mg, 0.15 mmol) and dimethylthiocarbamoyl chloride (445 mg, 3.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.37) to give the product **171q** (881 mg, 1.58 mmol, 53%) as an orange solid.

M.p. (°C): 176-178.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.09 (s, 2H), 3.49 (s, 3H), 3.44 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 183.4, 153.9, 147.0, 93.5, 91.5, 43.8, 39.5.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2935, 1544, 1409, 1394, 1216.
MS (EI, 70 eV, %) m/z = 432 (100), 178 (17), 88 (55), 72 (40).
HRMS (EI, 70 eV) m/z: calc. for **$C_7H_2I_3OS$**: 514.6960; found: 514.7058.

Synthesis of 2-((benzyloxy)methoxy)-1,3,5-triiodobenzene (171r)

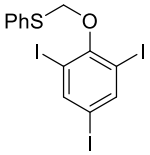


Compound **171r** was prepared *via* **TP5** using 2,4,6-triiodophenol (1.18 g, 2.50 mmol), NaH (60% dispersion in mineral oil, 110 mg, 2.75 mmol) and dry DMF (7 mL). After stirring at 0 °C for 30 min, benzyl chloromethyl ether (0.41 mL, 3.00 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.43) to give the product **171r** (1.40 g, 2.37 mmol, 95%) as an orange solid.

M.p. (°C): 80-82.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.08 (s, 2H), 7.46 – 7.28 (m, 5H), 5.25 (s, 2H), 5.02 (s, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 156.9, 147.6, 137.3, 128.6, 128.1 (2 C), 98.3, 92.7, 89.7, 72.7.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2941, 1436, 1394, 1158, 923.
MS (EI, 70 eV, %) m/z = 562 (10), 472 (11), 91 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}I_3O_2$**: 591.7893; found: 591.7886.

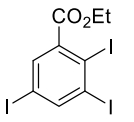
Synthesis of phenyl((2,4,6-triiodophenoxy)methyl)sulfane (171s)



Compound **171s** was prepared *via* **TP5** using 2,4,6-triiodophenol (1.18 g, 2.50 mmol), NaH (60% dispersion in mineral oil, 110 mg, 2.75 mmol) and dry DMF (5 mL). After stirring at 0 °C for 30 min, (chloromethyl)(phenyl)sulfane (0.40 mL, 3.00 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.57) to give the product **171s** (1.22 g, 2.06 mmol, 82%) as an off-white solid.

M.p. (°C): 101-103.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.03 (s, 2H), 7.68 – 7.55 (m, 2H), 7.42 – 7.20 (m, 3H), 5.42 (s, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 157.3, 147.6, 134.8, 131.5, 129.1, 127.6, 92.7, 90.2, 78.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3447, 3052, 1436, 1137, 737.
MS (EI, 70 eV, %) m/z = 467 (17), 124 (17), 123 (100), 45 (17).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_9I_3OS$**: 593.7508; found: 593.7496.

Synthesis of ethyl 2,3,5-triiodobenzoate (171t)[211]



2,3,5-triiodobenzoic acid (10.0 g, 20.0 mmol) and EtOH (60 mL) were placed in a round bottom flask equipped with a reflux condenser and a stirring bar. H_2SO_4 (96%, 3 mL) was added and the mixture was heated to reflux overnight. The reaction solution was allowed to cool down to room temperature

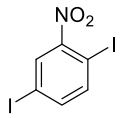
[211] Adapted procedure from: X. Yang, T. Rotter, C. Piazza, P. Knochel, *Org. Lett.* **2003**, *5*,1229.

overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was recrystallized from pentane/MeOH to give the product **171t** (6.39 g, 12.1 mmol, 61%) as an off-white solid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.29 (d, *J* = 2.0 Hz, 1H), 7.72 (d, *J* = 2.0 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.3, 148.8, 141.9, 137.0, 113.4, 106.6, 93.8, 62.7, 14.2.

The spectra matched those of the literature.[211]

Synthesis of 1,4-diiodo-2-nitrobenzene (171u)[51b]

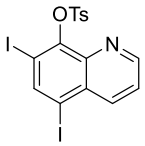


A 50 mL round-bottom flask, equipped with a magnetic stirring bar and a dropping funnel was charged with water (5.7 mL) and H_2SO_4 (96%, 5.25 mL). Glacial acetic acid (5.25 mL) and 4-iodo-2-nitroaniline (1.98 g, 7.50 mmol) were added at 0 °C. Afterwards, a solution of $NaNO_2$ (569 mg, 8.25 mmol, in 2.25 mL H_2O) was added dropwies over a period of 1 h. On completion of the addition the mixture was stirred for 30 min and a solution of KI (1.50 g, 9.00 mmol, in 2.25 mL H_2O) was added dropwise with a strong evolution of gas (N_2). On completion of addition the sticky mixture was heated to 60 °C for 1 h, cooled again to 0 °C and diethyl ether was added until all precipitate was dissolved and the reaction mixture was poured into saturated $NaHCO_3$(aq) solution (30 mL) in a separatory funnel. After extraction with diethyl ether (2 x 30 ml) the organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was recrystallized from ethanol to give compound **171u** (2.13 g, 5.68 mmol, 76%) as a yellow-orange powder.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.14 (d, *J* = 2.0 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 1H), 7.56 (dd, *J* = 8.3, 2.0 Hz, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 153.6, 143.2, 142.5, 134.2, 93.0, 85.7.

The spectra matched those of the literature.[51b]

Synthesis of 5,7-diiodoquinolin-8-yl 4-methylbenzenesulfonate (174a)[30]

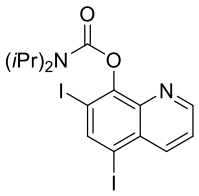


5,7-diiodoquinolin-8-ol (3.97 g, 10.0 mmol) was dissolved in dry THF (10 mL) and NaOH (3.75 M in H_2O, 8.8 mL, 33.0 mmol) was added. Tosyl chloride (2.29 g, 12.0 mmol) was then added at 0 °C and the mixture was stirred at room temperature overnight. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was washed with pentane to give the product **174a** (5.30 g, 9.60 mmol, 96%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.72 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.49 (s, 1H), 8.30 (dd, *J* = 8.6, 1.6 Hz, 1H), 8.00 – 7.92 (m, 2H), 7.49 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 2H), 2.49 (s, 3H). **^{13}C-NMR (101 MHz, $CDCl_3$, ppm)** δ = 151.6, 149.9, 145.6, 145.3, 142.6, 140.4, 135.4, 131.2, 129.6, 129.1, 123.9, 97.0, 92.7, 22.0.

The spectra matched those of the literature.[30]

Synthesis of 5,7-diiodoquinolin-8-yl diisopropylcarbamate (174b)[209]



2-hydroxy-3,5-diiodobenzonitrile (3.90 g, 10.0 mmol) was dissolved in dry pyridine (10 mL) in a round bottom flask equipped with an air condenser and a stirring bar. DMAP (120 mg, 1.00 mmol) and diisopropyl carbamoyl chloride (1.64 g, 10.0 mmol) were then added at 25 °C and the mixture was heated to reflux for 2 days. The mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), diluted with water (10 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.17) to give the product **174b** (1.47 g, 2.80 mmol, 28%) as a white solid.

M.p. (°C): 121-123.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.82 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.46 (s, 1H), 8.28 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.47 (dd, *J* = 8.5, 4.2 Hz, 1H), 4.27 – 4.15 (m, 1H), 4.15 – 4.05 (m, 1H), 1.50 (dd, *J* = 11.7, 6.8 Hz, 6H), 1.34 (t, *J* = 6.2 Hz, 6H).

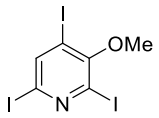
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 152.4, 151.4, 151.0, 144.7, 142.6, 140.3, 131.0, 123.5, 94.5, 92.7, 47.1, 47.1, 22.2, 21.7, 20.8, 20.6.

IR (ATR, cm^{-1}) ṽ = 2968, 1708, 1304, 1204, 1038, 745.

MS (EI, 70 eV, %) m/z = 398 (10), 397 (100), 369 (6), 270 (21), 269 (8), 242 (21), 241 (11), 143 (11), 128 (42), 115 (22), 114 (17), 87 (6), 86 (72), 43 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{18}I_2N_2O_2$**: 523.9458; found: 523.9455.

Synthesis of 2,4,6-triiodo-3-methoxypyridine (174c)



Compound **174c** was prepared *via* **TP5** using 2,4,6-triiodopyridin-3-ol (2.84 g, 6.00 mmol), NaH (60% dispersion in mineral oil, 264 mg, 6.60 mmol) and dry DMF (12 mL). After stirring at 0 °C for 30 min, MeI (0.45 mL, 7.20 mmol) was added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.29) to give the product **174c** (1.40 g, 2.89 mmol, 48%) as a yellowish solid.

M.p. (°C): 112-114.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.04 (s, 1H), 3.89 (s, 3H).

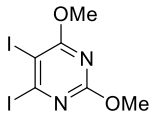
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 157.7, 143.8, 113.8, 109.6, 102.4, 61.3.

IR (ATR, cm^{-1}) ṽ = 3075, 1733, 1419, 1394, 1202.

MS (EI, 70 eV, %) m/z = 487 (100), 360 (53), 345 (21), 330 (38), 233 (27), 190 (41), 127 (29).

HRMS (EI, 70 eV) m/z: calc. for **$C_6H_4I_3NO$**: 486.7427; found: 486.7419.

Synthesis of 4,5-diiodo-2,6-dimethoxypyrimidine (174e)[212]



A dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirring bar and a septum, was charged with TMPMgCl·LiCl[13] (11.0 mmol, 1.12 M in THF, 9.8 mL, 1.1 equiv) and 2,4-dimethoxypyrimidine (10.0 mmol, 1.40 g, 1.0 equiv) dissolved in dry THF (10 mL) was added dropwise at –40 °C. The reaction mixture was stirred for 12 h at this temperature and the completion of the deprotonation was checked by GC-analysis of reaction aliquots quenched with iodine using decane as internal standard. Iodine (11.0 mmol, 2.80 g, 1.2 equiv) was added and the reaction mixture was stirred for 2 h at –30 °C. The mixture was warmed to –30 °C and TMPMgCl·LiCl (15.0 mmol, 1.12 M, 13.4 mL, 1.5 equiv) was added dropwise. The mixture was warmed to 0 °C and stirred for 2 h. Iodine (20.0 mmol, 5.14 g, 2.0 equiv) was added at 25 °C and the mixture was stirred for 3 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ (60 mL) solution at 0 °C, extracted with EtOAc (3 x 50 mL), the organic layer was washed with brine and dried over Na_2SO_4. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.63) to give the product **174e** (3.68 g, 9.39 mmol, 94%) as a white solid.

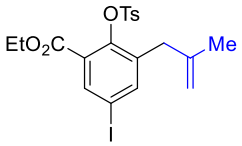
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 3.99 (s, 3H), 3.97 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 169.1, 163.7, 142.0, 84.3, 56.0, 55.8.

The spectra matched those of the literature.[212]

[212] Adapted procedure from: M. Mosrin, N. Boudet, P. Knochel, *Org. Biomol. Chem.* **2008**, *6*, 3237.

5.4 Preparation of Compounds 173 to 176

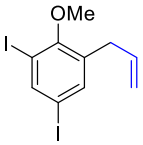
Synthesis of ethyl 5-iodo-3-(2-methylallyl)-2-(tosyloxy)benzoate (173a)



Allylated tosylate **173a** was prepared *via* **TP6** using ethyl 3,5-diiodo-2-(tosyloxy)benzoate (**171a**, 229 mg, 0.40 mmol) and dry toluene (0.80 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.24 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (7.60 mg, 40 µmol) and methallyl bromide (49 µL, 0.48 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 92:8, R_f = 0.28) to give the product **173a** (123 mg, 246 µmol, 61%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.02 (d, *J* = 2.3 Hz, 1H), 7.86 – 7.69 (m, 2H), 7.63 (d, *J* = 2.3 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 2H), 4.84 (t, *J* = 1.7 Hz, 1H), 4.68 – 4.54 (m, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.94 (s, 2H), 2.47 (s, 3H), 1.53 (t, *J* = 1.1 Hz, 3H), 1.38 (t, *J* = 7.2 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 164.4, 145.9, 145.7, 142.7, 142.3, 138.5, 137.3, 133.1, 130.1, 129.5, 128.6, 114.4, 91.5, 62.1, 37.5, 22.1, 21.9, 14.2.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2979, 1729, 1285, 1178, 1088.
MS (EI, 70 eV, %) m/z = 345 (21), 299 (29), 219 (14), 218 (100), 173 (14), 172 (52), 155 (18), 116 (13), 115 (21), 91 (63), 65 (10).
HRMS (EI, 70 eV) m/z: calc. for **$C_{20}H_{21}IO_5S$**: 500.0154; found: 500.0155.

Synthesis of 1-allyl-3,5-diiodo-2-methoxybenzene (173b)

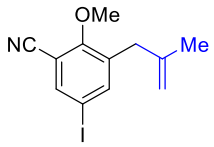


Anisole **173b** was prepared *via* **TP6** using 2,4,6-triiodoanisole (**171b**, 243 mg, 0.50 mmol) and dry toluene (5.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (7.60 mg, 40 µmol) and allyl bromide (52 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product

was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.33) to give the product **173b** (186 mg, 465 µmol, 93%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.95 (d, *J* = 2.1 Hz, 1H), 7.46 (d, *J* = 2.1 Hz, 1H), 5.91 (ddt, *J* = 16.8, 10.1, 6.6 Hz, 1H), 5.31 – 4.97 (m, 2H), 3.76 (s, 3H), 3.40 (dt, *J* = 6.5, 1.6 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 158.0, 145.2, 139.6, 136.7, 135.9, 117.3, 93.5, 89.0, 61.3, 34.5.
IR (ATR, cm^{-1}) ṽ = 2933, 1456, 1411, 1224, 996.
MS (EI, 70 eV, %) m/z = 400 (74), 371 (40), 258 (83), 257 (37), 244 (82), 146 (80), 132 (10), 131 (100), 115 (43), 103 (67), 102 (15), 89 (15), 77 (19).
HRMS (EI, 70 eV) m/z: calc. for **$C_{10}H_{10}I_2O$**: 399.8821; found: 399.8815.

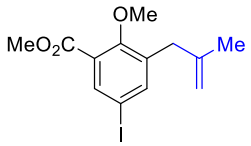
Synthesis of 5-iodo-2-methoxy-3-(2-methylallyl)benzonitrile (173c)



Benzonitrile **173c** was prepared *via* **TP6** using 3,5-diiodo-2-methoxybenzonitrile (**171c**, 193 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol_2Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (9.50 mg, 50 µmol) and methallyl bromide (60 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.38) to give the product **173c** (131 mg, 418 µmol, 84%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.73 (d, *J* = 2.3 Hz, 1H), 7.67 (d, *J* = 2.3 Hz, 1H), 4.88 (d, *J* = 0.9 Hz, 1H), 4.74 – 4.52 (m, 1H), 3.99 (s, 3H), 3.29 (s, 2H), 1.71 (t, *J* = 1.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.8, 144.3, 143.2, 140.1, 136.4, 115.4, 113.3, 107.7, 86.0, 62.3, 37.3, 22.5.
IR (ATR, cm^{-1}) ṽ = 2935, 2232, 1470, 1422, 1221.
MS (EI, 70 eV, %) m/z = 313 (100), 284 (28), 186 (90), 171 (78), 170 (37), 157 (65), 156 (86), 154 (26), 143 (38), 115 (51).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{12}INO$**: 312.9964; found: 312.9957.

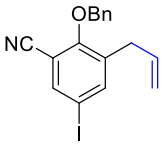
Synthesis of methyl 5-iodo-2-methoxy-3-(2-methylallyl)benzoate (173d)



Methyl benzoate **173d** was prepared *via* **TP6** using methyl 3,5-diiodo-2-methoxybenzoate (**171d**, 209 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (9.50 mg, 50 µmol) and methallyl bromide (60 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.58) to give the product **173d** (132 mg, 381 µmol, 76%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.98 (d, *J* = 2.3 Hz, 1H), 7.64 (d, *J* = 2.3 Hz, 1H), 4.87 (s, 1H), 4.65 (s, 1H), 3.91 (s, 3H), 3.79 (s, 3H), 3.33 (s, 2H), 1.72 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 165.5, 158.6, 143.9, 143.3, 138.5, 137.2, 126.7, 113.1, 86.9, 62.7, 52.6, 37.3, 22.6.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2980, 1715, 1658, 1265, 1101, 712.
MS (EI, 70 eV, %) m/z = 346 (44), 315 (14), 314 (100), 313 (30), 299 (22), 286 (16), 283 (49), 259 (12), 188 (13), 187 (95), 172 (45), 171 (11), 159 (18), 145 (21), 144 (30), 129 (31), 128 (39), 116 (24), 115 (41), 91 (11).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{15}IO_3$**: 346.0066; found: 346.0061.

Synthesis of 3-allyl-2-(benzyloxy)-5-iodobenzonitrile (173e)



Benzonitrile **173e** was prepared *via* **TP6** using 2-(benzyloxy)-3,5-diiodobenzonitrile (**171e**, 231 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (9.50 mg, 50 µmol) and allyl bromide (52 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.24) to give the product **173e** (146 mg, 389 µmol, 78%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.78 (d, *J* = 2.2 Hz, 1H), 7.69 (dd, *J* = 2.2, 0.7 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.43 – 7.35 (m, 3H), 5.81 (ddt, *J* = 16.7, 10.0, 6.5 Hz, 1H), 5.16 (s, 2H), 5.13 (dq, *J* = 10.1, 1.4 Hz, 1H), 5.05 (dq, *J* = 17.0, 1.6 Hz, 1H), 3.31 (dt, *J* = 6.6, 1.5 Hz, 2H).

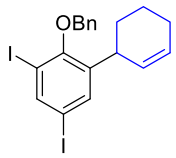
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.0, 144.1, 140.1, 137.3, 135.7, 135.1, 128.9, 128.8, 128.7, 117.8, 115.6, 108.6, 86.6, 77.1, 33.6.

IR (ATR, cm^{-1}) ṽ = 3066, 2232, 1445, 1211, 696.

MS (EI, 70 eV, %) m/z = 283 (2), 157 (3), 117 (6), 102 (2), 92 (8), 91 (100), 65 (5).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{14}INO$**: 375.0120; found: 375.0108.

Synthesis of 2'-(benzyloxy)-3',5'-diiodo-1,2,3,4-tetrahydro-1,1'-biphenyl (173f)



Benzyl ether **173f** was prepared *via* **TP6** using 2-(benzyloxy)-1,3,5-triiodobenzene (**171f**, 281 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (9.50 mg, 50 µmol) and 3-bromocyclohexene (69 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.44) to give the product **173f** (147 mg, 285 µmol, 57%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.98 (d, *J* = 2.1 Hz, 1H), 7.52 (d, *J* = 7.1 Hz, 2H), 7.48 (d, *J* = 2.1 Hz, 1H), 7.41 (td, *J* = 6.1, 1.3 Hz, 2H), 7.39 – 7.33 (m, 1H), 5.94 – 5.88 (m, 1H), 5.50 (dd, *J* = 10.0, 2.5 Hz, 1H), 4.97 (d, *J* = 10.7 Hz, 1H), 4.86 (d, *J* = 10.8 Hz, 1H), 3.74 (ddt, *J* = 8.6, 5.7, 2.8 Hz, 1H), 2.14 – 2.01 (m, 2H), 2.01 – 1.93 (m, 1H), 1.75 – 1.67 (m, 1H), 1.62 – 1.55 (m, 1H), 1.50 – 1.43 (m, 1H).

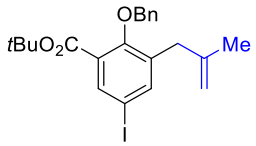
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 156.2, 145.0, 143.7, 138.7, 136.6, 129.6, 129.2, 128.7, 128.5, 128.2, 93.8, 89.5, 75.9, 36.0, 31.7, 24.9, 21.3.

IR (ATR, cm^{-1}) ṽ = 2924, 1430, 1219, 972, 695.

MS (EI, 70 eV, %) m/z = 425 (19), 423 (3), 359 (5), 298 (5), 207 (6), 152 (3), 128 (4), 115 (6), 92 (8), 91 (100), 89 (3), 65 (4).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{18}I_2O$**: 515.9447; found: 515.9441.

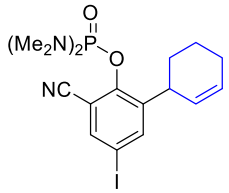
Synthesis of tert-butyl 2-(benzyloxy)-5-iodo-3-(2-methylallyl)benzoate (173g)



Tert-butyl benzoate **173g** was prepared *via* **TP6** using tert-butyl 2-(benzyloxy)-3,5-diiodobenzoate (**171g**, 214 mg, 0.40 mmol) and dry toluene (0.80 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.24 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (7.60 mg, 40 µmol) and methallyl bromide (49 µL, 0.48 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.56) and HPLC to give the product **173g** (163 mg, 351 µmol, 88%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.87 (d, *J* = 2.3 Hz, 1H), 7.60 (d, *J* = 2.3 Hz, 1H), 7.51 – 7.40 (m, 2H), 7.39 – 7.35 (m, 2H), 7.35 – 7.30 (m, 1H), 4.93 (s, 2H), 4.85 (t, *J* = 1.7 Hz, 1H), 4.62 (dt, *J* = 2.2, 1.0 Hz, 1H), 3.26 (s, 2H), 1.81 – 1.63 (m, 3H), 1.56 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 164.6, 156.4, 144.0, 142.4, 137.9, 137.3, 137.1, 129.5, 128.6, 128.2, 127.9, 113.2, 87.2, 82.3, 76.8, 37.4, 28.3, 22.6.
IR (ATR, cm^{-1}) ṽ = 2975, 1718, 1292, 1140, 696.
MS (EI, 70 eV, %) m/z = 408 (18), 131 (17), 91 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{22}H_{25}IO_3$**: 464.0848; found: 464.0852.

Synthesis of *bis*-(*N*,*N*-dimethylamido)-*O*-2-cyclohex-3'-ene-4-iodo-6-cyanophenylphosphate (173h)

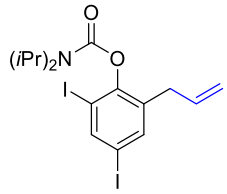


Phosphoramide **173h** was prepared *via* **TP6** using *bis*-(*N*,*N*-dimethylamido)-*O*-2,4-diiodo-6-cyanophenylphosphate (**171h**, 202 mg, 0.40 mmol) and dry toluene (0.80 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.24 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (15 mg, 80 µmol) and 3-bromocyclohexene (55 µL, 0.48 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column

chromatography (*iso*hexane:ethyl acetate = 1:1, R_f = 0.20) to give the product **173h** (113 mg, 246 µmol, 62%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.86 – 7.57 (m, 2H), 5.97 (dtd, *J* = 9.9, 3.7, 2.4 Hz, 1H), 5.68 – 5.50 (m, 1H), 3.93 (ddt, *J* = 8.3, 5.6, 2.8 Hz, 1H), 2.80 (d, *J* = 0.7 Hz, 6H), 2.77 (d, *J* = 0.7 Hz, 6H), 2.17 – 2.06 (m, 2H), 2.07 – 1.97 (m, 1H), 1.74 – 1.66 (m, 1H), 1.65 – 1.55 (m, 1H), 1.42 (dddd, *J* = 13.3, 10.4, 8.2, 3.0 Hz, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 150.6 (d, *J* = 7.0 Hz), 143.4 (2 C), 139.9 (d, *J* = 1.7 Hz), 130.2, 128.4, 115.4 (d, *J* = 1.4 Hz), 109.5 (d, *J* = 3.1 Hz), 88.2 (d, *J* = 2.5 Hz), 36.9 (dd, *J* = 12.0, 4.6 Hz), 35.2 (d, *J* = 0.8 Hz), 31.1, 24.9, 21.0.
IR (ATR, cm^{-1}) ṽ = 2928, 1448, 1231, 993, 751.
MS (EI, 70 eV, %) m/z = 459 (21), 415 (5), 352 (12), 258 (5), 207 (6), 182 (4), 153 (13), 135 (100), 127 (8), 92 (9), 44 (9).
HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{23}IN_3O_2P$**: 459.0573; found: 459.0569.

Synthesis of 2-allyl-4,6-diiodophenyl diisopropylcarbamate (173i)

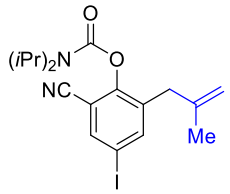


Carbamate **173i** was prepared *via* **TP6** using 2,4,6-triiodophenyl diisopropylcarbamate (**171i**, 240 mg, 0.40 mmol) and dry toluene (0.80 mL). Then, *p*Tol_2Zn·2LiOR (**167** 0.24 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (15 mg, 80 µmol) and allyl bromide (42 µL, 0.48 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.18) to give the product **173i** (145 mg, 283 µmol, 71%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.97 (d, *J* = 2.0 Hz, 1H), 7.48 (d, *J* = 2.1 Hz, 1H), 5.85 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.22 – 4.99 (m, 2H), 4.26 (p, *J* = 6.8 Hz, 1H), 3.86 (p, *J* = 6.7 Hz, 1H), 3.36 – 3.13 (m, 2H), 1.48 – 1.21 (m, 12H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 151.1, 150.3, 144.9, 139.1, 137.0, 135.0, 117.5, 94.2, 90.6, 47.4, 46.6, 35.3, 21.8, 21.6, 20.7, 20.6.
IR (ATR, cm^{-1}) ṽ = 2969, 2361, 1717, 1419, 1316.

MS (EI, 70 eV, %) m/z = 386 (11), 257 (15), 132 (26), 131 (25), 128 (80), 127 (11), 103 (17), 86 (100), 77 (13), 43 (20).
HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{21}I_2NO_2$**: 512.9662; found: 512.9662.

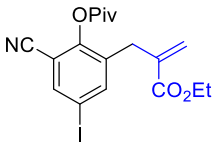
Synthesis of 2-cyano-4-iodo-6-(2-methylallyl)phenyl diisopropylcarbamate (173j)



Compound **173j** was prepared *via* **TP6** using 2-cyano-4,6-diiodophenyl diisopropylcarbamate (**171j**, 199 mg, 0.40 mmol) and dry toluene (0.80 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.26 mL, 0.26 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (15 mg, 80 µmol) and methallyl bromide (48 µL, 0.48 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 97:3, R_f = 0.37) to give the product **173j** (152 mg, 357 µmol, 89%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.80 (d, *J* = 2.1 Hz, 1H), 7.74 (d, *J* = 2.1 Hz, 1H), 4.89 (t, *J* = 1.6 Hz, 1H), 4.68 (t, *J* = 1.6 Hz, 1H), 4.14 (dq, *J* = 12.4, 6.9 Hz, 1H), 3.93 (p, *J* = 6.9 Hz, 1H), 3.23 (s, 2H), 1.90 – 1.55 (m, 3H), 1.35 (d, *J* = 7.0 Hz, 6H), 1.31 (d, *J* = 6.9 Hz, 6H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 152.0, 151.3, 143.9, 142.2, 139.4, 137.0, 114.4, 113.8, 110.8, 88.8, 47.3, 47.2, 38.2, 22.3, 21.4, 20.5.
IR (ATR, cm^{-1}) ṽ = 2971, 1723, 1424, 1315, 1195.
MS (EI, 70 eV, %) m/z = 299 (21), 284 (12), 128 (100), 86 (84), 43 (46).
HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{23}IN_2O_2$**: 426.0804; found: 426.0799.

Synthesis of ethyl 2-(3-cyano-5-iodo-2-(pivaloyloxy)benzyl)acrylate (173k)

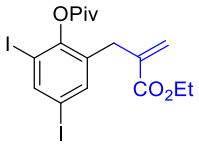


Pivalate **173k** was prepared *via* **TP6** using 2-cyano-4,6-diiodophenyl pivalate (**171k**, 182 mg, 0.40 mmol) and dry toluene (0.80 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.22 mL, 0.22 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (15 mg, 80 µmol) and ethyl 2-(bromomethyl)acrylate (67

µL, 0.48 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.42) to give the product **173k** (86 mg, 195 µmol, 49%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.94 – 7.80 (m, 1H), 7.75 (dd, *J* = 2.3, 1.0 Hz, 1H), 6.31 (d, *J* = 1.3 Hz, 1H), 5.40 (d, *J* = 1.7 Hz, 1H), 4.20 (qd, *J* = 7.2, 1.2 Hz, 2H), 3.49 (d, *J* = 1.6 Hz, 2H), 1.38 (d, *J* = 1.7 Hz, 9H), 1.26 (td, *J* = 7.0, 1.2 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 175.6, 166.1, 151.2, 144.1, 139.9, 137.2, 135.6, 127.8, 113.9, 110.3, 89.5, 61.3, 39.5, 31.7, 27.1, 14.3.
IR (ATR, cm^{-1}) ṽ = 2977, 1714, 1456, 1185, 1077.
MS (EI, 70 eV, %) m/z = 357 (30), 312 (11), 311 (100), 282 (10), 184 (8), 156 (8).
HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{20}INO_4$**: 441.0437; found: 441.0434.

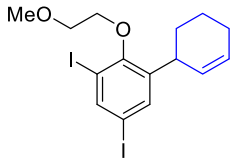
Synthesis of ethyl 2-(3,5-diiodo-2-(pivaloyloxy)benzyl)acrylate (173l)



Pivalate **173l** was prepared *via* **TP6** using 2,4,6-triiodophenyl pivalate (**171l**, 222 mg, 0.40 mmol) and dry toluene (0.80 mL). Then, *p*Tol_2Zn·2LiOR (**167**, 0.24 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (15 mg, 80 µmol) and ethyl 2-(bromomethyl)acrylate (67 µL, 0.48 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 97:3, R_f = 0.24) to give the product **173l** (166 mg, 306 µmol, 77%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.02 (d, *J* = 2.0 Hz, 1H), 7.46 (d, *J* = 2.0 Hz, 1H), 6.30 (q, *J* = 1.1 Hz, 1H), 5.36 (q, *J* = 1.4 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.45 (s, 2H), 1.38 (s, 9H), 1.27 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 175.2, 166.4, 150.1, 145.6, 139.6, 137.6, 134.8, 127.5, 93.3, 91.0, 61.2, 39.6, 32.7, 27.4, 14.3.
IR (ATR, cm^{-1}) ṽ = 2974, 1756, 1714, 1436, 1092.
MS (EI, 70 eV, %) m/z = 458 (44), 413 (12), 412 (100), 285 (18), 257 (12), 57 (15).
HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{20}I_2O_4$**: 541.9451; found: 541.9455.

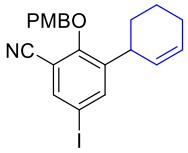
Synthesis of 3',5'-diiodo-2'-(2-methoxyethoxy)-1,2,3,4-tetrahydro-1,1'-biphenyl (173m)



Methoxyethylether **173m** was prepared *via* **TP6** using 1,3,5-triiodo-2-(2-methoxyethoxy)benzene (**171m**, 265 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuI (9.50 mg, 50 µmol) and 3-bromocyclohexene (69 µL, 0.60 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.37) to give the product **173m** (181 mg, 374 µmol, 75%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.93 (d, *J* = 2.1 Hz, 1H), 7.45 (d, *J* = 2.1 Hz, 1H), 6.06 – 5.76 (m, 1H), 5.66 – 5.31 (m, 1H), 4.10 (dt, *J* = 10.2, 4.6 Hz, 1H), 3.96 (dt, *J* = 10.0, 4.7 Hz, 1H), 3.83 (dt, *J* = 5.7, 2.8 Hz, 1H), 3.78 (t, *J* = 4.7 Hz, 2H), 3.46 (s, 3H), 2.09 (td, *J* = 5.5, 2.7 Hz, 2H), 2.02 (dtt, *J* = 12.4, 5.9, 2.5 Hz, 1H), 1.73 (ddt, *J* = 9.8, 6.2, 3.3 Hz, 1H), 1.68 – 1.60 (m, 1H), 1.44 (dddd, *J* = 12.9, 11.1, 8.5, 3.1 Hz, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 156.4, 144.9, 143.6, 138.6, 129.4 (2 C), 93.5, 89.4, 73.3, 71.7, 59.4, 35.6, 31.8, 25.0, 21.4.
IR (ATR, cm^{-1}) ṽ = 2926, 1431, 1222, 1125, 1044.
MS (EI, 70 eV, %) m/z = 426 (75), 425 (52), 359 (38), 312 (39), 298 (100), 270 (38), 230 (39), 198 (78), 172 (76), 171 (61), 157 (37), 152 (38), 144 (47), 141 (37), 128 (70), 115 (98).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{18}I_2O_2$**: 483.9396; found: 483.9391.

Synthesis of 5-iodo-2-((4-methoxybenzyl)oxy)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carbonitrile (173n)

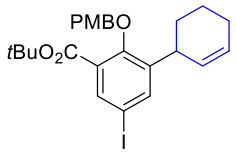


Benzonitrile **173n** was prepared *via* **TP6** using 3,5-diiodo-2-((4-methoxybenzyl)oxy)benzonitrile (**171n**, 160 mg, 0.327 mmol) and dry toluene (0.66 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.19 mL, 0.19 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuI (6.22 mg, 32.7 µmol) and 3-

bromocyclohexene (45 µL, 0.39 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.36) to give the product **173n** (140 mg, 314 µmol, 96%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.75 (d, *J* = 2.2 Hz, 1H), 7.67 (d, *J* = 2.3 Hz, 1H), 7.50 – 7.31 (m, 2H), 7.01 – 6.83 (m, 2H), 5.93 (dtd, *J* = 10.0, 3.7, 2.4 Hz, 1H), 5.62 – 5.33 (m, 1H), 5.11 (d, *J* = 1.4 Hz, 2H), 3.82 (s, 3H), 3.70 (ddt, *J* = 8.4, 5.6, 2.8 Hz, 1H), 2.07 (qd, *J* = 5.2, 2.7 Hz, 2H), 1.88 (dtd, *J* = 12.8, 6.3, 2.8 Hz, 1H), 1.66 (dtd, *J* = 11.8, 8.9, 6.0 Hz, 1H), 1.61 – 1.50 (m, 1H), 1.46 – 1.33 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 160.2, 158.8, 143.8, 143.0, 139.8, 130.5, 130.2, 128.4, 127.9, 115.9, 114.2, 108.6, 86.7, 77.3, 55.5, 34.8, 31.2, 24.9, 21.1.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2929, 1514, 1447, 1249, 1174.
MS (EI, 70 eV, %) m/z = 121 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{21}H_{20}INO_2$**: 445.0539; found: 445.0529.

Synthesis of tert-butyl 5-iodo-2-((4-methoxybenzyl)oxy)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxylate (173o)



Tert-butyl benzoate **173o** was prepared *via* **TP6** using tert-butyl 3,5-diiodo-2-((4-methoxybenzyl)oxy)benzoate (**171o**, 226 mg, 0.40 mmol) and dry toluene (0.80 mL). Then, *p*Tol_2Zn·2LiOR (**167**, 0.24 mL, 0.24 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuI (7.60 mg, 40 µmol) and 3-bromocyclohexene (55 µL, 0.48 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.41) to give the product **173o** (186 mg, 357 µmol, 89%) as a yellowish oil.

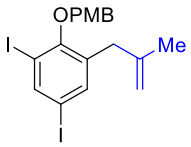
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.83 (d, *J* = 2.3 Hz, 1H), 7.58 (d, *J* = 2.4 Hz, 1H), 7.42 – 7.29 (m, 2H), 7.06 – 6.76 (m, 2H), 6.04 – 5.80 (m, 1H), 5.50 – 5.35 (m, 1H), 5.03 – 4.88 (m, 1H), 4.84 (d, *J* = 10.6 Hz, 1H), 3.82 (s, 3H), 3.73 (ddt, *J* = 8.4, 5.5, 2.8 Hz, 1H), 2.06 (ddt, *J* = 9.2, 6.3, 3.1 Hz, 2H), 1.93 – 1.80 (m, 1H), 1.73 – 1.66 (m, 1H), 1.58 (s, 9H), 1.56 – 1.50 (m, 1H), 1.44 – 1.37 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 164.7, 159.7, 155.7, 143.9, 141.1, 137.5, 129.7, 129.5, 129.4, 129.3, 129.2, 114.0, 87.3, 82.2, 77.1, 55.5, 34.7, 31.5, 28.3, 25.0, 21.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2974, 1721, 1514, 1247, 1143.

MS (EI, 70 eV, %) m/z = 121 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{25}H_{29}IO_4$**: 520.1111; found: 520.1100.

Synthesis of 1,5-diiodo-2-((4-methoxybenzyl)oxy)-3-(2-methylallyl)benzene (173p)



Diiodobenzene **173p** was prepared *via* **TP6** using 1,3,5-triiodo-2-((4-methoxybenzyl)oxy)benzene (**171p**, 296 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuI (19 mg, 100 µmol) and methallyl bromide (60 µL, 0.60 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.22) and HPLC to give the product **173p** (194 mg, 373 µmol, 75%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.00 (d, *J* = 2.1 Hz, 1H), 7.64 – 7.33 (m, 3H), 6.98 – 6.80 (m, 2H), 4.89 (t, *J* = 1.8 Hz, 1H), 4.81 (s, 2H), 4.74 – 4.53 (m, 1H), 3.83 (s, 3H), 3.32 (s, 2H), 1.69 (t, *J* = 1.1 Hz, 3H).

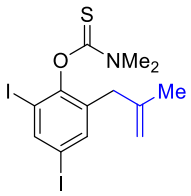
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.9, 156.9, 145.3, 143.8, 139.9, 136.7, 130.2, 128.7, 114.1, 113.4, 94.0, 89.1, 75.3, 55.5, 38.4, 22.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2932, 1611, 1514, 1439, 1246.

MS (EI, 70 eV, %) m/z = 400 (22), 394 (26), 258 (20), 207 (67), 159 (55), 131 (25), 127 (23), 121 (100), 115 (24), 108 (35), 91 (27), 77 (25).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{18}I_2O_2$**: 519.9396; found: 519.9394.

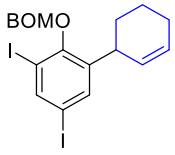
Synthesis of *O*-(2,4-diiodo-6-(2-methylallyl)phenyl) dimethylcarbamothioate (173q)



Dimethylcarbamothioate **173q** was prepared *via* **TP6** using *O*-(2,4,6-triiodophenyl) dimethylcarbamothioate (**171q**, 224 mg, 0.40 mmol) and dry toluene (0.80 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.24 mL, 0.24 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (7.60 mg, 40 µmol) and methallyl bromide (49 µL, 0.48 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.31) to give the product **173q** (112 mg, 230 µmol, 57%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.00 (d, *J* = 2.1 Hz, 1H), 7.51 (d, *J* = 2.0 Hz, 1H), 5.09 – 4.83 (m, 1H), 4.71 (dt, *J* = 2.1, 1.0 Hz, 1H), 3.48 (s, 3H), 3.38 (s, 3H), 3.30 (d, *J* = 15.5 Hz, 1H), 3.17 (d, *J* = 15.5 Hz, 1H), 1.68 (t, *J* = 1.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 184.7, 152.5, 145.0, 142.7, 139.4, 137.0, 113.5, 94.4, 91.3, 43.7, 39.8, 39.2, 22.4.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2933, 1533, 1393, 1210, 1108.
MS (EI, 70 eV, %) m/z = 361 (14), 360 (100), 233 (14), 88 (53), 72 (36).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{15}I_2NOS$**: 486.8964; found: 486.8962.

Synthesis of 2'-((benzyloxy)methoxy)-3',5'-diiodo-1,2,3,4-tetrahydro-1,1'-biphenyl (173r)

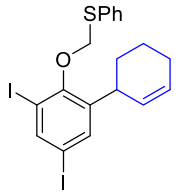


Diiodobenzene **173r** was prepared *via* **TP6** using 2-((benzyloxy)methoxy)-1,3,5-triiodobenzene (**171r**, 296 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuI (19 mg, 100 µmol) and 3-bromocyclohexene (69 µL, 0.60 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl

acetate = 95:5, R_f = 0.47) and HPLC to give the product **173r** (203 mg, 372 µmol, 74%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.96 (d, *J* = 2.1 Hz, 1H), 7.47 (d, *J* = 2.1 Hz, 1H), 7.41 – 7.29 (m, 5H), 6.01 – 5.80 (m, 1H), 5.53 (dq, *J* = 9.8, 2.3 Hz, 1H), 5.19 (d, *J* = 6.0 Hz, 1H), 5.15 (d, *J* = 6.1 Hz, 1H), 4.88 (d, *J* = 3.5 Hz, 2H), 3.90 (ddt, *J* = 8.3, 5.6, 2.8 Hz, 1H), 2.15 – 1.99 (m, 3H), 1.74 – 1.64 (m, 1H), 1.55 (ddt, *J* = 10.9, 7.1, 2.4 Hz, 1H), 1.50 – 1.39 (m, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 155.7, 144.9, 143.9, 138.5, 137.2, 129.5, 129.3, 128.7, 128.1, 128.0, 98.5, 94.0, 89.6, 72.0, 35.9, 31.5, 25.0, 21.3.
IR (ATR, cm^{-1}) ṽ = 2929, 1431, 1215, 1078, 946.
MS (EI, 70 eV, %) m/z = 425 (29), 91 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{20}H_{20}I_2O_2$**: 545.9553; found: 545.9548.

Synthesis of (((3,5-diiodo-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-yl)oxy)methyl)(phenyl) sulfane (173s)



Diiodobenzene **173s** was prepared *via* **TP6** using phenyl((2,4,6-triiodophenoxy)methyl)sulfane (**171s**, 297 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuI (19 mg, 100 µmol) and 3-bromocyclohexene (69 µL, 0.60 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9:1, R_f = 0.21) and HPLC to give the product **173s** (149 mg, 272 µmol, 54%) as a white solid.

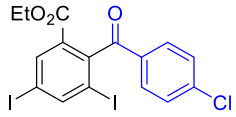
M.p. (°C): 192-194.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.20 – 7.96 (m, 2H), 7.88 (d, *J* = 2.1 Hz, 1H), 7.78 – 7.68 (m, 1H), 7.62 (dd, *J* = 8.5, 7.0 Hz, 2H), 7.45 (d, *J* = 2.1 Hz, 1H), 5.92 (dq, *J* = 9.8, 3.5 Hz, 1H), 5.46 (dq, *J* = 10.0, 2.4 Hz, 1H), 5.04 (d, *J* = 10.5 Hz, 1H), 4.83 (d, *J* = 10.5 Hz, 1H), 3.60 (ddt, *J* = 8.5, 5.7, 2.8 Hz, 1H), 2.05 (tq, *J* = 5.5, 2.8 Hz, 2H), 1.86 (dtd, *J* = 12.7, 6.2, 2.6 Hz, 1H), 1.64 (dqd, *J* = 12.5, 5.1, 2.8 Hz, 1H), 1.59 – 1.44 (m, 1H), 1.34 (ddt, *J* = 12.9, 10.5, 5.5 Hz, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 154.0, 145.3, 143.4, 139.0, 136.9, 134.7, 130.1, 129.5 (2C), 128.4, 91.5, 91.1, 84.8, 35.5, 31.6, 24.8, 21.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2924, 1446, 1330, 1151, 740.

MS (EI, 70 eV, %) m/z = 439 (20), 438 (100), 410 (27), 383 (10), 359 (13), 128 (21), 127 (13), 115 (11), 79 (11), 77 (17), 44 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{13}I_2O$**: 438.9056; found: 438.9044.

Synthesis of ethyl 2-(4-chlorobenzoyl)-3,5-diiodobenzoate (173t)



Ethyl diiodobenzoate **173t** was prepared *via* **TP6** using ethyl 2,3,5-triiodobenzoate (**171t**, 264 mg, 0.50 mmol) and dry toluene (5.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (9.50 mg, 50 µmol) and 4-chlorobenzoyl chloride (193 µL, 1.50 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.28) to give the product **173t** (151 mg, 279 µmol, 56%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.43 (q, *J* = 1.6 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.55 – 7.34 (m, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 1.14 (t, *J* = 7.2 Hz, 3H).

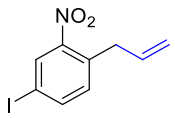
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 195.0, 163.2, 151.0, 145.0, 140.2, 139.2, 134.1, 131.5, 130.7, 129.4, 95.2, 94.2, 62.5, 13.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2980, 1717, 1265, 921, 747.

MS (EI, 70 eV, %) m/z = 540 (19), 429 (46), 401 (56), 150 (19), 141 (32), 139 (100), 111 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{11}ClI_2O_3$**: 539.8486; found: 539.8490.

Synthesis of 1-allyl-4-iodo-2-nitrobenzene (173u)

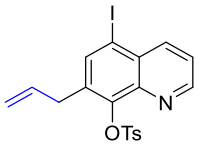


Nitrobenzene **173u** was prepared *via* **TP6** using 1,4-diiodo-2-nitrobenzene (**171u**, 188 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.35 mL, 0.35 mmol) was added at –15 °C. After stirring at –15 °C for 20 min, CuI (9.50 mg, 50 µmol) and allyl bromide (69 µL, 0.80 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up,

the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.40) to give the product **173u** (107 mg, 370 µmol, 74%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.22 (d, *J* = 1.8 Hz, 1H), 7.84 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 5.92 (ddt, *J* = 16.7, 10.1, 6.5 Hz, 1H), 5.13 (dq, *J* = 10.1, 1.4 Hz, 1H), 5.08 (dq, *J* = 17.1, 1.6 Hz, 1H), 3.62 (dt, *J* = 6.5, 1.5 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 149.8, 142.0, 134.7, 134.5, 133.6, 133.4, 117.8, 90.7, 36.7.
IR (ATR, cm^{-1}) ṽ = 3079, 2916, 1521, 1342, 804.
MS (EI, 70 eV, %) m/z = 288 (23), 272 (36), 259 (24), 145 (70), 133 (62), 117 (58), 115 (100), 89 (40).
HRMS (EI, 70 eV) m/z: calc. for **$C_9H_8INO_2$**: 288.9600; found: 288.9551.

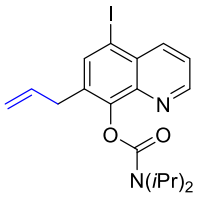
Synthesis of 7-allyl-5-iodoquinolin-8-yl 4-methylbenzenesulfonate (176a)



Quinoline **176a** was prepared *via* **TP6** using 5,7-diiodoquinolin-8-yl 4-methylbenzenesulfonate (**174a**, 276 mg, 0.50 mmol) and dry toluene (5.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (9.50 mg, 50 µmol) and allyl bromide (52 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 80:20, R_f = 0.36) to give the product **176a** (125 mg, 269 µmol, 54%) as a yellow solid.

M.p. (°C): 128-130.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.71 – 8.60 (m, 1H), 8.28 (dd, *J* = 8.5, 1.5 Hz, 1H), 8.03 (s, 1H), 8.01 – 7.94 (m, 2H), 7.41 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 5.94 (ddt, *J* = 17.9, 9.3, 6.7 Hz, 1H), 5.20 – 5.18 (m, 1H), 5.16 (dq, *J* = 6.7, 1.6 Hz, 1H), 3.64 (dt, *J* = 6.7, 1.5 Hz, 2H), 2.48 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 151.0, 145.1, 144.8, 142.8, 140.2, 139.3, 136.3, 134.9, 134.4, 130.1, 129.5, 129.0, 122.9, 118.0, 96.4, 34.7, 21.9.
IR (ATR, cm^{-1}) ṽ = 2922, 1363, 1173, 1068, 750.
MS (EI, 70 eV, %) m/z = 401 (27), 386 (33), 183 (53), 182 (54), 155 (24), 154 (100), 128 (20), 127 (31), 91 (72), 65 (28).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_9INO$**: 309.9729; found: 309.9714.

Synthesis of 7-allyl-5-iodoquinolin-8-yl diisopropylcarbamate (176b)



Quinoline **176b** was prepared *via* **TP6** using 5,7-diiodoquinolin-8-yl 4-methylbenzenesulfonate (**174b**, 262 mg, 0.50 mmol) and dry toluene (10 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuI (19 mg, 100 µmol) and allyl bromide (52 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.22) to give the product **176b** (138 mg, 315 µmol, 63%) as a white solid.

M.p. (°C): 65-67.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.80 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.26 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.98 (s, 1H), 7.40 (dd, *J* = 8.5, 4.1 Hz, 1H), 5.99 (ddt, *J* = 16.7, 10.0, 6.6 Hz, 1H), 5.19 – 5.12 (m, 2H), 4.24 – 4.04 (m, 2H), 3.54 (d, *J* = 6.6 Hz, 2H), 1.46 (d, *J* = 6.8 Hz, 6H), 1.33 (d, *J* = 6.8 Hz, 6H).

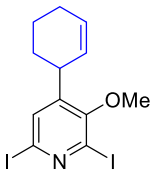
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 153.5, 150.8, 146.8, 143.0, 140.0, 139.0, 135.5, 134.3, 129.8, 122.6, 117.2, 110.2, 93.7, 46.9, 34.5, 21.8, 20.7.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2968, 1706, 1427, 1281, 1144.

MS (EI, 70 eV, %) m/z = 311 (25), 297 (12), 296 (100), 184 (12), 182 (14), 169 (18), 167 (6), 166 (21), 154 (24), 128 (38), 127 (6), 86 (79), 43 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{23}IN_2O_2$**: 438.0804; found: 438.0805.

Synthesis of 4-(cyclohex-2-en-1-yl)-2,6-diiodo-3-methoxypyridine (176c)

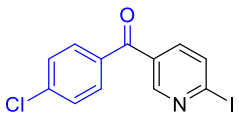


Pyridine **176c** was prepared *via* **TP6** using 2,4,6-triiodo-3-methoxypyridine (**174c**, 243 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuI (19 mg, 100 µmol) and 3-bromocyclohexene (69 µL, 0.60 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After

work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.26) to give the product **176c** (168 mg, 381 µmol, 76%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.43 (s, 1H), 6.09 – 5.87 (m, 1H), 5.58 – 5.40 (m, 1H), 3.85 (s, 3H), 3.78 – 3.60 (m, 1H), 2.11 (ddt, *J* = 7.9, 5.0, 2.6 Hz, 2H), 2.02 (dtd, *J* = 12.6, 6.1, 2.8 Hz, 1H), 1.78 – 1.68 (m, 1H), 1.68 – 1.59 (m, 1H), 1.45 (dddd, *J* = 12.9, 10.6, 8.4, 3.2 Hz, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 155.7, 151.3, 134.8, 130.7, 127.3, 116.0, 110.0, 62.3, 35.7, 30.9, 24.8, 21.0.
IR (ATR, cm^{-1}) ṽ = 2924, 1448, 1312, 987, 749.
MS (EI, 70 eV, %) m/z = 442 (11), 441 (100), 426 (10), 186 (10), 172 (7), 116 (7), 115 (7).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{13}I_2NO$**: 440.9087; found: 440.9077.

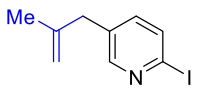
Synthesis of (4-chlorophenyl)(6-iodopyridin-3-yl)methanone (176da)



Iodopyridine **176da** was prepared *via* **TP6** using 2,5-diiodopyridine (166 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuI (57 mg, 0.30 mmol) and 4-chlorobenzoyl chloride (193 µL, 1.50 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.31) to give the product **176da** (115 mg, 335 µmol, 67%).

M.p. (°C): 131-133.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.68 (dd, *J* = 2.5, 0.8 Hz, 1H), 7.91 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.80 – 7.64 (m, 3H), 7.58 – 7.40 (m, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 193.0, 151.5, 140.3, 138.2, 135.2, 134.8, 132.3, 131.4, 129.3, 123.1.
IR (ATR, cm^{-1}) ṽ = 2923, 1651, 1567, 1072, 752.
MS (EI, 70 eV, %) m/z = 309 (13), 308 (100), 232 (8), 207 (10), 204 (11), 141 (23), 139 (70), 111 (8).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_7ClINO$**: 342.9261; found: 342.9253.

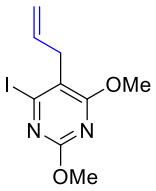
Synthesis of 2-iodo-5-(2-methylallyl)pyridine (176db)



Allylated pyridine **176db** was prepared *via* **TP6** using 2,5-diiodopyridine (166 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 25 °C. After stirring at 25 °C for 10 min, CuI (9.50 mg, 50 µmol) and methallyl bromide (60 µL, 0.60 mmol) were added at 0 °C and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.27) to give the product **176db** (93 mg, 359 µmol, 72%) as a colorless oil.

^{1}H-NMR (400 MHz, CDCl$_3$, ppm) δ = 8.20 (d, *J* = 2.6 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.17 (dd, *J* = 8.1, 2.6 Hz, 1H), 4.85 (t, *J* = 1.7 Hz, 1H), 4.72 – 4.68 (m, 1H), 3.24 (s, 2H), 1.67 (t, *J* = 1.1 Hz, 3H).
^{13}C-NMR (101 MHz, CDCl$_3$, ppm) δ = 151.5, 143.4, 138.5, 135.0, 134.6, 115.3, 113.4, 41.0, 22.2.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2933, 1447, 1375, 1070, 894.
MS (EI, 70 eV, %) m/z = 259 (51), 150 (10), 132 (100), 130 (15), 117 (39), 115 (11).
HRMS (EI, 70 eV) m/z: calc. for **C$_9$H$_{10}$IN**: 258.9858; found: 258.9851.

Synthesis of 5-allyl-4-iodo-2,6-dimethoxypyrimidine (176e)



Pyrimidine **176e** was prepared *via* **TP6** using 4,5-diiodo-2,6-dimethoxypyrimidine (**174e**, 196 mg, 0.50 mmol) and dry toluene (1.00 mL). Then, *p*Tol$_2$Zn·2LiOR (**167**, 0.30 mL, 0.30 mmol) was added at 0 °C. After stirring at 0 °C for 20 min, CuI (9.50 mg, 50 µmol) and allyl bromide (52 µL, 0.60 mmol) were added and the reaction solution was allowed to warm to room temperature overnight. After work-up, the crude product was purified *via* column chromatography (*iso*hexane, R_f = 0.67) to give the product **176e** (112 mg, 366 µmol, 73%) as a colorless oil.

^{1}H-NMR (400 MHz, CDCl$_3$, ppm) δ = 5.81 (ddt, *J* = 17.6, 9.7, 6.0 Hz, 1H), 5.11 – 5.04 (m, 1H), 5.04 (t, *J* = 1.7 Hz, 1H), 3.96 (s, 3H), 3.96 (s, 3H), 3.36 (dt, *J* = 6.1, 1.7 Hz, 2H).
^{13}C-NMR (101 MHz, CDCl$_3$, ppm) δ = 167.5, 162.4, 134.1, 133.6, 118.2, 116.3, 55.3, 54.8, 35.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2954, 1529, 1365, 1219, 1016.

MS (EI, 70 eV, %) m/z = 306 (100), 305 (51), 291 (33), 277 (36), 275 (18), 179 (93), 177 (12), 164 (21), 163 (24), 149 (15), 122 (52), 121 (17), 119 (10), 107 (18), 94 (42), 83 (10), 81 (10), 78 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_9H_{11}IN_2O_2$**: 305.9865; found: 305.9862.

6 Iron-Catalyzed Cross-Coupling of Functionalized Benzylmanganese Halides with Alkenyl Iodides, Bromides and Triflates

6.1 Typical Procedures

Typical Procedure for the Preparation of Benzylic Manganese Chlorides 177a–177k (TP 7)

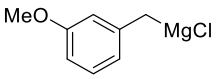
A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with magnesium turnings (583 mg, 24.0 mmol, 2.40 equiv), followed by freshly distilled THF (5.00 mL) or MTBE (6.25 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (12.5 mL, 12.5 mmol, 1.20 equiv, 1.00 M in THF). The solution was then cooled to –5 °C. Subsequently, the corresponding benzyl chloride (**178a**–**178k**, 10.0 mmol, 1.00 equiv) was added drop by drop and the reaction mixture was stirred at –5 °C until a complete conversion of the starting material was observed. The reaction progress was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots. When the metalation was completed, the black solutions of the benzylmanganese chlorides **177a**–**177k** were separated from the magnesium turnings using a syringe and subsequently transferred into another pre-dried and argon-flushed *Schlenk*-tube, which was cooled to –5 °C. To determine the concentration of the manganese chlorides **177a**–**177k** a titration against iodine in freshly distilled THF was performed.

Typical Procedure for the Fe-catalyzed Cross-Coupling Reactions of Benzylic metallic species 177a–177k, 181, 182 with different Elecrophiles 179a–179n (TP 8)

A pre-dried and argon-flushed *Schlenk*-tube equipped with a magnetic stirring bar and a rubber septum was charged with $FeCl_2$ (4.20 mg, 33.0 µmol, 10 mol%), the corresponding electrophile (**179a**–**179n**, 333 µmol, 1.00 equiv), tetradecane as internal standard (20 µL) and freshly distilled THF (0.30 mL) as solvent. The reaction mixture was cooled to 0 °C and the benzylic metallic species solution (**177a**–**177k**, **181**, **182**, 1.20 equiv) was added dropwise. After the addition was complete, the reaction mixture was allowed to warm to 25 °C and the completion of the cross-coupling reaction was monitored by GC-analysis of hydrolyzed aliquots. Thereupon, a saturated aqueous solution of NH_4Cl was added and the aqueous layer was extracted with EtOAc (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude products by flash column chromatography afforded the desired cross-coupling reaction products (**180a**–**180z**).

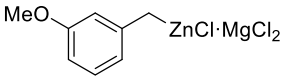
6.2 Starting Materials and Organometallic Reagents

Preparation of 3-methoxybenzylmagnesium chloride (181)



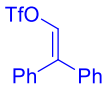
A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with magnesium turnings (292 mg, 12.0 mmol), followed by freshly distilled THF (4.00 mL). 3-methoxybenzyl chloride (**178a**, 783 mg, 5.00 mmol) diluted in THF (10.0 mL) was added to the reaction mixture: 1.00 mL was added until the solution gets warm then an autopulsed syringe was used (rate: 0.02 mL/min). Iodine (10.0 mg, 40.0 µmol) was added to activate the magnesium turnings. The reaction mixture was stirred at room temperature until a complete conversion of the starting material was observed. The reaction progress was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots. When the metalation was completed, the solution of the benzylmagnesium chloride was separated from the magnesium turnings using a syringe and subsequently transferred into another pre-dried and argon-flushed *Schlenk*-tube. To determine the concentration of the magnesium chloride**,** a titration against iodine in freshly distilled THF was performed. 3-methoxybenzylmagnesium chloride (**181**) was obtained (0.27 M, 48%).

Preparation of 3-methoxybenzylzinc chloride (182):



A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (318 mg, 7.50 mmol) and heated up to ca. 450 °C for 5 min under high vacuum using a heat gun. After cooling to room temperature under vigourous stirring, $ZnCl_2$ (900 mg, 6.60 mmol) was added under argon, the *Schlenk*-tube was heated to ca. 320 °C for 5 min under vacuum using a heat gun, cooled to room temperature and charged with magnesium turnings (340 mg, 14.4 mmol). Freshly distilled THF (5.00 mL) and 3-methoxybenzyl chloride (**178a**, 940 mg, 6.00 mmol) were added and the reaction mixture was stirred at room temperature until a complete conversion of the starting material was observed. The completion of the metalation was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots. When the oxidative insertion was complete, the solution 3-methoxybenzylzinc chloride was separated from the resulting salts *via* a syringe equipped with a filter and transferred to another pre-dried and argon-flushed *Schlenk*-tube, before being titrated against iodine. 3-methoxybenzylzinc chloride (**182**) was obtained (0.39 M, 42%).

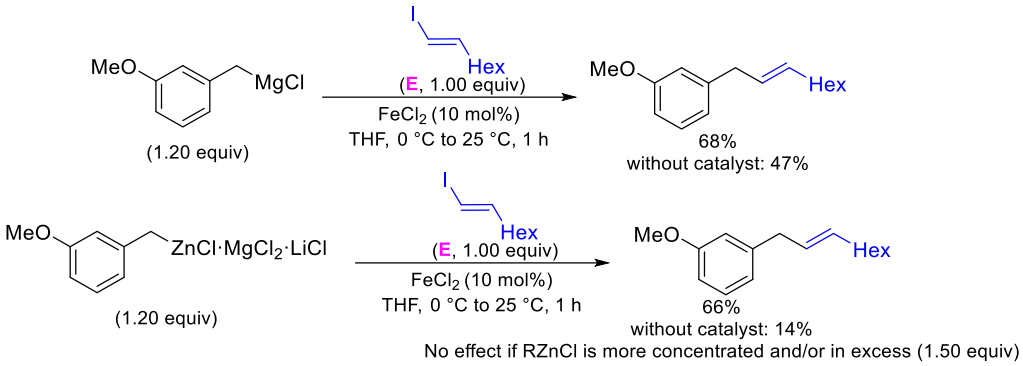
Synthesis of 2,2-diphenylvinyl trifluoromethanesulfonate (179e)



For this reaction, 2,2-diphenylacetaldehyde (5.00 g, 4.52 mL, 25.5 mmol), potassium *tert*-butoxide (4.05 g, 36.1 mmol) and THF (150 mL) were used. The reaction mixture was refluxed for 4 h and quenched with *N*-phenyl-bis(trifluoromethanesulfonimide) (10.9 g, 30.6 mmol). Purification by flash column chromatography (*iso*hexane, $R_f = 0.34$) afforded the desired product **179e** (4.47 g, 13.6 mmol, 54%) as a yellowish oil.

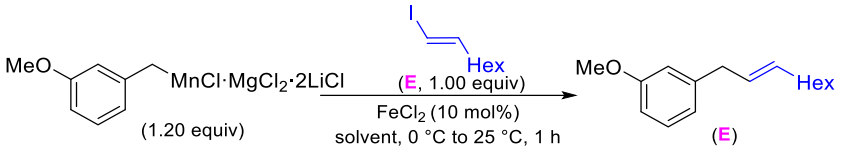
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.45 – 7.33 (m, 6H), 7.31 – 7.22 (m, 4H), 7.05 (s, 1H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 136.6, 134.3 (2C), 132.0, 129.8, 129.1, 128.9 (2C), 128.6 (2C), 118.6 (q, J = 321.2 Hz).
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –73.7.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1446, 1422, 1244, 1205, 1165, 1137, 1035, 1014, 947, 914, 828, 807, 775, 759, 694.
MS (EI, 70 eV, %) m/z = 195 (60), 167 (100), 165 (79), 152 (39).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{11}F_3O_3S$**: 328.0381; found 328.0373.

6.3 Additional Results and Screening Table



Scheme 63: Screening of other organometallic species.

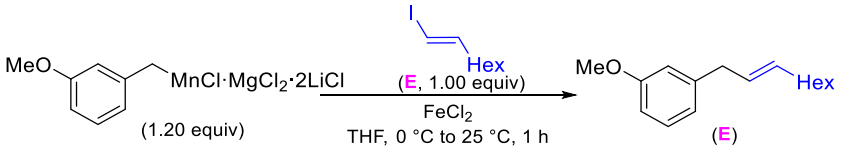
Table 21: Cosolvent screening of the reaction between benzylic manganese chlorides and (*E*)-1-iodooctene.



Entry	THF:NMP	Yield [%][a]
1	1:1	97
2	3:1	93
3	THF only	97

[a] Yield determined by GC-analysis of water quenched reaction aliquots.

Table 22: Catalyst loading screening of the reaction between benzylic manganese chlorides and (*E*)-1-iodooctene.

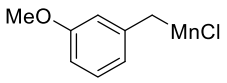


Entry	[$FeCl_2$] (mol%)	Yield [%][a]
1	10	98
2	5.0	73
3	2.5	79
4	1.0	79

[a] Yield determined by GC-analysis of water quenched reaction aliquots.

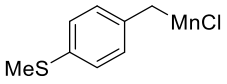
6.4 Preparation of Benzylic Manganese Reagents 177

Preparation of 3-methoxybenzylmanganese chloride (177a)



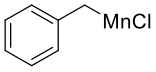
Based on **TP7**, magnesium turnings (583 mg, 24.0 mmol), THF (5.00 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (12.5 mL, 12.5 mmol, 1.00 M in THF) were used. Subsequently, 3-methoxybenzyl chloride (**178a**, 1.45 mL, 10.0 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 1 h at the given temperature. The concentration of 3-methoxybenzylmanganese chloride (**177a**) was determined against iodine in THF (0.39 M, 78%).

Preparation of 4-(methylthio)benzylmanganese chloride (177b)



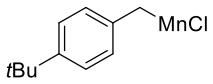
Based on **TP7**, magnesium turnings (350 mg, 14.4 mmol), THF (3.00 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (7.50 mL, 7.50 mmol, 1.00 M in THF) were used. Subsequently, 4-(methylthio)benzyl chloride (**178b**, 0.91 mL, 6.00 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 1 h at the given temperature. The concentration of 4-(methylthio)benzylmanganese chloride (**177b**) was determined against iodine in THF (0.36 M, 69%).

Preparation of benzylmanganese chloride (177c)



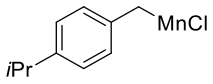
Based on **TP7**, magnesium turnings (583 mg, 24.0 mmol), THF (5.00 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (12.5 mL, 12.5 mmol, 1.00 M in THF) were used. Subsequently, benzylchloride (**178c**, 1.15 mL, 10.0 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 0.5 h at the given temperature. The concentration of benzylmanganese chloride (**177c**) was determined against iodine in THF (0.34 M, 65%).

Preparation of 4-*tert*butylbenzylmanganese chloride (177d)



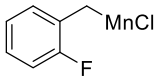
Based on **TP7**, magnesium turnings (180 mg, 7.20 mmol), THF (3.00 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (3.80 mL, 3.80 mmol, 1.00 M in THF) were used. Subsequently, 1-(*tert*-butyl)-4-(chloromethyl)benzene (**178d**, 0.58 mL, 3.00 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 1 h at the given temperature. The concentration of 4-(*tert*-butyl)benzylmanganese chloride (**177d**) was determined against iodine in THF (0.37 M, 84%).

Preparation of 4-isopropylbenzylmanganese chloride (177e)



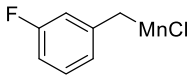
Based on **TP7**, magnesium turnings (350 mg, 14.4 mmol), THF (3.00 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (7.50 mL, 7.50 mmol, 1.00 M in THF) were used. Subsequently, 4-isopropylbenzyl chloride (**178e**, 0.66 mL, 6.00 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 1.5 h at the given temperature. The concentration of 4-isopropylbenzylmanganese chloride (**177e**) was determined against iodine in THF (0.37 M, 68%).

Preparation of 2-fluorobenzylmanganese chloride (177f)



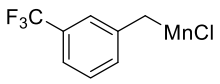
Based on **TP7**, magnesium turnings (175 mg, 7.20 mmol), THF (1.50 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (3.80 mL, 3.80 mmol, 1.00 M in THF) were used. Subsequently, 2-fluorobenzyl chloride (**178f**, 0.36 mL, 3.00 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 1.5 h at the given temperature. The concentration of 2-fluorobenzylmanganese chloride (**177f**) was determined against iodine in THF (0.40 M, 67%).

Preparation of 3-fluorobenzylmanganese chloride (177g)



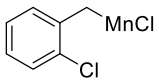
Based on **TP7**, magnesium turnings (175 mg, 7.20 mmol), THF (1.50 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (3.80 mL, 3.80 mmol, 1.00 M in THF) were used. Subsequently, 3-fluorobenzyl chloride (**178g**, 0.36 mL, 3.00 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 0.5 h at the given temperature. The concentration of 3-fluorobenzylmanganese chloride (**177g**) was determined against iodine in THF (0.30 M, 68%).

Preparation of 3-(trifluoromethyl)benzylmanganese chloride (177h)



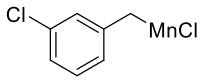
Based on **TP7**, magnesium turnings (175 mg, 7.20 mmol), MTBE (1.90 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (3.80 mL, 3.80 mmol, 1.00 M in THF) were used. Subsequently, 3-(trifluoromethyl)benzyl chloride (**178h**, 0.47 mL, 3.00 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 1 h at the given temperature. The concentration of 3-(trifluoromethyl)benzylmanganese chloride (**177h**) was determined against iodine in THF (0.31 M, 58%).

Preparation of 2-chlorobenzylmanganese chloride (177i)



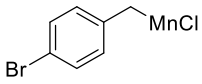
Based on **TP7**, magnesium turnings (583 mg, 24.0 mmol), MTBE (6.25 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (12.5 mL, 12.5 mmol, 1.00 M in THF) were used. Subsequently, 2-chlorobenzyl chloride (**178i**, 1.16 mL, 10.0 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 1 h at the given temperature. The concentration of 2-chlorobenzylmanganese chloride (**177i**) was determined against iodine in THF (0.22 M, 44%).

Preparation of 3-chlorobenzylmanganese chloride (177j)



Based on **TP7**, magnesium turnings (350 mg, 14.4 mmol), THF (3.00 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (7.50 mL, 7.50 mmol, 1.00 M in THF) were used. Subsequently, 3-chlorobenzyl chloride (**178j**, 0.78 mL, 6.00 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 1.5 h at the given temperature. The concentration of 3-chlorobenzylmanganese chloride (**177j**) was determined against iodine in THF (0.47 M, 86%).

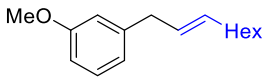
Preparation of 4-bromobenzylmanganese chloride (177k)



Based on **TP7**, magnesium turnings (180 mg, 7.20 mmol), THF (3.00 mL) and a solution of $MnCl_2 \cdot 2LiCl$ (3.80 mL, 3.80 mmol, 1.00 M in THF) were used. Subsequently, 1-bromo-4-(chloromethyl)benzene (**178k**, 620 mg, 3.00 mmol) was added dropwise at –5 °C and the reaction mixture was stirred for 2 h at the given temperature. The concentration of 4-bromo-benzylmanganese chloride (**177k**) was determined against iodine in THF (0.22 M, 50%).

6.5 Synthesis of Compounds 180

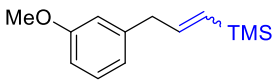
Synthesis of (*E*)-1-methoxy-3-(non-2-en-1-yl)benzene (180a)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), (*E*)-1-iodooctene (**179a**, 79.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 3-methoxybenzylmanganese chloride (**177a**, 1.03 mL, 400 µmol, 0.39 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane, R_f = 0.41) afforded the desired cross-coupling reaction product **180a** (75.0 mg, 323 µmol, 97%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.24 – 7.18 (m, 1H), 6.81 – 6.77 (m, 1H), 6.76 – 6.73 (m, 2H), 5.61 – 5.47 (m, 2H), 3.80 (s, 3H), 3.31 (d, *J* = 5.1 Hz, 2H), 2.08 – 1.98 (m, 2H), 1.42 – 1.33 (m, 2H), 1.33 – 1.23 (m, 6H), 0.93 – 0.83 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.7, 142.9, 132.5, 129.4, 128.6, 121.0, 114.3, 111.3, 55.3, 39.2, 32.7, 31.9, 29.6, 29.0, 22.8, 14.3.
IR (ATR, cm^{-1}) ṽ = 2955, 2924, 2854, 1601, 1585, 1488, 1465, 1454, 1435, 1257, 1148, 1046, 966, 874, 771, 726, 693.
MS (EI, 70 eV, %) m/z = 232 (80), 175 (11), 161 (31), 150 (10), 147 (87), 136 (16), 134 (100), 128 (10), 122 (99), 117 (17), 91 (48).
HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{24}O$**: 232.1827; found 232.1821.

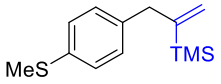
Synthesis of (3-(3-methoxyphenyl)prop-1-en-1-yl)trimethylsilane (180b)



In relation to **TP8**, for this reaction $FeCl_2$ (13.0 mg, 100 µmol), 2-bromovinyltrimethylsilane (**179b**, *Z/E* = 10:90, 0.15 mL, 1.00 mmol) and freshly distilled THF (1.00 mL) were used. The reaction mixture was cooled to 0 °C and 3-methoxybenzylmanganese chloride (**177a**, 3.08 mL, 1.20 mmol, 0.39 M) was added dropwise before the mixture was allowed to warm to 25 °C for 12 h. Purification by flash column chromatography (SiO_2, *iso*hexane:ethyl acetate= 99:1, R_f = 0.54) afforded the desired cross-coupling reaction product **180b** (202 mg, *Z/E* = 6:94, 920 µmol, 92%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.26 (dd, *J* = 14.1, 6.3 Hz, 1H), 7.02 – 6.66 (m, 3H), 6.45 (dt, *J* = 13.8, 7.4 Hz, 0.06H), 6.18 (dt, *J* = 18.8, 6.4 Hz, 0.93H), 5.75 (dt, *J* = 18.4, 1.5 Hz, 0.93H), 5.73 (t, *J* = 1.5 Hz, 0.06H), 3.83 (s, 3H), 3.46 (dd, *J* = 6.2, 1.0 Hz, 2H), 0.18 – 0.02 (m, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.8, 146.7, 145.0, 142.1, 141.8, 131.8, 130.4, 129.6, 129.5, 121.3, 121.0, 114.6, 114.3, 111.6, 111.5, 55.3, 43.4, 39.7, 38, 0.5, –1.1.
IR (ATR, cm^{-1}) ṽ = 2954, 2898, 2834, 1600, 1584, 1490, 1466, 1454, 1436, 1316, 1286, 1258, 1246, 1162, 1150, 1052, 1046, 990, 938, 860, 834, 766, 748, 692.
MS (EI, 70 eV, %) m/z = 220 (28), 205 (100), 193 (12), 190 (60), 175 (47), 146 (71), 121 (15), 115 (23), 91 (13), 75 (14), 73 (58), 59 (18).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{20}OSi$**: 220.1283; found 220.1277.

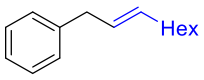
Synthesis of trimethyl(3-(4-(methylthio)phenyl)prop-1-en-2-yl)silane (180c)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), (1-bromovinyl)trimethylsilane (**179c**, 60.0 mg, 333 µmol) and freshly distilled THF (0.3 mL) were used. The reaction mixture was cooled to 0 °C and 4-(methylthio)benzylmanganese chloride (**177b**, 1.11 mL, 400 µmol, 0.36 M) was added dropwise before the mixture was allowed to warm to 25 °C for 12 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.83) afforded the desired cross-coupling reaction product **180c** (73.0 mg, 308 µmol, 92%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.19 (d, *J* = 8.3 Hz, 2H), 7.10 – 7.05 (m, 2H), 5.49 – 5.40 (m, 2H), 3.42 (d, *J* = 1.3 Hz, 2H), 2.47 (s, 3H), 0.00 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 151.4, 137.4, 135.5, 129.9, 126.9, 126.0, 42.3, 16.4, –1.3.
IR (ATR, cm^{-1}) ṽ = 2955, 2921, 1492, 1436, 1404, 1258, 1247, 1093, 922, 836, 800, 759, 691.
MS (EI, 70 eV, %) m/z = 236 (83), 221 (79), 206 (11), 191 (15), 181 (11), 137 (37), 115 (21), 73 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{20}SSi$**: 236.1055; found 236.1047.

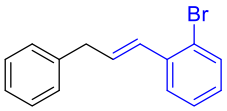
Synthesis of (*E*)-non-2-en-1-ylbenzene (180d)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), (*E*)-1-iodooctene (**179a**, 79.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and benzylmanganese chloride (**177c**, 1.18 mL, 400 µmol, 0.34 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane, R_f = 0.73) afforded the desired cross-coupling reaction product **180d** (52.0 mg, 256 µmol, 77%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.34 – 7.25 (m, 2H), 7.23 – 7.17 (m, 3H), 5.65 – 5.43 (m, 2H), 3.34 (d, *J* = 5.8 Hz, 2H), 2.07 – 1.97 (m, 2H), 1.43 – 1.33 (m, 2H), 1.30 (ddd, *J* = 10.5, 4.5, 2.2 Hz, 6H), 0.93 – 0.81 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 141.3, 132.3, 128.8, 128.6, 128.4, 126.0, 39.2, 32.7, 31.9, 29.6, 29.0, 22.8, 14.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2955, 2926, 2856, 1741, 1720, 1706, 1495, 1453, 965, 746, 696.
MS (EI, 70 eV, %) m/z = 202 (10), 129 (12), 117 (71), 115 (28), 104 (100), 91 (43).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{22}$**: 202.1722; found 202.1714.

Synthesis of (*E*)-1-bromo-2-(3-phenylprop-1-en-1-yl)benzene (180e)

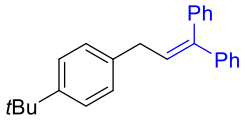


According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), (*E*)-1-bromo-2-(2-iodovinyl)benzene (**179d**, 103 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and benzylmanganese chloride (**177c**, 1.18 mL, 400 µmol, 0.34 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane, R_f = 0.54) afforded the desired cross-coupling reaction product **180e** (79.0 mg, 289 µmol, 87%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.50 (ddd, *J* = 17.3, 7.9, 1.5 Hz, 2H), 7.36 – 7.28 (m, 2H), 7.28 – 7.19 (m, 4H), 7.05 (td, *J* = 7.7, 1.7 Hz, 1H), 6.81 (dt, *J* = 15.6, 1.6 Hz, 1H), 6.28 (dt, *J* = 15.6, 7.0 Hz, 1H), 3.59 (dd, *J* = 7.1, 1.5 Hz, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 139.9, 137.4, 133.0, 132.4, 130.1, 128.8, 128.7, 128.5, 127.5, 127.1, 126.4, 123.4, 39.6.
IR (ATR, cm^{-1}) ṽ = 3408, 3062, 3028, 1696, 1587, 1496, 1467, 1454, 1438, 1265, 1200, 1023, 964, 745, 697.
MS (EI, 70 eV, %) m/z = 272 (16), 193 (100), 191 (25), 189 (15), 178 (73), 165 (22), 115 (98), 91 (11).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}Br$**: 272.0201; found 272.0196.

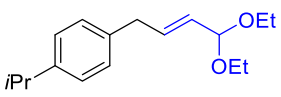
Synthesis of (3-(4-(tert-butyl)phenyl)prop-1-ene-1,1-diyl)dibenzene (180f)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), 2,2-diphenylvinyl trifluoromethanesulfonate (**179e**, 109 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 4-tertbutylbenzylmanganese chloride (**177d**, 1.08 mL, 400 µmol, 0.37 M) was added dropwise before the mixture was allowed to warm to 25 °C for 12 h. Purification by flash column chromatography (*iso*hexane, R_f = 0.59) afforded the desired cross-coupling reaction product **180f** (103 mg, 315 µmol, 95%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.39 (dd, *J* = 7.1, 1.2 Hz, 2H), 7.33 (dd, *J* = 7.9, 1.9 Hz, 3H), 7.28 – 7.21 (m, 7H), 7.16 (d, *J* = 8.3 Hz, 2H), 6.29 (t, *J* = 7.6 Hz, 1H), 3.46 (d, *J* = 7.6 Hz, 2H), 1.32 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 148.9, 142.6, 142.4, 140.0, 138.0, 130.1, 128.4, 128.2 (2C), 128.1, 127.5, 127.2, 127.1, 125.5, 35.5, 34.5, 31.5.
IR (ATR, cm^{-1}) ṽ = 2961, 2868, 1699, 1661, 1606, 1600, 1514, 1494, 1446, 1363, 1318, 1276, 1176, 1109, 1026, 1019, 829, 762, 697.
MS (EI, 70 eV, %) m/z = 326 (13), 269 (100), 191 (87), 178 (15), 115 (12), 91 (15).
HRMS (EI, 70 eV) m/z: calc. for **$C_{25}H_{26}$**: 326.2035; found 326.2024.

Synthesis of (*E*)-1-(4,4-diethoxybut-2-en-1-yl)-4-isopropylbenzene (180g)

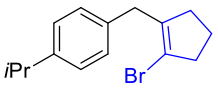


According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), (*E*)-1-bromo-3,3-diethoxyprop-1-ene (**179f**, 70.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was

cooled to 0 °C and 4-isopropylbenzylmanganese chloride (**177e**, 1.08 mL, 400 µmol, 0.37 M) was added dropwise before the mixture was allowed to warm to 25 °C for 12 h. Purification by flash column chromatography (*iso*hexane:triethylamine = 97:3, R_f = 0.50) afforded the desired cross-coupling reaction product **180g** (69.0 mg, 263 µmol, 79%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.17 – 7.09 (m, 4H), 5.27 (dt, *J* = 1.9, 0.9 Hz, 1H), 4.87 (q, *J* = 1.7 Hz, 1H), 4.73 (s, 1H), 3.52 (ddq, *J* = 60.2, 9.4, 7.1 Hz, 4H), 3.37 (d, *J* = 1.4 Hz, 2H), 2.88 (p, *J* = 6.9 Hz, 1H), 1.23 (dd, *J* = 8.2, 7.0 Hz, 12H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 146.7, 146.1, 136.6, 129.4, 126.4, 114.5, 102.6, 61.6, 37.5, 33.8, 24.2, 15.3.
IR (ATR, cm^{-1}) ṽ = 2962, 2928, 2873, 1513, 1326, 1116, 1098, 1052, 1020, 1008, 979, 915, 849, 808.
MS (EI, 70 eV, %) m/z = 173 (100), 145 (60), 129 (27), 117 (15).
HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{26}O_2$**: 262.1933; found 262.1924.

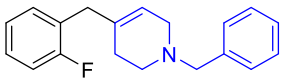
Synthesis of 1-((2-bromocyclopent-1-en-1-yl)methyl)-4-isopropylbenzene (180h)



Adapted from **TP8** (1.00 equiv of benzylic manganese chloride instead of 1.20 equiv); for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), 1,2-dibromocyclopent-1-ene (**179g**, 75.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 4-isopropylbenzylmanganese chloride (**177e**, 0.90 mL, 333 µmol, 0.37 M) was added dropwise before the mixture was allowed to warm to 25 °C for 12 h. Purification by flash column chromatography (*iso*hexane, R_f = 0.73) afforded the desired cross-coupling reaction product **180h** (54.0 mg, 193 µmol, 58%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.18 – 7.10 (m, 4H), 3.46 (s, 2H), 2.89 (p, *J* = 6.9 Hz, 1H), 2.67 (t, *J* = 7.2 Hz, 2H), 2.23 (t, *J* = 7.1 Hz, 2H), 1.90 (p, *J* = 7.5 Hz, 2H), 1.25 (d, *J* = 6.8 Hz, 6H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 146.8, 140.1, 136.1, 128.6, 126.6, 116.6, 40.1, 36.1, 33.8 (2C), 24.2, 21.7.
IR (ATR, cm^{-1}) ṽ = 2959, 2925, 2868, 1710, 1622, 1512, 1463, 1431, 1420, 1315, 1176, 1082, 1054, 1020, 935, 841, 817, 808.
MS (EI, 70 eV, %) m/z = 278 (10), 199 (70), 171 (29), 157 (55), 155 (43), 153 (16), 143 (29), 141 (18), 129 (100), 117 (13), 115 (23), 91 (19), 79 (13).
HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{19}Br$**: 278.0670; found 278.0647.

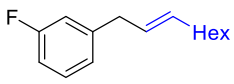
Synthesis of ethyl 1-benzyl-4-(2-fluorobenzyl)-1,2,3,6-tetrahydropyridine (180i)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), 1-benzyl-4-bromo-1,2,3,6-tetrahydropyridine (**179h**, 84.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 2-fluorobenzylmanganese chloride (**177f**, 1.00 mL, 400 µmol, 0.40 M) was added dropwise before the mixture was allowed to warm to 25 °C for 12 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 85:15, R_f = 0.35) afforded the desired cross-coupling reaction product **180i** (79.0 mg, 281 µmol, 84%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.30 – 7.21 (m, 4H), 7.21 – 7.07 (m, 3H), 7.03 – 6.90 (m, 2H), 5.29 (dt, *J* = 3.3, 1.7 Hz, 1H), 3.51 (s, 2H), 3.25 (s, 2H), 2.91 (dt, *J* = 3.7, 2.2 Hz, 2H), 2.49 (t, *J* = 5.8 Hz, 2H), 2.03 (dt, *J* = 5.9, 3.4 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 161.4 (d, *J* = 245.2 Hz), 138.4, 134.7, 131.4 (d, *J* = 4.8 Hz), 129.4, 128.3, 127.9 (d, *J* = 8.1 Hz), 127.2, 126.5 (d, *J* = 16.0 Hz), 124.0 (d, *J* = 3.6 Hz), 121.0, 115.3 (d, *J* = 22.3 Hz), 62.8, 53.0, 49.9, 36.0 (d, *J* = 2.9 Hz), 29.1.
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –118.2.
IR (ATR, cm^{-1}) ṽ = 2908, 2798, 2749, 1584, 1491, 1454, 1364, 1229, 1149, 1112, 1094, 1028, 970, 827, 753, 729, 698.
MS (EI, 70 eV, %) m/z = 172 (68), 109 (11), 91 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{20}FN$**: 281.1580; found 281.1494.

Synthesis of (*E*)-1-fluoro-3-(non-2-en-1-yl)benzene (180j)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), (*E*)-1-iodooctene (**179a**, 79.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 3-fluorobenzylmanganese chloride (**177g**, 1.33 mL, 400 µmol, 0.30 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane, R_f = 0.80) afforded the desired cross-coupling reaction product **180j** (69.0 mg, 313 µmol, 94%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.28 – 7.20 (m, 1H), 6.96 (d, *J* = 7.7 Hz, 1H), 6.89 (t, *J* = 8.4 Hz, 2H), 5.60 – 5.44 (m, 2H), 3.33 (d, *J* = 3.7 Hz, 2H), 2.04 (dt, *J* = 10.4, 6.2 Hz, 2H), 1.45 – 1.19 (m, 8H), 0.94 – 0.84 (m, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 163.1 (d, *J* = 245.1 Hz), 143.9 (d, *J* = 7.1 Hz), 133.0, 129.8 (d, *J* = 8.3 Hz), 128.0, 124.2 (d, *J* = 2.8 Hz), 115.4 (d, *J* = 21.0 Hz), 112.8 (d, *J* = 21.1 Hz), 38.9 (d, *J* = 1.7 Hz), 32.7, 31.9, 29.5, 29.0, 22.8, 14.2.

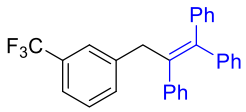
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –113.9.

IR (ATR, cm^{-1}) ṽ = 2956, 2927, 2856, 1615, 1586, 1487, 1467, 1448, 1266, 1249, 1139, 966, 948, 871, 778, 754, 723, 685.

MS (EI, 70 eV, %) m/z = 135 (27), 122 (100), 109 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{21}F$**: 220.1627; found 220.1620.

Synthesis of (3-(3-(trifluoromethyl)phenyl)prop-1-ene-1,1,2-triyl)tribenzene (180k)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), (2-bromoethene-1,1,2-triyl)tribenzene (**179i**, 112 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 3-(trifluoromethyl)benzylmanganese chloride (**177h**, 1.29 mL, 400 µmol, 0.31 M) was added dropwise before the mixture was allowed to warm to 25 °C for 12 h. Purification by flash column chromatography (*iso*hexane, R_f = 0.18) afforded the desired cross-coupling reaction product **180k** (120 mg, 290 µmol, 87%) as a white solid.

M.p. (°C): 121-123.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.39 – 7.23 (m, 9H), 7.13 – 6.99 (m, 8H), 6.97 – 6.93 (m, 2H), 3.92 (s, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 143.0, 142.6, 142.5, 141.7, 141.2, 137.2, 132.1 (d, *J* = 1.1 Hz), 130.8, 130.5 (d, *J* = 31.8 Hz), 130.0, 129.4, 128.7, 128.5, 128.1, 127.7, 127.2, 126.6, 126.3, 125.7 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 272.9 Hz), 122.8 (d, *J* = 3.9 Hz), 41.4.

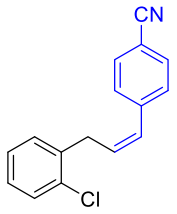
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –62.7.

IR (ATR, cm^{-1}) ṽ = 1489, 1445, 1330, 1311, 1281, 1160, 1154, 1120, 1095, 1079, 1031, 1001, 956, 922, 908, 872, 814, 800, 780, 764, 748, 712, 695, 659.

MS (EI, 70 eV, %) m/z = 414 (78), 336 (100), 323 (28), 283 (12), 267 (19), 265 (19), 259 (12), 255 (30), 252 (44), 239 (34), 191 (20), 189 (12), 178 (45), 176 (15), 167 (93), 165 (59), 152 (27), 126 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{28}H_{21}F_3$**: 414.1595; found 414.1592.

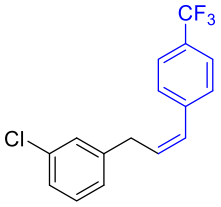
Synthesis of (*Z*)-4-(3-(2-chlorophenyl)prop-1-en-1-yl)benzonitrile (180l)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), (*Z*)-4-(2-bromovinyl)benzonitrile (**179j**, 70.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 2-chlorobenzylmanganese chloride (**177i**, 1.82 mL, 400 µmol, 0.22 M) was added dropwise before the mixture was allowed to warm to 25 °C for 12 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.30) afforded the desired cross-coupling reaction product **180l** (83.0 mg, 327 µmol, 98%) as a white solid.

M.p. (°C): 100-102.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.69 – 7.58 (m, 2H), 7.47 – 7.32 (m, 3H), 7.25 – 7.12 (m, 3H), 6.62 (dd, *J* = 11.6, 1.9 Hz, 1H), 5.97 (dt, *J* = 11.6, 7.5 Hz, 1H), 3.73 (dd, *J* = 7.5, 1.8 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 141.8, 137.5, 134.1, 132.3 (2C), 129.9, 129.7, 129.4 (2C), 128.0, 127.2, 119.1, 110.6, 32.7.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2230, 1474, 1215, 1052, 858, 744, 668.
MS (EI, 70 eV, %) m/z = 253 (10), 218 (100), 216 (12), 203 (21), 190 (11), 140 (48), 115 (27).
HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{12}ClN$**: 253.0658; found 253.0651.

Synthesis of (*Z*)-1-chloro-3-(3-(4-(trifluoromethyl)phenyl)allyl)benzene (180m)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), (*Z*)-1-(2-iodovinyl)-4-(trifluoromethyl)benzene (**179k**, 99.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 3-chlorobenzylmanganese chloride (**177j**, 0.85 mL, 400 µmol, 0.47 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane, R_f = 0.46) afforded the desired cross-coupling reaction product **180m** (97.0 mg, 327 µmol, 98%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.61 (d, *J* = 8.1 Hz, 2H), 7.43 – 7.37 (m, 2H), 7.26 – 7.19 (m, 3H), 7.09 (ddq, *J* = 7.4, 1.5, 0.8 Hz, 1H), 6.65 (d, *J* = 11.6 Hz, 1H), 5.94 (dt, *J* = 11.6, 7.6 Hz, 1H), 3.63 (dd, *J* = 7.6, 1.8 Hz, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 142.3, 140.6 (d, *J* = 1.4 Hz), 134.6 (2C), 131.8, 130.0, 129.6 (2C), 129.1 (q, *J* = 32.5 Hz), 128.6, 126.6 (d, *J* = 6.0 Hz), 125.4 (q, *J* = 3.8 Hz), 124.32 (d, *J* = 271.9 Hz), 34.3.

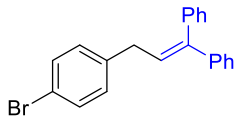
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –62.5.

IR (ATR, cm^{-1}) ṽ = 1618, 1597, 1574, 1476, 1321, 1161, 1109, 1080, 1066, 1016, 849, 778, 747, 734, 684.

MS (EI, 70 eV, %) m/z = 296 (12), 261 (100), 246 (19), 227 (12), 221 (11), 192 (26), 189 (16), 183 (59), 149 (14), 115 (61).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{12}ClF_3$**: 296.0580; found 296.0572.

Synthesis of (3-(4-bromophenyl)prop-1-ene-1,1-diyl)dibenzene (180n)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), 2,2-diphenylvinyl trifluoromethanesulfonate (**179e**, 109 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 4-bromobenzylmanganese chloride (**177k**, 1.82 mL, 400 µmol, 0.22 M) was added dropwise before the mixture was allowed to warm to 25 °C for 12 h. Purification by flash column chromatography (*iso*hexane, R_f = 0.39) afforded the desired cross-coupling reaction product **180n** (50.0 mg, 143 µmol, 43%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.42 – 7.35 (m, 4H), 7.35 – 7.25 (m, 2H), 7.25 – 7.19 (m, 6H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.20 (t, *J* = 7.6 Hz, 1H), 3.41 (d, *J* = 7.6 Hz, 2H).

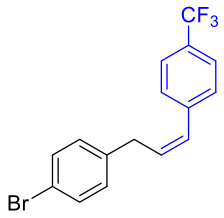
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 143.1, 142.3, 140.0, 139.7, 131.6, 130.3, 129.9, 128.5, 128.3, 127.5, 127.4, 127.3, 127.0, 119.9, 35.4.

IR (ATR, cm^{-1}) ṽ = 3057, 3026, 2924, 1710, 1700, 1659, 1590, 1486, 1446, 1402, 1318, 1277, 1070, 1011, 800, 754, 696.

MS (EI, 70 eV, %) m/z = 348 (10), 272 (16), 270 (17), 269 (38), 192 (47), 191 (100), 190 (11), 189 (22), 178 (38), 165 (29), 91 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{21}H_{17}Br$**: 348.0514; found 348.0506.

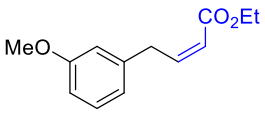
Synthesis of (*Z*)-1-bromo-4-(3-(4-(trifluoromethyl)phenyl)allyl)benzene (180o)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), (*Z*)-1-(2-iodovinyl)-4-(trifluoromethyl)benzene (**179k**, 99.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 4-bromobenzylmanganese chloride (**177k**, 1.82 mL, 400 µmol, 0.22 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane, R_f = 0.56) afforded the desired cross-coupling reaction product **180o** (60.0 mg, 176 µmol, 53%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.60 (d, *J* = 8.2 Hz, 2H), 7.46 – 7.35 (m, 4H), 7.11 – 7.04 (m, 2H), 6.63 (d, *J* = 11.5 Hz, 1H), 5.93 (dt, *J* = 11.5, 7.6 Hz, 1H), 3.60 (dd, *J* = 7.6, 1.7 Hz, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 140.6 (d, *J* = 1.3 Hz), 139.2, 132.1, 131.8, 130.1, 129.4, 129.1 (q, *J* = 32.5 Hz),129.0, 125.4 (q, *J* = 3.8 Hz), 124.3 (d, *J* = 272.0 Hz), 120.2, 34.1.
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –62.5.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 1618, 1487, 1322, 1162, 1120, 1109, 1066, 1011, 855, 817, 797, 744.
MS (EI, 70 eV, %) m/z = 340 (10), 261 (57), 246 (21), 221 (14), 191 (42), 189 (27), 183 (58), 171 (10), 169 (11), 165 (20), 159 (10), 151 (18), 133 (12), 115 (100), 102 (11), 91 (21), 89 (28), 69 (12).
HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{12}BrF_3$**: 340.0074; found 340.0066.

Synthesis of ethyl (*Z*)-Ethyl 4-(3-methoxyphenyl)but-2-enoate (180p)



In relation to **TP8**, for this reaction $FeCl_2$ (13.0 mg, 100 µmol), (*Z*)-ethyl 3-iodoacrylate (**179l**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.00 mL) were used. The reaction mixture was cooled to 0 °C and 3-methoxybenzylmanganese chloride (**177a**, 3.08 mL, 1.20 mmol, 0.39 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.23) afforded the desired cross-coupling reaction product **180p** (218 mg, 980 µmol, 98%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.22 (t, *J* = 7.5 Hz, 1H), 6.89 – 6.71 (m, 3H), 6.34 (dt, *J* = 11.4, 7.5 Hz, 1H), 5.85 (dt, *J* = 11.4, 1.8 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 4.00 (dd, *J* = 7.5, 1.7 Hz, 2H), 3.80 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).

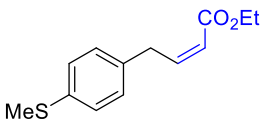
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.5, 160.0, 147.9, 141.2, 129.7, 121.1, 120.1, 114.5, 111.9, 60.1, 55.3, 35.3, 14.4.

IR (ATR, cm^{-1}) ṽ = 2980, 2938, 2836, 1714, 1642, 1600, 1584, 1490, 1466, 1454, 1438, 1410, 1388, 1314, 1284, 1258, 1198, 1160, 1148, 1112, 1094, 1038, 996, 932, 910, 862, 822, 780, 760, 696.

MS (EI, 70 eV, %) m/z = 220 (32), 174 (69), 163 (12), 160 (15), 147 (100), 145 (67), 131 (43), 117 (13), 115 (48), 103 (24), 91 (36), 77 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{16}O_3$**: 220.1099; found 220.1091.

Synthesis of (*Z*)-ethyl 4-(4-(methylthio)phenyl)but-2-enoate (180q)



In relation to **TP8**, for this reaction $FeCl_2$ (13.0 mg, 100 µmol), (*Z*)-ethyl 3-iodoacrylate (**179l**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.00 mL) were used. The reaction mixture was cooled to 0 °C and 4-methylthiobenzylmanganese chloride (**177b**, 3.33 mL, 1.20 mmol, 0.36 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 19:1, R_f = 0.56) afforded the desired cross-coupling reaction product **180q** (180 mg, 760 µmol, 76%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.24 – 7.19 (m, 2H), 7.18 – 7.13 (m, 2H), 6.31 (dt, *J* = 11.4, 7.6 Hz, 1H), 5.85 (dt, *J* = 11.4, 1.8 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.98 (dd, *J* = 7.6, 1.7 Hz, 2H), 2.47 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H).

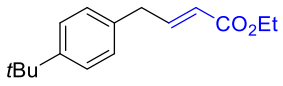
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.5, 147.8, 136.4 (2C), 129.3, 127.4, 120.2, 60.2, 34.7, 16.4, 14.4.

IR (ATR, cm^{-1}) ṽ = 2982, 2922, 1712, 1642, 1494, 1478, 1464, 1438, 1412, 1386, 1296, 1234, 1192, 1160, 1114, 1094, 1036, 1018, 968, 926, 912, 842, 806, 734, 722.

MS (EI, 70 eV, %) m/z = 236 (54), 207 (15), 190 (82), 179 (21), 163 (17), 161 (100), 147 (18), 144 (27), 128 (21), 121 (11), 115 (78).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{16}O_2S$**: 236.0871; found 236.0864.

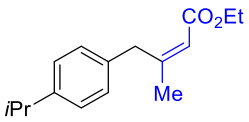
Synthesis of ethyl (*E*)-4-(4-(tert-butyl)phenyl)but-2-enoate (180r)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), ethyl (*E*)-3-iodoacrylate (**179m**, 76.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 4-tertbutylbenzylmanganese chloride (**177d**, 1.08 mL, 400 µmol, 0.37 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.26) afforded the desired cross-coupling reaction product **180r** (45.0 mg, 183 µmol, 55%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.35 (s, 1H), 7.33 (s, 1H), 7.15 – 7.06 (m, 3H), 5.82 (dt, *J* = 15.5, 1.7 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.49 (dd, *J* = 6.9, 1.6 Hz, 2H), 1.36 – 1.27 (m, 12H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.7, 149.7, 147.7, 134.8, 128.6, 125.7, 122.3, 60.4, 38.1, 34.6, 31.5, 14.4.
IR (ATR, cm^{-1}) ṽ = 2962, 2906, 2870, 1717, 1655, 1513, 1464, 1366, 1320, 1265, 1196, 1154, 1110, 1040, 984, 842, 828, 815, 803, 715.
MS (EI, 70 eV, %) m/z = 246 (26), 231 (100), 203 (24), 185 (61), 157 (49), 144 (30), 129 (19), 117 (19), 115 (17).
HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{22}O_2$**: 246.1620; found 246.1612.

Synthesis of ethyl (*Z*)-4-(4-isopropylphenyl)-3-methylbut-2-enoate (180s)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), ethyl (*Z*)-3-iodobut-2-enoate (**179n**, 80.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 4-isopropylbenzylmanganese chloride (**177e**, 1.08 mL, 400 µmol, 0.37 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 98:2, R_f = 0.27) afforded the desired cross-coupling reaction product **180s** (64.0 mg, 260 µmol, 78%) as a yellowish oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.21 – 7.05 (m, 4H), 5.76 (d, *J* = 1.3 Hz, 1H), 4.19 (d, *J* = 7.1 Hz, 2H), 3.98 (s, 2H), 2.87 (p, *J* = 6.9 Hz, 1H), 1.80 (d, *J* = 1.3 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 6H).

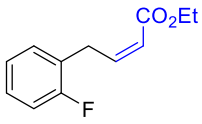
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.7, 158.1, 146.9, 136.3, 129.0, 126.6, 117.0, 59.8, 38.6, 33.8, 24.8, 24.2, 14.5.

IR (ATR, cm^{-1}) ṽ = 2960, 1712, 1649, 1512, 1442, 1376, 1242, 1161, 1136, 1097, 1050, 1020, 864, 844, 800.

MS (EI, 70 eV, %) m/z = 246 (10), 158 (100), 131 (24), 129 (36), 115 (14), 91 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{22}O_2$**: 246.1620; found 246.1613.

Synthesis of (*Z*)-Ethyl 4-(2-fluorophenyl)but-2-enoate (180t)



In relation to **TP8**, for this reaction $FeCl_2$ (13.0 mg, 100 µmol), (*Z*)-ethyl 3-iodoacrylate (**179l**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.00 mL) were used. The reaction mixture was cooled to 0 °C and 2-fluorobenzylmanganese chloride (**177f**, 3.00 mL, 1.20 mmol, 0.40 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 19:1, R_f = 0.54) afforded the desired cross-coupling reaction product **180t** (202 mg, 970 µmol, 97%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.41 – 7.17 (m, 2H), 7.17 – 6.83 (m, 2H), 6.36 (dt, *J* = 11.4, 7.5 Hz, 1H), 5.89 (dt, *J* = 11.4, 1.8 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.08 (d, *J* = 7.5 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.4, 161.2 (d, *J* = 245.6 Hz), 146.5, 130.9 (d, *J* = 4.7 Hz), 128.3 (d, *J* = 8.0 Hz), 126.5 (d, *J* = 15.9 Hz), 124.3 (d, *J* = 3.6 Hz), 120.6, 115.5 (d, *J* = 21.8 Hz), 60.2, 28.7 (d, *J* = 3.1 Hz), 14.4.

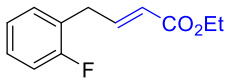
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –118.2.

IR (ATR, cm^{-1}) ṽ = 2982, 1716, 1646, 1586, 1492, 1456, 1412, 1388, 1298, 1286, 1230, 1198, 1180, 1162, 1114, 1098, 1032, 864, 846, 818, 754.

MS (EI, 70 eV, %) m/z = 208 (38), 180 (27), 162 (66), 151 (21), 135 (75), 133 (100), 123 (10), 115 (36), 109 (23), 83 (15).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{13}O_2F$**: 208.0900; found 208.0891.

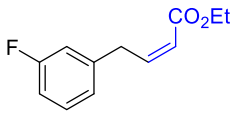
Synthesis of ethyl (*E*)-4-(2-fluorophenyl)but-2-enoate (180u)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), ethyl (*E*)-3-iodoacrylate (**179m**, 76.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 2-fluorobenzylmanganese chloride (**177f**, 1.00 mL, 400 µmol, 0.40 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 95:5, R_f = 0.29) afforded the desired cross-coupling reaction product **180u** (46.0 mg, 221 µmol, 66%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.19 – 7.07 (m, 2H), 7.06 – 6.94 (m, 3H), 5.73 (dtd, *J* = 15.6, 1.7, 0.6 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.48 (dt, *J* = 6.7, 1.5 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.5, 161.1 (d, *J* = 246.1 Hz), 145.8, 131.0 (d, *J* = 4.4 Hz), 128.7 (d, *J* = 8.1 Hz), 124.9 (d, *J* = 15.9 Hz), 124.4 (d, *J* = 3.7 Hz), 122.8, 115.6 (d, *J* = 21.8 Hz), 60.5, 31.7 (d, *J* = 3.2 Hz), 14.4.
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –118.1.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2982, 2932, 1716, 1654, 1585, 1492, 1456, 1368, 1332, 1267, 1230, 1202, 1157, 1098, 1037, 982, 830, 754, 701.
MS (EI, 70 eV, %) m/z = 208 (36), 180 (37), 173 (15), 162 (58), 153 (14), 151 (11), 135 (100), 133 (51), 125 (12), 115 (36), 109 (15).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{13}FO_2$**: 208.0900; found 208.0889.

Synthesis of (*Z*)-Ethyl 4-(3-fluorophenyl)but-2-enoate (180v)



In relation to **TP8**, for this reaction $FeCl_2$ (13.0 mg, 100 µmol), (*Z*)-ethyl 3-iodoacrylate (**179l**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.00 mL) were used. The reaction mixture was cooled to 0 °C and 3-fluorobenzylmanganese chloride (**177g**, 4.00 mL, 1.20 mmol, 0.30 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 19:1, R_f = 0.51) afforded the desired cross-coupling reaction product **180v** (148 mg, 710 µmol, 71%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.49 – 7.21 (m, 1H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.94 (ddd, *J* = 10.8, 8.8, 2.0 Hz, 2H), 6.34 (dt, *J* = 11.4, 7.6 Hz, 1H), 5.90 (dt, *J* = 11.4, 1.8 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.05 (dd, *J* = 7.6, 1.5 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.4, 163.1 (d, *J* = 245.8 Hz), 146.9, 142.1 (d, *J* = 7.3 Hz), 130.1 (d, *J* = 8.3 Hz), 124.4 (d, *J* = 2.8 Hz), 120.7, 115.6 (d, *J* = 21.3 Hz), 113.4 (d, *J* = 21.0 Hz), 60.2, 34.9 (d, *J* = 1.9 Hz), 14.4.

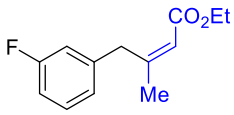
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –113.3.

IR (ATR, cm^{-1}) ṽ = 2984, 1714, 1644, 1616, 1588, 1488, 1466, 1448, 1412, 1388, 1298, 1284, 1270, 1250, 1196, 1162, 1136, 1096, 1076, 1038, 1028, 952, 926, 892, 862, 824, 782, 766, 692.

MS (EI, 70 eV, %) m/z = 208 (34), 180 (13), 162 (50), 151 (16), 135 (100), 133 (93), 115 (28), 109 (19), 83 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{13}O_2F$**: 208.0900; found 208.0892.

Synthesis of ethyl (*Z*)-4-(3-fluorophenyl)-3-methylbut-2-enoate (180w)



According to **TP8**, for this reaction $FeCl_2$ (4.20 mg, 33.0 µmol), ethyl (*Z*)-3-iodobut-2-enoate (**179n**, 80.0 mg, 333 µmol) and freshly distilled THF (0.30 mL) were used. The reaction mixture was cooled to 0 °C and 3-fluorobenzylmanganese chloride (**177g**, 1.33 mL, 400 µmol, 0.30 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.30) afforded the desired cross-coupling reaction product **180w** (51.0 mg, 230 µmol, 69%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.26 – 7.19 (m, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.96 (dt, *J* = 10.0, 1.9 Hz, 1H), 6.90 (td, *J* = 8.3, 2.1 Hz, 1H), 5.83 – 5.77 (m, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.02 (s, 2H), 1.79 (d, *J* = 1.3 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.5, 163.1 (d, *J* = 245.4 Hz), 156.8, 141.5 (d, *J* = 7.4 Hz), 129.9 (d, *J* = 8.4 Hz), 124.8 (d, *J* = 2.8 Hz), 117.7, 115.9 (d, *J* = 21.3 Hz), 113.3 (d, *J* = 21.2 Hz), 59.9, 38.6 (d, *J* = 1.6 Hz), 24.7, 14.4.

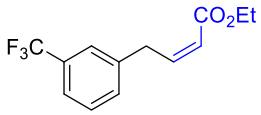
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –113.6.

IR (ATR, cm^{-1}) ṽ = 2981, 1709, 1651, 1614, 1588, 1486, 1445, 1371, 1351, 1243, 1168, 1136, 1096, 1075, 1050, 951, 859, 783, 760, 690.

MS (EI, 70 eV, %) m/z = 222 (10), 176 (100), 148 (57), 133 (21), 128 (10), 109 (20).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{15}FO_2$**: 222.1056; found 222.1079.

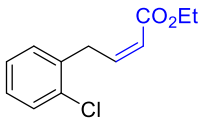
Synthesis of (*Z*)-Ethyl 4-(3-(trifluoromethyl)phenyl)but-2-enoate (180x)



In relation to **TP8**, for this reaction $FeCl_2$ (13.0 mg, 100 µmol), (*Z*)-ethyl 3-iodoacrylate (**179l**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.00 mL) were used. The reaction mixture was cooled to 0 °C and 3-(trifluoromethyl)benzylmanganese chloride (**177h**, 3.90 mL, 1.20 mmol, 0.31 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.23) afforded the desired cross-coupling reaction product **180x** (130 mg, 500 µmol, 50%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.83 – 7.35 (m, 4H), 6.32 (dt, *J* = 11.4, 7.6 Hz, 1H), 5.91 (dt, *J* = 11.4, 1.7 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 4.09 (dd, *J* = 7.6, 1.6 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.3, 146.5, 140.5, 132.2, 131.1 (q, *J* = 32.1 Hz), 129.2, 125.4 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 272.3 Hz), 123.4 (q, *J* = 3.8 Hz), 121.0, 60.3, 34.9, 14.4.
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –62.6.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2984, 1716, 1646, 1450, 1412, 1388, 1330, 1238, 1194, 1160, 1120, 1096, 1072, 1038, 1002, 936, 918, 900, 868, 822, 798, 762, 702, 656.
MS (EI, 70 eV, %) m/z = 258 (55), 230 (50), 213 (61), 210 (12), 201 (13), 193 (30), 185 (59), 183 (34) 181 (11), 175 (11), 173 (13), 165 (87), 164 (50), 161 (32), 159 (22), 146 (16), 133 (22), 115 (100), 109 (15).
HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{13}O_2F_3$**: 258.0868; found 258.0858.

Synthesis of (*Z*)-Ethyl 4-(2-chlorophenyl)but-2-enoate (180y)



In relation to **TP8**, for this reaction $FeCl_2$ (13.0 mg, 100 µmol), (*Z*)-ethyl 3-iodoacrylate (**179l**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.00 mL) were used. The reaction mixture was cooled to 0 °C and 2-chlorobenzylmanganese chloride (**177i**, 5.45 mL, 1.20 mmol, 0.22 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 99:1, R_f = 0.26) afforded the desired cross-coupling reaction product **180y** (113 mg, 500 µmol, 50%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.36 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.30 (dd, *J* = 7.2, 2.1 Hz, 1H), 7.23 – 7.13 (m, 2H), 6.33 (dt, *J* = 11.4, 7.4 Hz, 1H), 5.88 (dt, *J* = 11.4, 1.8 Hz, 1H), 4.19 (ddd, *J* = 10.8, 9.2, 4.5 Hz, 4H), 1.32 (t, *J* = 7.1 Hz, 3H).

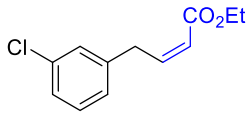
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.4, 146.3, 137.4, 134.2, 130.8, 129.6, 128.0, 127.2, 120.7, 60.2, 33.1, 14.4.

IR (ATR, cm^{-1}) ṽ = 2982, 2928, 1714, 1644, 1474, 1444, 1410, 1386, 1298, 1286, 1234, 1192, 1162, 1126, 1096, 1052, 1032, 926, 842, 806, 750, 680, 668.

MS (EI, 70 eV, %) m/z = 224 (51), 215 (16), 213 (11), 193 (12), 179 (100), 178 (45), 167 (11), 165 (19), 151 (16), 149 (19), 144 (13), 127 (23), 125 (75), 115 (39), 89 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{13}O_2Cl$**: 224.0604; found 224.0614.

Synthesis of (*Z*)-Ethyl 4-(3-chlorophenyl)but-2-enoate (180z)



In relation to **TP8**, for this reaction $FeCl_2$ (13.0 mg, 100 µmol), (*Z*)-ethyl 3-iodoacrylate (**179l**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.00 mL) were used. The reaction mixture was cooled to 0 °C and 3-chlorobenzylmanganese chloride (**177j**, 2.55 mL, 1.20 mmol, 0.47 M) was added dropwise before the mixture was allowed to warm to 25 °C for 1 h. Purification by flash column chromatography (*iso*hexane:ethyl acetate = 19:1, R_f = 0.54) afforded the desired cross-coupling reaction product **180z** (163 mg, 730 µmol, 73%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.42 – 7.18 (m, 3H), 7.14 (dd, *J* = 7.0, 1.8 Hz, 1H), 6.32 (dt, *J* = 11.4, 7.6 Hz, 1H), 5.90 (dt, *J* = 11.4, 1.7 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.03 (dd, *J* = 7.6, 1.7 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.4, 146.8, 141.6, 134.5, 130.0, 128.9, 127.0, 126.7, 120.7, 60.3, 34.8, 14.4.

IR (ATR, cm^{-1}) ṽ = 2982, 1714, 1644, 1598, 1574, 1476, 1430, 1410, 1388, 1298, 1286, 1236, 1194, 1160, 1114, 1094, 1080, 1036, 1000, 932, 860, 886, 818, 780, 756, 736, 702, 682.

MS (EI, 70 eV, %) m/z = 224 (28), 179 (23), 178 (35), 167 (16), 153 (18), 151 (53), 149 (30), 144 (25), 138 (14), 133 (10), 125 (14), 116 (22), 115 (100), 103 (12), 89 (16).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{13}O_2Cl$**: 224.0604; found 224.0597.

7 Iron-Catalyzed Cross-Coupling of Functionalized *Bis*-(aryl)manganese Nucleophiles with Alkenyl Halides

7.1 Typical Procedures

Typical Procedure for the One-Pot Preparation of *Bis*-(aryl)manganese Reagents 181a–181g (TP 9)

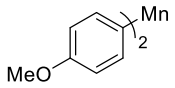
A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (0.610 g, 14.4 mmol, 2.40 equiv), heated to 450 °C under high vacuum and then cooled to room temperature. After being switched to argon, the same procedure was applied after $MnCl_2$ was added (453 mg, 3.60 mmol, 0.60 equiv). After cooling to room temperature, magnesium turnings were added (0.350 g, 14.4 mmol, 2.40 equiv), followed by freshly distilled THF (12 mL). After the reaction mixture was cooled to −5 °C, the aryl bromides **182a**–**182g** were then added drop by drop (6.0 mmol, 1.00 equiv) and the reaction mixture was stirred until a complete conversion of the starting material was observed. The reaction progress was monitored by GC-analysis of hydrolyzed and iodolyzed aliquots. When the metalation was completed, the concentration of the *bis*-(aryl)manganese species was determined by titration against iodine in freshly distilled THF. The black solutions of the aryl reagents **181a**–**181g** were then separated from the magnesium turnings using a syringe and subsequently transferred into another pre-dried and argon-flushed *Schlenk*-tube, which was cooled to −5 °C. After a titration against iodine in freshly distilled THF was performed, the reagent was ready to be used for Cross-Couplings.

Typical Procedure for the Fe-catalyzed Cross-Coupling Reactions of *Bis*-(aryl)manganese Reagents 181a–181g with different Elecrophiles 183a–183e (TP 10)

A pre-dried and argon-flushed *Schlenk*-tube equipped with a magnetic stirring bar and a rubber septum was charged with $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), the corresponding electrophile (**183a**–**183e**, 1.00 mmol, 1.00 equiv), tetradecane as internal standard (50 µL) and freshly distilled THF (1.0 mL) as solvent. The reaction mixture was cooled to 0 °C and the *bis*-(aryl)manganese solution (**181a**–**181g**, 0.60 equiv) was added dropwise whereupon a color change to dark brown could be recognized. After the addition was complete, the reaction mixture was stirred for a given time at room temperature. Thereupon, a saturated aqueous solution of NH_4Cl was added and the aqueous layer was extracted with EtOAc (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Crude products purified by flash column chromatography, affording the desired cross-coupling reaction products (**184a**–**184n**). Yield of **180l** determined by GC and ^{1}H-NMR.

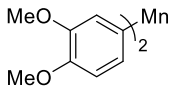
7.2 Preparation of *Bis*-(aryl)manganese Reagents 181

Preparation of *Bis*-(4-methoxyphenyl)manganese (181a)



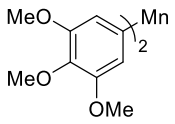
Based on **TP9**, LiCl (814 mg, 19.2 mmol, 2.40 equiv), magnesium turnings (467 mg, 19.2 mmol), $MnCl_2$ (605 mg, 4.8 mmol), THF (16.0 mL) and 1-bromo-4-methoxybenzene (**182a**, 1.496 g, 1.00 mL, 8.0 mmol) were used. After stirring for 1 h at the given temperature, the concentration of *bis*-(4-methoxyphenyl)manganese (**181a**) was determined against iodine in THF (0.25 M, 87%).

Preparation of *Bis*-(3,4-dimethoxyphenyl)manganese (181b)



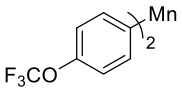
Based on **TP9**, LiCl (305 mg, 7.2 mmol), magnesium turnings (175 mg, 7.2 mmol), $MnCl_2$ (227 mg, 1.8 mmol), THF (6.0 mL) and 5-bromo-1,2-dimethoxybenzene (**182b**, 868 mg, 3.0 mmol) were used. After stirring for 2 h, the concentration of *bis*-(3,4-dimethoxyphenyl)manganese (**181b**) was determined against iodine in THF (0.15 M, 30%).

Preparation of *Bis*-(3,4,5-trimethoxyphenyl)manganese (181c)



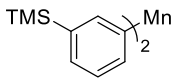
Based on **TP9**, LiCl (814 mg, 19.2 mmol), magnesium turnings (467 mg, 19.2 mmol), $MnCl_2$ (605 mg, 4.8 mmol), THF (16.0 mL) and 5-bromo-1,2,3-trimethoxybenzene (**182c**, 1.977 g, 8.0 mmol) were used. After stirring for 1 h at the given temperature, the concentration of *bis*-(3,4,5-trimethoxyphenyl)manganese (**181c**) was determined against iodine in THF (0.23 M, 68%).

Preparation of *Bis*-(4-(trifluoromethoxy)phenyl)manganese (181d)



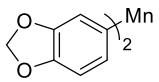
Based on **TP9**, LiCl (814 mg, 19.2 mmol), magnesium turnings (467 mg, 19.2 mmol), $MnCl_2$ (605 mg, 4.8 mmol), THF (16.0 mL) and 1-bromo-4-trifluoromethoxybenzene (**182d**, 1.496 g, 1.00 mL, 8.0 mmol) were used. After stirring for 1 h at the given temperature, the concentration of *bis*-(4-trifluoromethoxyphenyl)manganese (**181d**) was determined against iodine in THF (0.25 M, 74%).

Preparation of *Bis*-(3-(trimethylsilyl)phenyl)manganese (181e)



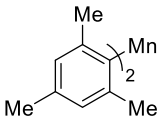
Based on **TP9**, LiCl (305 mg, 7.2 mmol), magnesium turnings (175 mg, 7.2 mmol), $MnCl_2$ (227 mg, 1.8 mmol), THF (6.0 mL) and (3-bromophenyl)trimethylsilane (**182e**, 688 mg, 0.57 mL, 3.0 mmol) were used. After stirring for 1 h at the given temperature, the concentration of *bis*-(3-(trimethylsilyl)phenyl)manganese (**181e**) was determined against iodine in THF (0.13 M, 52%).

Preparation of *Bis*-benzo[*d*][1,3]dioxol-5-ylmanganese (181f)



Based on **TP9**, LiCl (814 mg, 19.2 mmol), magnesium turnings (467 mg, 19.2 mmol), $MnCl_2$ (605 mg, 4.8 mmol), THF (16.0 mL) and 5-bromobenzo[*d*][1,3]dioxole (**182f**, 1.608 g, 0.95 mL, 8.0 mmol) were used. After stirring for 1 h at the given temperature, the concentration of *bis*-benzo[d][1,3]dioxol-5-ylmanganese (**181f**) was determined against iodine in THF (0.29 M, 79%).

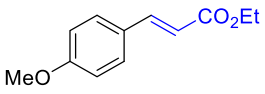
Preparation of *Bis*-(mesityl)manganese (181g)



Based on **TP9**, LiCl (814 mg, 19.2 mmol), magnesium turnings (467 mg, 19.2 mmol), $MnCl_2$ (605 mg, 4.8 mmol), THF (16.0 mL) and mesityl bromide (**182g**, 1.592 g, 1.22 mL, 8.0 mmol) were used. After stirring for 1.5 h at the given temperature, the concentration of *bis*-(mesityl)manganese (**181g**) was determined against iodine in THF (0.27 M, 83%).

7.3 Synthesis of Compounds 184

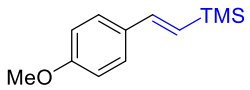
Synthesis of (*E*)-ethyl 3-(4-methoxyphenyl)acrylate (184a)



According to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), (*Z*)-ethyl 3-iodoacrylate (**183a**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(4-methoxyphenyl)manganese (**181a**, 3.0 mL, 1.20 mmol, 0.21 M) was added dropwise before the mixture was stirred for 1 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 19:1, R_f = 0.20) afforded the desired cross-coupling reaction product **184a** (0.163 g, 0.79 mmol, 79%) as a pale-yellow solid.

M.p. (°C): 50-52.
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.64 (d, *J* = 16.0 Hz, 1H), 7.47 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.30 (d, *J* = 16.0 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 167.4, 161.5, 144.4, 129.8, 127.3, 115.9, 114.4, 60.4, 55.5, 14.5.
IR (ATR, cm^{-1}) ṽ = 2972, 2930, 2898, 2870, 1708, 1632, 1604, 1512, 1458, 1442, 1372, 1316, 1302, 1288, 1252, 1206, 1164, 1096, 1026, 1006, 984, 930, 828, 778.
MS (EI, 70 eV, %) m/z = 206 (54), 178 (16), 162 (11), 161 (100), 134 (58), 133 (36), 118 (13), 89 (14).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{14}O_3$**: 206.0943; found 206.0937.

Synthesis of (*E*)-(4-methoxystyryl)trimethylsilane (184b)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), 2-bromovinyltrimethylsilane (**183b**, *Z*/*E* = 10/90, 179 mg, 0.15 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(4-methoxyphenyl)manganese (**181a**, 3.0 mL, 1.20 mmol, 0.21 M) was added dropwise before the mixture was stirred for 0.5 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 19:1, R_f = 0.71) afforded the desired cross-coupling reaction product **184b** (0.202 g, 0.98 mmol, 98%) as a pale-yellow solid.

M.p. (°C): 50-52.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.41 – 7.33 (m, 2H), 6.86 (m, 2H), 6.82 (d, *J* = 19.2 Hz, 1H), 6.31 (d, *J* = 19.1 Hz, 1H), 3.82 (s, 3H), 0.15 (s, 9H).

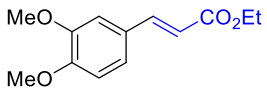
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 159.7, 143.1, 131.5, 127.7, 126.8, 114.0, 55.5, –1.0.

IR (ATR, cm^{-1}) ṽ = 2954, 2898, 2836, 1606, 1572, 1508, 1488, 1464, 1440, 1418, 1304, 1296, 1244, 1196, 1172, 1106, 1032, 992, 864, 832, 796, 748, 738, 726, 690.

MS (EI, 70 eV, %) m/z = 209 (12), 206 (42), 193 (20), 192 (10), 191 (100), 183 (12), 176 (10), 175 (37), 165 (36).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{18}OSi$**: 206.1127; found 206.1119.

Synthesis of (*E*)-ethyl 3-(3,4-dimethoxyphenyl)acrylate (184c)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), (*Z*)-ethyl 3-iodoacrylate (**183a**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(3,4-dimethoxyphenyl)manganese (**181b**, 4.0 mL, 0.60 mmol, 0.15 M) was added dropwise before the mixture was stirred for 0.5 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 8:2, R_f = 0.37) afforded the desired cross-coupling reaction product **184c** (0.165 g, 0.69 mmol, 69%) as a pale-yellow solid.

M.p. (°C): 55-57.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.61 (d, *J* = 15.9 Hz, 1H), 7.09 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.04 (d, *J* = 2.0 Hz, 1H), 6.85 (d, *J* = 8.3 Hz, 1H), 6.30 (d, *J* = 15.9 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 6H), 1.32 (t, *J* = 7.1 Hz, 3H).

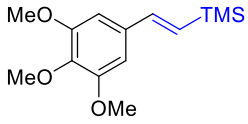
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 167.3, 151.2, 149.3, 144.6, 127.6, 122.7, 116.1, 111.1, 109.7, 60.5, 56.0 (2C), 14.5.

IR (ATR, cm^{-1}) ṽ = 2984, 2960, 2938, 2836, 1692, 1628, 1598, 1582, 1512, 1466, 1454, 1438, 1424, 1364, 1246, 1224, 1176, 1160, 1142, 1096, 1044, 1024, 986, 976, 968, 936, 870, 860, 802, 776, 752.

MS (EI, 70 eV, %) m/z = 237 (14), 236 (100), 191 (67), 164 (20), 105 (15), 70 (10), 61 (15), 44 (10), 43 (16), 42 (60).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{16}O_4$**: 236.1049; found 236.1042.

Synthesis of (*E*)-trimethyl(3,4,5-trimethoxystyryl)silane (184d)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), 2-bromovinyltrimethylsilane (**183b**, *Z/E* = 10/90, 179 mg, 0.15 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(3,4,5-trimethoxyphenyl)manganese (**181c**, 3.2 mL, 0.60 mmol, 0.22 M) was added dropwise before the mixture was stirred for 0.5 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 19:1, R_f = 0.29) afforded the desired cross-coupling reaction product **184d** (0.215 g, 0.80 mmol, 80%) as a white solid.

M.p. (°C): 44-46.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.79 (d, *J* = 19.0 Hz, 1H), 6.67 (s, 2H), 6.37 (d, *J* = 19.0 Hz, 1H), 3.87 (d, *J* = 17.1 Hz, 9H), 0.16 (s, 9H).

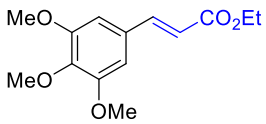
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 153.4, 143.5, 138.3, 134.2, 128.9, 103.5, 61.0, 56.2, –1.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3000, 2952, 2900, 2838, 2828, 1574, 1504, 1464, 1450, 1432, 1414, 1328, 1238, 1202, 1184, 1148, 1124, 1006, 996, 982, 862, 834, 804, 782, 742, 732, 690.

MS (EI, 70 eV, %) m/z = 267 (13), 266 (100), 251 (64), 239 (10), 236 (41), 235 (12), 221 (45), 220 (15), 219 (12), 205 (21), 194 (17), 179 (13), 161 (16), 89 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{22}O_3Si$**: 266.1338; found 266.1326.

Synthesis of (*E*)-ethyl 3-(3,4,5-trimethoxyphenyl)acrylate (184e)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), (*Z*)-ethyl 3-iodoacrylate (**183a**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(3,4,5-trimethoxyphenyl)manganese (**181c**, 3.2 mL, 0.60 mmol, 0.22 M) was added dropwise before the mixture was stirred for 0.5 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 19:1, R_f = 0.41) afforded the desired cross-coupling reaction product **184e** (0.151 g, 0.57 mmol, 57%) as a yellow-orange solid.

M.p. (°C): 70-72.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.59 (d, *J* = 15.9 Hz, 1H), 6.74 (s, 2H), 6.34 (d, *J* = 15.9 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.97 – 3.76 (m, 9H), 1.33 (t, *J* = 7.1 Hz, 3H).

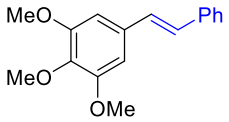
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.9, 153.4, 144.5, 140.1, 130.0, 117.5, 105.2, 61.0, 60.5, 56.1, 14.3.

IR (ATR, cm^{-1}) ṽ = 2974, 2944, 2928, 2838, 1700, 1632, 1582, 1504, 1470, 1452, 1432, 1414, 1340, 1310, 1272, 1242, 1174, 1148, 1118, 1034, 996, 982, 922, 872, 824, 790, 760.

MS (EI, 70 eV, %) m/z = 267 (14), 266 (100), 251 (55), 223 (15), 221 (19), 179 (11), 177 (21), 163 (21), 135 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{18}O_5$**: 266.1154; found 266.1142.

Synthesis of (*E*)-1,2,3-trimethoxy-5-styrylbenzene (184f)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), 2-bromovinylbenzene (**183c**, *Z/E* = 18:82, 183 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(3,4,5-trimethoxyphenyl)manganese (**181c**, 3.2 mL, 0.60 mmol, 0.22 M) was added dropwise before the mixture was stirred for 0.5 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 19:1, R_f = 0.12) afforded the desired cross-coupling reaction product **184f** (0.223 g, 0.82 mmol, 82%) as a pale-yellow solid.

M.p. (°C): 106-108.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.54 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.29 (tt, *J* = 6.8, 1.2 Hz, 1H), 7.18 – 6.95 (m, 2H), 6.77 (s, 2H), 3.95 (s, 6H), 3.91 (s, 3H).

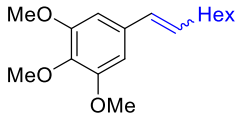
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 153.8, 138.4, 137.6, 133.5, 129.1, 129.0, 128.6, 128.0, 126.9, 104.1, 61.4, 56.6.

IR (ATR, cm^{-1}) ṽ = 2924, 2854, 1582, 1506, 1460, 1448, 1428, 1418, 1346, 1326, 1260, 1238, 1150, 1128, 1074, 1006, 984, 972, 846, 816, 784, 748, 692.

MS (EI, 70 eV, %) m/z = 271 (18), 270 (100), 256 (14), 255 (83), 195 (25), 181 (10), 180 (13), 167 (26), 165 (26), 153 (10), 152 (28), 141 (22), 115 (16).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{18}O_3$**: 270.1256; found 270.1251.

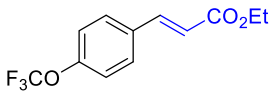
Synthesis of 1,2,3-trimethoxy-5-(oct-1-en-1-yl)benzene (184g)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), (*E*)-1-iodo-1-octene (**183d**, 238 mg, 0.17 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(3,4,5-trimethoxyphenyl)manganese (**181c**, 3.2 mL, 0.60 mmol, 0.22 M) was added dropwise before the mixture was stirred for 1 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 9:1, R_f = 0.36) afforded the desired cross-coupling reaction product **184g** (0.242 g, *Z/E* = 9/91, 0.87 mmol, 87%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 6.57 (s, 2H), 6.30 (d, *J* = 15.7 Hz, 1H), 6.14 (dt, *J* = 15.7, 6.8 Hz, 1H), 3.85 (d, *J* = 15.5 Hz, 9H), 2.26 – 2.10 (m, 2H), 1.71 – 1.19 (m, 8H), 0.89 (t, *J* = 6.9 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 153.4, 137.4, 133.9, 131.0, 129.7, 103.1, 61.1, 56.2, 33.1, 31.9, 29.5, 28.9, 22.8, 14.3.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2954, 2926, 2872, 2854, 1580, 1506, 1454, 1430, 1416, 1340, 1324, 1236, 1184, 1152, 1124, 1104, 1042, 1008, 960, 844, 808, 780, 688.
MS (EI, 70 eV, %) m/z = 281 (13), 279 (14), 278 (79), 263 (12), 225 (21), 207 (54), 196 (11), 195 (11), 182 (23), 181 (53), 179 (33), 177 (16), 176 (100), 175 (14), 167 (13), 161 (32), 153 (18), 151 (30), 133 (12), 115 (15), 91 (27), 79 (15), 77 (11), 67 (12).
HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{26}O_3$**: 278.1882; found 278.1871.

Synthesis of (*E*)-ethyl 3-(4-(trifluoromethoxy)phenyl)acrylate (184h)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), (*Z*)-ethyl 3-iodoacrylate (**183a**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(4-(trifluoromethoxy)phenyl)manganese (**181d**, 4.4 mL, 0.60 mmol, 0.14 M) was added dropwise before the mixture was stirred for 0.5 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 9:1, R_f = 0.50) afforded the desired cross-coupling reaction product **184h** (0.200 g, 0.77 mmol, 77%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.65 (d, *J* = 16.0 Hz, 1H), 7.59 – 7.48 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.41 (d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 166.8, 150.5 (q, *J* = 1.8 Hz), 142.9, 133.2, 129.6, 121.3, 120.5 (q, *J* = 258.0 Hz), 119.4, 60.8, 14.4.

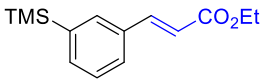
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –57.8.

IR (ATR, cm^{-1}) ṽ = 2986, 1710, 1642, 1606, 1588, 1508, 1418, 1368, 1312, 1248, 1210, 1154, 1106, 1036, 1018, 980, 946, 922, 884, 836, 810, 798, 700, 668.

MS (EI, 70 eV, %) m/z = 260 (37), 232 (16), 215 (11), 214 (100), 187 (13), 186 (28), 101 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{11}F_3O_3$**: 260.0660; found 260.0646.

Synthesis of (*E*)-ethyl 3-(3-(trimethylsilyl)phenyl)acrylate (184i)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), (*Z*)-ethyl 3-iodoacrylate (**183a**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(3-trimethylsilylphenyl)manganese (**181e**, 4.6 mL, 0.60 mmol, 0.13 M) was added dropwise before the mixture was stirred for 1 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 19:1, R_f = 0.44) afforded the desired cross-coupling reaction product **184i** (0.160 g, 0.64 mmol, 64%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.71 (d, *J* = 16.0 Hz, 1H), 7.66 (s, 1H), 7.56 – 7.49 (m, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 6.46 (d, *J* = 16.0 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.29 (s, 9H).

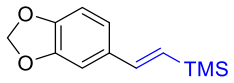
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 167.2, 145.1, 141.6, 135.4, 133.8, 133.3, 128.4, 128.4, 118.3, 60.6, 14.5, –1.1.

IR (ATR, cm^{-1}) ṽ = 2978, 2956, 1710, 1638, 1474, 1396, 1366, 1306, 1264, 1248, 1206, 1166, 1126, 1112, 1096, 1036, 982, 912, 900, 862, 834, 794, 752, 726, 684.

MS (EI, 70 eV, %) m/z = 251 (34), 248 (25), 234 (11), 233 (100), 205 (43), 187 (40), 131 (53), 115 (11), 75 (29), 73 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{20}O_2Si$**: 248.1233; found 248.1223.

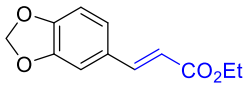
Synthesis of (*E*)-(2-(benzo[*d*][1,3]dioxol-5-yl)vinyl)trimethylsilane (184j)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), 2-bromovinyltrimethylsilane (**183b**, *Z/E* = 10:90, 179 mg, 0.15 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-benzo[*d*][1,3]dioxol-5-ylmanganese (**181f**, 2.5 mL, 0.60 mmol, 0.28 M) was added dropwise before the mixture was stirred for 0.5 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 19:1, R_f = 0.74) afforded the desired cross-coupling reaction product **184j** (0.171 g, 0.78 mmol, 78%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.00 (d, *J* = 1.7 Hz, 1H), 6.87 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.78 (d, *J* = 18.9 Hz, 1H), 6.77 (s, 1H), 6.27 (d, *J* = 19.1 Hz, 1H), 5.95 (s, 2H), 0.15 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 148.2, 147.6, 143.1, 133.3, 127.4, 121.5, 108.3, 105.6, 101.2, –1.0.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2954, 2894, 1594, 1502, 1488, 1444, 1354, 1244, 1204, 1186, 1120, 1096, 1038, 982, 942, 928, 862, 834, 786, 758, 742, 728, 690.
MS (EI, 70 eV, %) m/z = 220 (67), 206 (10), 205 (100), 189 (20), 179 (10), 175 (63), 165 (10), 149 (17), 148 (10), 147 (26), 145 (17).
HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{16}O_2Si$**: 220.0920; found 220.0911.

Synthesis of (*E*)-ethyl 3-(benzo[*d*][1,3]dioxol-5-yl)acrylate (184k)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), (*Z*)-ethyl 3-iodoacrylate (**183a**, 226 mg, 0.13 mL, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-benzo[*d*][1,3]dioxol-5-ylmanganese (**181f**, 2.5 mL, 0.60 mmol, 0.28 M) was added dropwise before the mixture was stirred for 1 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 19:1, R_f = 0.25) afforded the desired cross-coupling reaction product **184k** (0.186 g, 0.84 mmol, 84%) as a white solid.

M.p. (°C): 68-70.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.58 (d, *J* = 15.9 Hz, 1H), 6.95 (ddd, *J* = 78.4, 42.1, 4.8 Hz, 3H), 6.25 (d, *J* = 15.9 Hz, 1H), 6.00 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).

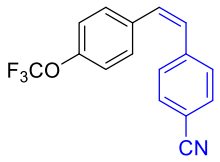
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 167.3, 149.7, 148.5, 144.4, 129.0, 124.5, 116.4, 108.7, 106.6, 101.7, 60.5, 14.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2922, 2854, 1702, 1640, 1610, 1504, 1490, 1474, 1448, 1440, 1368, 1356, 1242, 1192, 1174, 1142, 1118, 1096, 1028, 1002, 926, 854, 804.

MS (EI, 70 eV, %) m/z = 221 (13), 220 (100), 192 (23), 191 (18), 175 (80), 174 (12), 173 (11), 148 (64), 147 (23), 146 (18), 145 (82), 117 (33), 89 (45), 63 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{12}O_4$**: 220.0736; found 220.0728.

Synthesis of (*Z*)-4-(4-(trifluoromethoxy)styryl)benzonitrile (184m)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), 4-(2-bromovinyl)benzonitrile (**183e**, *Z*/*E* = 98:2, 208 mg, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(4-(trifluoromethoxy)phenyl)manganese (**181d**, 4.4 mL, 0.60 mmol, 0.14 M) was added dropwise before the mixture was stirred for 1 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 99:1, R_f = 0.18) afforded the desired cross-coupling reaction product **184m** (0.214 g, 0.74 mmol, 74%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.58 – 7.45 (m, 2H), 7.37 – 7.28 (m, 2H), 7.24 – 7.15 (m, 2H), 7.13 – 7.03 (m, 2H), 6.72 (d, *J* = 12.2 Hz, 1H), 6.62 (d, *J* = 12.2 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 148.7, 141.7, 134.9, 132.3, 131.8, 130.4, 129.6, 129.4, 121.0, 120.5 (d, *J* = 257.5 Hz), 118.9, 111.0.

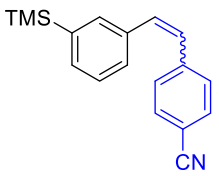
^{19}F-NMR (377 MHz, $CDCl_3$, ppm) δ = –57.8.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2228, 1605, 1507, 1407, 1252, 1210, 1198, 1156, 1110, 1018, 948, 922, 885, 832, 813, 779, 760, 741, 670.

MS (EI, 70 eV, %) m/z = 290 (17), 289 (98), 249 (11), 205 (17), 204 (100), 203 (32), 202 (36), 190 (31), 177 (21), 165 (16).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{10}F_3NO$**: 289.0714; found 289.0708.

Synthesis of 4-(3-(trimethylsilyl)styryl)benzonitrile (184n)



In relation to **TP10**, for this reaction $Fe(acac)_3$ (35 mg, 0.10 mmol, 10 mol%), 4-(2-bromovinyl)benzonitrile (**183e**, *Z/E* = 98:2, 208 mg, 1.00 mmol) and freshly distilled THF (1.0 mL) were used. The reaction mixture was cooled to 0 °C and *bis*-(3-trimethylsilylphenyl)manganese (**181e**, 4.6 mL, 0.60 mmol, 0.13 M) was added dropwise before the mixture was stirred for 1 h at the given temperature. Purification by flash column chromatography (*iso*hexane:EtOAc = 99:1, R_f = 0.30) afforded the desired cross-coupling reaction product **184n** (0.182 g, *Z/E* = 7:3, 0.66 mmol, 66%) as a pale-yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.67 – 7.46 (m, 3.3H), 7.41 – 7.31 (m, 3H), 7.28 – 7.16 (m, 2H), 7.10 (d, *J* = 16.4 Hz, 0.3H), 6.67 (ddd, *J* = 74.6, 12.2 Hz, 1.4H).
^{13}C-NMR (101 MHz, $CDCl_3$, ppm) δ = 142.5, 142.1, 141.4, 140.8, 135.6, 135.4, 134.0, 133.8, 133.7, 132.9, 132.8, 132.6, 132.3, 132.1, 129.7, 129.4, 128.4, 128.4, 128.0, 127.1, 127.0, 126.7, 119.2, 119.1, 110.6, 110.5, –1.0, –1.2.
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2954, 2226, 1603, 1504, 1414, 1403, 1377, 1261, 1248, 1176, 1112, 965, 926, 898, 884, 858, 831, 801, 750, 712, 689.
MS (EI, 70 eV, %) m/z = 280 (27), 277 (40), 263 (17), 262 (100).
HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{19}NSi$**: 277.1287; found 277.1280.