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New Preparation of Functionalized Indoles and Azaindoles *via* an Intramolecular Copper-mediated Carbomagnesiation of Ynamides, Regioselective *in situ* Trapping Metalation of Arenes and Heteroarenes with TMPLi in the Presence of Metal Salts and Synthesis of SF_5-Substituted Aromatics and Heterocycles

von

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Erklärung

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Eidesstattliche Versicherung

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Parts of this PhD thesis have been published

Communications

1) Annette Frischmuth, Andreas Unsinn, Klaus Groll, Heinz Stadtmüller, Paul Knochel: Preparations and Reactions of SF_5-Substituted Aryl and Heteroaryl Derivatives *via* Mg and Zn Organometallics, *Chemistry - A European Journal* **2012**, *18* (33), 10234-10238.

2) Annette Frischmuth, Paul Knochel: Preparation of Functionalized Indoles and Azaindoles *via* an Intramolecular Copper-mediated Carbomagnesiation of Ynamides, *Angewandte Chemie International Edition* **2013**, *52* (38), 10084-10088.

3) Annette Frischmuth, Maitane Fernández, Nadja M. Barl, Florian Achrainer, Hendrik Zipse, Guillaume Berionni, Herbert Mayr, Konstantin Karaghiosoff and Paul Knochel: New *in situ* Trapping Metalations of Functionalized Arenes and Heteroarenes with TMPLi in the Presence of $ZnCl_2$ and other Metal Salts, *Angewandte Chemie International Edition* **2014**, *53* (30), 7928-7932.

"Das Leben ist wert, gelebt zu werden, sagt die Kunst, die schönste Verführerin; das Leben ist wert, erkannt zu werden, sagt die Wissenschaft."

Friedrich Nietzsche

Meiner Mutter

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LIST OF ABBREVIATIONS

Ac	acetyl
acac	acetylacetonate
AcOH	acetic acid
Alk	alkyl
aq	aqueous
Ar	aryl
Bu	butyl
calc.	calculated
conc.	concentrated
Cy	cyclohexyl
dba	*trans*,*trans*-dibenzylideneacetone
DBE	1,2-dibromoethane
dist.	distilled
DMG	directed metalation group
DMSO	dimethyl sulfoxide
D*o*M	directed *ortho* metalation
δ	chemical shifts in ppm
E	electrophile
EDG	electron-donating group
EI	electron impact ionization
equiv	equivalent
ESI	electrospray ionization
Et	ethyl
EWG	electron-withdrawing group
FG	functional group
GC	gas chromatography
h	hour
*i*hexane	*iso*-hexane
Hal	halogen
HRMS	high resolution mass spectrometry
*i*Pr	*iso*propyl
IR	infra-red
J	coupling constant (NMR)
LDA	lithium di*iso*propylamide
M	molarity
m	*meta*
m.p.	melting point
Me	methyl
Met	metal
min	minute
mmol	millimole
MS	mass spectrometry
MWI	microwave irradiation
NBS	*N*-bromosuccinimide
NMP	*N*-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
o	*ortho*
Oct	octyl
p	*para*
PEPPSI-*i*Pr	[1,3-bis(2,6-di(*iso*propyl)-phenyl)imidazol-2-ylidene] (3-chloropyridyl)-palladium(II) dichloride
Ph	phenyl
ppm	parts per million
R	organic substituent
sat.	saturated
*s*Bu	*sec*-butyl
SPhos	2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl
TBAF	tetra-*n*-butylammonium fluoride
TBDMS	*tert*-butyldimethylsilyl
*t*Bu	*tert*-butyl
Tf	triflate
tfp	tris-(2-furyl)phosphine
THF	tetrahydrofuran
TIPS	tri(*iso*propylsilyl)
TLC	thin layer chromatography
TMP	2,2,6,6-tetramethyl-piperidyl
TMPH	2,2,6,6-tetramethylpiperidine
TMS	trimethylsilyl
Ts	4-toluenesulfonyl
X	halide or pseudohalide

A. INTRODUCTION

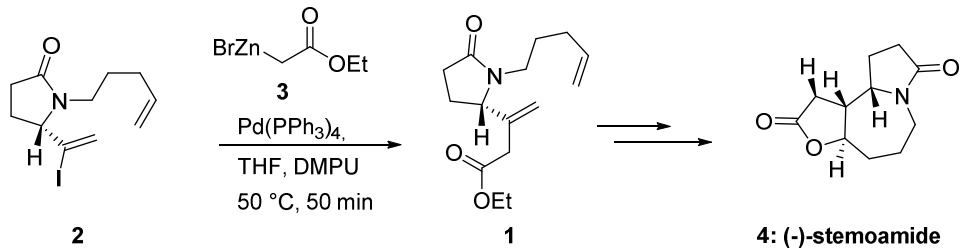
1. Overview

Already 1760, Louis-Claude Cadet de Gassicourt produced the first organometallic compound while trying to prepare invisible inks by the treatment of arsenic-containing cobalt ores with various acids. The so-called „Cadet`s fuming liquid" contained cacodyl oxide $[(CH_3)_2As]_2O$, which is today known as the first organometallic compound.[1] The next organometallic compounds that were reported are Zeise`s salt as the first platinum / olefin complex and Frankland`s diethyl zinc.[2] At the beginning of the 20th century Victor *Grignard* set another milestone in the history of organometallic chemistry by preparing the first organomagnesium compound.[3] Since that time, organometallic chemistry became an important part of the organic and inorganic chemistry and 20 Nobel-Prize laureates worked in this field of research.[4] Nowadays, metalorganic compounds play a special role in synthetic organic chemistry, and organic chemists can choose from an ever growing toolbox of organometallic reagents, because nearly every metal in the periodic table has found some valuable applications in organic chemistry.[5] On the one hand very reactive organometallics, such as organolithium, -sodium or -potassium reagents show an excellent reactivity towards many electrophiles, but they are incompatible with sensitive functional groups.[6] On the other hand organoboron, –indium or tin reagents show, due to a very covalent carbon-metal bond, a higher stability and functional group tolerance.[7] For this reason, they need either harsh reaction conditions or appropriate catalysts in order to react with electrophiles.[5, 8] Organomagnesium, -zinc and –copper reagents strike a balance between those extrems. Because of their high reactivity even at low temperatures and sufficient reactivity towards various electrophiles as well as high tolerance towards functional groups, organomagnesium reagents have an exceptional position in organometallic chemistry. Organocopper reagents possess also a well-balanced reactivity, but a main drawback is still their thermal instability and that they have to be prepared by transmetallation of other organometallic species. Organozinc reagents provide improved chemo- and regioselectivity and higher stability compared to *Grignard* reagents. Otherwise, they are less reactive and so less used in total synthesis.[9] Their moderate reactivity toward standard organic electrophiles is compensated by their high reactivity in transition metal-catalyzed cross-coupling reactions. As a result of a relatively fast transmetalation, Pd-catalyzed *Negishi*[10] cross-coupling reactions usually go on faster and under milder conditions than the corresponding *Stille* and *Suzuki* cross-couplings.

An application of a *Negishi* coupling is shown in Scheme 1, the formation of sp^2-sp^3 carbon-carbon bond with high stereoselectivity is performed *via* Pd-catalyzed *Negishi* cross-coupling reaction. *β, γ-*

[1] D. Seyferth, *Organometallics* **2001**, *20*, 1488.
[2] a) E. Frankland, *Liebigs Ann. Chem.* **1848**, *71*, 171; b) E. Frankland, *J. Chem. Soc.* **1848**, *2*, 263.
[3] V. *Grignard*, *Compt. Rend. Acad. Sc. Paris* **1900**, *130*, 1322.
[4] *Grignard*, Sabatier, Ziegler, Natta, Wilkinson, Fischer, Lipscomb, Brown, Wittig, Fukui, Hoffmann, Knowles, Noyori, Sharpless, Chauvin, Grubbs, Schrock, Heck, Negishi, Suzuki.
[5] For an overview, see: *Handbook of Functionalized Organometallics* (Ed.: P. Knochel), Wiley-VCH, Weinheim, **2005**.
[6] J. Clayden, *Organolithiums: Selectivity for Synthesis* (Ed. J.E. Baldwin), Pergamon Press, Oxford, **2002**.
[7] a) *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials* (Ed. D.G. Hall), Wiley-VCH, Weinheim, **2011**; b) Z.-L. Shen, S.-Y. Wang, Y.-K. Chok, Y.-H. Xu, T.-P. Loh, *Chem. Rev.* **2013**, *113*, 271.
[8] E. Negishi, *Organometallics in Organic Synthesis*, Wiley, New York, **1980**.
[9] K.C. Nicolaou, P. Bulger, S. Sarlah, *Angew. Chem. Int. Ed.* **2005**, *44*, 4442.
[10] E. Negishi, A.O. King, N. Okukado, *J. Org. Chem.* **1977**, *42*, 1821.

Unsaturated ester **1** is produced *via* coupling of vinyl iodide **2** and *Reformatsky* nucleophile **3** in 78% yield in a key step in the total synthesis of (-)-stemoamide (**4**) (Scheme 1).[11]



Scheme 1: Synthesis of (-)-stemoamide (**4**) as an example of a *Negishi* cross-coupling reaction.

2. Preparation of Organometallic Reagents

2.1 Oxidative Insertion

The most common and oldest method to prepare organometallic reagents is the direct oxidative insertion of elemental metal into a halogen-carbon bond. In 1849, it was first reported by *Frankland***,** who prepared dialkylzinc reagents by reacting zinc metal with alkyl halides.[12] The final breakthrough was made by *Grignard* in 1900, who generated the first organomagnesium reagents also *via* insertion of elemental magnesium into a carbon-halide bond in diethyl ether, which upon reaction with aldehydes and ketones afforded secondary and tertiary alkcohols, respectively.[13] Soon after its discovery, the *Grignard* reaction became one of the most manifold C-C bond forming tools. The exact mechanism of this reaction is still not entirely elucidated, but radical pathways are generally accepted.[14] One of the major drawbacks of the first magnesium insertions is the need of high reaction temperatures, which limit the functional group tolerance. In addition only a small number of alkyl or aryl halides react easily with magnesium, since the magnesium metal is passivized by a layer of magnesium oxide or magnesium hydroxide. To remove them, suitable activation reagents (either 1,2-dibromoethane or diisobutylaluminium hydride) have to be added.[15] To avoid these problems, *Rieke* developed highly reactive metal powders, which also enables such compounds to be transformed into *Grignard* reagents. These "*Rieke* metals" can be prepared by reduction of an anhydrous metal chloride with an alkali metal such as lithium, sodium or potassium in THF and also react with aryl or alkyl bromides at very low temperatures (Scheme 2).[16]

[11] S. Torssell, E. Wanngren, P. Somfai, *J. Org. Chem.* **2007**, *72*, 4246.

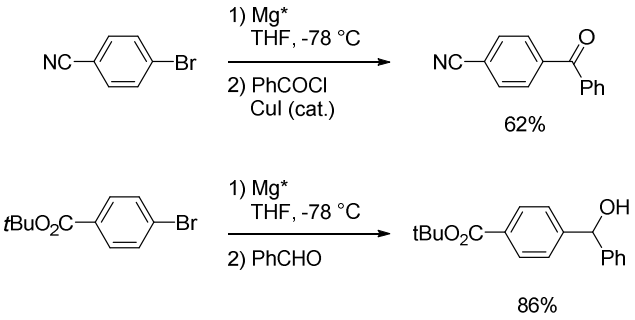
[12] a) E. Frankland, *Ann. Chem.* **1849**, *71*, 171; b) E. Frankland, *Ann. Chem.* **1849**, *71*, 213.

[13] V. *Grignard*, *C. R. Acad. Sci.* **1900**, 1322.

[14] a) H.M. Walborksy, *Acc. Chem. Res.* **1990**, *23*, 286. b) J.F. Garst, *Acc. Chem. Res.* **1991**, *24*, 95; c) J.F. Garst, M.P. Soriaga, *Coord. Chem. Rev.* **2004**, *248*, 623.

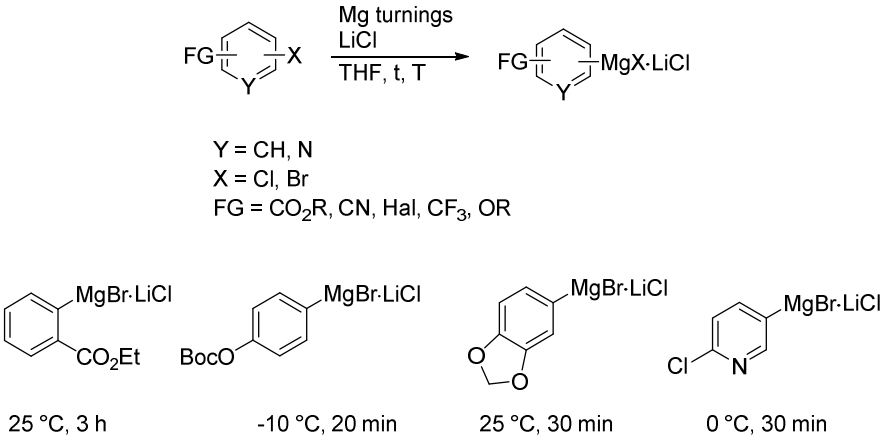
[15] a) D.J. am Ende, P.J. Clifford, D.M. DeAntonis, C. SantaMaria, S.J. Brenek, *Org. Process Res. Dev.* **1999**, *3*, 319; b) U. Tilstam, H. Weinmann, *Org. Process Res. Dev.* **2002**, *6*, 906.

[16] a) R.D. Rieke, L.-C. Chao, *Syn. React. Inorg. Metal-Org. Chem.* **1974**, *4*, 101; b) R.D. Rieke, *Acc. Chem. Res.* **1977**, *10*, 301; c) R.D. Rieke, *Science* **1989**, *246*, 1260; d) L. Zhu, R.M. Wehmeyer, R.D. Rieke, *J. Org. Chem.* **1991**, *56*, 1445; R.D. Rieke, M.V. Hanson, *Tetrahedron* **1997**, *53*, 1925; f) R.D. Rieke, *Aldrichim. Acta* **2000**, *33*, 52; g) J. Lee, R. Velarde-Ortiz, A. Guijarro, J.R.Wurst, R.D. Rieke, *J. Org. Chem.* **2000**, *65,* 5428.



Scheme 2: Preparation and reaction of functionalized *Grignard* reagents using "*Rieke* magnesium".

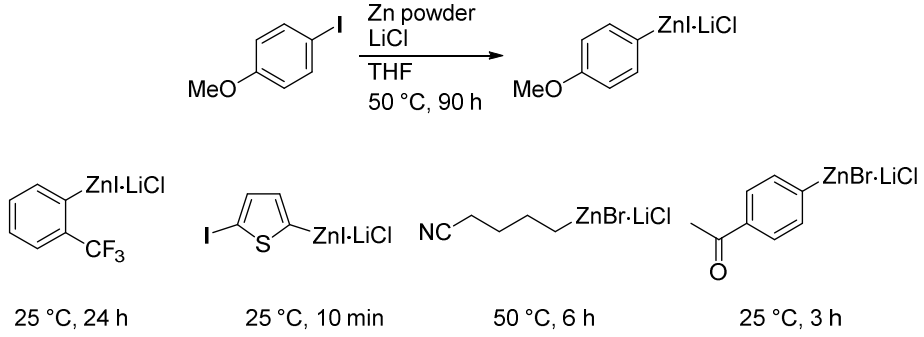
However, this method still has some drawbacks, the "*Rieke* metals" always have to be freshly prepared, the functional group tolerance is still limited and low temperatures are necessary. Recently, *Knochel* and coworkers developed a convenient methodology to generate aryl and heteroaryl magnesium and zinc organometallics from aryl and heteroaryl halides by a direct metal insertion in the presence of LiCl (Scheme 3, Scheme 4).[17] The latter facilitates the insertion reaction in several ways and allows it to proceed more selectively and under mild conditions.[18]



Scheme 3: Selected examples for LiCl promoted Mg insertion.

[17] Zn reagents: a) A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040; b) N. Boudet, S. Sase, P. Sinha, C.-Y. Liu, A. Krasovskiy, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 12358; c) A. Metzger, M.A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1107; Mg reagents: d) F.M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 6802; e) F.M. Piller, A. Metzger, M.A. Schade, B.A. Haag, A. Gavryushin, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 7192.

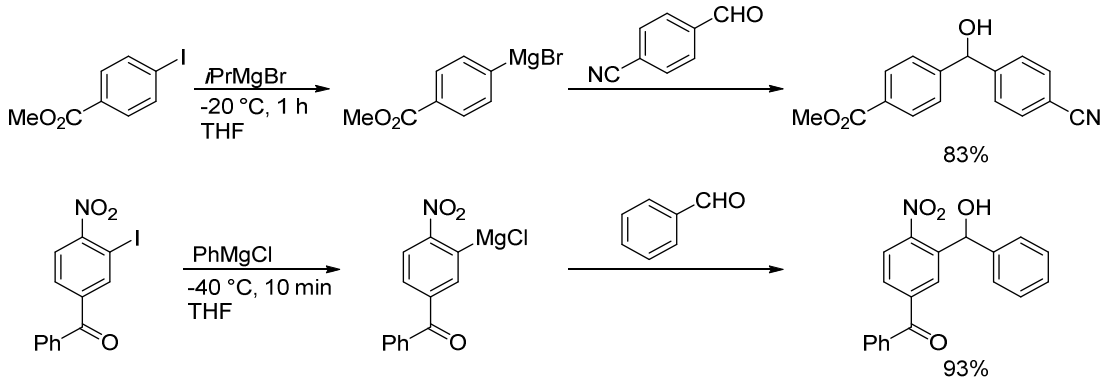
[18] a) L. Gupta, A.C. Hoepker, K.J. Singh, D.B. Collum, *J. Org. Chem*. **2009**, *74*, 2231; b) Y. Ma, A.C. Hoepker, L. Gupta, M.F. Faggin, D.B. Collum, *J. Am. Chem. Soc*. **2010**, *132*, 15610; c) D.R. Armstrong, A.R. Kennedy, R.E. Mulvey, J.A. Parkinson, S.D. Robertson, *Chem. Sci.* **2012**, *3*, 2700.



Scheme 4: Selected examples for LiCl promoted Zn insertion.

2.2 Halogen-Metal Exchange Reactions

A more practical preparation of organomagnesium compounds with high functional group tolerance, avoiding many of the drawbacks of the direct insertion, is the halogen-magnesium exchange reaction. Starting from an aryl bromide or iodide and an alkyl-metal reagent, the driving force for this reaction class is the formation of an organometallic reagent possessing a higher stability than the exchange reagent itself ($sp > sp^2_{vinyl} > sp^2_{aryl} > sp^3_{prim} > sp^3_{sec}$).[19] Based on the preliminary work of *Prévost*[20] in 1931 and *Villieras* in 1967,[21] *Knochel* could demonstrate the potential of the iodine-magnesium exchange with substrates even bearing sensitive functional groups by preparing arylmagnesium reagents *via* treating aryl iodides with *i*PrMgBr, *i*Pr_2Mg and in the case of very electron poor aromatics with PhMgCl (Scheme 5).[22]

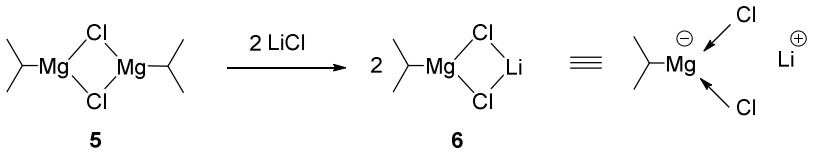


Scheme 5: Preparation of polyfunctional *Grignard* reagents starting from aryl iodides.

This method was further improved by the addition of stoichiometric amounts of LiCl to *i*PrMgCl (**5**) to form the exchange reagent *i*PrMgCl·LiCl (**6**), the so called "turbo-*Grignard*", that shows an extremely high exchange reactivity towards aryl iodides and bromides at low temperatures and therefore reduces undesired side reactions.[23] This behavior might be due to deaggregation of *i*PrMgCl (**5**) and the

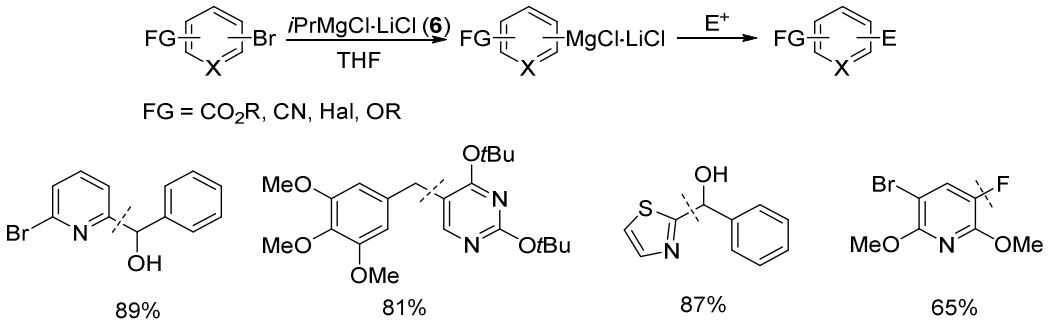
[19] D. Hauk, S. Lang, A. Murso, *Org. Process Res. Dev*. **2006**, *10*, 733.
[20] C. Prévost, *Bull. Soc. Chim. Fr.* **1931**, *49*, 1372.
[21] a) J. Villiéras, *Bull. Chem. Soc. Fr.* **1967**, *5*, 1520. b) J. Villiéras, B. Kirschleger, R. Tarhouni, M. Rambaud, *Bull. Chem. Soc. Fr.* **1986**, *24*, 470.
[22] a) L. Boymond, M. Rottländer, G. Cahiez, P. Knochel, *Angew. Chem. Int. Ed.* **1998**, *37*, 1701. b) I. Sapountzis, P. Knochel, *Angew. Chem. Int. Ed.* **2002**, *41*, 1610.
[23] A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333.

formation of the monomeric magnesiate species *i*PrMgCl$_2^-$Li$^+$ (**6**) (Scheme 6). Furthermore, the LiCl also increases the solubility of the *Grignard* reagent.



Scheme 6: Effect of LiCl on *Grignard* reagent *i*PrMgCl (**5**).

A huge variety of aromatic and heteroaromatic bromides could now be converted into the corresponding magnesium reagents and react with electrophiles. However, this increased reactivity does not limitate the functional group tolerance (Scheme 7).[24]



Scheme 7: Preparation and reactivity of functionalized *Grignard* reagents by bromine-magnesium exchange using the Turbo-*Grignard* reagent (*i*PrMgCl·LiCl (**6**)) and reaction with electrophiles.

2.3 Directed Metalation

Besides these two halogen-metal conversions, the directed metalation using alkyl metals or metal amide bases is the third major way to generate organometallics. In contrast to metal insertion as well as halogen-metal exchange reactions, there is no need for a halogen precursor, usually iodine or bromine. The huge advantage lies in the unlimited availability of the corresponding precursor, which only has to have a carbon-hydrogen-bond.

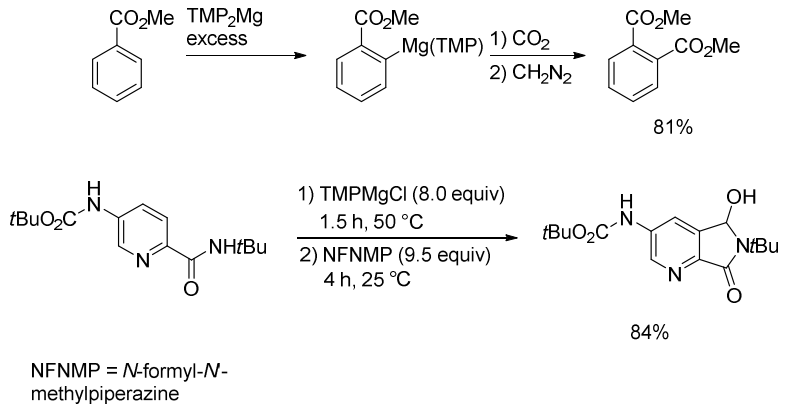
In 1939-40, the independant discovery by *Gilman* and *Bebb*[25] and *Wittig* and *Fuhrmann*[26] of anisole *ortho* deprotonation by *n*-BuLi constituted a forerunner for a new conceptual framework in synthetic aromatic chemistry. These pioneering results of the directed *ortho*-metalation (D*o*M) process initiated fundamental reactivity, studies by *Gilman*[27] and, in the early 1960`s, by *Hauser* and his coworkers,[28] who also systematically expanded the scope of directed metalation groups (DMGs). The D*o*M reaction comprises the deprotonation of a site *ortho* to a heteroatom-containing DMG by a strong base leading to an *ortho*-lithiated species. The complementary technique of halogen-metal exchange, also

[24] a) A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *41*, 1610. b) A. Krasovskiy, B.F. Straub, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 159. c) H. Ren, P. Knochel, *Chem. Commun.* **2006**, 726; d) C.-Y. Liu, P. Knochel, *Org. Lett.* **2005**, *7*, 2543. e) F. Kopp, A. Krasovskiy, P. Knochel, *Chem. Commun.* **2004**, 2288.
[25] H. Gilman, R.L. Bebb, *J. Am. Chem. Soc.* **1939**, *61*, 109.
[26] G. Wittig, G. Fuhrmann, *Chem. Ber.* **1940**, *73*, 1197.
[27] H. Gilman, J.W. Morton, *Org. React. (N.Y.)* **1954**, *8*, 258.
[28] a) W.H. Puterbaugh, C.R. Hauser, *J. Org. Chem.* **1964**, *29*, 853; b) D.W. Slocum, D.I. Sugarman, *Adv. Chem. Ser.* **1974**, *No. 130*, 227.

discovered by *Gilman*[29] and *Wittig*,[30] furnished further impulse to this area.[31] In the 1970`s, the industrial use of alkyllithium bases as polymerization catalysts[32] led to their commercial availability and allowed the metalation technique to be practiced widely.[33] Non-nucleophilic, sterically hindered lithium bases, such as lithium di*iso*propylamide (LDA), which was first used by *Hamell* and *Levine*[34] in 1950, and TMPLi (TMP=2,2,6,6-tetramethylpiperidyl), first described in two different publications by *Rickborn* and *Kow*[35] in 1972, were established. The directed *ortho*-lithiation was especially promoted by the work of *Snieckus* and coworkers, who introduced carbamates, amides, and a variety of ethers as convenient DMGs.[33, 36]

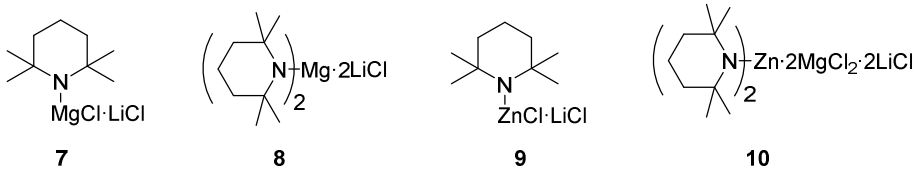
However, the major drawback of the use of alkyllithium reagents and lithium amides is the high reactivity of the bases used, which can lead to undesired side reactions like, for example *Chichibabin* addition,[37] and attacks on functional groups. Furthermore, they have to be prepared *in situ* since their stability in THF is limited and most lithiations require very low temperatures (-78 to -100 °C). Alternatively, the use of magnesium amide bases is generally preferred when dealing with more sensitive functional groups. Already 1947 *Hauser* and coworkers established magnesium amide bases of the type R_2NMgX and $(R_2N)_2Mg$;[38] based on *Meunier`s* original discoveries.[39] *Eaton* and later *Mulzer* used the more sterically demanding amides TMPMgX and TMP_2Mg (TMP = 2,2,6,6-tetramethylpiperidyl) for the metalation of aromatic carboxamides, esters, pyridinecarboxamides and carbamates (Scheme 8).[40] Despite pioneering and extensive studies on the directed magnesiation of arenes and heteroarenes, they still suffer from several limitations. One major drawback is their low solubility due to aggregation, and the need of large excesses of both base and electrophile.[41]

[29] H. Gilman, A.L. Jacoby, *J. Org. Chem.* **1938**, *3*, 108.
[30] G. Wittig, U. Pockels, H. Droge, *Chem. Ber.* **1938**, *71*, 1903.
[31] W.E. Parsham, C.K. Bradsher, *Acc. Chem. Res.* **1982**, *15*, 300.
[32] a) A.W. Langer, *Adc. Chem. Ser.* **1974**, *No.* 130; b) A.F. Halesa, D.N. Schulz, D.P. Tate, V.D. Mochel, *Adv. Organomet. Chem.* **1980**, *18*, 55.
[33] V. Snieckus, *Chem. Rev.* **1990**, *90*, 879.
[34] M. Hamell, R. Levine, *J. Org. Chem.* **1950**, *15*, 162.
[35] a) C.L. Kissel, B. Rickborn, *J. Org. Chem.* **1972**, *37*, 2060; b) M.W. Rathke, R. Kow, *J. Am. Chem. Soc.* **1972**, *94*, 6854.
[36] a) V. Snieckus*, Pure & Appl. Chem.* **1990**, *62*, 2047; b) T. K. Macklin, J. Panteleev, V. Snieckus, *Angew. Chem. Int. Ed.* **2008**, *47*, 2097.
[37] A.E. Chichibabin, O.A. Zeide, *J. Russ. Phys. Chem.* **1914**, *46*, 1216.
[38] a) C.R. Hauser, H. G. Walker, *J. Am. Chem. Soc.* **1947**, *69*, 295; b) C.R. Hauser, F.C. Frostick, *J. Am. Chem. Soc.* **1949**, *71*, 1350.
[39] L. Meunier, *C. R. Hebd. Seances Acad. Sci.* **1903**, *136*, 758.
[40] a) P.E. Eaton, C.H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016; b) W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *J. Org. Chem.* **1995**, *60*, 8414.
[41] W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *J. Org. Chem.* **1995**, *60*, 8414.



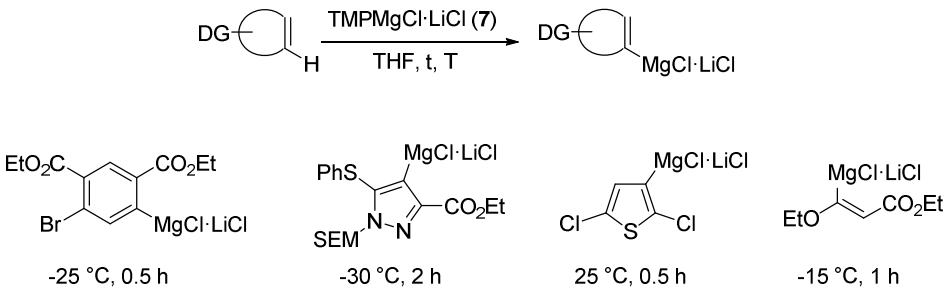
Scheme 8: Early examples of metalation by TMP-magnesium amides.

A high improvement was the development of highly chemoselective TMP mixed metal/Li amides such as TMPMgCl·LiCl[42] (**7**), TMPZnCl·LiCl[43] (**8**), $TMP_2Mg·2LiCl$[44] (**9**) and $TMP_2Zn·2MgCl_2·2LiCl$[45] (**10**) (Scheme 9), which allow the selective metalation of sensitive aromatic compounds and heterocycles. This new generation of bases is highly soluble in THF, easily prepared, and offers additionally long term stability under inert atmosphere at room temperature.



Scheme 9: TMP-derived, mixed metal/Li amide bases.

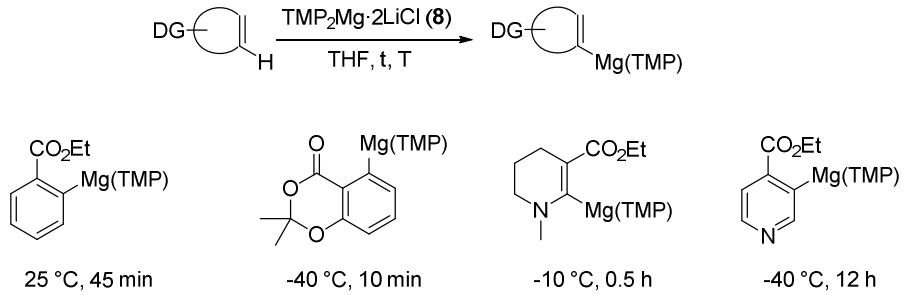
Especially the sterically hindered TMPMgCl·LiCl (**7**), obtained by mixing TMPH with turbo-*Grignard* **6**, proved to be an excellent reagent to deprotonate a large variety of functionalized aromatics and heteraromatics (Scheme 10).[46]



Scheme 10: Magnesiation of various aromatic and non-aromatic substrates by using TMPMgCl·LiCl (**7**).

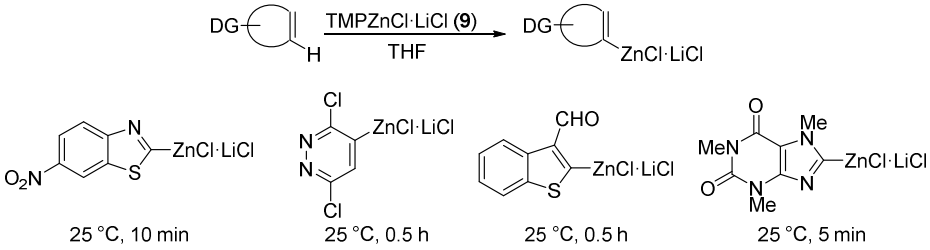
[42] A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958.
[43] a) M. Mosrin, P. Knochel, *Org. Lett.* **2009**, *11*, 1837; b) M. Mosrin, T. Bresser, P. Knochel, *Org. Lett.* **2009**, *11,* 3406; c) M. Mosrin, G. Monzon, T. Bresser, P. Knochel, *Chem. Commun.* **2009**, 5615.
[44] a) G.C. Clososki, C.J. Rohbogner, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7681; b) C.J. Rohbogner, G.C. Clososki, P. Knochel, *Angew. Chem. Int. Ed.* **2008**, *47*, 1503; c) C.J. Rohbogner, A.J. Wagner, G.C. Clososki, P. Knochel *Org. Synth.* **2009**, *86*, 374.
[45] a) S.H. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7685; b) S.H. Wunderlich, P. Knochel, *Org. Lett.* **2008**, *10*, 4705.
[46] For a review see: B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem. Int. Ed*. **2011**, *50*, 9794.

For moderately activated aromatics and heteroaromatics, $TMP_2Mg \cdot 2LiCl$ (**8**) was developed by mixing TMPLi with TMPMgCl·LiCl (**7**) featuring an improved kinetic basicity (Scheme 11).

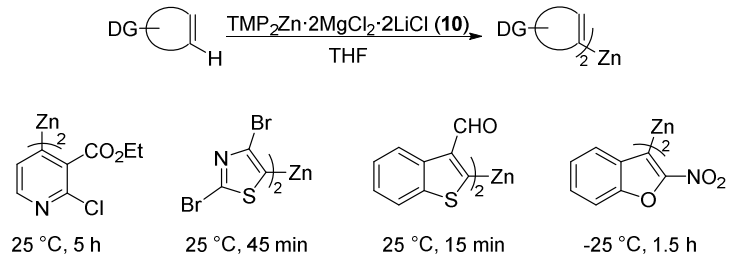


Scheme 11: Magnesiation of various aromatic and non-aromatic substrates by using $TMP_2Mg \cdot 2LiCl$ (**8**).

Despite the high tolerance toward nitriles, esters, and aryl ketones, there are still a number of functional groups, that are not compatible with TMPMgCl·LiCl (**7**) or $TMP_2Mg \cdot 2LiCl$ (**8**). For example, molecules bearing an aldehyde or nitro group, or sensitive heterocycles do not undergo directed magnesiations due to degradation. By transmetalating TMPLi or TMPMgCl·LiCl (**7**) with $ZnCl_2$, the mild zinc amides TMPZnCl·LiCl (**9**)[43, 47] and $TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (**10**),[45, 48] respectively, can be readily prepared. These bases can be used for the mild zincation of a variety of sensitive substrates (Scheme 12, Scheme 13).



Scheme 12: Zincation of various functionalized aromatics using TMPZnCl·LiCl (**9**).

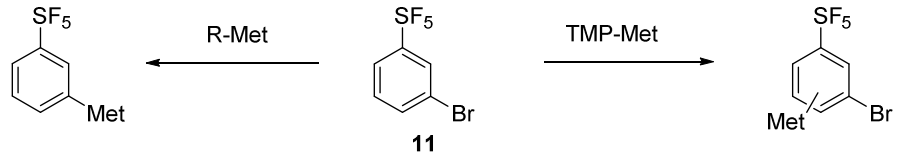


Scheme 13: Zincation of various sensitive heterocycles using $TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (**10**).

[47] a) T. Bresser, M. Mosrin, G. Monzon, P. Knochel, *J. Org. Chem.* **2010**, *75*, 4686; b) T. Bresser, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 1914.
[48] a) M. Mosrin, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 1468; b) M. Kienle, C. Dunst, P. Knochel, *Org. Lett.* **2009**, *11*, 5158; c) A. Unsinn, P. Knochel, *Chem. Commun.* **2012**, *48*, 2680.

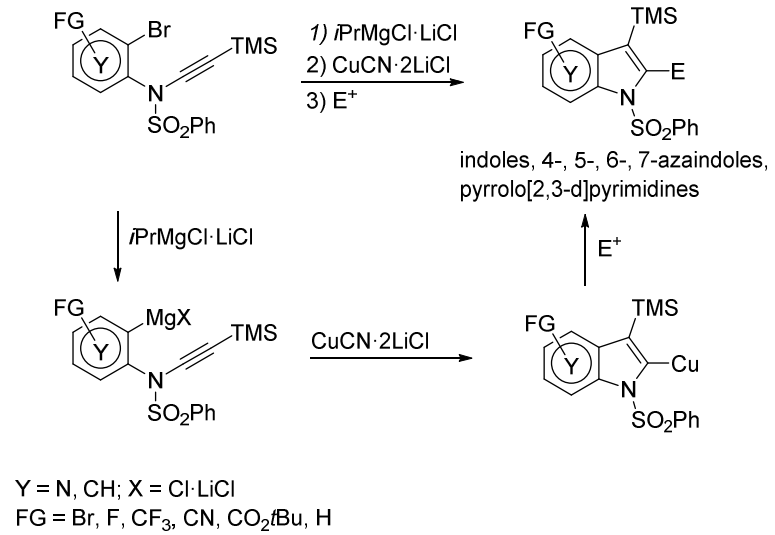
3. Objectives

The aim of the first project was the development of new SF_5-substituted Mg- and Zn-organometallics using established methods like the halogen-metal exchange reaction or the directed metalation. In general, fluorinated compounds gain a high attention in pharmaceutical, agrochemical and material research because of their physico-chemical and pharmacological properties. The CF_3-group plays already an important role in a lot of biological active molecules. A very similar, but rarely known substituent is the SF_5-group. Despite some lithium reagents, almost no SF_5-substituted Mg- and Zn-organometallics are known in the literature. Hence, a Br/Mg-exchange reaction or a directed metalation starting from commercially available 3-bromo-pentafluorosulfanyl benzene (**11**) should be developed (Scheme 14). Additionally, the synthesis of different heterocycles should be achieved.



Scheme 14: Preparation of SF_5-substituted organometallics.

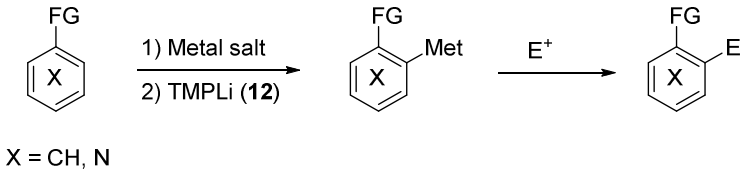
Based on the synthetic method for the preparation of functionalized benzo[*b*]thiophenes and benzo[*b*]thieno[2,3-*d*]thiophenes,[49] developed by *Kunz* and *Knochel*, a new methodology for the preparation of indoles as well as azaindoles should be evolved. Starting from functionalized bromo-ynamides a bromine-magnesium exchange reaction should be carried out, followed by a copper-mediated ring closing reaction. Subsequent allylation or acylation reactions should explore the scope of the methodology affording highly diversified indoles as well as azaindoles and pyrrolo[2,3-*d*]pyrimidines (Scheme 15).



Scheme 15: Preparation of indoles, azaindoles and pyrrolo[2,3-*d*]pyrimidines *via* copper-mediated carbomagnesiation of ynamides.

[49] T. Kunz, P. Knochel, *Angew Chem. Int. Ed.* **2012**, *51*, 1958.

Finally, the metalation of functionalized, sensitive aromatics and heteroaromatics with TMPLi (**12**) in the presence of metal salts was investigated. By using different metal salts it should be possible to get access to different organometallic species, which can then undergo further functionalization reactions with different electrophiles (Scheme 16).



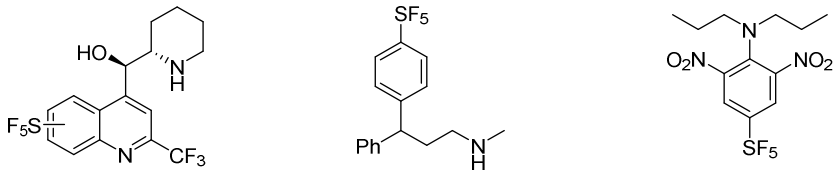
Scheme 16: Metalation of sensitive substrates with TMPLi (**12**) in the presence of metal salts.

B. RESULTS & DISCUSSION

1. Preparations and Reactions of SF_5-substituted Aryl and Heteroaryl Derivatives via Mg and Zn Organometallics

1.1 Introduction

The physico-chemical and pharmacological properties of organic molecules are often significantly modified by the incorporation of fluorine atoms.[50] Therefore, the preparation of fluoro- or trifluoromethyl-substituted aromatics and heteroaromatics has become an active research field.[51] Recently, it has been shown that the replacement of CF_3-groups with SF_5-substituents may increase the biological activity of pharmacologically active substances (Scheme 17).[52]



SF_5-Mefloquin SF_5-Fluoxetin SF_5-Trifluralin

Scheme 17: SF_5-Analoga of Mefloquin, Fluoxetin and Trifluralin.

Also, due to its specific physico-chemical properties[53] and to the increased availability of SF_5-substituted starting materials,[54] this fluorous group is beginning to find many applications in material sciences.[52] [55] A noteworthy feature of the SF_5-substituent includes its remarkable chemical stability. Aromatic SF_5-substituted compounds tolerate even harsh acidic conditions; their hydrolytic stability equals that of the CF_3-group. However, synthetic methods leading to SF_5-substituted aryl and heteroaryl derivatives are rare.[56]

One major difference between the SF_5-group and the trifluoromethyl function is its susceptibility toward reduction by some organometallic reagents. The attempt to lithiate 1-bromo-4-

[50] a) C. Isanbor, D. O'Hagan, *J. Fluorine Chem.* **2006**, *127*, 303; b) K.L. Kirk, *J. Fluorine Chem.* **2006**, *127*, 1013; c) J.-P. Bégué, D. Bonnet-Delpon, *J. Fluorine Chem.* **2006**, *127*, 992.

[51] a) A.M. Sipyagin, C.P. Bateman, Y.-T. Tan, J.S. Thrasher, *J. Fluorine Chem.* **2001**, *112*, 287; b) M. Schlosser, *Angew. Chem* **2006**, *118*, 5558; *Angew. Chem. Int. Ed.* **2006**, *45*, 5432; c) A.T. Parsons, S.L. Buchwald, *Nature* **2011**, *480*, 184; d) X. Mu, T. Wu, H.-Y. Wang, Y.-L. Guo, G. Liu, *J. Am. Chem. Soc.* **2011**, *134*, 878; e) N.D. Litvinas, P.S. Fier, J.F. Hartwig, *Angew. Chem.* **2012**, *124*, 551; *Angew. Chem. Int. Ed.* **2012**, *51*, 536; f) T. L. Liu, X. Shao, Y. Wu, Q. Shen, *Angew. Chem.* **2012**, *124*, 555; *Angew. Chem. Int. Ed.* **2012**, *51*, 540.

[52] a) J.T. Welch, D.S. Lim, *Bioorg. Med. Chem.* **2007**, *15*, 6659; b) P. Wipf, T. Mo, S. Geib, D. Caridha, G. Dow, L. Gerena, N. Roncal, E. Milner, *Org. Biomol. Chem.* **2009**, 4163; c) B. Stump, C. Eberle, W.B. Schweizer, M. Kaiser, R. Brun, R.L. Kraut-Siegel, D. Lentz, F. Diederich, *ChemBioChem* **2009**, *10*, 79; d) D.S. Lim, J.S. Choi, C.S. Pak, J.T. Welch, *J. Pestic. Sci.* **2007**, *32*, 255.

[53] P. Kirsch, Modern Fluoroorganic Chemistry. Synthesis, Reactivity and Applications; Wiley-VCH: Weinheim, **2004**.

[54] a) W.A. Sheppard, *J. Am. Chem. Soc.* **1960,** *82*, 4751; b) J.R. Case, N.H. Ray, H.L. Roberts, *J. Chem. Soc.* **1961**, 2066; c) W.A. Sheppard, *J. Am. Chem. Soc.* **1962,** *84*, 3072; d) R.D. Bowden, P.J. Comina, M.P. Greenhall, B.M. Kariuki, A. Loveday, D. Philp, *Tetrahedron* **2000**, *56*, 3399; e) A.M. Sipyagin, C.P. Bateman, Y.-T. Tan, J.S. Thrasher, *J. Fluorine Chem.* **2001**, *112*, 287; f) S. Ait-Mohand, W.R. Dolbier Jr., *Org. Lett.* **2002**, *4*, 3013; g) R.W. Winter, G.L. Gard, *J. Fluorine Chem.* **2004**, *125*, 549; h) T.A. Sergeeva, W.R. Dolbier Jr., *Org. Lett.* **2004**, *6,* 2417; i) V.K. Brel, *J. Fluorine Chem.* **2007**, *128*, 862.

[55] a) P. Kirsch, M. Bremer, *Angew. Chem.* **2000**, *112*, 4384; *Angew. Chem. Int. Ed.* **2000**, *39*, 4216; b) V.K. Brel, *J. Fluorine Chem.* **2007**, *128*, 862; d) D.S. Lim, J.S. Choi, C.S. Pak, J.T. Welch, *J. Pestic. Sci.* **2007**, *32*, 255.

[56] a) J.T. Welch, D.S. Lim, *Bioorg. Med. Chem.* **2007**, *15*, 6659; b) P. Wipf, T. Mo, S. Geib, D. Caridha, G. Dow, L. Gerena, N. Roncal, E. Milner, *Org. Biomol. Chem.* **2009**, 4163; c) B. Stump, C. Eberle, W.B. Schweizer, M. Kaiser, R. Brun, R.L. Kraut-Siegel, D. Lentz, F. Diederich, *ChemBioChem* **2009**, *10*, 79.

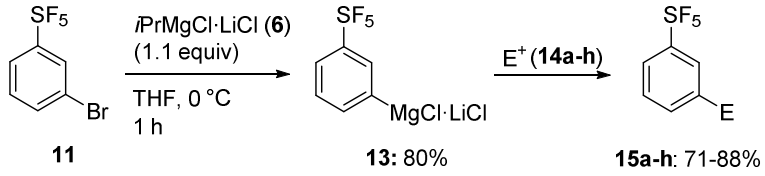
(pentafluorosulfanyl)-benzene (**11**) with *n*BuLi in THF at -78 °C resulted merely in the immediate formation of a variety of reduction products. In contrast, by using *t*BuLi in diethyl ether at -78 °C, the desired lithium intermediate was formed without side reactions and could be applied for many different transformations.[57] Because of the known disadvantages of lithium reagents, it would be of great interest to prepare SF_5-substituted organomagnesium and –zinc reagents. For the synthesis of these organometallics the halogen-magnesium exchange using *i*PrMgCl·LiCl (**6**) and directed metalation with TMP-metal bases were studied.

1.2 Preparation using Halogen-Magnesium Exchange

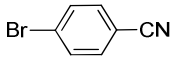
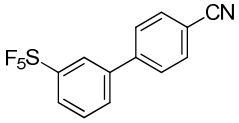
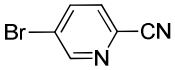
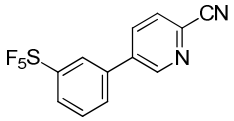
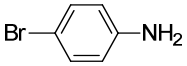
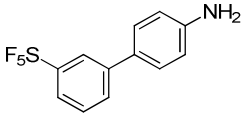
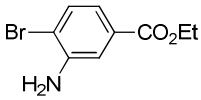
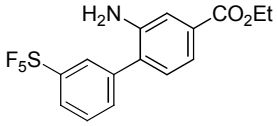
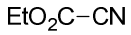
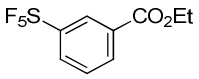
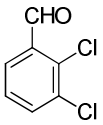
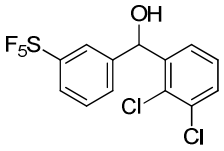
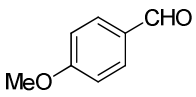
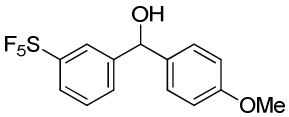
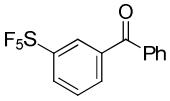
First, a Br/Mg-exchange reaction with the commercially available 1-bromo-3-(pentafluorosulfanyl)-benzene (**11**) using *i*PrMgCl·LiCl (**6**) was studied (Table 1). The aryl bromide **11** furnished after treatment with *i*PrMgCl·LiCl (**6**, 1.1 equiv) the arylmagnesium halide **13** within 1 h at 0 °C in 80% yield.[58] This magnesium reagent **13** reacted with various electrophiles in good yields. Thus, after a transmetalation with $ZnCl_2$, a Pd-catalyzed cross-coupling with 4-bromobenzonitrile (**14a**) or 5-bromopicolinonitrile (**14b**) (2% PEPPSI-*i*Pr[59]) furnished the functionalized SF_5-substituted biphenyls **15a** and **15b** in 79-83% yield (Table 1, entries 1-2).

Remarkably, the *Grignard* reagent **13** underwent, after a transmetalation with $ZnCl_2$, *Negishi* cross-couplings[60] with aryl bromides bearing unprotected anilines,[61] such as 4-bromoaniline (**14c**) or 3-amino-4-bromo-benzoic acid ethyl ester (**14d**) providing the functionalized amines **15c** and **15d** in 71-88% yield (entries 3-4). The acylation of the Mg-reagent **13** with ethyl cyanoformate (**14e**) yielded the SF_5-substituted ester **15e** in 80% yield (entry 5). Addition of **13** to electron-poor aldehydes, such as 2,3-dichlorobenzaldehyde (**14f**) as well as electron-rich aldehydes such as 4-methoxybenzaldehyde (**14g**) led to the SF_5-functionalized alcohols **15f** and **15g** in 81-84% yield (entries 6-7). After transmetalation with CuCN·2LiCl (1.1 equiv),[62] substitution with benzoyl chloride (**14h**) provided the ketone **15h** in 84% yield (entry 8).

Table 1: Products of type **15** obtained by Br/Mg-exchange with *i*PrMgCl·LiCl (**6**) followed by reaction with various electrophiles.



[57] P. Kirsch, M. Bremer, M. Heckmeier, K. Tarumi, *Angew. Chem. Int. Ed.* **1999**, *38*, 1989.
[58] The yield was determined by iodolysis of reaction aliquots using iodine in THF.
[59] a) C.J. O'Brien, E.A.B. Kantchev, C. Valente, N. Hadei, G.A. Chass, A. Lough, A.C. Hopkinson, M.G. Organ, *Chem. Eur. J.* **2006**, *12*, 4743; b) M.G. Organ, S. Avola, I. Dubovyk, N. Hadei, E.A.B. Kantchev, C.J. O'Brien, C. Valente, *Eur. J. Chem.* **2006**, *12*, 4749.
[60] a) E. Negishi, L.F. Valente, M. Kobayashi, *J. Am. Chem. Soc.* **1980**, *102*, 3298; b) E. Negishi, *Acc. Chem. Res.* **1982**, *15*, 340.
[61] a) G. Manolikakes, M.A. Schade, C. Munoz Hernandez, H. Mayr, P. Knochel, *Org. Lett.* **2008**, *10*, 2765; b) G. Manolikakes, Z. Dong, H. Mayr, J. Li, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 1324.
[62] P. Knochel, M.C.P. Yeh, S.C. Berk, J. Talbert, *J. Org. Chem.* **1988**, *53*, 2390.

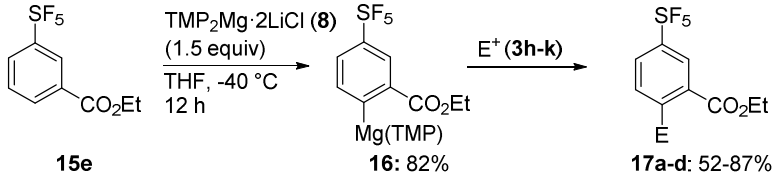
Entry	Electrophile	Product	Yield[a] [%]
1			83[b]
	14a	**15a**	
2			79[b]
	14b	**15b**	
3			88[c]
	14c	**15c**	
4			71[c]
	14d	**15d**	
5			80
	14e	**15e**	
6			81[e]
	14f	**15f**	
7			84
	14g	**15g**	
8			84[d]
	14h	**15h**	

[a] Isolated yields of analytically pure product. [b] Cross-coupling conditions: $ZnCl_2$ (1.1 equiv) / 2% PEPPSI-*i*Pr. [c] Cross-coupling conditions: $ZnCl_2$ (1.1 equiv) / 2% $Pd(OAc)_2$, 4% S-Phos, 23 °C, 12 h. [d] CuCN·2LiCl (1.1 equiv) was added. [e] Product prepared by Klaus Groll.

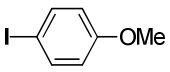
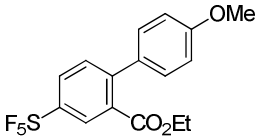
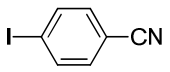
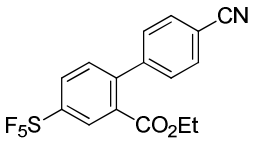
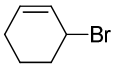
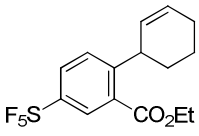
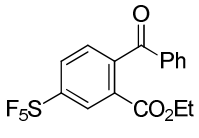
1.3 Preparation using Directed Metalation

Also, the SF_5-substituent showed a good compatibility in the performance of directed metalations using $TMP_2Mg \cdot 2LiCl$ (**8**). Thus, the treatment of the SF_5-substituted benzoic acid ethyl ester **15e** with $TMP_2Mg \cdot 2LiCl$ (**8**) led to the functionalized arylmagnesium reagent **16** after 12 h at -40 °C in ca. 82% yield (Table 2). After transmetalation with $ZnCl_2$ (1.1 equiv) the resulting zinc reagent underwent a *Negishi* cross-coupling with 1-iodo-4-methoxybenzene (**14i**) or 4-iodobenzonitrile (**14j**) in the presence of 2mol% $Pd(dba)_2$ and 4mol% tfp[63] (23 °C, 12 h), providing the SF_5-substituted biphenyl derivatives **17a** and **17b** in 52-83% yield (Table 2, entries 1-2). A copper-catalyzed allylation (20% $CuCN \cdot 2LiCl$) with 3-bromocyclohexene (**14k**) provided the trisubstituted benzene **15c** in 70% yield (entry 3). Furthermore, a Cu^I-mediated acylation with benzoyl chloride (**14h**) led to the corresponding ketoester **17d** in 87% yield (entry 4).

Table 2: Products of type **17** obtained by directed metalation of the ethyl benzoate **15e** using $TMP_2Mg \cdot 2LiCl$ (**8**) followed by quenching with electrophiles.



15e **16:** 82% **17a-d:** 52-87%

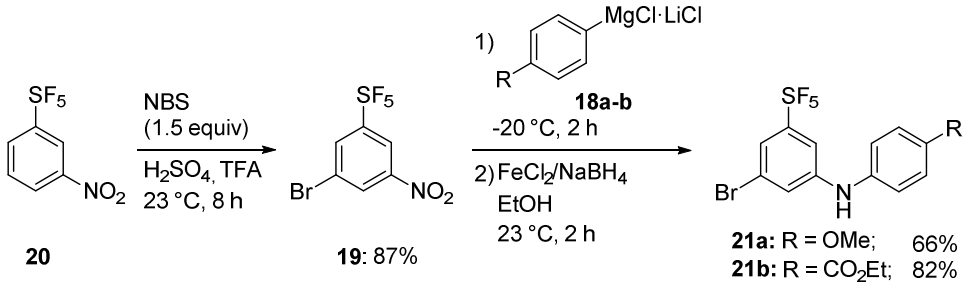
Entry	Electrophile	Product	Yield[a] [%]
1			52[b]
	14i	**17a**	
			83[b]
	14j	**17b**	
3			70[c]
	14k	**17c**	
4	PhCOCl		87[d]
	14h	**17d**	

[a] Isolated yields of analytically pure product. [b] Cross-coupling conditions: $ZnCl_2$ (1.1 equiv) / 2% $Pd(dba)_2$, 4% tfp, 23 °C, 12 h. [c] 20% $CuCN \cdot 2LiCl$ was added. [d] $CuCN \cdot 2LiCl$ (1.1 equiv) was added.

[63] Y. Takahashi, T. Ito, S. Sakai, Y. Ishii, *J. Chem. Soc. Chem. Commun.* **1970**, 1065; b) V. Farina, B. Krishnan, *J. Am. Chem. Soc.* **1991**, *113*, 9585; b) V. Farina, S. Kapadia, B. Krishnan, C. Wang, L.S. Liebeskind, *J. Org. Chem.* **1994**, *59*, 5905.

1.4 Preparation of SF_5-substituted Diarylamines

Arylamines are an important class of pharmaceuticals, due to their ability to undergo highly specific interactions with proteins. Recently, *Knochel* and coworkers showed that the amination of arylmagnesium reagents with nitroarenes provides after reductive workup polyfunctional diarylamines.[64] This method proved to be well suited for the preparation of SF_5-substituted diarylamines. Br/Mg-exchange on 1-iodo-4-methoxybenzene or 4-iodobenzoic acid ethyl ester with *i*PrMgCl·LiCl (**6**) (THF, -20 °C, 0.5 h) produced the corresponding functionalized Mg-reagents **18a-b**. These organometallics reacted smoothly with 1-bromo-3-nitro-5-pentafluorosulfanylbenzene (**19**), prepared[65] from 3-nitro-5-pentafluorosulfanyl-benzene (**20**). After reductive treatment with $FeCl_2/NaBH_4$, the SF_5-substituted diarylamines **21a-b** were obtained in 66-82% yield (Scheme 18).

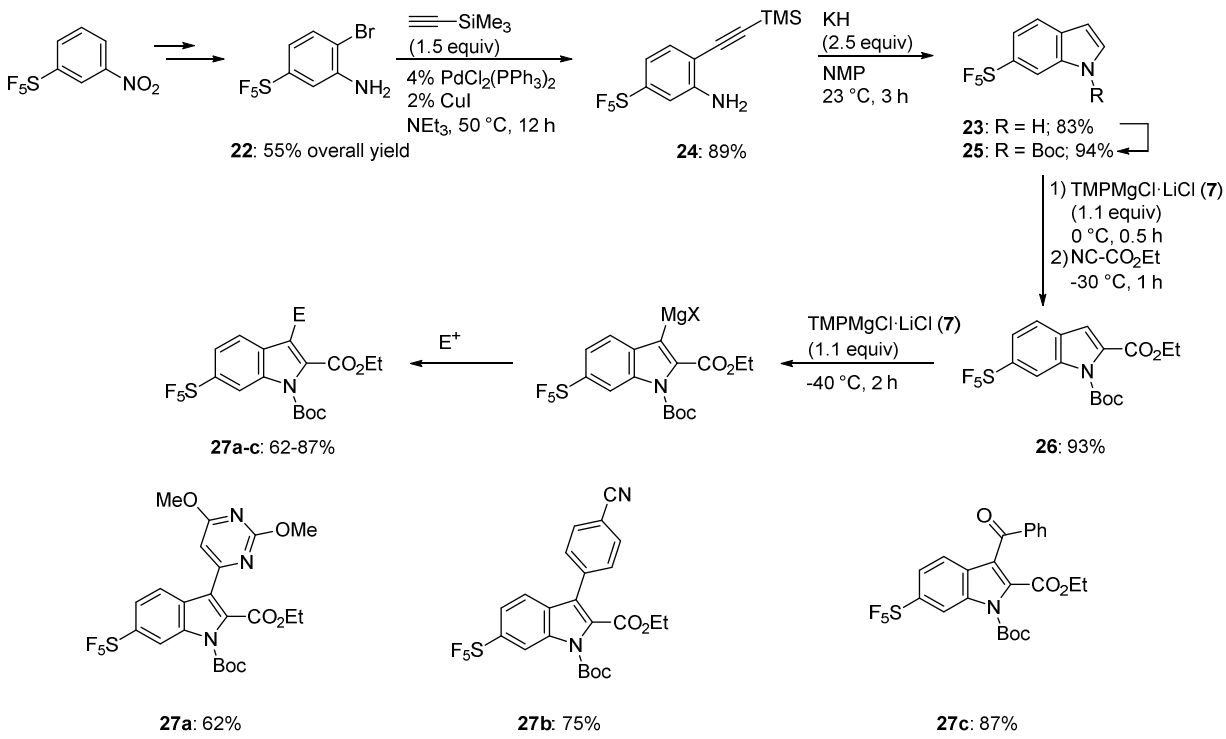


Scheme 18: Synthesis of diarylamines **21a-b** using arylmagnesium halides **18a-b** and the SF_5-substituted nitroarene **19**.

1.5 Preparation of SF_5-substituted Indoles

Heterocyclic building blocks are ubiquitous in medicinal chemistry. Therefore, SF_5-substituted functionalized indoles were synthesized. Starting from 2-bromo-5-(pentafluorosulfanyl)aniline[66] (**22**), the synthesis of 6-pentafluorosulfanyl-1*H*-indole (**23**) was achieved in two steps (Scheme 2). First, a Sonogashira cross-coupling[67] was performed by treating 2-bromoaniline **22** with (trimethylsilyl)acetylene (1.5 equiv, 50 °C, 12 h) providing the SF_5-substituted 2-((trimethylsilyl)ethynyl)aniline (**24**) in 89% yield. A subsequent cyclization reaction was performed by treatment with KH (2.5 equiv) in NMP (23 °C, 3 h) to afford the indole **23** in 83% yield.[68] The indole **23** was readily protected at nitrogen with Boc_2O leading to the N-Boc indole **25** in 94% yield (Scheme 19).

[64] a) I. Sapountzis, P. Knochel, *J. Am. Chem. Soc.* **2002**, *124*, 9390; b) F. Kopp, I. Sapountzis, P. Knochel, S*ynlett* **2003**, 885.
[65] Prepared according to the literature procedure: J. Duan, L. H. Zhang, W. R. Dolbier, Jr., *Synlett* **1999**, 1245.
[66] Prepared according to the literature procedure: J. T. Welch, D. S. Lim, *Bioorg Med. Chem.* **2007**, *15*, 6659.
[67] a) S. Takahashi, Y. Kuroyama, K. Sonogashira, N. Hagihara, *Synthesis* **1980**, 627; b) T. Sakamoto, M. Shiraiwa, Y. Kondo, H. Yamanaka, *Synthesis* **1983**, 312.
[68] a) A.L. Rodriguez, W. Dohle, P. Knochel, *Angew. Chem.* **2000**, *112*, 2607; *Angew. Chem. Int. Ed.* **2000**, *39*, 2488; b) C. Koradin, W. Dohle, A.L. Rodriguez, B. Schmid, P. Knochel, *Tetrahedron* **2003**, *59*, 1571; c) A.H. Stoll, P. Knochel, *Org. Lett.* **2007**, *10*, 113.



Scheme 19: Synthesis of the SF_5-substituted indole **23** and further functionalization of position 2 and 3 of the N-protected indole **25** by using TMPMgCl·LiCl (**7**).

Further functionalization of the *N*-protected indole **25** could be achieved using TMPMgCl·LiCl (**7**). The magnesiation of **25** was selective at position 2 of the indole ring with TMPMgCl·LiCl (**7**) (1.1 equiv, 0 °C, 0.5 h); subsequent trapping with cyanoformic acid ethyl ester (**14e**, 1.1 equiv, –30 °C, 1 h) afforded the *N*-protected ethyl 6-(pentafluorosulfanyl)-1*H*-indole-2-carboxylate **26** in 93% yield. Subsequent treatment of the indole **26** with TMPMgCl·LiCl (**7**) (1.1 equiv, -40 °C, 2 h) led to a fast magnesiation at position 3. After the transmetalation with $ZnCl_2$ (1.1 equiv), *Negishi* cross-coupling reactions (2mol% PEPPSI-*i*Pr, 23 °C, 10 h) with 4-iodo-2,6-dimethoxypyrimidine or 4-iodobenzonitrile provided the corresponding indoles **27a**-**b** in 62-75% yield. Alternatively, a transmetalation with CuCN·2LiCl (1.0 equiv) allows an efficient benzoylation (PhCOCl (1.2 equiv), -40 °C, 12 h) affording smoothly the 2,3-disubstituted indole **27c** in 87% yield (Scheme 19).

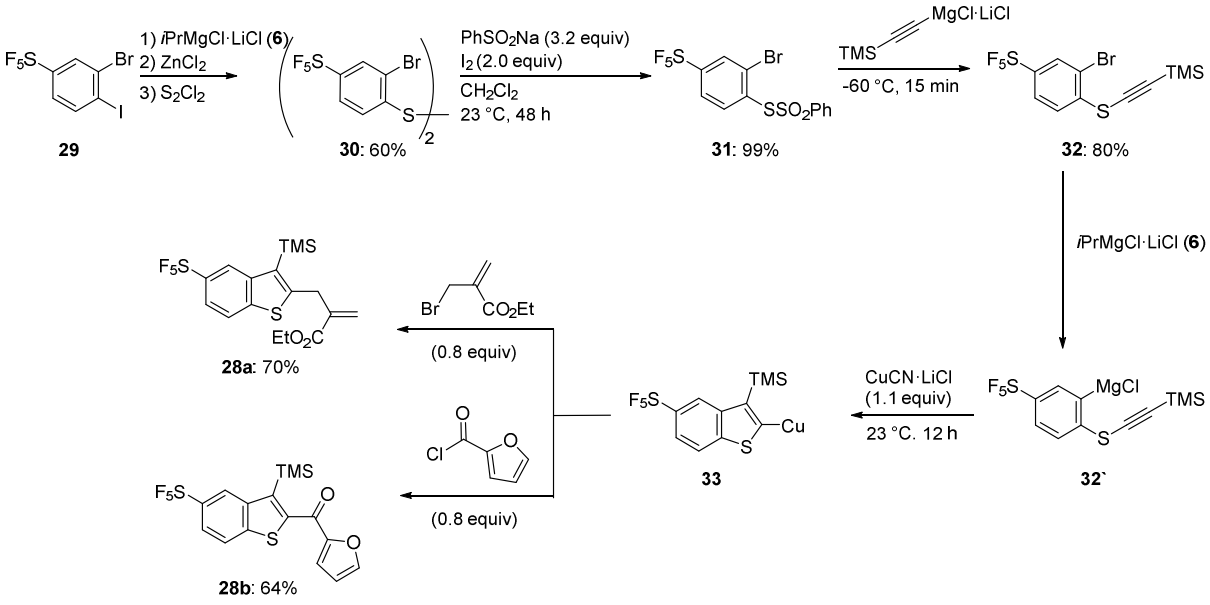
1.6 Preparation of SF_5-substituted Benzo[*b*]thiophenes

Besides indoles, benzo[*b*]thiophenes are of particular interest, as they are potential drug candidates[69] and are also widespread in material science.[70] Functionalized benzo[*b*]thiophenes can be prepared by the intramolecular copper-catalyzed carbomagnesiation of alkynyl(aryl)thioethers.[49] Herein, this

[69] a) C.D. Jones, M.G. Jevnikar, A.J. Pike, M.K. Peters, L.J. Black, A.R. Thompson, J.F. Falcone, J.A. Clemes, *J. Med. Chem.* **1984**, *27*, 1057; b) K.G. Pinney, A.D. Bounds, K.M. Dingeman, V.P. Mocharla, G.R. Pettit, R. Bai, E. Hamel, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1081; c) M.-J. R. P. Queiroz, R. C. Calhelha, L.A. Vale-Silva, E. Pinto, M. Sao-José Nascimento, *Eur. J. Med. Chem.* **2009**, *44*, 1893.

[70] a) T.Y. Zhang, J. O`Toole, C.S. Proctor, *Sulfur Rep.* **1999**, *22*, 1; b) I. McCulloch, M. Heeney, M.L. Chabinyc, D. DeLongchamp, R.J. Kline, M. Cçlle, W. Duffy, D. Fischer, D. Gundlach, B. Hamadani, R. Hamilton, L. Richter, A. Salleo, M. Shkunov, D. Sparrowe, S. Tierney, W. Zhang, *Adv. Mater.* **2009**, *21*, 1091.

method was applied to the synthesis of SF_5-substituted, functionalized benzo[*b*]thiophenes of type **28** (Scheme 20). The readily available SF_5-substituted 1,2-bromoiodoarene **29** was converted to the corresponding organic disulfide **30** by a I/Mg-exchange reaction (*i*PrMgCl·LiCl (**6**), -80 °C, 10 min), subsequent transmetalation with $ZnCl_2$ and reaction with sulfur monochloride.[71] The sulfonothioate **31** was obtained by treating the disulfide **30** with iodine and sodium benzenesulfinate.[72] This sulfonothioate reacted with trimethylsilylethynylmagnesium chloride providing the desired alkynyl(aryl)thioether **32** in 80% yield. Thus, the treatment of the thioether **32** with *i*PrMgCl·LiCl (**6**) (1.1 equiv, 23 °C, 1 h) provided the corresponding magnesium reagent **32`**. In the presence of stoichiometric amounts of CuCN·2LiCl cyclization occurred at 23 °C within 12 h producing the copper reagent **33**. A subsequent allylation reaction with 2-(bromomethyl)acrylic acid ethyl ester (0.8 equiv) afforded the polyfunctional benzothiophene **28a** in 70% yield. Similarly, the acylation with furan-2-carbonyl chloride (0.8 equiv) provided the acylated benzothiophene **28b** in 64% yield.



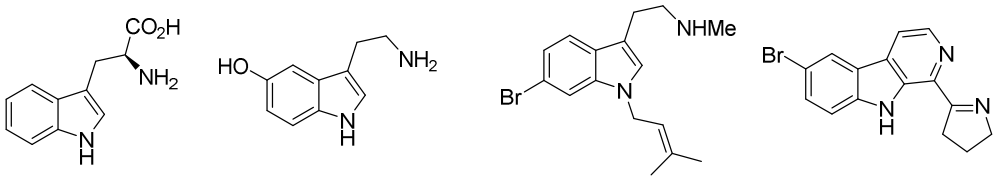
Scheme 20: Reaction sequence towards the SF_5-substituted alkynyl(aryl)thioether **32** and subsequent cyclization/allylation and acylation reaction sequence.

[71] T.J. Korn, P. Knochel, *Synlett* **2005**, 1185.
[72] K. Fujiki, N. Tanifuji, Y. Sasaki, T. Yokoyama, *Synthesis* **2002**, 343.

2. Preparation of Functionalized Indoles, Azaindoles and Pyrrolo[2,3-*d*]pyrimidines *via* an Intramolecular Copper-mediated Carbomagnesiation of Ynamides

2.1 Introduction

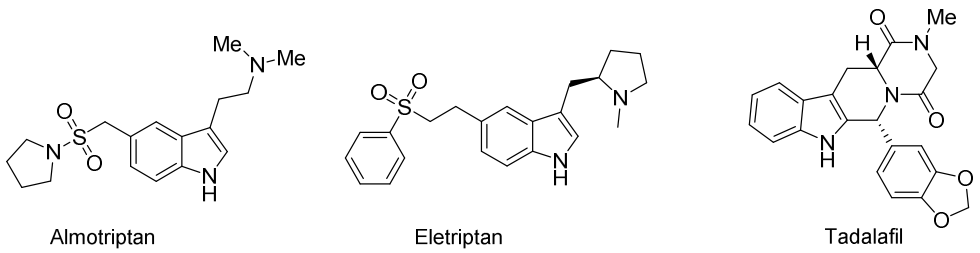
The indole ring system belongs to one of the most abundant and important heterocycles. It is a key substructure in a multitude of naturally occurring molecules, including the amino acid tryptophan, the neurotransmitter serotonin, and a plethora of others (Scheme 21).[73] Deformylflustrabromine B for example was isolated from the marine bryozoan *Flustra foliacea*.[74]. Also Eudistomin H, isolated from the caribbean tunicate *Eudistoma olivaceum*[75] shows antiviral and microbial activity.[76]



Scheme 21: Natural products containing the indole moiety.

Additionally, it is a key structural element for a vast number of biologically active molecules (pharmaceuticals and agrochemicals).[77] Almotriptan and Eletriptan for instance are used as antimigraine agents. Tadalafil is a PDE5 inhibitor marketed by Eli Lilly for treating erectile dysfunction under the name Cialis, and under the name Adcirca for the treatment of pulmonary arterial hypertension (Scheme 22).[78] The widespread utility of indoles has stimulated the development of numerous methodologies for their synthesis.[79]

[73] E. Fattorusso, O. Taglialatela-Scafati, *Modern Alkaloids*, Wiley-VCH, Weinheim **2008**.
[74] L. Peters, A.D. Wright, A. Krick, G.M. König, *J. Chem. Ecol.* **2004**, *30*, 1165.
[75] K.L. Rinehart, J. Kobayashi, G.C. Harbour, R.G. Hughes, S.A. Mizsak, T.A. Scahiel, *J. Am. Chem. Soc.* **1984**, *106*, 1524.
[76] C.M. Irland, B.R. Copp, M.P. Foster, L.A. McDonald, D.C. Radisky, J.C. Swersey, *Marine Biotechnology*, (Eds.D.H. Attaway, O.R. Zaborsky) Plenum: New York, **1993**.
[77] a) M. Inman, C.J. Moody, *Chem. Sci.* **2013**, *4*, 29; b) M. Somei, F. Yamada, *Nat. Prod. Rep.* **2005**, *22*, 73, c) P.S. Baran, A.C. Guerrero, B. D. Hafensteiner, N. B. Ambhaikar, *Angew. Chem. Int. Ed.* **2005**, *44*, 3892, d) T. Yamashita, N. Kawai, H. Tokuyama, T. Fukuyama, *J. Am. Chem. Soc.* **2005**, *127*, 15038; e) C.F. Nising, *Chem. Soc. Rev.* **2010**, *3*, 591.
[78] A. Kleemann, J. Engel, B. Kutscher, D. Reichert, Pharmaceutical Substances, Thieme, 5th edition 2009
[79] Review on indole synthesis: a) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2005**, *105*, 2873; b) G. R. Humphrey, J. T. Kuethe, *Chem. Rev.* **2006**, *106*, 2875; c) M. Platon, R. Amardeil, L. Djakovitch, J.-C. Hierso, *Chem. Soc. Rev.* **2012**, *41*, 3929; d) D. Liu, G. Zhao, L. Xiang, *Eur. J. Org. Chem.* **2010**, 3975; e) B. Witulski, C. Alayrac, L. Tevzadze-Saeftel, *Angew. Chem.* **2003**, *115*, 4392; *Angew. Chem. Int. Ed.* **2003**, *42*, 4257; f) C. Bressy, D. Alberico, M. Lautens, *J. Am. Chem. Soc.* **2005**, *127*, 13148; g) P. Thansandote, D.G. Hulcoop, M. Langer, M. Lautens, *J. Org. Chem.* **2009**, *74*, 1673; h) L. Ackermann, *Org. Lett.* **2005**, *7*, 439. i) S. Barfüßer, H.K. Potukuchi, L. Ackermann, *Adv. Synth. Catal.* **2009**, *351*, 1064; j) J. Barluenga, and C. Valdés, *Five-Membered Heterocycles: Indole and Related Systems*, in *Modern Heterocyclic Chemistry* (Eds J. Alvarez-Builla, J.J. Vaquero and J. Barluenga), Wiley-VCH, Weinheim **2011**.



Scheme 22: Bioactive molecules containing the indole moiety.

Also, the closely related azaindoles have recently received a lot of attention due to their potential biological properties.[80] Among the natural substances where the azaindole core is present,[81] it is also a part of synthetic analogues of naturally occurring indoles.[82] And especially highly functionalized 7-azaindoles have become major goals for medicinal chemistry studies.[83] In addition, azaindoles have also found applications in material science and coordination chemistry.[84] Most of the conventional indole scaffold preparations cannot be extended to the azaindole system. A frequently employed strategy for azaindole synthesis is to start with substituted pyridines and to build up the pyrrole ring. Due to the electron-deficient nature of the pyridine ring, many classical indole preparations do either not proceed or are not efficient.[85]

Next to the standard four nucleotides, there are a number of nucleotide modifications in the RNA. Queuosine and Archaeosine are two of these modifications, which possess a carbon atom at position 7 instead of a nitrogen atom. In addition, they sparked a lot of interest in the pharmaceutical industry. Ruxolitinib for example is a drug for the treatment of intermediate or high-risk myelofibrosis, a type of bone marrow cancer (Scheme 23).[86, 87]

[80] a) J.J. Song, J.T. Reeves, F. Gallou, Z. Tan, N.K. Yee, C. H. Senanayake, *Chem. Soc. Rev.* **2007**, *36*, 1120; b) L. Xu, I.R. Lewis, S.K. Davidson, J.B. Summers, *Tetrahedron Lett.* **1998**, *39*, 5159; c) M. Nazaré, C. Schneider, A. Lindenschmidt, D. W. Will, *Angew. Chem.* **2004**, *115*, 4626; *Angew. Chem. Int. Ed.* **2004**, *43*, 4526; d) V. Kumar, J.A. Dority, E.R. Bacon, B. Singh, G.Y. Lesher, *J. Org. Chem.* **1992**, *57*, 6995; e) J.A. Turner, *J. Org. Chem.* **1983**, *48*, 3401; f) D. Wensbo, A. Eriksson, T. Jeschke, U. Annby, S. Gronowitz, *Tetrahedron Lett.* **1993**, *34*, 2823; g) S.S. Park, J.-K. Choi, E.K. Yum, *Tetrahedron Lett.* **1998**, *39*, 627; h) M. Amjad, D.W. Knight, *Tetrahedron Lett.* **2004**, *45*, 539; i) S. Cacchi, G. Fabrizi, L.M. Parisi, *J. Comb. Chem.* **2005**, *7*, 510; j) C. Harcken, Y. Ward, D. Thomson, D. Riether, *Synlett* **2005**, 3121; k) M. Layek, Y.S. Kumar, A. Islam, R. Karavarapu, A. Sengupta, D. Halder, K. Mukkanti, M. Pal, *Med. Chem. Commun.* **2011**, *2*, 478; l) S. Zhang, W-X. Zhang, Z. Xi, *Chem. Eur. J.* **2010**, *16*, 8419; m) D. Thomae, M. Jeanty, J. Coste, G. Guillaumet, F. Suzenet, *Eur. J. Org. Chem.* **2013**, *16*, 3328; n) F. Popowycz, S. Routier, B. Joseph, J.-Y. Merour, *Tetrahedron* **2007**, *63*, 1031; o) F. Popowycz, J.-Y. Merour, B. Joseph, *Tetrahedron* **2007**, *63*, 8689; p) J.-Y. Merour, S. Routier, F. Suzenet, B. Joseph, Tetrahedron **2013**, *69*, 4767; q) F. Saab, V. Beneteau, F. Schoentgen, J.-Y. Merour, S. Routier, *Tetrahedron* **2010**, *66*, 102; r) C. Schneider, E. David, A.A. Toutov, V. Snieckus, *Angew. Chem.* **2012**, *124*, 2776; *Angew. Chem. Int. Ed.* **2012**, *51*, 2722.

[81] N.B. Perry, L. Ettouati, M. Litaudon, J.W. Blunt, M.H.G. Munro, *Tetrahedron* **1994**, *50*, 3987

[82] C. Marminon, A. Pierré, B. Pfeiffer, V. Pérez, S. Leonce, P. Renard, M. Prudhomme, *Bioorg. Med. Chem.* **2003**, *11*, 679.

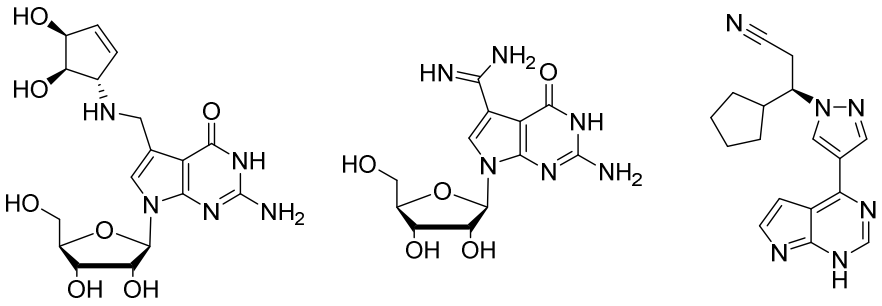
[83] C.N. Hodge, P.E. Aldrich, Z.R. Wasserman, C.H. Fernandez, G.A. Nemeth, *J. Med. Chem.* **1999**, *42*, 819.

[84] a) S.-B. Zhao, S. Wang, *Chem. Soc. Rev.* **2010**, *39*, 3142; b) K.L. Garner, L.F. Parkes, J.D. Piper, J.A.G. Williams, *Inorg. Chem.* **2010**, *49*, 476; c) D. Pogozhev, S. A. Baudron, G. Rogez, M. W. Hosseini, *Polyhedron* **2013**, *52*, 1329.

[85] F. Popowycz, S. Routier, B. Joseph, J.-Y. Merour, *Tetrahedron* **2006**, *63*, 1031.

[86] R.A. Mesa, U. Yasothan, P. Kirkpatrick, *Nature Reviews Drug Discovery* **2012**, *11*, 103.

[87] Alan R. Katritzky, *Comprehensive heterocyclic chemistry*, (Ed: Alan R. Katritzky) Elsevier Books, **2008**.



Scheme 23: RNA nucleosides Quenosine and Archaeosine.

A synthetic method which can give access to the preparation of indoles, to the various isomeric azaindoles (4-, 5-, 6-, or 7-azaindoles) as well as to pyrrolo[2,3-*d*]pyrimidines would be highly desirable.

Recently, *Kunz* and *Knochel* described a general preparation of functionalized benzo[*b*]thiophenes and benzo[*b*]thieno[2,3-*d*]thiophenes *via* an intramolecular catalytic carbocupration[88] reaction.[49] Carbocuprations are very powerful addition reactions for the construction of complex stereodefined organic molecules[89] and their intramolecular version is very attractive for constructing heterocyclic organometallics.[90]

The aim of this work was to develop a mild and general one-pot preparation of indoles, azaindoles and pyrrolo[2,3-*d*]pyrimidines of type **34** *via* a new 5-endo-dig[91] copper-mediated intramolecular carbometalation of magnesiated derivatives of type **35**, leading to cuprated heterocyclic intermediates of type **36** which after quenching with various electrophiles afford functionalized *N*-heterocycles of type **34** (Scheme 24). The magnesiated intermediates were readily prepared from the corresponding bromo-ynamides[92] of type **37** using a bromine-magnesium exchange.

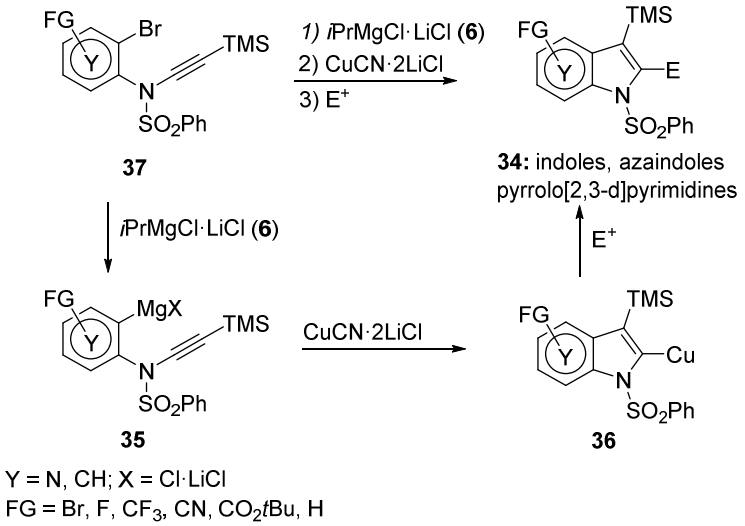
[88] a) J.P. Das, H. Chechik, I. Marek, *Nat. Chem*. **2009**, *1*, 128; b) A. Abramovitch, I. Marek, *Eur. J. Org. Chem*. **2008**, 4924; c) Y. Minko, M. Pasco, H. Chechik, I. Marek, *Beilstein J. Org. Chem.* **2013**, *9*, 526; For reviews on carbocupration reactions see also: d) J.F. Normant, A. Alexakis, *Synthesis* **1981**, 841; e) A. Basheer, I. Marek, *Beilstein J. Org. Chem*. **2010**, *6*, No. 77; f) N. Chinkov, D. Tene, I. Marek in *Metal-Catalyzed Cross-Coupling Reactions* (Ed.: F. Diederich, A. de Meijere), 2nd ed., Wiley-VCH, Weinheim, **2004**; g) N. Krause in *Modern Organocopper Chemistry* (Ed.: N. Krause), Wiley-VCH, Weinheim, **2002**.

[89] a) C. Germon, A. Alexakis, J. F. Normant, *Synthesis* **1984**, 40; b) E. Nakamura, S. Mori, *Angew. Chem.* **2000**, *112*, 3902; *Angew. Chem. Int. Ed.* **2000**, *39*, 3750; c) A. Alexakis, J. E. Bäckvall, N. Krause, O. Pàmies, M. Diéguez, *Chem. Rev.* **2008**, *108*, 2796; d) Y. Minko, M. Pasco, L. Lercher, I. Marek, *Nature Protocols*, **2013**, *8*, 749; e) L. Ackermann, *Angew. Chem.* **2011**, *123,* 3926; *Angew. Chem. Int. Ed.* **2011**, *50*, 3842; f) R. Jeyachandran, H. K. Potukuchi, L. Ackermann, *Beilstein J. Org. Chem.* **2012**, *8*, 1771; g) F. Monnier, M. Taillefer, *Angew. Chem.* **2009**, *121*, 7088; *Angew. Chem. Int. Ed.* **2009**, *48*, 6954; h) G. Lefevre, G. Franc, A. Tlili, C. Adamo, M. Taillefer, I. Ciofini, A. Jutand, *Organometallics* **2012***, 31*, 7694; A. Tlili, F. Monnier, M. Taillefer, *Chem. Commun.* **2012**, *48*, 6408; i) G. Danoun, A. Tlili, F. Monnier, M. Taillefer, *Angew. Chem.* 2012, *124*, 12987; *Angew. Chem. Int. Ed.* **2012**, *51*, 12815.

[90] a) Z. Shen, X. Lu, *Adv. Synth. Cat.* **2009**, *351*, 3107; b) V. Kavala, D. Janreddy, M. J. Raihan, C.-W. Kuo, C. Ramesh, C.-F. Yao, *Adv. Synth. Catal.* **2012**, *354*, 2229.

[91] a) I. L. Kruse, J. E. Baldwin, *J. Chem. Soc., Chem. Commun.* **1976**, *18*, 734; b) R. C. Thomas, I. L. Kruse, L. Silberman, E. J. Baldwin, *J. Org. Chem.* **1977**, *42*, 3846.

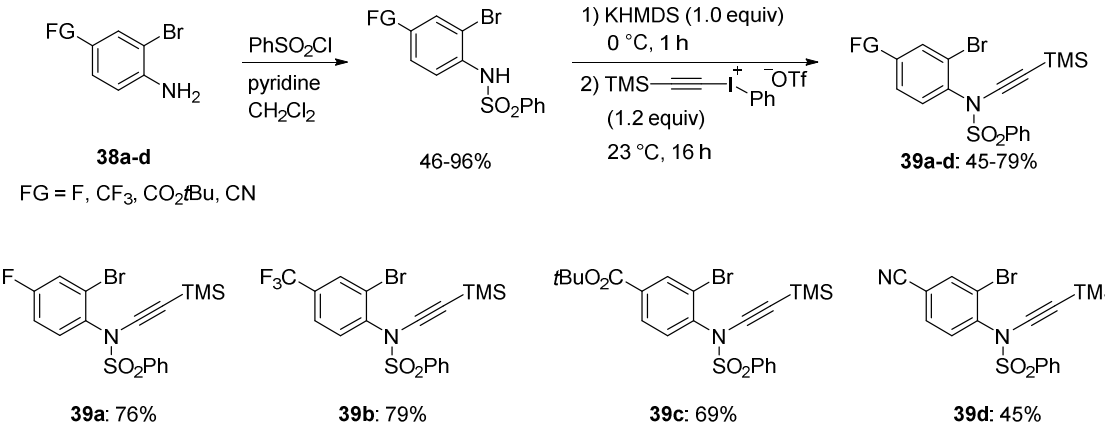
[92] Review: a) G. Evano, A. Coste, K. Jouvin, *Angew. Chem.* **2010**, *122*, 2902; *Angew. Chem. Int. Ed.* **2010**, *49*, 2840; b) K. A. DeKorver, H. Li, A.G. Lohse, R. Hayashi, Z. Lu, Y. Zhan, R. P. Hsung*, Chem. Rev.* **2010**, *110*, 5064; c) A. Coste, G. Karthikeyan, F. Couty, G. Evano, *Angew. Chem.* **2009**, *121*, 4445; *Angew. Chem. Int. Ed.* **2009**, *48*, 4381; d) K. Jouvin, J. Heimburger, G. Evano, *Chem. Sci.* **2012**, *3*, 756; e) J.Y. Kim, S.H. Kim, S. Chang, *Tetrahedron Lett.* **2008**, *49*, 1745; f) F. Nissen, V. Richard, C. Alayrac, B. Witulski, *Chem. Commun.* **2011**, *47*, 6656; g) S. Balieu, K. Toutah, L. Carro, L.-M. Chamoreau, H. Rousselière, C. Courillon, *Tetrahedron Lett.* **2011**, *52*, 2876.



Scheme 24: Preparation of indoles, 4-, 5-, 6-, and 7-azaindoles and pyrrolo[2,3-*d*]pyrimidines *via* copper-mediated carbomagnesiation of ynamides of type **37**.

2.2 Preparation of Functionalized Indoles

First, the intramolecular carbocupration for the preparation of polyfunctional indoles was tested. The required bromo-ynamides are available in two straightforward steps starting from the corresponding 2-bromoanilines (**38a-d**). After *N*-sulfonylation of the anilines **38a-d** and *N*-ethynylation using KHMDS (KHMDS = potassium hexamethyldisilazane) and phenyl((trimethylsilyl)ethynyl)iodonium triflate[93] afforded the corresponding ynamides **39a-d** in 45-79% (Scheme 25).[94]



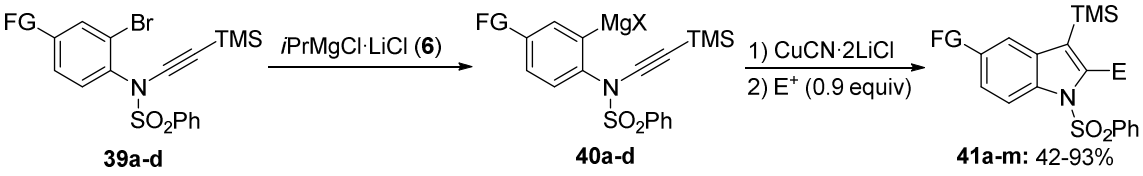
Scheme 25: TMS-substituted ynamides of type **39**.

Additional treatment of the ynamide **39a** with *i*-PrMgCl·LiCl (**6**) provided the corresponding magnesium reagent **40a** within 0.5 h at -10 °C in over 90% yield.[95] In the presence of a catalytic

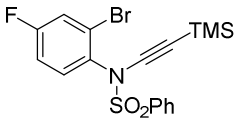
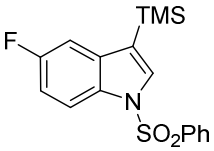
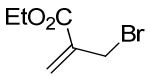
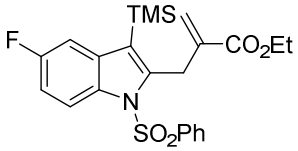
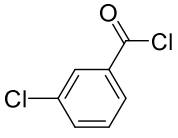
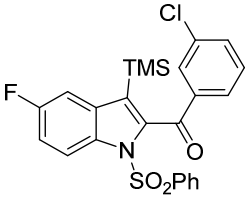
[93] a) T. Kitamura, J. Matsuyuki, H. Taniguchi, *Synthesis* **1994**, 147; b) T. Kitamura, M. Kotani, Y. Fujiwara, *Synthesis* **1998**, 1416.
[94] a) P. Murch, B.L. Williamson, P.J. Stang, *Synthesis* **1994**, 1255; b) B. Witulski, T. Stengel, *Angew. Chem.* **1998**, *110*, 495; *Angew. Chem. Int. Ed.* **1998**, *37*, 489; c) K. Tanaka, K. Takeishi, *Synthesis* **2007**, 2920.
[95] The yield was determined by iodolysis of reaction aliquots using iodine in THF.

amount of CuCN·2LiCl[96] (30 mol%) a smooth cyclization occurred (23 °C, 24 h)[97] producing a 2-metalated indole derivative (of type **36**; Scheme 24) After quenching with water the fluorine-substituted indole **41a** could be obtained in 93% yield (Table 3, entry 1). A subsequent allylation reaction with ethyl 2-(bromomethyl)acrylate[98] (0.9 equiv) afforded the polyfunctional indole **41b** in 92% yield (entry 2). Similarly, an acylation with 3-chlorobenzoyl chloride furnished the 2-acylated indole **41c** in 92% yield (entry 3). The CF_3-substituted ynamide **39b** reacted smoothly with *i*PrMgCl·LiCl (**6**) (-20°C, 15min) to give the corresponding magnesium reagent **40b**. However, in this case the addition of one equivalent of CuCN·2LiCl was necessary to achieve a complete ring closure (23 °C, 8 h). Alternatively, microwave irradiation[99] of the reaction mixture (50 °C, max. 100 W) allows to complete the ring closure within 1.5 h. The resulting 2-metalated indole reacted with various electrophiles in good yields. Thus, hydrolysis, an acylation with cyclopropanecarbonyl chloride or 4-methylbenzoyl chloride provided the desired ketones **41d-f** in 76-85% yield (entries 4-6). Similarly, the allylation with 3-bromocyclohexene afforded the functionalized indole **41g** in 65% yield (entry 7).

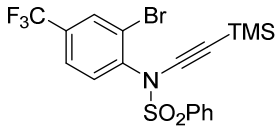
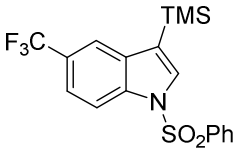
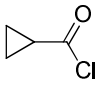
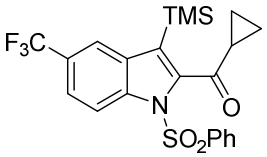
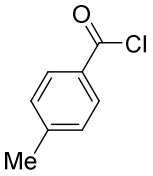
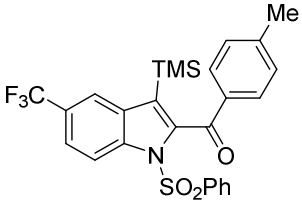
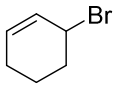
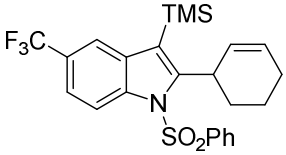
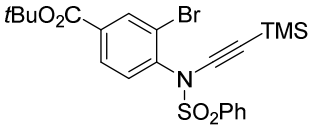
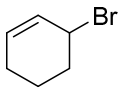
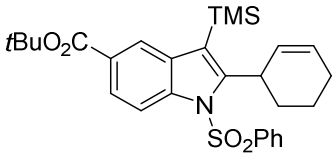
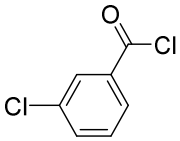
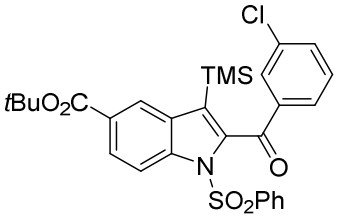
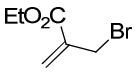
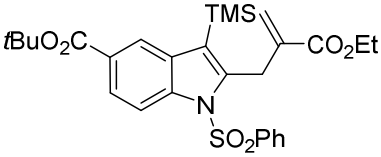
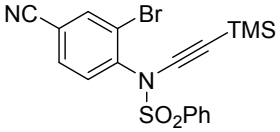
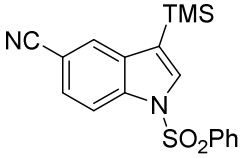
Table 3: Preparation of functionalized indoles of type **41** by a copper-mediated carbomagnesiation of ynamides of type **39** and subsequent reaction with electrophiles.

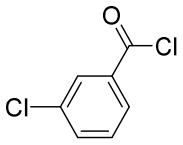
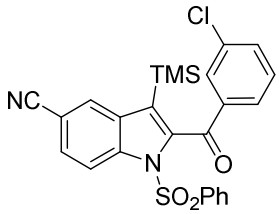
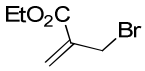
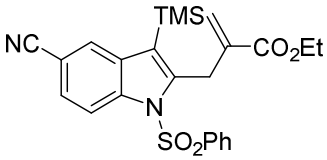


39a-d **40a-d** **41a-m:** 42-93%

Entry	Substrate	Electrophile[a]	Product[b]
1		H_2O	
	39a		**41a:** 93%
2	**39a**		
			41b: 92%
3	**39a**		
			41c: 92%

[96] P. Knochel, M.C.P. Yeh, S.C. Berk, J. Talbert, *J. Org. Chem*. **1988**, *53*, 2390.
[97] In the absence of the copper salt, no cyclization is observed.
[98] a) M. Rambaud, J. Villiéras, *Synthesis* **1984**, 406; b) J. Villiéras, M. Rambaud, *Org. Synth.* **1988**, *66*, 220.
[99] C.O. Kappe, *Angew. Chem.* **2004**, *116*, 6408; *Angew. Chem. Int. Ed.* **2004**, *43*, 6250.

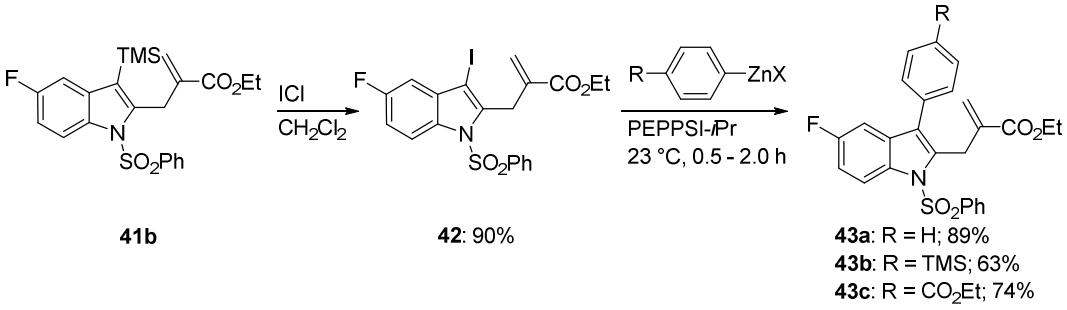
4		H_2O	
	39b		**41d:** 76%
5	**39b**		
			41e: 85%
6	**39b**		
			41f: 78%
7	**39b**		
			41g: 65%
8			
	39c		**41h:** 62%
9	**39c**		
			41i: 93%
10	**39c**		
			41j: 48%
11		H_2O	
	39d		**41k:** 66%

12	**39d**		 **41l:** 68%
13	**39d**		 **41m:** 42%

[a] 0.9 equiv of electrophile were used. [b] Isolated yields of analytically pure product.

In the case of the cyano-substituted ynamide **39d**, the Br/Mg-exchange with *i*-PrMgCl·LiCl (**6**) was complete at -5 °C in 0.5 h and for the more sensitive ester-substituted ynamide **39c**, the exchange was carried out at -20 °C in 1 h. The use of stoichiometric amounts of CuCN·2LiCl avoids side reactions in both cases. Again an alternative microwave irradiation (50 °C, max. 100 W) allows to complete the ring closure within 0.75-1 h (instead of 23 °C, 16 h). A subsequent allylation or acylation of the ester-substituted reagent **39c** afforded the derived indoles **41h-j** in 48-93% yield (Table 3, entries 8-10). Likewise, hydrolysis, acylation or allylation of the corresponding cyano-substituted 2-metalled heterocycle gave the indoles **41k-m** in 42-68% yield. (entries 11-13).

The TMS-substituent in indoles of type **41** can be used for further functionalization in position 3. Thus, the TMS-substituted indole **41b** was converted to the iodide **42** in 90% yield[100] (Scheme 26). This iodoindole **42** undergoes *Negishi* cross-coupling reactions with various zinc reagents[17, 23] using 3mol% PEPPSI-*i*Pr to provide the 2,3 disubstituted indoles **43a-c** in 63-89% yield (Scheme 26).

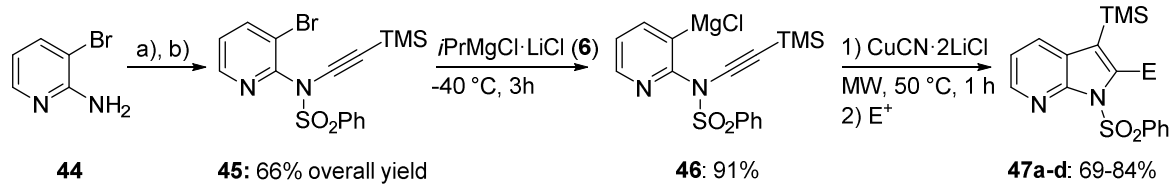


Scheme 26: Transformation of the TMS-substituted indole **41b** to the 3-iodoindole **42** and additional *Negishi* cross-couplings.

[100] Z. Bo, A.D. Schlüter, *J. Org. Chem*. **2002**, *67*, 5327.

2.3 Preparation of Functionalized Azaindoles

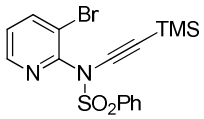
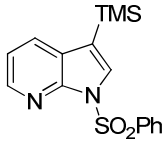
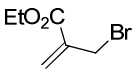
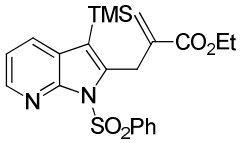
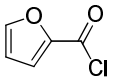
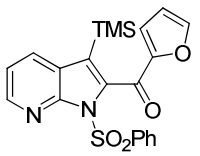
Remarkably, this versatile indole synthesis was successfully extended to the preparation of 4-, 5-, 6-, or 7-azaindoles. Thus, for the synthesis of 7-azaindoles, commercial 2-amino-3-bromopyridine (**44**) was used as starting material. The synthesis of the corresponding ynamide **45** was achieved in two steps as described above (66% overall yield). The treatment of ynamide **45** with *i*-PrMgCl·LiCl (**6**) (1.1 equiv, -45 °C, 1 h) provided the heteroaryl-magnesium reagent **46** in ca. 91% yield. A subsequent microwave irradiation using CuCN·2LiCl (1.0 equiv) at 50 °C allowed to complete the ring closure within 1 h (Scheme 27).

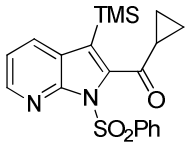


Scheme 27: Preparation of functionalized 7-azaindoles of type **47** by a copper-mediated carbomagnesiation of ynamide **45**. Reagents and conditions: a) $PhSO_2Cl$ (1.2 equiv), pyridine (3.0 equiv), CH_2Cl_2, 23 °C, 72 h, 80%; b) KHMDS (1.0 equiv), toluene, 0 °C, 1 h, then phenyl((trimethylsilyl)ethynyl)iodonium triflate (1.2 equiv), 23 °C, 16 h, 82%.

After quenching with water the corresponding 7-azaindole **47a** was isolated in 79% yield (Table 4, entry 1). Alternatively, allylation or acylation could be readily performed with ethyl 2-(bromomethyl)acrylate, furoyl chloride or cyclopropanecarbonyl chloride to provide the desired 7-azaindoles **47b-d** in 69-84% yield (entry 2-4).

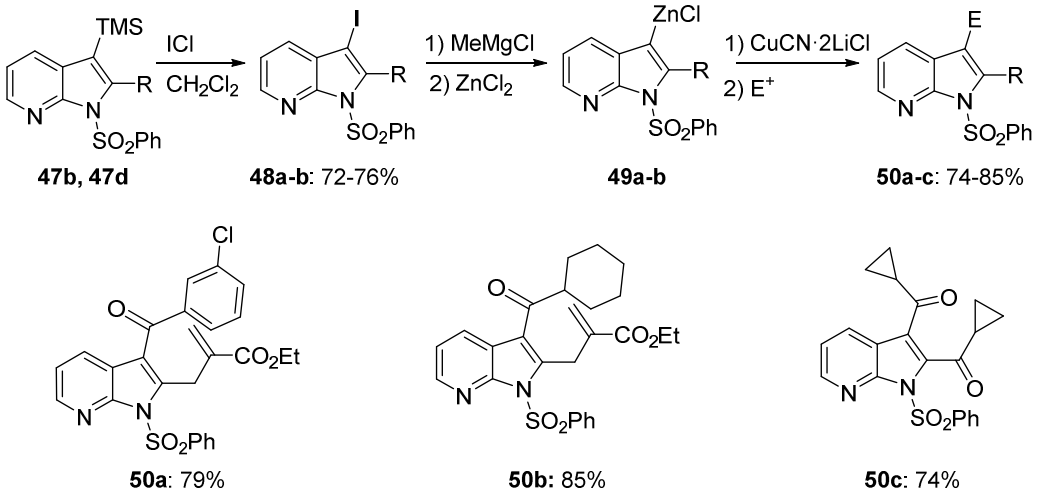
Table 4: Functionalized 7-azaindoles of type **47** obtained by the copper-mediated carbomagnesiation of ynamide **45** and subsequent reaction with various electrophiles.

Entry	Substrate	Electrophile[a]	Product	Yield[b] [%]
1		H_2O		79
	45		**47a**	
2	**45**			84
			47b	
3	**45**			69
			47c	

4	**45**		 **47d**	84

[a] 0.9 equiv of electrophile were used. [b] Isolated yield of analytically pure product.

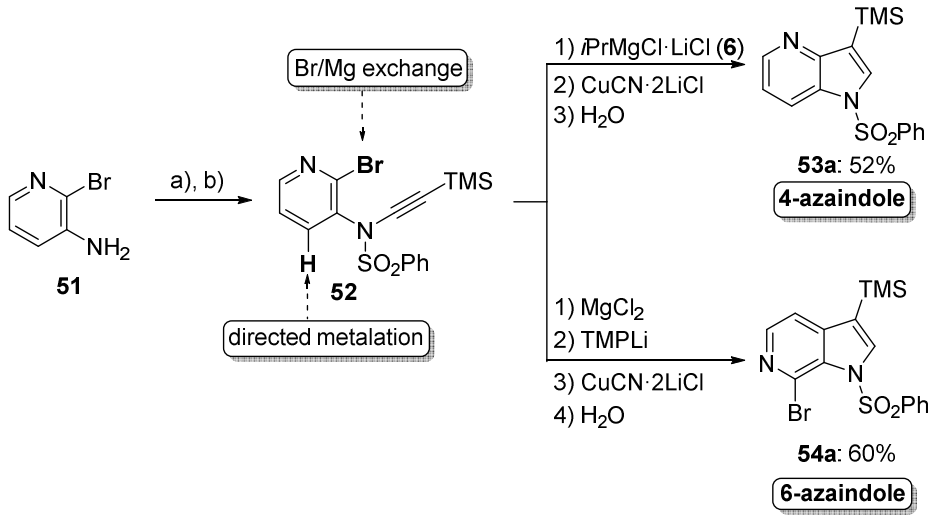
Further functionalization of 7-azaindoles **47b** and **47d** could be achieved *via* a transformation of the TMS-group to the corresponding iodides **48a** and **48b** using ICl in 64-72% yield (Scheme 28). Subsequent I/Mg exchange reaction with MeMgCl (1.1 equiv, -78 °C, 0.5 h)[101] followed by transmetalation with $ZnCl_2$ furnished the functionalized Zn-reagents **49a-b** which reacted smoothly with 3-chlorobenzoyl chloride, cyclohexanecarbonyl chloride or cyclopropanecarbonyl chloride to give the 2,3-disubstituted azaindoles **50a-c** in 74-85% yield (Scheme 28).



Scheme 28: 2,3-Disubstituted 7-azaindoles of type **50** obtained by transformation of the TMS-substituted 7-azaindoles **47b** and **47d**.

Also the subclass of 4- and 6-azaindoles are readily available using this new method. The standard two-step conversion of the commercial 2-bromopyridin-3-amine (**51**) provides the desired ynamide **52** in 56% overall yield. This precursor **52** undergoes a Br/Mg exchange reaction with *i*PrMgCl·LiCl (**6**) (1.5 equiv, -40 °C, 24 h) at position 2 providing after copper-mediated ring closure the 4-azaindole **53a** in 52% yield (Scheme 29). Remarkably, starting from the same ynamide **52**, the present methodology allows also the preparation of 6-azaindoles using a directed metalation mediated by TMPLi (**12**).[102] Thus, the 2,3-substituted pyridine **52** was conveniently metalated with TMPLi (1.1 equiv) in the presence of $MgCl_2$ (1.2 equiv) at –78 °C within 0.5 h at position 4. A subsequent copper-mediated cyclization (23 °C, 48 h) followed by hydrolysis afforded the 6-azaindole **54a** in 60% yield.

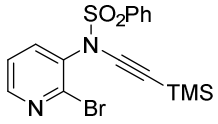
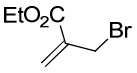
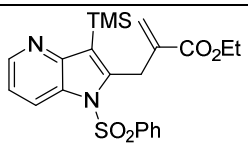
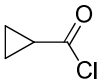
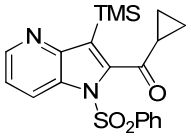
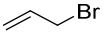
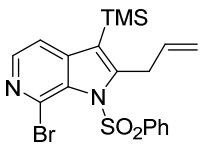
[101] I/Mg exchange reaction with *i*-PrMgCl·LiCl even at -90 °C led to a fast decomposition of the organometallic reagent.
[102] a) H. Gilman, W. Langham, A.L. Jacoby, *J. Am. Chem. Soc.* **1939**, *61*, 106; b) G. Wittig, G. Fuhrmann, *Ber. Dtsch. Chem. Ges.* **1940**, *73*, 1197; c) T.K. Macklin, J. Panteleev, V. Snieckus, *Angew. Chem.* **2008**, *120*, 2127; *Angew. Chem. Int. Ed.* **2008**, *47*, 2097.



Scheme 29: Reaction pathways allowing the conversion of ynamide **52** to 4-azaindole **53a** or 6-azaindole **54a**. Reagents and conditions: a) $PhSO_2Cl$ (1.2 equiv), pyridine (3.0 equiv), CH_2Cl_2, 23 °C, 1 h, 76%; b) KHMDS (1.0 equiv), toluene, 0 °C, 1 h, then phenyl((trimethylsilyl)ethynyl)iodonium triflate (1.2 equiv), 23 °C, 16 h, 74%.

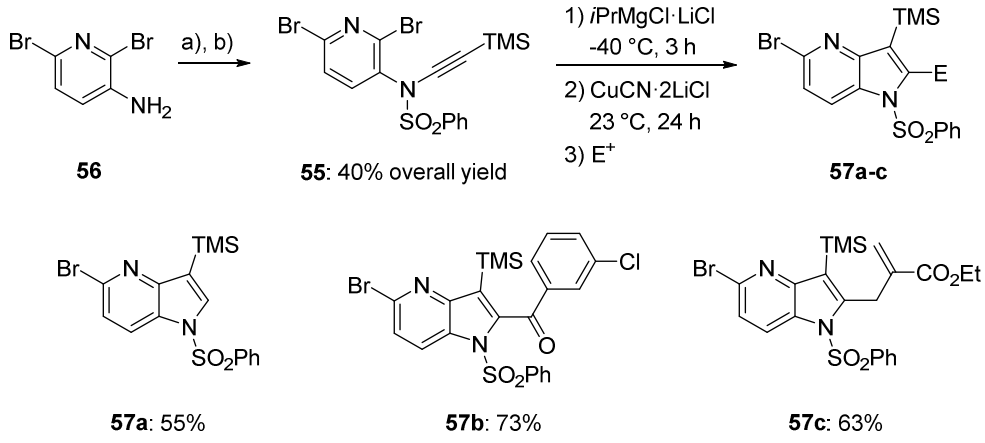
Beside hydrolysis, further functionalization of position 2 would be desirable. As a result of the challenging Br/Mg exchange reaction (-40 °C, 24 h, 80% conversion), successive allylation and acylation reactions provided only moderate yields (**53b-c**: 36-45%) (Table 5, entries 1-2). In the case of the directed metalation by TMPLi (**12**) an allylation with allylbromide gave the 6-azaindole **54b** in 67% yield (entry 3).

Table 5: Functionalized 4- and 6-azaindoles of type **53** and **54** obtained by the copper-mediated carbomagnesiation of ynamide **52** and subsequent reaction with various electrophiles.

Entry	Substrate	Electrophile[a]	Product	Yield[b] [%]
1	 **52**		 **53b**	36
2	**52**		 **53c**	45
3	**52**		 **54b**	67

[a] 0.9 equiv of electrophile were used. [b] Isolated yield of analytically pure product.

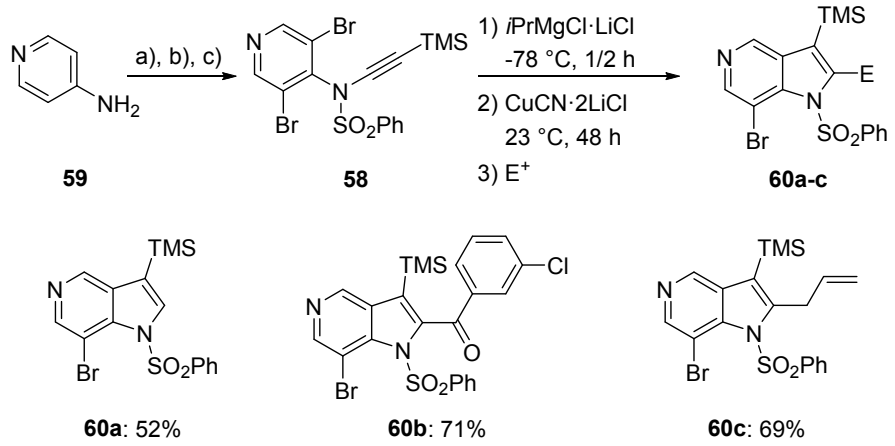
To provide access to further functionalized 4-azaindoles, the cyclization sequence was performed starting from 2,6-dibromo-3-aminopyridine (**56**). The required ynamide **55** is available in two straightforward steps starting from pyridine[103] **56** (40% overall yield, Scheme 30). A Br/Mg exchange performed on **55** with *i*PrMgCl·LiCl (**6**) at -40 °C within 3 h afforded after copper-mediated ring closure (23 °C, 24 h) and subsequent hydrolysis, acylation with 3-chlorobenzoyl chloride or allylation with ethyl 2-(bromomethyl)acrylate the polyfunctional 4-azaindoles **57a-c** in 55-73% yield (Scheme 30). Interestingly, the bromine substituent at position 5 provides a convenient handle for further functionalization.



Scheme 30: Preparation of functionalized 4-azaindoles of type **57** by a copper-mediated carbomagnesiation of ynamide **55**. Reagents and conditions: a) $PhSO_2Cl$ (1.2 equiv), pyridine (3.0 equiv), CH_2Cl_2, 0-23 °C, 12 h, 65%; b) KHMDS (1.0 equiv), toluene, 0 °C, 1 h, then phenyl((trimethylsilyl)ethynyl)iodonium triflate (1.2 equiv), 23 °C, 16 h, 62%.

The methodology was extended to the synthesis of 5-azaindoles. Thus, ynamide **58**, prepared in the standard way in three steps from the commercial 4-aminopyridine (**59**) underwent a smooth Br/Mg exchange reaction with *i*PrMgCl·LiCl (**6**) at -78 °C in 0.5 h. CuCN·2LiCl mediated cyclization (1.0 equiv, 23 °C, 48 h) gave after aqueous workup the 5-azaindole **60a** (Scheme 31). Furthermore, a functionalization of position 2 was achieved by allylation with allyl bromide as well as acylation with 3-chlorobenzoyl chloride to give the new azaindoles **60b-c** in 69-71% yield.

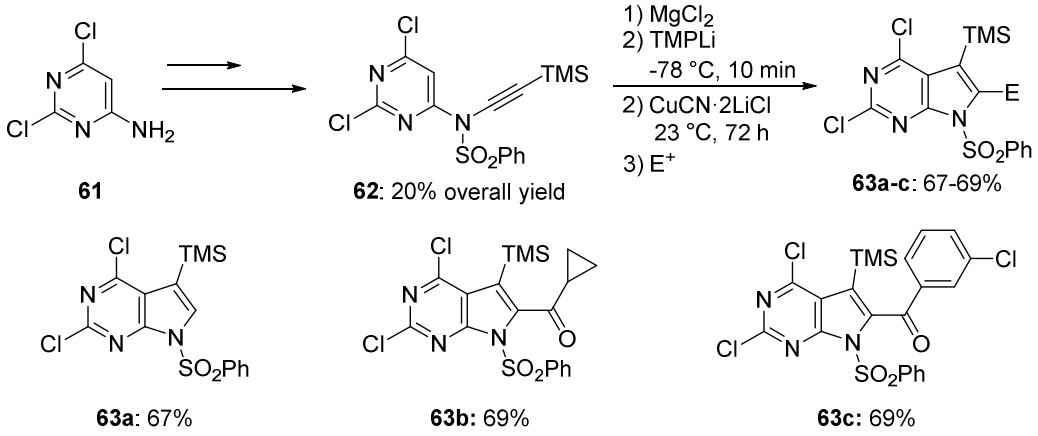
[103] V. Canibano, J.F. Rodriguez, M. Santos, M.A. Sanz-Tejedor, M.C. Carreno, G. Gonzalez, J.L. Garcia-Ruano, *Synthesis* **2001**, 2175.



Scheme 31: Preparation of functionalized 5-azaindoles of type **60** by a copper-mediated carbomagnesiation of ynamide **58**. Reagents and conditions: a) NBS (2.0 equiv), CCl_4, 24 h 23 °C, 70%; b) NaH (2.0 equiv), $PhSO_2Cl$ (1.0 equiv), THF, 0-23 °C, 12 h, 51%; c) KHMDS (1.0 equiv), toluene, 0 °C, 1 h, then phenyl((trimethylsilyl)-ethynyl)iodonium triflate (1.2 equiv), 23 °C, 16 h, 39%.

2.4 Preparation of Functionalized Pyrrolo[2,3-*d*]pyrimidine

Finally, the method was used for the synthesis of pyrrolo[2,3-*d*]pyrimidines. The standard two-step conversion of the commercial 2,6-dichloropyrimidin-4-amine (**61**) provided the desired ynamide **62** in 20% overall yield (Scheme 32). The ynamide **62** was conveniently metalated with TMPLi (**12**) in the presence of $MgCl_2$ at –78 °C within 0.5 h at position 5. A subsequent copper-mediated cyclization (23 °C, 72 h) followed by hydrolysis, acylation or allylation afforded the pyrrolo[2,3-*d*]pyrimidines **63a-c** in 67-69% yield (Scheme 32).

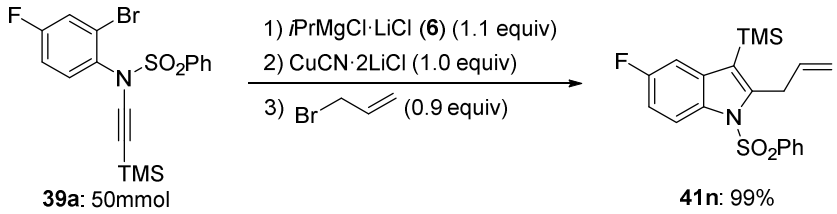


Scheme 32: Preparation of functionalized Pyrrolo[2,3-*d*]pyrimidines of type **63** by a copper-mediated carbomagnesiation of ynamide **62**.

2.5 Scaleable Preparation of Functionalized Indoles and Azaindoles *via* an Intramolecular Copper-mediated Carbomagnesiation of Ynamides

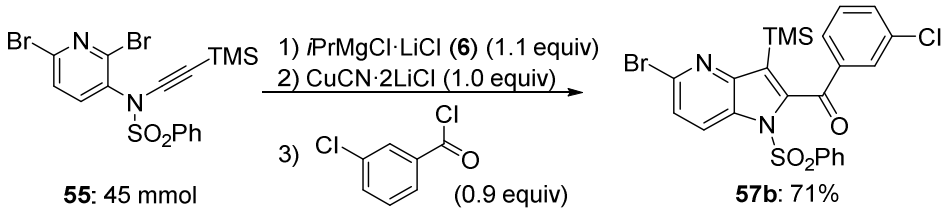
Several indoles and azaindoles are efficiently prepared in THF *via* intramolecular copper-mediated carbometalation of magnesiated derivatives, leading to cuprated heterocyclic intermediates which after quenching with various electrophiles afford functionalized *N*-heterocycles. These reactions are carried out at 45-50 mmol scale with comparable yields as obtained for small scales.

Thus, a large-scale Br/Mg exchange reaction with *i*PrMgCl·LiCl (**6**) was performed using ynamide **39a**. Ynamide **39a** is available in two straightforward steps starting from the corresponding 2-bromoaniline **38a** according to 2.2 (Scheme 25). Treatment of the ynamide **39a** with *i*PrMgCl·LiCl (**6**) (1.1 equiv) provided the corresponding magnesium reagent within 0.5 h at -10 °C (same exchange reaction rate as for reactions performed at 1 mmol scale; exchange reaction progress checked by iodolysis and hydrolysis of reaction aliquots and HPLC analysis). After dilution of the reaction mixture with THF (0.1 M), CuCN·2LiCl (1.0 equiv) was added at -10 °C. The cyclization step was then carried out at 23 °C for 30 h (compared to 24 h for 1 mmol scale) producing a 2-metalated indole derivative. The resulting mixture was cooled to 0 °C, and reacted afterwards with allyl bromide (0.9 equiv). After a slow warming of the reaction mixture to 23 °C within 16 h, the indole **41n** was obtained in an excellent yield of 99% (Scheme 33). To avoid side reactions all cyclization reactions were carried out with one equivalent of CuCN·2LiCl.



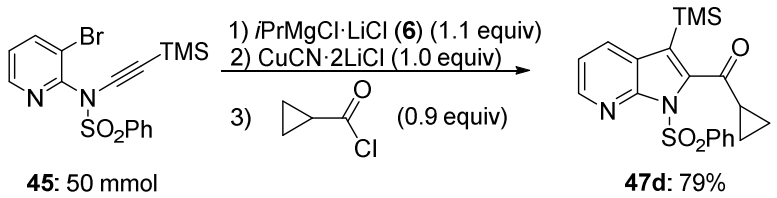
Scheme 33: Large scale preparation of functionalized indole **41n** by a copper-mediated carbomagnesiation of ynamide **39a**.

The scalability of the procedure was also applied on the preparation of 4-azaindole **57g**. Starting from commercial 3-aminopyridine, ynamide **55** was synthesized in three straightforward steps (2.3; Scheme 30). The ynamide **55** underwent a Br/Mg exchange reaction with *i*PrMgCl·LiCl (**6**) (1.1 equiv), leading to the magnesium species within 3 h at -40 °C (same exchange reaction rate as for reactions performed at a 1 mmol scale). After dilution of the reaction mixture with THF (0.1 M), a copper-mediated ring closure (CuCN·2LiCl, 1.0 equiv) was complete after 24 h at 23 °C. After cooling down to 0 °C, an acylation with 3-chlorobenzoyl chloride (0.9 equiv) proceeded while the reaction mixture is slowly warmed to reach 23 °C over 16 h to give 4-azaindole **57b** in 71% yield (Scheme 34; compared to 73% yield at a 1 mmol scale). Purification by flash column chromatography could be avoided by recrystallization in *iso*hexan/EtOAc.



Scheme 34: Large scale preparation of 4-azaindole **57b** by a copper-mediated carbomagnesiation of ynamide **55**.

Finally, the large scale synthesis of a 2-substituted 7-azaindole **47d** was carried out. Thus, commercial 2-amino-3-bromopyridine was used as starting material. The synthesis of the corresponding ynamide **45** was achieved in two steps according to 2.3 (Scheme 27). The treatment of ynamide **45** with *i*PrMgCl·LiCl (**6**) (1.1 equiv) provided the heteroaryl-magnesium reagent within 1 h at -45 °C (same exchange rate as for reaction performed at a 1 mmol scale). After addition of 400 mL of THF (0.1 M), CuCN·2LiCl (1.0 equiv) was added at -45 °C. The cyclization step was then carried out at 23 °C in 36 h (compared to 24 h in 1 mmol scale). The resulting mixture is cooled to 0 °C. Then, cyclopropane carbonyl chloride (0.9 equiv) was added dropwise. The desired 7-azaindole **47d** was obtained in 79% yield (Scheme 35; compared to 84% in 1 mmol scale).



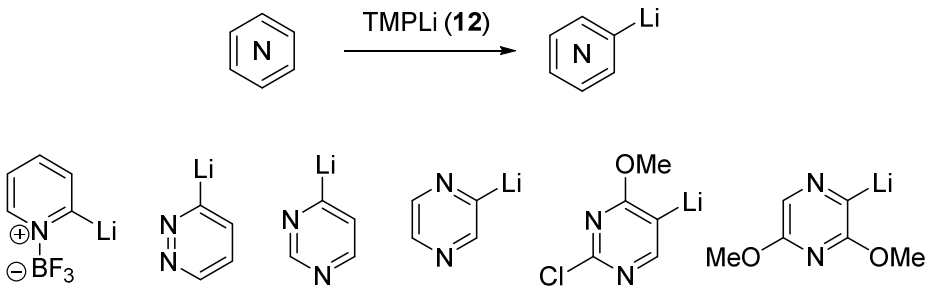
Scheme 35: Large scale preparation of 7-azaindole **47d** by a copper-mediated carbomagnesiation of ynamide **45**.

3. New *in situ* Trapping Metalations of Functionalized Arenes and Heteroarenes with TMPLi in the Presence of $ZnCl_2$ and other Metal Salts

3.1 Introduction

The lithiation of arenes and heteroarenes constitutes a powerful method to functionalize these molecules.[6, 33, 104] TMPLi (**12**) was first considered in 1972 in the base-induced rearrangement of epoxides[105] and as a sterically hindered base for deprotonation at a carbon center adjacent to a boron atom.[106] Since then, this strong base was extensively used for the selective lithiation of a wide range of arenes.

For the deprotonation of electron-deficient aromatic heterocycles, the use of TMPLi (**12**) is often necessary, since alkyllithiums prefer addition to the electron-deficient ring over deprotonation. Starting from ortholithiation of pyridine itself (promoted by BF_3) to pyridazines, pyrazines and pyrimidines it is possible to generate a multitude of different heterocyclic lithium species (Scheme 36).[107]



Scheme 36: Lithiation of various functionalized aromatics using TMPLi (**12**).

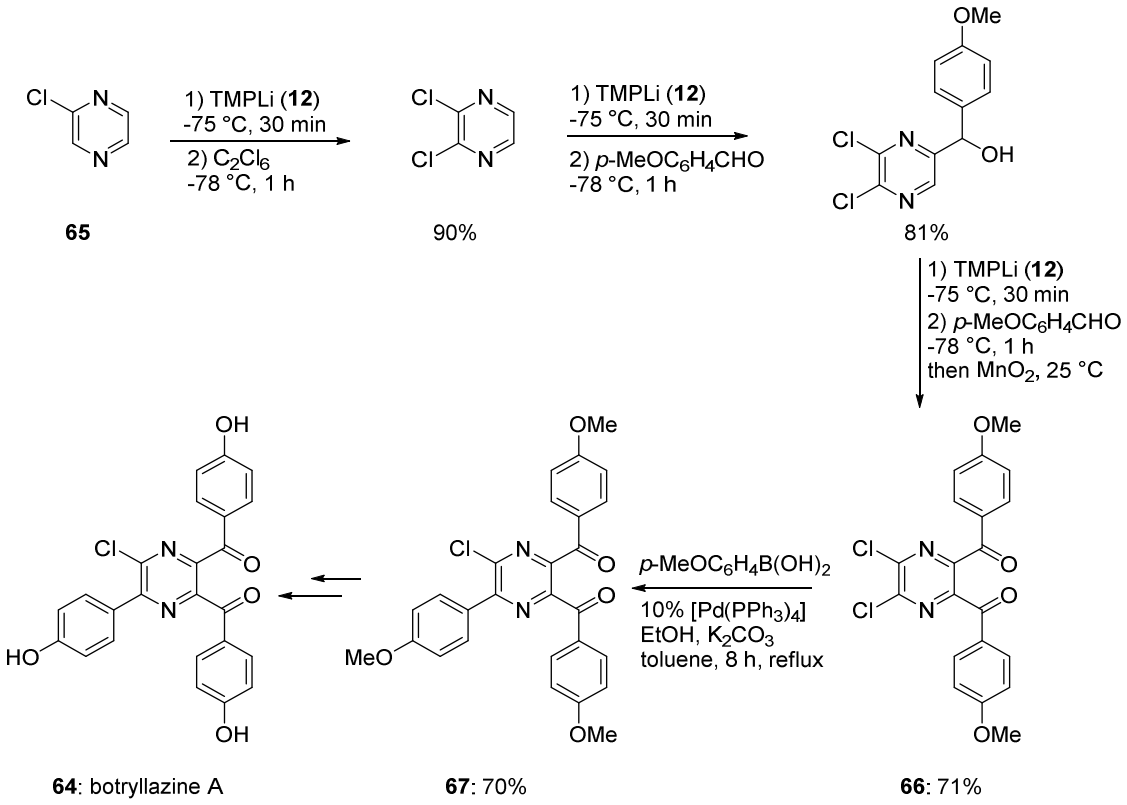
In 2005, *Turck*, *Quéguiner*, and co-workers described a synthesis of the antitumor alkaloid botryllazine A (**64**) (Scheme 37). Starting from commercially available 2-chloropyrazine (**65**), this synthesis involved consecutive regioselective lithiations with TMPLi (**12**). Three successive lithiation sequences afforded the diketone **66**. Thereafter, a *Suzuki* cross-coupling reaction provided the tetrasubstituted pyrazine **67** in 70% yield. After two further steps, botryllazine A (**64**) could be obtained in an overall yield of 25%.

[104] a) P. Beak, V. Snieckus, *Acc. Chem. Res.* **1982**, *15*, 306; b) M. Schlosser, Organometallics in Synthesis, 3rd ed. (Ed.: M. Schlosser), Wiley, New York, **2013**, Chapter 1; c) Fieser and Fieser`s reagents for organic synthesis, Wiley, Hoboken, **2011**, and earlier volumes; d) R.E. Mulvey, S.D. Robertson, *Angew. Chem.* **2013**, *125*, 11682; *Angew. Chem. Int. Ed.* **2013**, *52*, 11470; e) C. Unkelbach, D.F. O`Shea, C. Strohmann, *Angew. Chem.* **2014**, *126*, 563; *Angew. Chem. Int. Ed.* **2014**, *53*, 553; f) A. Salomone, F.M. Perna, A. Falcicchio, S.O. Nilsson Lill, A. Moliterni, R. Michel, S. Florio, D. Stalke, V. Capriati, *Chem. Sci.* **2014**, *5*, 528.

[105] C.L. Kissel, B. Rickborn, *J. Org. Chem.* **1972**, *37*, 2060.

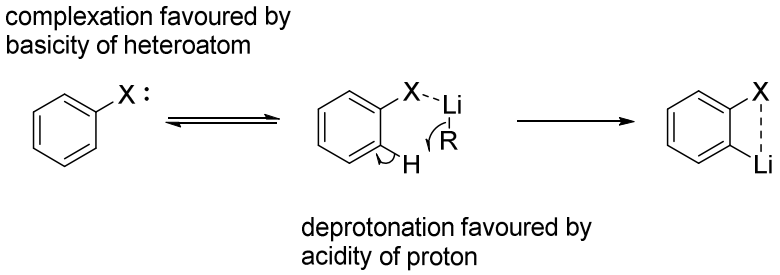
[106] M.W. Rathke, R. Kow, *J. Am. Chem. Soc.* **1972**, *94*, 6854.

[107] a) S.V. Kesser, P. Singh, *Chem. Rev.* **1997**, *97*, 721; b) E. Vedejs, X.J. Chen, *J. Am. Chem. Soc.* **1996**, *118*, 1809; c) N. Plé, A. Turck, K. Couture, G. Quéguiner, *J. Org. Chem.* **1995**, *60*, 3781; d) N. Plé, A. Turck, F. Bardin, G. Quéguiner, *J. Heterocyclic Chem.* **1992**, *29*, 467; e) W. Liu, J.A. Walker, J.J. Chen, D.S. Wise, B.L. Townend, *Tetrahedron Lett.* **1996**, *37*, 5325.



Scheme 37: Synthesis of the antitumor alkaloid botryllazine A (**64**).

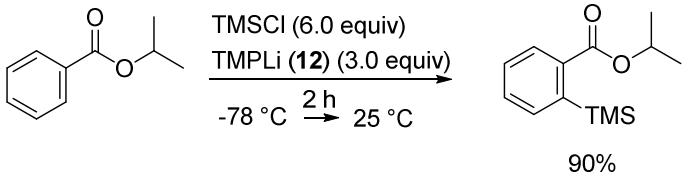
Ortholithiation - the directed metalation of an aromatic ring adjacent to a heteroatom-containing functional group - has overtaken classical electrophilic aromatic substitution as the principal means of making regiospecifically substituted aromatic rings. In general, ortholithiation consist of two steps (complex-formation and deprotonation) in which two features (rate and regioselectivity of lithiation) are controlled by coordination between organolithium and a heteroatom and acidity of the proton to be removed (Scheme 38).6



Scheme 38: Ortholithiation.

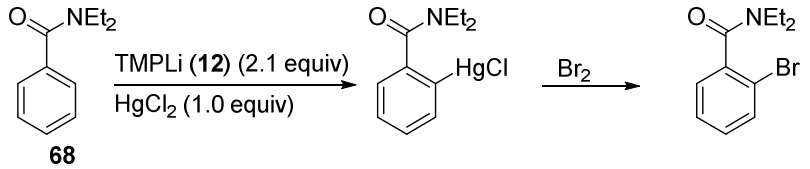
Nevertheless, the scope for the lithiation of complex molecules with TMPLi (**12**) is limited; highly reactive lithium derivatives are produced which often have little compatibility with sensitive functional groups (esters, cyano or nitro groups) especially when attached to electron-deficient N-heterocycles.

There are two different ways to avoid these drawbacks. *Krizan* and *Martin* reported the deprotonation of aryl carboxylic esters with TMPLi (**12**) by *in situ* trapping of the aryl lithium species with TMSCl (Scheme 39).[108] This way also more sensitive groups like esters could be tolerated.



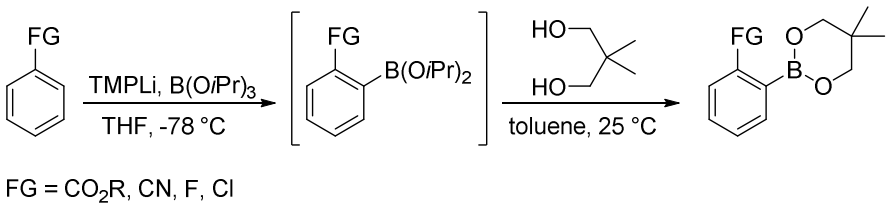
Scheme 39: Deprotonation of aryl carboxylic esters with TMPLi (**12**) by *in situ* trapping with TMSCl.

Eaton and *Martin* found a procedure to metalate *N,N*-diethylbenzamide (**68**) with TMPLi (**12**) in the presence of $HgCl_2$ (Scheme 40). [109] Also dilithiation was possible by using a large amount of TMPLi (**12**) and $HgCl_2$. However, the utility of the method is reduced by difficulties of purification and their characterization. Since the arylmercury compounds were transformed into the corresponding aryl bromides to have a preparative utility.



Scheme 40: Deprotonation of *N,N*-Diethylbenzamide (**68**) with TMPLi (**12**) in the presence of $HgCl_2$.

2001, *Vedsø* and *Begtrup* reported the synthesis of *ortho*-substituted arylboronic esters *via ortho*-lithiation and *in situ* trapping of the corresponding lithium species with tri*iso*propyl borate (Scheme 41).[110]

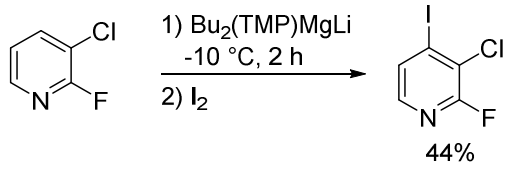


Scheme 41: Preparation of organoboron reagents via transmetalation.

A more general route to improve the reaction scope is the use of less reactive bases of Mg and Zn.[111] Since *Wittig* and co-workers introduced the first magnesiate, Ph_3MgLi, prepared by combination of Ph_2Mg and PhLi, in 1951,[112] several magnesiate species were developed. The first use of a magnesiate

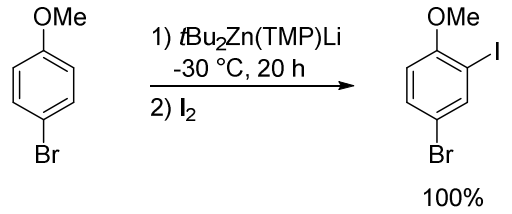
[108] T.D. Krizan, J.C. Martin, *J. Am. Chem. Soc.* **1983**, *105*, 6155.
[109] P.E. Eaton, R.M. Martin, *J. Org. Chem.* **1988**, *53*, 2728.
[110] J. Kristensen, M. Lysén, P. Vedsø, M. Begtrup, *Org. Lett.* **2001**, *3*, 1435.
[111] a) R.E. Mulvey, F. Mongin, M. Uchiyama, Y. Kondo, *Angew. Chem.* **2007**, *119*, 3876; *Angew. Chem. Int. Ed.* **2007**, *46*, 3802; b) A. Harrison-Marchand, F. Mongin, *Chem. Rev.* **2013**, *113*, 7470; c) E. Crosbie, A.R. Kennedy, R.E. Mulvey, S.D. Robertson, *Dalton Trans.* **2012**, *41*, 1832; d) Y. Kondo, M. Shilai, M. Uchiyama, T. Sakamoto, *J. Am. Chem. Soc.* **1999**, *121*, 3539; e) F. Mongin, A. Bucher, J.P. Bazureau, O. Bayh, H. Awad, F. Trécourt, *Tetrahedron Lett.* **2005**, *46*, 7989.
[112] a) G. Wittig, F.J. Meyer, G. Lange, *Justus Liebigs Ann. Chem.* **1951**, *571*, 167; b) G. Wittig, *Angew. Chem.* **1958**, *70*, 65.

as a deprotonating agent was reported in 1992.[113] *Mongin* and coworkers developed a series of lithium magnesates for instance Bu_3MgLi, $(TMP)_3MgLi$, Bu_4MgLi_2, $Bu_3(TMP)MgLi_2$ and $Bu_2Mg(TMP)Li$. With these bases it is possible to deprotonate halogenated pyridines[114] (Scheme 42) as well as thiophenes[115], furans[116] and oxazoles[117].



Scheme 42: Metalation of 2-fluoro-3-chloropyridine with $Bu_2Mg(TMP)Li$.

Lithium zincates can adopt two possible formulations: R_3ZnLi and R_4ZnLi_2.[118] *Kondo* and co-workers reported in 1999 the synthesis of tBu$_2$Zn(TMP)Li. This deprotonation agent was chemoselectively used for various arenes (Scheme 43), pyridines, thiophenes, quinolines, isoquinolines and furans. [119] Major drawback of this metalation system is the low reactivity of the formed zinc species with most electrophiles.

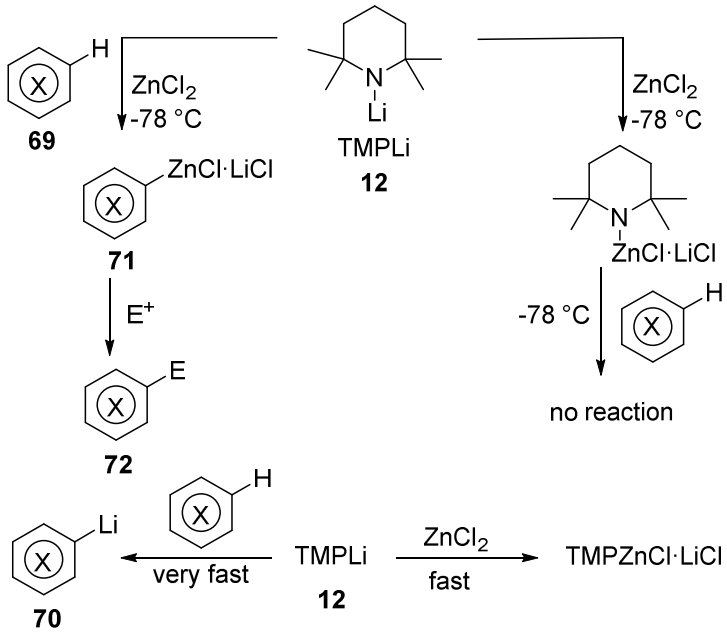


Scheme 43: Zincation of 4-bromoanisole with tBu$_2$Zn(TMP)Li.

3.2 *In situ* Trapping Metalation of Functionalized Arenes and Heteroarenes with TMPLi in the Presence of $ZnCl_2$

The aim of this work was to develop a metalation of functionalized N-heteroarenes and acceptor-substituted benzenes by the concomitant use of TMPLi (**12**) and various metal salts such as $MgCl_2$, $ZnCl_2$ or CuCN. This new method could give a practical access to Mg-, Zn- or Cu-organometallics.

[113] G. Castaldi, G. Borsotti, Eur. Patent 491326A2, **1992** [*Chem. Abstr.* **1992,** *117*, 150667].
[114] H. Awad, F. Mongin, F. Trécourt, G. Quéguiner, F. Marsais, F. Blanco, B. Abarca, R. Ballesteros, *Tetrahedron Lett.* **2004**, *45*, 6697; b) H. Awad, F. Mongin, F. Trécourt, G. Quéguiner, F. Marsais, *Tetrahedron Lett.* **2004**, *45*, 7873.
[115] O. Bayh, H. Awad, F. Mongin, C. Hoarau, F. Trécourt, G. Quéguiner, F. Marsais, F. Blanco, B. Abarca, R. Ballesteros, *Tetrahedron Lett.* **2005**, *61*, 4779.
[116] F: Mongin, A. Bucher, J.P. Bazureau, O. Bayh, H. Awad, F. Trécourt, *Tetrahedron Lett.* **2005**, *46*, 7989.
[117] O. Bayh, H. Awad, F. Mongin, C. Hoarau, L. Bischoff, F. Trécourt, G. Quéguiner, F. Marsais, F. Blanco, B. Abarca, R. Ballesteros, *J. Org. Chem.* **2005**, *70*, 5190.
[118] See review: A.E.H. Wheatley, *New J. Chem.* **2004**, *28*, 435.
[119] a) Y. Kondo, M. Shilai, M. Uchiyama, T. Sakamoto, *J. Am. Chem. Soc.* **1999**, *121*, 3539; b) M. Uchiyama, Y. Matsumoto, D. Nobuto, T. Furuyamam, K. Yamaguchi, K. Morokuma, *J. Am. Chem. Soc.* **2006**, *128*, 8748.



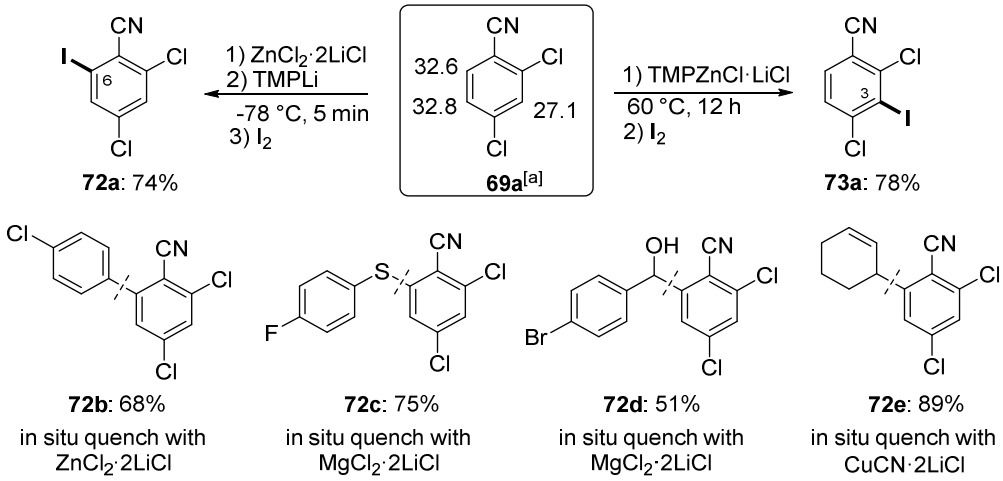
Scheme 44: Reaction of a mixture of $ZnCl_2$ and aromatic or heterocyclic substrate **69** with TMPLi (**12**) at -78 °C leading to zinc reagents of type **71** *via* a lithiation-transmetalation sequence.

The lithiation of functionalized carbocycles or heterocyclic arenes of type **69** with TMPLi (**12**) would provide the unstable lithiated species **70**. The performance of this lithiation in the presence of $ZnCl_2$ (or $MgCl_2$ and CuCN) may result in an *in situ* trapping of the lithiated arene **70** to yield the zinc reagent **71**, which now has an excellent thermal stability and can be readily trapped with electrophiles leading to various products of type **72**. To be successful, such a method requires that the metalation of **69** with TMPLi (**12**) is faster than the transmetalation of TMPLi (**12**) to TMPZnCl·LiCl (**9**). It should be noticed that TMPZnCl·LiCl (**9**) is unreactive toward metalation of **69** at -78 °C (Scheme 44). Herein, the realization of this *in situ* trapping method is reported and the advantages of this lithiation-transmetalation procedure for generating highly functionalized zinc organometallics, difficult to prepare otherwise, is demonstrated. It will also be shown that these lithiations can be used to provide metalated intermediates with a different regioselectivity to the one produced with TMPZnCl·LiCl (**9**) or $TMP_2Zn·2LiCl$ (**10**). This synthetic approach can be extended from $ZnCl_2$ to $MgCl_2$ or CuCN producing valuable magnesium or copper intermediates.

3.3 Regioselectivity switch by *in situ* Trapping Metalation of Functionalized Arenes and Heteroarenes with TMPLi in the Presence of different metal salts

First, the metalation of 2,4-dichlorobenzonitrile (**69a**; Scheme 45) was examined. A calculation of the relative acidity of H(3), H(5) and H(6) shows that H(3) is ca. 10^6 times more acidic than H(5) and

H(6).[120] Thus, the reaction of **69a** with a moderately powerful base such as TMPZnCl·LiCl (**9**) only allowed a metalation at position 3 leading exclusively after iodolysis to the 3-iodinated benzonitrile **73a** in 78% isolated yield.



Scheme 45: Regioselectivity switch in the metalation of **69a** by TMPLi (**12**) in the presence of metal salts or TMPZnCl·LiCl. [a] Calculated pKa values for H(3), H(5) and H(6).

Since the cyano group is a good *ortho*-directing group,[33, 121] a kinetic metalation of **69a** at position 6 using a very strong lithium base is expected. Thus, a mixture of **69a** and $ZnCl_2 \cdot 2LiCl$ (1.1 equiv) was treated with a THF solution of TMPLi (**12**, 1.5 equiv, ca. 0.6 M) at -78 °C. After 5 min, the metalation of **69a** is complete furnishing after iodolysis the 6-iodobenzonitrile **72a** in 74% yield (Scheme 45). The complexation of $ZnCl_2$ with LiCl enhances the solubility and often increases the reaction yields ca. 10-20%. The metalation regioselectivity is excellent (ca. 95:5) and is complementary to the metalation with TMPZnCl·LiCl (**9**), which proceeds at position 3. Independently generated $TMP_2Zn \cdot 2LiCl$ (**10**) or "$(TMP)_3ZnLi \cdot 2LiCl$"[122] either does not metalate **69a** at -78 °C or metalates with low regioselectivity (position 3 : position 6 = 4:1) with only 29% conversion after 10 min. Besides iodolysis, the resulting arylzinc derived from **69a** was submitted to a *Negishi* cross-coupling with 1-chloro-4-iodobenzene (0.9 equiv) leading to the biphenyl **72b** in 68% yield. All of the *in situ* trapping reactions favor the metalation at position 6. Although this new *in situ* trapping is very satisfactory using $ZnCl_2 \cdot 2LiCl$, the method to the preparation of some other useful organometallic intermediates was extended. Thus, mixing **69a** with $MgCl_2 \cdot 2LiCl$ (1.1 equiv) and adding TMPLi (**12**, 1.5 equiv, -78 °C, 5 min) produced the corresponding magnesium reagent which by reaction with $ArSSO_2Ph$ (Ar = *p*-FC_6H_4) or 4-bromobenzaldehyde afforded the thioether **72c** in 75% yield or the

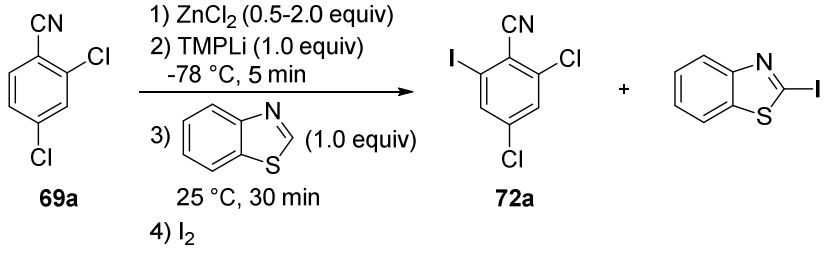
[120] For detailed information see: A. Frischmuth, M. Fernández, N.M. Barl, F. Achrainer, H. Zipse, G. Berionni, H. Mayr, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2014**, DOI: 10.1002/anie.201403688.

[121] M.C. Whisler, S. MacNeil, V. Snieckus, P. Beak, *Angew. Chem.* **2004**, *116*, 2256; *Angew. Chem. Int. Ed.* **2004**, *43*, 2206.

[122] a) A. Seggio, F. Chevallier, M. Vaultier, F. Mongin, *J. Org. Chem.* **2007**, *72*, 6602; b) J.-M. L`Helgoual`ch, A. Seggio, F. Chevallier, M. Yonehara, E. Jeanneau, M. Uchiyama, F. Mongin, *J. Org. Chem.* **2008**, *73*, 177; c) K. Snégaroff, S. Komagawa, F. Chevallier, P.C. Gros, S. Golhen, T. Roisnel, M. Uchiyama, F. Mongin, *Chem. Eur. J.* **2010**, *16*, 8191; d) F. Chevallier, Y.S. Halauko, C. Pecceu, I.F. Nassar, T.U. Dam, T. Roisnel, V.E. Matulis, O.A. Ivashkevich, F. Mongin, *Org. Biomol. Chem.* **2011**, *9*, 4671; e) P. Garcia-Alvarez, R.E. Mulvey, J.A. Parkinson, *Angew. Chem.* **2011**, *123*, 9842; *Angew. Chem. Int. Ed.* **2011**, *50*, 9668.

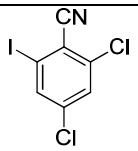
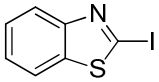
alcohol **72d** in 51% yield, respectively. An *in situ* quench with CuCN·2LiCl is also possible and produces valuable copper intermediates. Thus, performing the metalation of **69a** by TMPLi (**12**) in the presence of CuCN·2LiCl (1.1 equiv) provided the corresponding copper(I)-intermediate, which reacted smoothly with 3-bromocyclohexene (0.9 equiv) to afford **72e** in 89% yield.

To issue a quantitative statement about the reaction of TMPLi (**12**) in the presence of $ZnCl_2$, competition experiments were performed. An estimate for the relative reactivities of **69a** and $ZnCl_2$ was derived from the reaction series shown in schemes 1-4, where the quantity of $ZnCl_2$ was increased from 0.5 to 2.0 equivalents, while **69a** and TMPLi (**12**) were kept at a 1:1 ratio. While increasing amounts of $ZnCl_2$, the concentration of metalated **69a** decreased from 82% (0.5 equiv of $ZnCl_2$) to 50% (2.0 equiv of $ZnCl_2$) while the concentration of TMPZnCl·LiCl, derived from the amount of metalated benzothiazole, increased from <1% to 16%. The 50/16 ratio of **72a** vs. iodothiazole obtained at a 2:1 ratio of $ZnCl_2$ vs. **69a** shows that the reaction of TMPLi (**12**) with $ZnCl_2$ is at least 6 times slower than the metalation of **1a**. The same conclusion can be drawn from the 56:14 ratio of these compounds at a 1.5:1 ratio of $ZnCl_2$ vs. **69a**. A more quantitative evaluation of these experiments is not possible because some material is missing in the mass balance and the relative rate of the reaction of lithiated **69a** with $ZnCl_2$ is unknown. The percentage of conversion is always larger than the amount of isolated iodoarene.



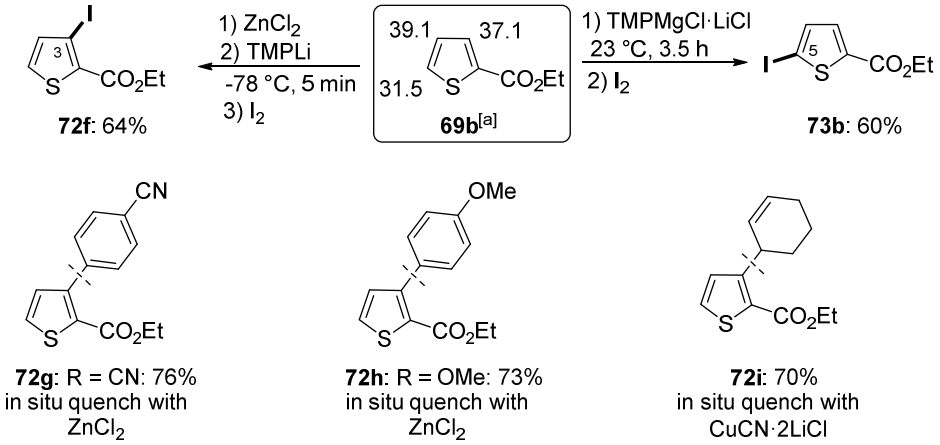
Scheme 46: Competition experiments for the metalation of **69a**.

Table 6: Results of the metalation of 2,4-dichlorobenzonitrile **69a** with TMPLi (**12**, 1.0 equiv) in the presence of $ZnCl_2$ (0.5-2.0 equiv) at -78 °C, addition of benzothiazole (1.0 equiv) at 23 °C, and additional quenching with iodine.

$ZnCl_2$ [equiv]		
0.5	82%	<1%
1.0	76%	6%
1.5	56%	14%
2.0	50%	16%

Analogous switches of regioselectivity switch were observed for several aromatic systems. The new *in situ* trapping procedure has also been applied to the metalation of heterocyclic ring positions which are notoriously difficult to metalate. Thus, as expected ethyl thiophene-2-carboxylate **69b** undergoes a smooth magnesiation at position 5 with TMPMgCl·LiCl (**7**) (Scheme 47). Metalation at this position is favored for thermodynamic reasons, since H(5) is the most acidic hydrogen in the molecule. This high

tendency to metalate position 5 can be overcome by an *in situ* quench using $ZnCl_2$ and TMPLi (**12**). Within 5 min at -78 °C, the metalation of **69b** is complete producing the C(3)-zincated thiophene as major regioisomer (C(3) : C(5) = 75 : 25). Interestingly, the complexation of $ZnCl_2$ with additional LiCl lowers this regioselectivity. After iodolysis the thienyl iodide **72f** is obtained in 64% yield. By adding $ZnCl_2$, *Negishi* cross-couplings with electron-poor iodides such as 4-iodobenzonitrile as well as electron-rich iodides such as 4-iodoanisole give, after chromatographic separation, 2,3-disubstituted thiophenes **72g** and **72h** in 73-76% yield. Performing the *in situ* trapping with CuCN·2LiCl allows an allylation with 3-bromocyclohexene (0.7 equiv) furnishing **72i** in 70% yield (Scheme 47).



Scheme 47: Regioselectivity switch in the metalation of **69b** by TMPLi (**12**) in the presence of metal salts or TMPMgCl·LiCl (**7**). [a] Calculated pKa values for H(3), H(4), and H(5).

3.4 *In situ* Trapping Metalation of Functionalized Heteroarenes with TMPLi in the Presence of different metal salts

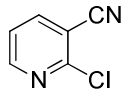
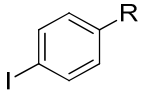
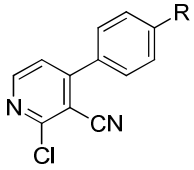
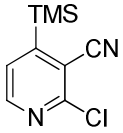
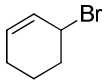
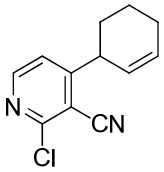
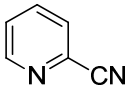
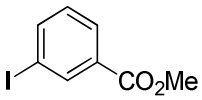
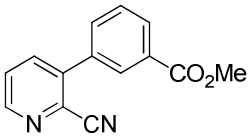
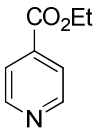
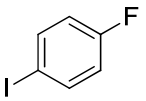
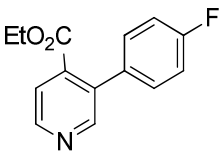
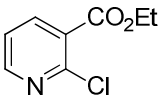
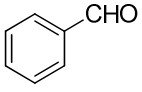
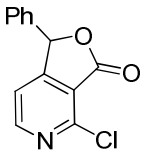
This *in situ* trapping method also allows a smooth metalation of sensitive heterocycles. For instance, the direct magnesiation or lithiation of 2-chloro-3-cyanopyridine (**74a**) is difficult. Attempts to use TMPLi (**12**), $TMP_2Mg·2LiCl$ (**8**) or TMPMgCl·LiCl (**7**) for deprotonation led to decomposition. Only $TMP_2Zn·2MgCl_2·2LiCl$ (**10**) allows the zincation of **74a** at 23 °C in 48 h in good yield. In contrast, metalation with TMPLi (**12**) in the presence of $ZnCl_2·2LiCl$ allows to prepare the same zinc species within 5 min at -78 °C.[123] After *Negishi* cross-coupling with methyl 4-iodobenzoate or 1-iodo-4-(trifluoromethyl)benzene the 4-arylated pyridines **75a** and **75b** were isolated in 72-90% yield (Table 7, entries 1-2). Using TMPLi (**12**) in the presence of $MgCl_2·2LiCl$ allows a smooth silylation of **74a** with TMSCl providing the pyridine **75c** in 96% yield (entry 3). The performance of an *in situ* quench using CuCN·2LiCl furnishes after allylation the pyridine **75d** in 96% yield (entry 4). Other cyano-, ester-, or nitro-substituted pyridines as well as an ester-substituted furan such as **74b,**[124] **74c-f**, for which the

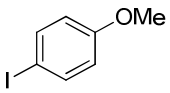
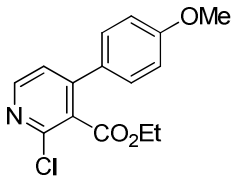
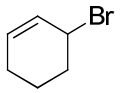
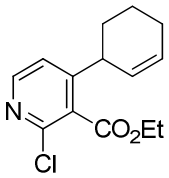
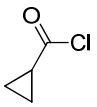
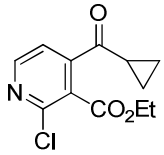
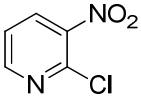
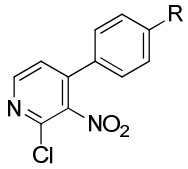
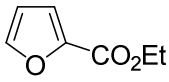
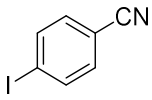
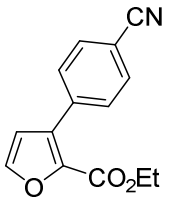
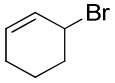
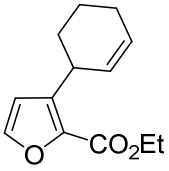
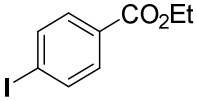
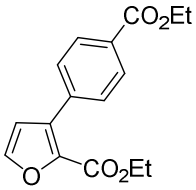
[123] ^{13}C NMR experiments showed the same zinc species for both experiments. For details see Experimental Part.

[124] Using TMPLi in the presence of $MgCl_2$ and quenching with iodine gives 2-cyano-3-iodopyridine in 72% yield; alternatively with TMPLi at -78 °C and quenching with iodine gives 53% yield. T. Cailly, F. Fabis, S. Lemaître, A. Bouillon, S. Rault *Tetrahedron Lett.* **2005**, *46*, 135.

lithiated derivatives are prone to decomposition and have to be handled at low temperature, the *in situ* quench with $MgCl_2 \cdot 2LiCl$, $ZnCl_2 \cdot 2LiCl$ or $CuCN \cdot 2LiCl$ and TMPLi (**12**) offers a simple preparative alternative and furnishes directly within 5 min the corresponding organometallic intermediates which undergo additions to aldehydes, *Negishi* cross-couplings, allylations or acylations in 64-94% yield (entries 5-15).

Table 7: Products **75** obtained by metalation with TMPLi (**12**) in the presence of $MgCl_2$, $ZnCl_2$ or CuCN and quenching with electrophiles.

Entry	Substrate	Electrophile	Product[a]	Yield[a]
				
1	**74a**	R = CO_2Me	**75a**	90%[b][f][h]
2	**74a**	R = OMe	**75b**	72%[b][f]
3	**74a**	TMSCl	 **75c**	96%[c][h]
4	**74a**		 **75d**	96%[e][h]
5	 **74b**		 **75e**	84%[b][f]
6	 **74c**		 **75f**	79%[b][f]
7	 **74d**		 **75g**	94%[d][h]

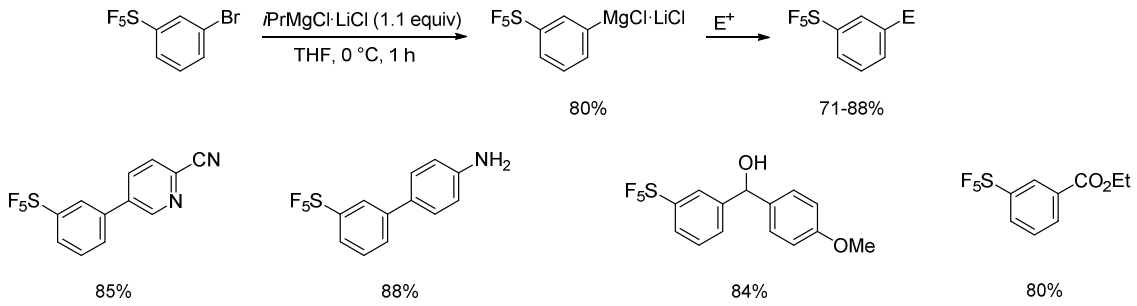
8	**74d**		 **75h**	86%[b][f][h]
9	**74d**		 **75i**	86%[e][h]
10	**74d**		 **75j**	94%[e][h]
11	 **74e**	R = CF_3	 **75k**	80%[b][f]
12	**74e**	R = CN	**75l**	70%[b][f]
13			 **75m**	70%[g]
14	**74f**		 **75n**	81%[g]
15	**74f**		 **75o**	64%[g]

[a] Isolated yield of analytically pure product. [b] $ZnCl_2 \cdot 2LiCl$ was added. [c] $MgCl_2 \cdot 2LiCl$ was added. [d] $MgCl_2$ was added. [e] $CuCN \cdot 2LiCl$ was added. [f] Obtained by a palladium-catalyzed cross-coupling with 2% $[Pd(dba)_2]$ and 4% P(2-furyl)$_3$, [g] $ZnCl_2$ was added. [h] Products prepared by Dr. Maitane Fernández.

4. Summary

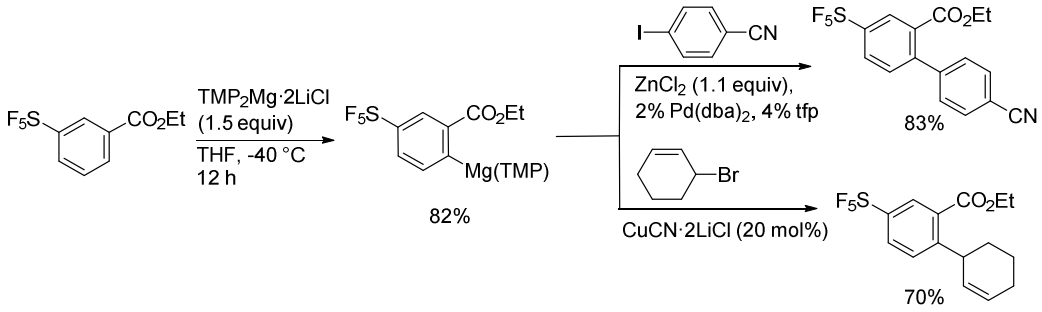
4.1 Preparations and Reactions of SF_5-substituted Aryl and Heteroaryl Derivatives via Mg and Zn Organometallics

A range of polyfunctional SF_5-substituted aromatic and heterocyclic compounds using zinc and magnesium intermediates were prepared. The commercial available 1-(bromo)-3-(pentafluorosulfanyl)benzene could be transformed into the magnesium intermediate using *i*PrMgCl·LiCl (**6**) furnishing after treatment with different electrophiles various SF_5-substituted arenes in good yields.



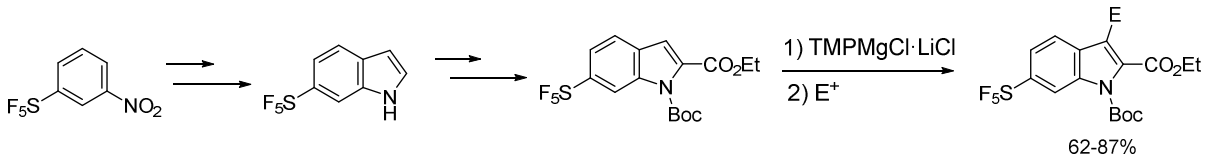
Scheme 48: Products obtained by Br/Mg-exchange with *i*PrMgCl·LiCl (**6**) followed by reaction with various electrophiles.

The treatment of the SF_5-substituted benzoic acid ethyl ester with $TMP_2Mg·2LiCl$ (**8**) led to a functionalized arylmagnesium reagent, which could used for further functionalization.



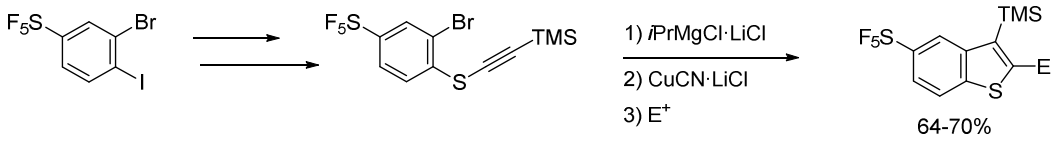
Scheme 49: Further functionalization using $TMP_2Mg·2LiCl$ (**8**).

By starting from commercial 1-nitro-3-(pentafluorsulfanyl)benzene it was possible to build up an SF_5-substituted indole. This indole could be further functionalized at position 2 and 3 by using TMPMgCl·LiCl (**7**).



Scheme 50: Synthesis of functionalized SF_5-substituted indoles.

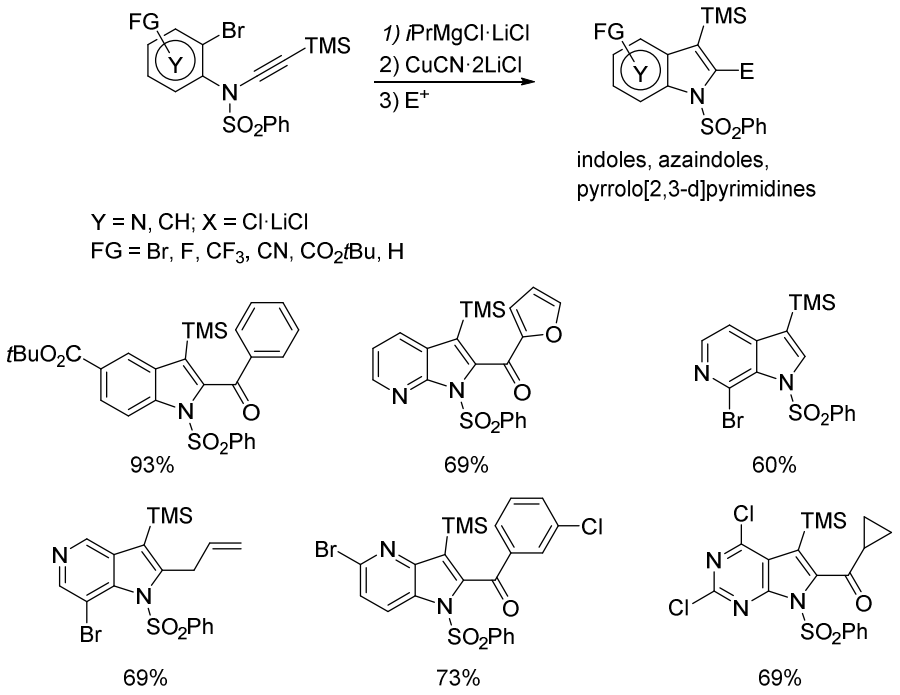
At last, performing a bromine-magnesium exchange reaction starting from a SF_5-substituted alkinyl(aryl)thioether, followed by a copper-mediated ring closing reaction, lead to SF_5-substituted benzo[*b*]thiophenes in good yields.



Scheme 51: Synthesis of functionalized SF_5-substituted benzo[*b*]thiophenes.

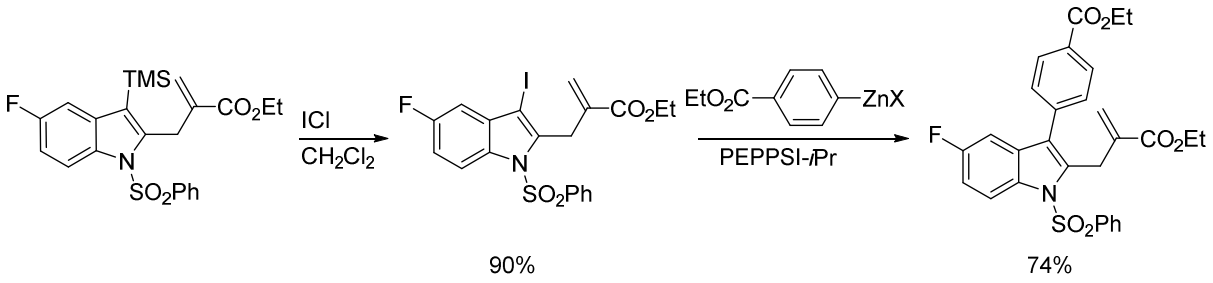
4.2 Preparation of Functionalized Indoles, Azaindoles and Pyrrolo[2,3-*d*]pyrimidines *via* an Intramolecular Copper-mediated Carbomagnesiation of Ynamides

A mild and general intramolecular copper-mediated carbomagnesiation procedure for the synthesis of functionalized indoles as well as 4-, 5-, 6-, and 7-azaindoles and pyrrolo[2,3-*d*]pyrimidines starting from the readily available ynamides was developed (Scheme 52). Further functionalization of these *N*-heterocycles with various electrophiles gave access to highly functionalized *N*-heterocycles in good yields. The use of *i*PrMgCl·LiCl (**6**) for the generation of the key magnesium intermediate tolerated a wide range of functional groups in the cyclization process.



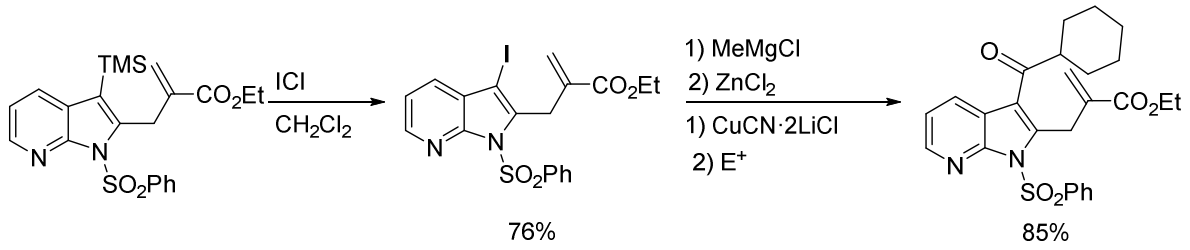
Scheme 52: Preparation of indoles, azaindoles and pyrrolo[2,3-*d*]pyrimidines by a copper-mediated cyclization reaction starting from bromo-ynamides.

Further transformations of these N-heterocycles lead to highly functionalized indoles as well as azaindoles. After transformation of the TMS-group to an iodine, it was possible to apply the corresponding indole as an electrophile in *Negishi* cross-couplings (Scheme 53).



Scheme 53: Further functionalization of position 3.

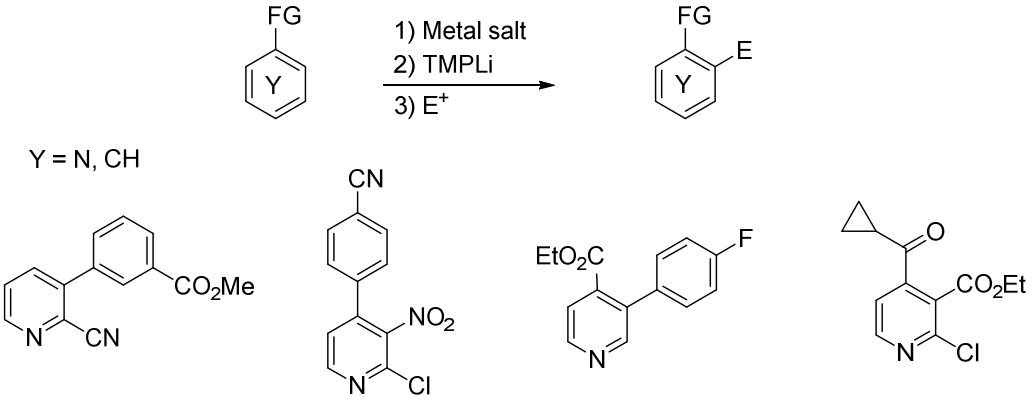
Starting from 7-azaindole **48a** it was possible to perform a I/Mg exchange reaction, followed by transmetalation with $ZnCl_2$. Copper-mediated acylation reactions lead to 2,3-substituted azaindoles in good yields (Scheme 54).



Scheme 54: Further functionalization of position 3.

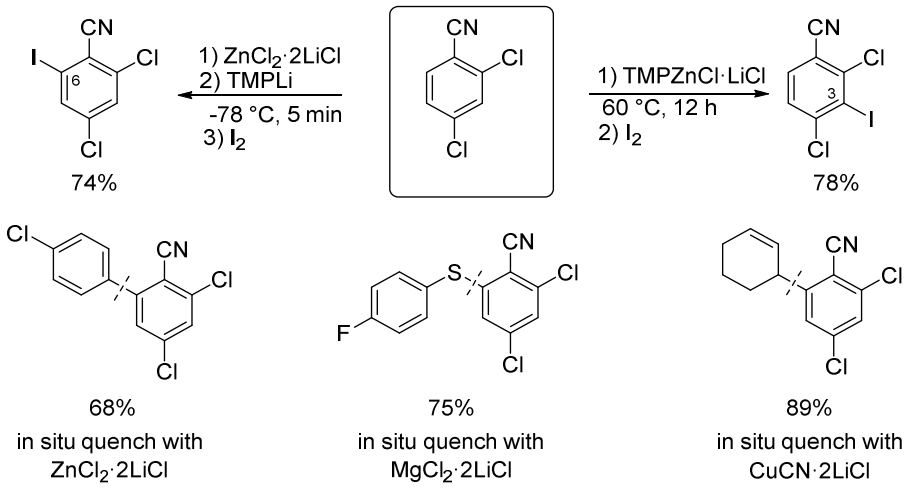
4.3 New *in situ* Trapping Metalations of Functionalized Arenes and Heteroarenes with TMPLi in the Presence of $ZnCl_2$ and other Metal Salts

The faster deprotonation of arenes and heteroarenes with TMPLi compared to transmetalation of TMPLi with Mg-, Zn- or Cu-halides has allowed to develop an *in situ* quench method, in which functionalized aromatic or heteroaromatic substrates mixed with Mg-, Zn- or Cu-halides have been metalated within 5 min by TMPLi at -78 °C leading after transmetalation to various functionalized Mg-, Zn- or Cu-derivatives. The method allows to metalate smoothly a range of functionalized pyridines and related heterocycles more efficiently and in higher yields as well conventional metalations (Scheme 55).



Scheme 55: *In situ* trapping metalation with TMPLi in the presence of metal salts.

In several cases, a different regioselectivity of the metalation is observed than in standard metalation procedures providing previously not accessible organometallics. For example using a moderately powerful base such as TMPZnCl·LiCl, 2,4-dichlorobenzonitrile only allows a metalation at position 3. Since the cyano group is a good *ortho*-directing group, a kinetic metalation at position 6 using the very strong base TMPLi is feasible. Mixing 2,4-dichlorobenzonitrile with Mg-, Zn- or Cu-halides and additional metalation with TMPLi lead after transmetalation to various functionalized Mg-, Zn- or Cu-derivatives, which react with various electrophiles (Scheme 56).



Scheme 56: Metalation of 2,4-dichlorobenzonitrile in position 3 or 6.

C. EXPERIMENTAL SECTION

1. General Considerations

If not otherwise stated, all reactions have been carried out using standard *Schlenk*-techniques in flame-dried glassware under nitrogen or argon. Prior to use, syringes and needles have been purged with the respective inert gas.

1.1 Solvents

Solvents were dried according to standard procedures by distillation over drying agents and stored under argon.

Et_2O was predried over $CaCl_2$ and dried with the solvent purification system SPS-400-2 from INNOVATIVE TECHNOLOGIES INC.

NMP (*N*-methylpyrrolidinone) was refluxed over CaH_2 and distilled from CaH_2.

Pyridine was dried over KOH and distilled.

THF (tetrahydrofuran) was continuously refluxed and freshly distilled from Na/benzophenone ketyl under nitrogen and stored over 4 Å molecular sieve under an argon atmosphere.

Toluene was predried over $CaCl_2$, distilled from CaH_2 and stored over 4 Å molecular sieve under an argon atmosphere.

Triethylamine was dried over KOH and distilled.

Solvents for reaction workup and for column chromatography were distilled prior to use.

1.2 Preparation of Reagents

Commercially available reagents were used without further purification unless otherwise stated. Liquid aldehydes and acid chlorides were distilled prior to use.

TMPH was distilled under argon prior to use.

Preparation of CuCN·2LiCl[125] solution:

CuCN·2LiCl solution (1.0 M in THF) was prepared by drying CuCN (7.17 g, 80 mmol) and LiCl (6.77 g, 160 mmol) in a *Schlenk*-tube under vacuum at 140 °C for 5 h. After cooling, dry THF (80 mL) was added and stirring was continued until all salts were dissolved.

Preparation of $ZnCl_2$ solution:

$ZnCl_2$ solution (1.0 M in THF) was prepared by drying $ZnCl_2$ (136.3 g, 100 mmol) in a *Schlenk*-flask under vacuum at 140 °C for 5 h. After cooling, dry THF (100 mL) was added and stirring was continued until all salts were dissolved.

Preparation of $MgCl_2$ solution:

A dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirrer and a septum was charged with Mg turnings (2.55 g, 105 mmol) and THF (200 mL). 1,2-Dichloroethane (9.90 g, 100 mmol, 7.92 mL) was added dropwise over 1 h. The reaction mixture was stirred at 23 °C until gas evolution was complete.

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

Preparation of LiCl solution:

LiCl solution (0.7 M in THF) was prepared by drying LiCl (8.6 g, 202 mmol) in a *Schlenk*-tube under vacuum at 140 °C for 5 h. After cooling, dry THF (288 mL) was added and stirring was continued until all salts were dissolved.

Preparation of TMPMgCl·LiCl (7):[126]

In a dry and argon-flushed *Schlenk*-flask TMPH (2,2,6,6-tetramethylpiperidine, 14.8 g, 105 mmol) was added to *i*PrMgCl·LiCl (**6**) (71.4 mL, 1.40 M in THF, 100 mmol) at 23 °C and the mixture was stirred for 3 days at 23 °C. The freshly prepared TMPMgCl·LiCl (**7**) was titrated prior to use at 0 °C with benzoic acid using 4-(phenylazo)diphenylamine as indicator.

Preparation of $TMP_2MgCl·LiCl$ (8):[127]

$TMP_2Mg·2LiCl$ solution (0.6 M in THF) was prepared by the slow addition of *n*BuLi (4.26 mL, 2.35 M in hexane, 10 mmol) to a solution of TMPH (1.41 g, 10 mmol) in THF (10 mL) at -40 °C. After stirring for 30 min the mixture was warmed up to 0 °C and TMPMgCl·LiCl (**7**) (8.3 mL, 1.2 M in THF, 10 mmol) was added dropwise. The resulting mixture was stirred for 30 min, warmed up to 23 °C and the solvent was evaporated under vacuum (10^{-3} mbar). THF was then added slowly under vigorous stirring until the salts were completely dissolved.

Preparation of TMPLi (12):

TMPLi solution (0.63 M in THF) was prepared by slow addition of *n*BuLi (2.17 mL, 5.0 mmol, 2.3 M in hexane) to a solution of TMPH (706 mg, 0.85 mL, 5.0 mmol) in THF (5 mL) at -40 °C and stirred for 30 min at -40 °C.

***i*PrMgCl·LiCl** (**6**) was purchased as a solution in THF from Rockwood Lithium GmbH.

***n*BuLi** was purchased as a solution in hexane from Rockwood Lithium GmbH.

Content determination of organometallic reagent:

***n*BuLi** was titrated using *i*PrOH and 1,10-phenanthroline as indicator in THF. [128]

Organomagnesium reagents were titrated using I_2 in THF. [129]

$TMP_2Mg·2LiCl$ and **TMPMgCl·LiCl** were titrated with benzoic acid and 4-(phenylazo)diphenylamine as indicator in THF.[42]

TMPLi was titrated using N-Benzylbenzamide in THF.[130]

1.3 Analytical Data

Gas chromatography was performed with machines of type *Hewlett-Packard* 6890 or 5890 series II, using a column of type HP 5 (*Hewlett-Packard*, 5% phenylmethylpolysiloxane; length: 15 m, diameter: 0.25 mm; film thickness: 0.25 µm). The detection was accomplished by using a

[126] A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem.* **2006**, *118*, 3024; *Angew. Chem. Int. Ed.* **2006**, *45*, 2958.
[127] G. Clososki, C. Rohbogner, P. Knochel, *Angew. Chem.* **2007**, *119*, 7825; *Angew. Chem. Int. Ed.* **2007**, *46*, 7681.
[128] H.-S. Lin, A Paquette, *Synth. Commun.* **1994**, *24*, 2503.
[129] A. Krasovskiy, P. Knochel, *Synthesis* **2006**, *5*, 890.
[130] A.F. Burchat, J.M. Chong, N. Nielsen, *J. Organomet. Chem.***1997**, *542*, 281.

flame ionization detector. The carrier gas was nitrogen. Alkanes like dodecane or tetradecane were used as internal standards.

Infrared spectra were recorded from 4000-400 cm^{-1} on a Perkin 281 IR spectrometer. Samples were measured neat (ATR, Smiths Detection DuraSample IR II Diamond ATR). The absorption bonds are reported in wave numbers (cm^{-1}).

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

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

NMR spectra were recorded on *Varian* Mercury 200, *Bruker* AC 300, WH 400, or AMX 600 instruments. Chemical shifts are reported as δ-values in ppm relative to the solvent peak, i.e. chloroform-d (δ 7.26 ppm for ^{1}H-NMR and δ 77.0 ppm for ^{13}C-NMR), DMSO-d_6 (δ 2.50 ppm for ^{1}H-NMR and δ 39.5 ppm for ^{13}C-NMR). For the characterization of the observed signal multiplicities the following abbreviations were used: s (singlet), d (doublet), t (triplet), m (multiplet), q (quartet), quint (quintet), sxt (sextet), oct (octet), as well as br (broad).

Microwave irradiation was performed in a Biotage Initiator™ Unit (Biotage, Uppsala, Sweden) in a closed-vessel system.

1.4 Chromatography

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

- Phosphomolybdic acid (5.0 g), $Ce(SO_4)_2$ (2.0 g) and conc. H_2SO_4 (12.0 mL) in water (230 mL).
- Iodine absorbed on silica gel.
- $KMnO_4$ (0.3 g), K_2CO_3 (20 g) and KOH (0.3 g) in water (300 mL).

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

2. Preparations and Reactions of SF_5-substituted Aryl and Heteroaryl Derivatives via Mg and Zn Organometallics

2.1 Typical Procedures

Typical procedure (TP1): Halogen/Magnesium exchange reactions

A dry and argon flushed *Schlenk*-flask, equipped with a septum and a magnetic stirring bar was charged with the starting aryl halide in THF (approx. 1.0 M solution) and cooled to the indicated temperature. Then *i*PrMgCl·LiCl (**6**) (1.1 equiv) was added and the reaction mixture was stirred for the indicated time at this temperature until the reaction was complete (checked by GC-analysis of reaction aliquots quenched with a solution of I_2 in THF).

Typical procedure (TP2): Palladium-catalyzed cross-coupling reactions

In a dry argon flushed *Schlenk*-flask equipped with a septum and a magnetic stirring bar, the electrophile (0.7-0.9 equiv) was dissolved in THF (0.5 M solution) and PEPPSI-*i*Pr (2 mol%) was added. Then, 3-pentafluorosulfonyl-phenylzinc chloride (1.0 equiv), prepared by transmetalation with $ZnCl_2$ (1.1 equiv) from the corresponding organomagnesium reagent **13** (**TP1**, 1 h, 0 °C) was added, and the reaction mixture was stirred for the given time until GC-analysis showed full conversion of the electrophile. The reaction mixture was quenched with sat. aqueous NH_4Cl-solution and extracted three times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and the solvent removed *in vacuo*. The crude residue was purified by flash column chromatography on silica gel.

Typical procedure (TP3): Palladium-catalyzed cross-coupling reactions with aryl bromides bearing unprotected anilines

In a dry argon-flushed *Schlenk*-flask equipped with a septum and a magnetic stirring bar, the electrophile (0.8-0.9 equiv) was dissolved in THF (0.5 M solution) and $Pd(OAc)_2$ (2 mol%) and S-Phos (4 mol%) were added. Then, 3-pentafluorosulfonyl-phenylzinc chloride (1.0 equiv), prepared by transmetalation with $ZnCl_2$ (1.1 equiv) from the corresponding organomagnesium reagent **13** (**TP1**, 1 h, 0 °C) was added, and the reaction mixture was stirred for the given time until GC-analysis showed full conversion of the electrophile. The reaction mixture was quenched with sat. aqueous NH_4Cl-solution and extracted three times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and the solvent removed *in vacuo*. The crude residue was purified by flash column chromatography on silica gel.

Typical Procedure for allylation or acylation reactions (TP4):

To the freshly prepared magnesium reagent (1.0 equiv) was added CuCN·2LiCl (1.0 M in THF) and the reaction mixture was stirred for 15 min at the indicated temperature. The allyl bromide or acyl chloride (0.6-1.2 equiv) was added and the reaction mixture was stirred for the indicated time at the respective temperature. The reaction mixture was quenched with sat. aqueous NH_4Cl-solution, extracted three times with Et_2O, over Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel.

Typical procedure (TP5): Typical Procedure for the Metalation using TMP_2Mg·2LiCl

A dry and argon flushed *Schlenk*-flask, equipped with a septum and a magnetic stirring bar was charged with 3-(pentafluorosulfanyl)benzoic acid ethyl ester (**15e**, 1.0 equiv) in THF (0.5 M) and

cooled to −40 °C. $TMP_2Mg·2LiCl$ (1.5 equiv) was added dropwise and the reaction mixture stirred for the indicated time (the completion of the reaction was checked by GC-analysis of reaction aliquots quenched with a solution of I_2 in THF).

Typical procedure (TP6): Typical Procedure for the deprotonation using TMPMgCl·LiCl (7)

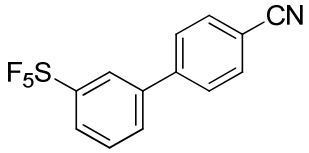
A dry and argon flushed *Schlenk*-flask, equipped with a septum and a magnetic stirring bar was charged with the starting material in THF (0.5 M) and cooled to the appropriate temperature. TMPMgCl·LiCl (**7**) (1.1 equiv) was added dropwise and the reaction mixture stirred for the indicated time (the completion of the reaction was checked by GC-analysis of reaction aliquots quenched with a solution of I_2 in THF).

Typical procedure (TP7): Palladium-catalyzed cross-coupling reactions

To the freshly prepared magnesium reagent, prepared by using **TP5** or **TP6**, was added $ZnCl_2$ (1.1 equiv) and the reaction mixture was stirred for 10 min at the indicated temperature. The catalytic system (PEPPSI-*i*Pr (2%), or $Pd(dba)_2$ (2%) and tfp (4%)) and the aryl halide (0.9-1.1 equiv) were added and the reaction mixture was warmed to 23 °C. After stirring for the indicated time the reaction mixture was quenched with sat. aqueous NH_4Cl-solution, extracted three times with Et_2O, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel.

2.2 Synthesis of Compounds of Type 15

3´-(Pentafluorosulfanyl)biphenyl-4-carbonitrile (15a)



The title compound was prepared from 1-bromo-3-(pentafluorosulfanyl)benzene (**11**; 283 mg, 1.0 mmol). A Br/Mg-exchange reaction was performed according to **TP1** with *i*PrMgCl·LiCl (**6**) (0.72 mL, 1.1 mmol, 1.53 M in THF) at 0 °C within 1 h. According to **TP2** the corresponding zinc reagent reacted for 12 h with 4-bromobenzonitrile (**14a**; 128 mg, 0.70 mmol). Flash column chromatographical purification (silica; pentane:Et_2O = 95:5) afforded **15a** as a colorless solid (176 mg, 0.58 mmol, 83%).

Mp.: 122-124 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.97 (t, J = 1.9 Hz, 1H), 7.87 – 7.75 (m, 3H), 7.75 – 7.58 (m, 2H), 7.71 – 7.68 (m, 1H), 7.62 (t, J = 8 Hz, 1H).

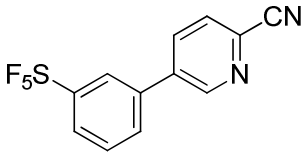
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 143.7, 143.5, 140.3 (d, J = 0.6 Hz), 132.9 – 132.8 (m, 2C), 130.3, 129.6, 127.9 (d, J = 2.8 Hz), 126.0 (t, J = 4.9 Hz), 125.0 – 124.7 (m), 118.5, 112.1.

^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 85.24 – 82.26 (m, 1F), 63.32 – 62.23 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2226 (w), 1604 (w), 1479 (w), 1398 (w), 1115 (w), 832 (s), 788 (s), 732 (w), 718 (w), 690 (w), 668 (w), 641 (w).

MS (EI, 70 eV): m/z (%) = 306 (M+H, 16), 305 (M^+, 100), 197 (36), 178 (22), 177 (29), 151 (26), 150 (10).
HRMS ($C_{13}H_8F_5NS$): calc.: 305.0298; found: 305.0277.

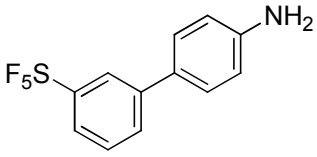
5-[3-(Pentafluorosulfanyl)phenyl]pyridine-2-carbonitrile (15b)



The title compound was prepared from 1-bromo-3-(pentafluorosulfanyl)benzene (**11**; 283 mg, 1.0 mmol). A Br/Mg-exchange reaction was performed according to **TP1** with *i*PrMgCl·LiCl (**6**) (0.72 mL, 1.1 mmol, 1.53 M in THF) at 0 °C within 1 h. According to **TP2** the corresponding zinc reagent reacted with 5-bromopicolinonitrile (**14b**; 165 mg, 0.90 mmol). The reaction time was 5 h. Flash column chromatographical purification (silica; isohexane:Et_2O = 3:1) afforded **15b** as a white solid (233 mg, 0.76 mmol, 85%).

Mp.: 136-138 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.97 (dd, J = 30.6 Hz, J = 2.1 Hz, 1H), 8.14 (t, J = 2.1 Hz, 1H), 7.93 (t, J = 1.8 Hz, 1H), 7.91 – 7.84 (m, 1H), 7.75 – 7.60 (m, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 155.5 – 154.3 (m), 151.6, 151.4, 137.6, 136.6, 135.4, 130.3, 130.0, 126.9 – 126.5 (m), 125.1 – 124.7 (m), 116.1, 110.5.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3776 (w), 3697 (w), 3079 (w), 3063 (w), 2238 (w), 1592 (w, 1432 (w), 1405 (w), 1342 (w), 1281 (w), 1220 (w), 1160 (w), 1116 (w), 1104 (w), 1066 (w), 1028 (w), 896 (m), 865 (m), 836 (vs), 823 (vs), 805 (s), 794 (s), 720 (m), 706 (m), 690 (m), 645 (w).
MS (ESI, 70 eV): m/z (%) = 348 (M+H+CH_3CN, 100), 307 (M+H, 40), 293 (6).
HRMS ($C_{12}H_7F_5N_2S$): calc.: 307.0328; found: 307.0322.

3'-(Pentafluorosulfanyl)biphenyl-4-amine (15c)



The title compound was prepared from 1-bromo-3-(pentafluorosulfanyl)benzene (**11**; 334 mg, 1.2 mmol). A Br/Mg-exchange reaction was performed according to **TP1** with *i*PrMgCl·LiCl (**6**) (0.90 mL, 1.3 mmol, 1.53 M in THF) at 0 °C within 1 h. According to **TP3** the corresponding zinc reagent reacted with 4-bromoaniline (**14c**; 172 mg, 1.0 mmol). The reaction time was 2 h. Flash column chromatographical purification (silica; isohexane:Et_2O:CH_2Cl_2 = 90:9:1) afforded **15c** as a yellow solid (260 mg, 0.88 mmol, 88%).

Mp.: 86-87 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.92 (t, J = 1.9 Hz, 1H), 7.80 – 7.60 (m, 2H), 7.60 – 7.34 (m, 3H), 6.91 – 6.60 (m, 2H), 3.79 (s, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 155.0 – 154.3 (m), 146.7, 142.2, 129.5, 129.3, 128.9, 128.2, 124.1 – 123.7 (m), 123.7 – 123.3 (m), 115.4.

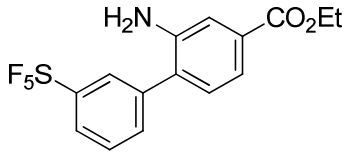
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 86.21 – 83.61 (m, 1F), 63.33 – 62.11 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1738 (m), 1723 (w), 1622 (w), 1599 (w), 1479 (w), 1366 (w), 1355 (w), 1287 (w), 1228 (w), 1217 (w), 824 (vs), 787 (s), 743 (m), 692 (w), 564 (vw).

MS (EI, 70 eV): m/z (%) = 296 (12), 295 (100), 167 (16), 86 (13), 71 (66), 57 (48), 56 (34), 55 (19).

HRMS ($C_{12}H_{10}F_5NS$): calc.: 295.0454; found: 295.0447.

2-Amino-3´-(pentafluorosulfanyl)biphenyl-4-carboxylic acid ethyl ester (15d)



The title compound was prepared from 1-bromo-3-(pentafluorosulfanyl)benzene (**11**; 334 mg, 1.2 mmol). A Br/Mg-exchange reaction was performed according to **TP1** with *i*PrMgCl·LiCl (**6**) (0.90 mL, 1.3 mmol, 1.53 M in THF) at 0 °C within 1 h. According to **TP3** the corresponding zinc reagent reacted with 3-amino-4-bromo-benzoic acid ethyl ester (**14d**; 244 mg, 1.0 mmol). The reaction time was 1 h. Flash column chromatographical purification (silica; isohexane:Et_2O = 1:1) afforded **15d** as a colorless solid (260 mg, 0.71 mmol, 71%).

Mp.: 129-131 °C

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.87 (dd, J = 2.0 Hz, 8.4 Hz, 1H), 7.85 – 7.83 (m, 1H), 7.80 (d, J = 2.0 Hz, 1H), 7.78 – 7.72 (m, 1H), 7.65 – 7.47 (m, 2H), 4.22 (s_{br}, 2H), 6.75 (d, J = 8.4, 1H), 4.32 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.4, 155.2 – 153.8 (m), 147.4, 139.4, 132.3, 131.3, 129.4, 126.6 - 126.7 (m), 125.0 - 125.2 (m), 124.5, 120.8, 115.0, 76.6, 60.6, 14.4.

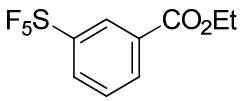
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 85.43 – 82.86 (m, 1F), 63.34 – 62.29 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3452 (w), 3358 (w), 2984 (vw), 1680 (m), 1626 (m), 1601 (m), 1508 (w), 1479 (w), 1434 (w), 1420 (vw), 1392 (vw), 1367 (w), 1336 (vw), 1311 (w), 1294 (m), 1281 (w), 1243 (m), 1166 (w), 1122 (w), 1108 (m), 1047 (w), 1026 (w), 984 (vw), 927 (vw), 912 (w), 894 (w), 849 (s), 832 (vs), 822 (vs), 793 (s), 770 (s), 749 (m), 738 (m), 696 (m), 682 (w), 643 (s), 612 (w), 593 (m), 576 (w), 570 (w).

MS (EI, 70 eV): m/z (%) = 368 (15), 367 (86), 323 (15), 322 (100), 167 (28), 166 (20), 74 (69), 59 (79), 45 (31).

HRMS ($C_{15}H_{14}F_5NO_2S$): calc.: 367.0665 found: 367.0660.

3-(Pentafluorosulfanyl)benzoic acid ethyl ester (15e)

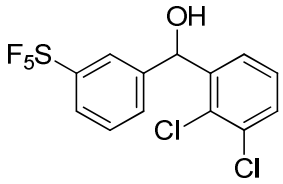


To a solution of 3-pentafluorosulfanyl-phenyl bromide (**11**; 566 mg 2.0 mmol) cooled to 0 °C, was added *i*PrMgCl·LiCl (**6**) (1.95 mL, 2.2 mmol, 1.13 M in THF) (**TP1**). The reaction mixture

was stirred for 1 h. The mixture was cooled to -30 °C, ethyl cyanoformate (**14e**; 198 mg, 2.0 mmol) was added and stirred for 1 h at -30 °C. The reaction mixture was quenched with sat. aqueous NH_4Cl-solution and extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent was removed *in vacuo*. Flash column chromatographical purification (silica; isohexane:Et_2O = 95:5) afforded **15e** as a colorless liquid (335 mg, 1.21 mmol, 61%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.48 – 8.43 (m, 1H), 8.22 (d, *J* = 7.7 Hz, 1H), 8.00 – 7.92 (m, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 1.44 (t, *J* = 7.2 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 164.8, 133.2, 132.5 – 132.4 (m), 131.6 – 131.4 (m), 130.1 – 129-9 (m), 128.9, 127.3 – 127.1 (m), 61.8, 14.3.
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 84.48 – 81.97 (m, 1F), 63.12 – 62.17 (m, 4F).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2987 (w), 1724 (m), 1438 (w), 1370 (w), 1301 (w), 1268 (m), 1177 (w), 1129 (w), 1102 (w), 1022 (w), 896 (w), 823 (s), 751 (m), 712 (m), 683 (w), 665 (w), 644 (w).
MS (EI, 70 eV): m/z (%) = 276 (M^+, 12), 248 (27), 231 (100), 152 (14), 95 (18), 89 (13), 76 (18), 75 (19).
HRMS ($C_9H_9F_5O_2S$): calc.: 276.0243; found: 276.0225.

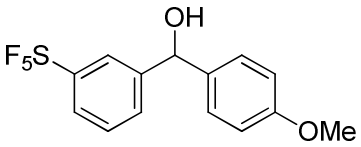
(2,3-Dichlorophenyl)[3-(pentafluorosulfanyl)phenyl]methanol (15f)



Prepared according to **TP1** from 1-bromo-3-(pentafluorosulfanyl)benzene (**11**; 283 mg, 1.0 mmol) and *i*PrMgCl·LiCl (**6**) (0.86 mL, 1.1 mmol, 1.28 M in THF) (exchange conditions: 0 °C, 1 h). 2,3-Dichlorobenzaldehyde (**14f**) (193 mg, 1.1 mmol) was added at 0 °C. The reaction mixture was quenched after 5 min at 23 °C with sat. NH_4Cl-solution (10 mL) and the resulting mixture was extracted 3 times with Et_2O. Flash column chromatographical purification (silica; isohexane:Et_2O = 3:1) afforded **15f** as a colorless oil (308 mg, 0.81 mmol, 81%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.89 (t, *J* = 1.9 Hz, 1H), 7.72 – 7.60 (m, 1H), 7.54 – 7.34 (m, 4H), 7.28 (t, *J* = 7.9 Hz, 1H), 6.27 (s, 1H), 2.55 (s_{br}, 1H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 154.8 – 153.7 (m), 153.9, 142.9, 142.4, 133.5, 130.7, 130.1, 128.9, 127.9, 126.0, 125.8 – 125.2 (m) 124.8 – 124.3 (m), 72.4.
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 86.09 – 82.41 (m, 1F), 63.65 – 61.58 (m, 4F).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3272 (w), 2964 (vw), 2924 (vw), 1706 (vw), 1604 (vw), 1584 (vw), 1565 (vw), 1482 (w), 1451 (w), 1438 (w), 1421 (w), 1326 (w), 1288 (w), 1241 (w) 1195 (w), 1180 (w), 1159 (w), 1112 (w), 1099 (w), 1061 (m), 1038 (w), 976 (vw), 913 (w), 896 (w), 836 (vs), 817 (vs), 793 (s), 781 (s), 743 (m), 726 (m), 690 (m), 643 (m), 625 (w), 615 (w), 594 (m), 572 (m), 559 (vw).
MS (EI, 70 eV): *m/z* (%) = 378 (3), 74 (63), 59 (100), 45 (73), 44 (22).
HRMS ($C_{13}H_9Cl_2F_5OS$): calc.: 377.9671; found: 377.9669.

(4-Methoxyphenyl)[3-pentafluorosulfanyl)phenyl]methanol (15g)



Prepared according to **TP1** from 1-bromo-3-(pentafluorosulfanyl)benzene (**11**; 283 mg, 1.0 mmol) and *i*PrMgCl·LiCl (**6**) (0.72 mL, 1.1 mmol, 1.53 M in THF) (exchange conditions: 0 °C, 1 h). 4-Methoxybenzaldehyde (**14g**; 150 mg, 1.1 mmol) was added at 0 °C. The reaction mixture was quenched after 5 min at 23 °C with sat. NH_4Cl-solution (10 mL) and the resulting mixture was extracted 3 times with Et_2O. Flash column chromatographical purification (silica; isohexane:Et_2O:CH_2Cl_2 = 6:2:2) afforded **15g** as a colorless liquid (285 mg, 0.84 mmol, 84%).

Mp.: 72-74 °C

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.88 (s, 1H), 7.70 – 7.62 (m, 1H), 7.52 – 7.37 (m, 2H), 7.32 – 7.21 (m, 2H), 6.94 – 6.86 (m, 2H), 5.83 (s, 1H), 3.81 (s, 3H), 2.48 (s_{br}, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 159.5, 154.5 – 153.6 (m), 145.2, 135.2, 129.5, 128.7, 128.1, 125.3 – 124.4 (m), 124.6 – 123.3 (m), 114.2, 75.1, 55.3.

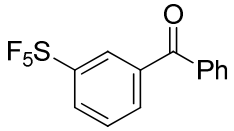
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 85.87 – 83.41 (m, 1F), 63.33 – 62.32 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3370 (w), 3306 (w), 3120 (vw), 3016 (vw), 2955 (vw), 2915 (vw), 2839 (vw), 1611 (w), 1586 (vw), 1513 (m), 1480 (w), 1465 (w), 1436 (w), 1336 (vw), 1303 (w), 1292 (w), 1265 (m), 1252 (m), 1188 (w), 1176 (m), 1112 (w), 1096 (w), 1030 (m), 1008 (w), 922 (w), 901 (m), 878 (w), 822 (vs), 806 (vs), 788 (s), 764 (s), 730 (m), 694 (w), 685 (w), 658 (w), 643 (m), 596 (w), 582 (w), 575 (w).

MS (EI, 70 eV): *m/z* (%) = 340 (38), 137 (46), 135 (24), 109 (41), 77 (13), 74 (78), 59 (100), 45 (45).

HRMS ($C_{14}H_{13}F_5O_2S$): calc.: 340.0556; found: 340.0552.

[3-(Pentafluorosulfanyl)phenyl](phenyl)methanone (15h)



The title compound was prepared from 1-bromo-3-(pentafluorosulfanyl)benzene (**11**; 556 mg, 2.0 mmol). A Br/Mg-exchange reaction was performed according to **TP1** with *i*PrMgCl·LiCl (**6**) (1.72 mL, 2.2 mmol, 1.27 M in THF) at 0 °C for 1 h. An acylation reaction was performed according to **TP4** using CuCN·2LiCl (2.4 mL, 2.4 mmol, 1.0 M in THF) and benzoyl chloride (**14h**; 197 mg, 1.4 mmol) at -40 °C within 12 h. Flash column chromatographical purification (silica; isohexane:Et_2O: = 95:5) afforded **15h** as a colorless solid (370 mg, 1.2 mmol, 86%).

Mp.: 64-65 °C

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.27 – 8.19 (m, 1H), 8.04 – 7.92 (m, 2H), 7.86 – 7.77 (m, 2H), 7.72 – 7.58 (m, 2H), 7.58 – 7.49 (m, 2H).

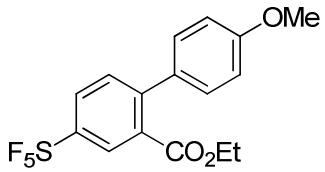
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 194.5, 154.2 – 153.6 (m), 138.4, 136.4, 133.2, 132.8, 130.0, 129.5 – 129.3 (m), 128.9, 128.6, 127.6 – 127.3 (m).

^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 84.44 – 81.80 (m, 1F), 63.21 – 62.17 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1653 (m), 1597 (w), 1432 (w), 1282 (m), 1159 (w), 1107 (w), 966 (m), 828 VS, 815 (vs), 788 (s), 739 (m), 715 (s), 699 (m), 682 (m), 648 (s).
MS (EI, 70 eV): *m/z* (%) = 309 (11), 308 (36), 105 (100), 77 (26).
HRMS ($C_{13}H_9F_5OS$): calc.: 308.0294; found: 308.0287.

2.3 Synthesis of Compounds of Type 17

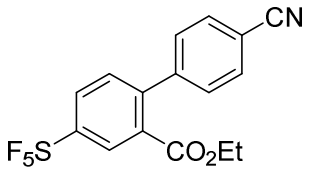
4´-Methoxy-4-(pentafluorosulfanyl)biphenyl-2-carboxylic acid ethyl-ester (17a)



The title compound was prepared from 3-(pentafluorosulfanyl)benzoic acid ethyl ester (**15e**; 280 mg, 1.0 mmol). The deprotonation was performed according to **TP5** using $TMP_2Mg \cdot 2LiCl$ (2.17 mL, 1.5 mmol, 0.7 M in THF) at -40 °C for 12 h. A cross-coupling reaction was performed according to **TP7** using $Pd(dba)_2$ (12 mg, 0.02 mmol), tfp (10 mg, 0.04 mmol) and 1-iodo-4-methoxybenzene (**14i**; 260 mg, 1.1 mmol), dissolved in THF (1.0 mL), during 12 h at 23 °C. Flash column chromatographical purification (silica; isohexane:Et_2O = 95:5) afforded **17a** as a colorless oil (200 mg, 0.52 mmol, 52%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.20 (d, J = 2.2 Hz, 1H), 7.89 (d_d, J = 8.6 Hz, J = 2.5 Hz, 1H), 7.48 (d, J = 8.6 Hz, 1H), 7.30 – 7.24 (m, 2H), 7.02 – 6.95 (m, 2H), 4.19 (q, J = 7.1 Hz, 2H), 3.88 (s, 3H), 1.12 (t, J = 7.2 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 167.2, 159.7, 152.3 – 152.1 (m), 145.3, 131.8, 131.7, 131.0, 129.5, 128.3 – 127.9 (m), 127.6 – 127.1 (m), 113.8, 61.6, 55.3, 13.7.
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 84.97 – 82.11 (m, 1F), 63.62 – 62.62 (m, 4F).
MS (EI, 70 eV): m/z (%) = 383 (M+H, 17), 382 (M^+, 100), 354 (17), 337 (42), 210 (14), 139 (11).
HRMS ($C_{16}H_{15}F_5O_3S$): calc.: 382.0662; found: 382.0647.

4´-Cyano-4-(pentafluorosulfanyl)biphenyl-2-carboxylic acid ethyl ester (17b)



The title compound was prepared from 3-(pentafluorosulfanyl)benzoic acid ethyl ester (**15e**; 280 mg, 1.0 mmol). The deprotonation was performed according to **TP5** using $TMP_2Mg \cdot 2LiCl$ (2.17 mL, 1.5 mmol, 0.7 M in THF) at -40 °C within 12 h. A cross-coupling reaction was performed according to **TP7** using $Pd(dba)_2$ (12 mg, 0.02 mmol), tfp (10 mg, 0.04 mmol) and 4-iodobenzonitrile (**14j**; 200 mg, 1.1 mmol), dissolved in THF (1.0 mL), during 12 h at 23 °C. Flash column chromatographical purification (silica; isohexane:Et_2O = 9:1) afforded **17b** as a colorless solid (315 mg, 0.83 mmol, 83%).

Mp.: 116-118 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.32 (d, J = 2.2 Hz, 1H), 7.94 (dd, J = 8.6 Hz, J = 2.5 Hz, 1H), 7.74 – 7.69 (m, 2H), 7.45 – 7.37 (m, 3H), 4.15 (q, J = 7.2 Hz, 2H), 1.08 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 165.7, 144.5, 144.1 (t, J = 1.5 Hz), 133.1, 131.9, 131.3, 131.0, 129.0, 128.9 – 128.6 (m), 128.3 – 128.0 (m), 118.4, 112.0, 61.9, 13.7.

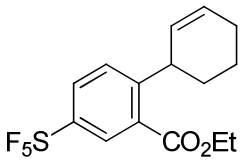
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 83.77– 81.47 (m, 1F), 63.24 – 62.49 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2233 (w), 1720 (w), 1703 (w), 1600 (w), 1368 (w), 1294 (m), 1275 (w), 1249 (w), 1156 (w), 1121 (w), 1007 (w), 900 (w), 833 (s), 791 (m), 728 (m), 670 (w), 646 (w).

MS (EI, 70 eV): m/z (%) = 377 (29), 349 (27), 333 (14), 332 (100), 205 (28), 177 (35).

HRMS ($C_{16}H_{12}F_5NSO_2$): calc.: 377.0509; found: 377.0505.

Ethyl 2-cyclohex-2-en-1-yl-5-(pentafluorosulfanyl)benzoate (17c)



The title compound was prepared from 3-(pentafluorosulfanyl)benzoic acid ethyl ester (**15e**; 276 mg, 1.0 mmol). The deprotonation was performed according to **TP5** using $TMP_2Mg\cdot 2LiCl$ (2.54 mL, 1.5 mmol, 0.59 M in THF) at -40 °C within 12 h. An allylation reaction was performed according to **TP4** using CuCN·2LiCl (0.2 mL, 0.2 mmol, 1.0 M in THF) and 3-bromocyclohex-1-ene (**14k**; 97 mg, 0.6 mmol) at -40 °C within 3 h. Flash column chromatographical purification (silica; isohexane:Et_2O: = 95:5) afforded **17c** as a yellow liquid (150 mg, 0.42 mmol, 70%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.20 (d, J = 2.5 Hz, 1H), 7.80 (dd, J = 2.5 Hz, 8.7 Hz, 1H), 7.50 (d, J = 8.7 Hz, 1H), 5.99 (ddd, J = 3.7 Hz, 6.1 Hz, 9.9 Hz, 1H), 5.63 (dd, J = 2.1 Hz, 10.1 Hz, 1H), 4.42 (q, J = 7.2 Hz, 2H), 4.36-4.26 (m, 1H), 2.27 – 2.05 (m, 3H), 1.84 – 1.58 (m, 2H), 1.51 (dd, J = 4.3 Hz, 8.5 Hz, 1H), 1.44 (dt, J = 3.5 Hz, 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.3, 152.1 – 150.6 (m), 151.5, 130.7, 129.6, 129.5, 129.1, 128.8 – 128.3 (m), 127.9 – 127.4 (m), 61.7, 37.9, 32.0, 24.9, 21.1, 14.2.

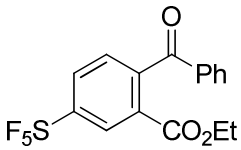
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 85.18– 82.75 (m, 1F), 63.40 – 62.49 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3022 (vw), 2985 (vw), 2935 (w), 2863 (vw), 2840 (vw), 1724 (m), 1601 (vw), 1486 (w), 1447 (w), 1434 (vw), 1391 (vw), 1368 (w), 1296 (w), 1273 (m), 1240 (m), 1220 (w), 1173 (w), 1157 (w), 1136 (w), 1115 (m), 1078 (m), 1019 (w), 985 (vw), 907 (m), 827 (vs), 786 (s), 731 (w), 717 (w), 668 (m), 625 (w), 612 (w), 597 (s), 580 (m), 570 (w).

MS (EI, 70 eV): m/z (%) = 356 (35), 311 (35), 310 (100), 309 (30), 291 (38), 183 (24), 182 (32), 165 (18), 155 (15), 71 (26), 57 (25).

HRMS ($C_{15}H_{17}F_5O_2S$): calc.: 356.0869; found: 356.0886.

5-(Pentafluorosulfanyl)-2-(phenylcarbonyl)benzoic acid ethyl ester (17d)



The title compound was prepared from 3-(pentafluorosulfanyl)benzoic acid ethyl ester (**15e**; 276 mg, 1.0 mmol). The deprotonation was performed according to **TP5** using $TMP_2Mg \cdot 2LiCl$ (2.54 mL, 1.5 mmol, 0.59 M in THF) at -40 °C within 12 h. An acylation reaction was performed according to **TP4** using $CuCN \cdot 2LiCl$ (1.5 mL, 1.5 mmol, 1.0 M in THF) and benzoyl chloride (**14h**; 105 mg, 0.75 mmol) at -40 °C within 2 h. Flash column chromatographical purification (silica; isohexane:Et_2O: = 9:1) afforded **17d** as a yellow liquid (247 mg, 0.65 mmol, 87%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.45 (d, J = 2.2 Hz, 1H), 8.01 (dd, J = 8.4 Hz, 2.4 Hz, 1H), 7.77 – 7.70 (m, 2H), 7.63 – 7.55 (m, 1H), 7.52 – 7.41 (m, 3H), 4.13 (q, J = 7.2 Hz, 2H), 1.07 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 195.0, 164.1, 154.8 – 153.5 (m), 144.7, 136.3, 133.7, 130.2, 129.9 – 129.5 (m), 129.4, 128.7, 128.2, 128.0 – 127.8 (m), 62.3, 13.6.

^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 83.55– 80.87 (m, 1F), 63.29 – 62.10 (m, 4F).

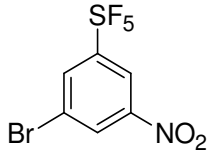
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3090 (vw), 2986 (vw), 1724 (m), 1677 (m), 1598 (w), 1583 (w), 1450 (w), 1368 (w), 1315 (w), 1297 (m), 1265 (s), 1152 (m), 1113 (m), 1081 (w), 1018 (w), 1002 (vw), 939 (w), 896 (m), 823 (vs), 789 (s), 743 (m), 729 (m), 704 (s), 668 (m), 649 (m), 618 (w), 598 (s), 577 (w).

MS (EI, 70 eV): m/z (%) = 380 (4), 336 (13), 335 (13), 303 (14), 274 (33), 105 (100), 77 (22).

HRMS ($C_{16}H_{13}F_5O_3S$): calc.: 380.0506; found: 380.0504.

2.4 Synthesis of Compounds of type 21

1-Bromo-3-nitro-5-(pentafluorosulfanyl)benzene[131] (19)



A round-bottom flask was charged with trifluoroacetic acid (1.5 mL), 3-nitro-(pentafluorosulfanyl)benzene (748 mg, 3.0 mmol), and H_2SO_4 (98%; 7.5 mL). The mixture was stirred vigorously, and *N*-bromosuccinimide (801 mg, 4.5 mmol) was added in portions over an 8 h period. After the appropriate reaction time, the mixture was poured into 50 mL of ice water, the organic layer separated, and the aqueous layer extracted 3 times with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and the solvent removed *in vacuo*. Flash column chromatographical purification (silica; isohexane:Et_2O = 9:1) afforded **19** as a yellow solid (851 mg, 2.6 mmol, 87%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.56 (t, J = 1.9 Hz, 1H), 8.54 (t, J = 1.8 Hz, 1H), 8.22 (t, J = 1.9 Hz, 1H).

[131] J. Duan, L. H. Zhang, W. R. Dolbier, Jr., *Synlett* **1999**, 1245-1246.

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 155.2 – 153.8 (m), 148.3, 134.9 – 134.6 (m), 129.7, 123.2 – 123.1 (m), 120.6 – 120.3 (m).

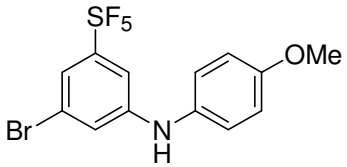
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 80.81 – 78.58 (m, 1F), 63.37 – 62.66 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3104 (w), 1604 (vw), 1582 (vw), 1538 (s), 1502 (vw), 1468 (vw), 1432 (w), 1420 (w), 1346 (s), 1302 (w), 1152 (w), 1120 (w), 1098 (w), 898 (m), 832 (vs), 736 (s), 726 (s), 686 (w), 662 (s).

MS (EI, 70 eV): m/z (%) = 329 (79), 327 (76), 283 (21), 281 (20), 175 (44), 173 (44), 163 (11), 155 (16), 153 (16), 99 (15), 94 (73), 93 (13), 89 (52), 83 (12), 75 (100), 74 (54), 71 (14), 69 (17), 57 (23), 56 (13), 55 (20), 43 (20), 43 (37), 41 (18).

HRMS ($C_6H_3BrF_5O_2NS$): calc.: 326.8988; found: 326.9000.

3-Bromo-*N*-(4-methoxyphenyl)-5-(pentafluorosulfanyl)aniline (21a)



In a dry and argon-flushed flask, equipped with a magnetic stirrer and a septum, 1-iodo-4-methoxybenzene (755 mg, 2.6 mmol) was dissolved in THF (5.0 mL) and cooled to -20 °C, and *i*PrMgCl (**5**) (2.2 mL, 2.8 mmol, 1.27 M in THF) was added dropwise. The I/Mg-exchange was complete after 30 min, and 1-bromo-3-nitro-5-(pentafluorosulfanyl)benzene (**19**; 328 mg, 1.0 mmol) was added. After 2 h stirring at -20 °C, the reaction mixture was quenched with EtOH (2.0 mL), and $FeCl_2$ (279 mg, 2.2 mmol) and $NaBH_4$ (42 mg, 1.1 mmol) were added. After 2 h of stirring at 23 °C, the reaction mixture was poured into water (20 mL). The aqueous phase was extracted 2 times with Et_2O. The combined organic fractions were washed with brine, dried over Na_2SO_4 and the solvent removed *in vacuo*. Flash column chromatographical purification (silica; isohexane:Et_2O: = 85:15) afforded **21a** as a yellow solid (267 mg, 0.66 mmol, 66%).

Mp.: 81-83 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.28 (s, 1H), 7.17 – 7.03 (m, 4H), 6.99 – 6.90 (m, 2H), 5.65 (s_{br}, 1H), 3.85 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 157.1 – 156.9 (m), 141.5, 132.8 – 132.6 (m), 130.9, 124.6, 122.8 – 122.6 (m), 119.5 – 119.2 (m), 118.9 – 118.5 (m), 115.2 – 114.9 (m), 111.0 – 111.7 (m), 55.5.

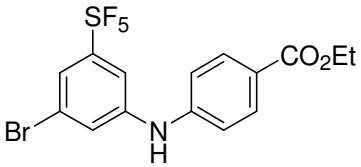
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 84.86 – 82.57 (m, 1F), 62.99 – 62.23 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3410 (w), 1592 (m), 1568 (w), 1510 (m), 1490 (w), 1452 (m), 1440 (w), 1416 (w), 1320 (w), 1300 (w), 1284 (w), 1244 (m), 1222 (w), 1180 (w), 1168 (w), 1112 (w), 1034 (w), 986 (w), 952 (w), 878 (w), 832 (vs), 806 (s), 774 (w), 728 (m), 678 (w), 654 (m), 644 (w).

MS (ESI, 70 eV): m/z (%) = 450 (25), 448 (30), 440 (100), 438 (67), 404 (32), 402 (31), 397 (1), 354 (1).

HRMS ($C_{13}H_{11}BrF_5NOS$): calc.: 403.9743; found: 403.9578.

4-{[3-Bromo-5-(pentafluorosulfanyl)phenyl]amino)}-benzoic acid ethyl ester (21b)



In a dry and argon-flushed flask, equipped with a magnetic stirrer and a septum, ethyl 4-iodobenzoate (755 mg, 2.6 mmol) was dissolved in THF (5.0 mL) and cooled to −20 °C, and *i*PrMgCl (**5**) (2.2 mL, 2.8 mmol, 1.27 M in THF) was added dropwise. The I/Mg-exchange was complete after 30 min, and 1-bromo-3-nitro-5-(pentafluorosulfanyl)benzene (**19**; 328 mg, 1.0 mmol) was added. After 2 h of stirring at -20 °C, the reaction mixture was quenched with EtOH (2.0 mL), and $FeCl_2$ (279 mg, 2.2 mmol) and $NaBH_4$ (42 mg, 1.1 mmol) were added. After 2 h of stirring at 23 °C, the reaction mixture was poured into water (20 mL). The aqueous phase was extracted 2 times with Et_2O. The combined organic fractions were washed with brine, dried over Na_2SO_4 and the solvent removed *in vacuo*. Flash column chromatographical purification (silica; isohexane:Et_2O = 6:1) afforded **21b** as a colorless solid (366 mg, 0.82 mmol, 82%).

Mp.: 166-168 °C.

^{1}H-NMR (300 MHz, DMSO-d$_6$): δ / ppm = 9.28 (s, 1H), 7.92 – 7.86 (m, 2H), 7.58 – 7.48 (m, 3H), 7.20 – 7.13 (m, 2H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.0 Hz, 3H).

^{13}C-NMR (75 MHz, DMSO-d$_6$): δ / ppm = 165.2, 154.5 – 153.7 (m), 145.8, 144.3, 132.8 – 132.6 (m), 131.1, 122.4, 122.2, 119.7 – 119.2 (m), 116.4, 113.8 – 113.3 (m), 60.2, 14.2.

^{19}F-NMR (280 MHz, DMSO-d$_6$): δ / ppm = 86.66 – 84.80 (m, 1F), 64.18 – 63.14 (m, 4F).

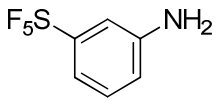
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3338 (w), 1680 (m), 1588 (m), 1536 (w), 1506 (w), 1476 (w), 1454 (w), 1434 (w), 1396 (w), 1368 (w), 1342 (w), 1314 (w), 1278 (m), 1244 (w), 1178 (m), 1110 (m), 1084 (m), 1020 (w), 956 (w), 832 (vs), 768 (m), 732 (m), 704 (w), 682 (w), 668 (w), 656 (m).

MS (EI, 70 eV): m/z (%) = 448 (15), 447 (100), 445 (96), 419 (28), 417 (27), 402 (94), 400 (91), 166 (25).

HRMS ($C_{15}H_{13}F_5O_2NBrS$): calc.: 444.9770; found: 444.9770.

2.5 Synthesis of Indoles 27

3-(Pentafluorosulfanyl)aniline[132]



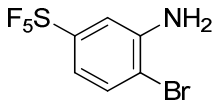
Hydrochloric acid (conc., 15 mL) was added dropwise to a suspension of 1-nitro-3-(pentafluorosulfanyl)benzene (7.53 g, 30.2 mmol) and Fe powder (10.13 g, 181.4 mmol) in EtOH (300 mL) under stirring at 0 °C. The resulting mixture was allowed to warm to room temperature and was stirred for 1.5 h. The remaining iron powder was removed by decantation and NH_3

[132] J. T. Welch, D. S. Lim, *Bioorg Med. Chem.* **2007**, *15*, 6659-6666.

(conc., 150 mL) was added to the resulting solution until pH 10 was adjusted. The solution was extracted 3 times with CH_2Cl_2. The combined extracts were washed with water (150 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (isohexane:EtOAc = 2:1) to afford 3-(pentafluorosulfanyl)aniline as orange oil (5.86 g, 26.7 mmol, 88%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.27 – 7.18 (m, 1H), 7.17 – 7.11 (m, 1H), 7.07 (t, J = 2.3 Hz, 1H), 6.83 – 6.75 (m, 1H), 3.84 (s_{br}, 2H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 155.2 – 154.6 (m), 146.7, 129.3, 117.7, 115.8 – 115.5 (m), 112.4 – 112.0 (m).
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 86.48 – 84.24 (m, 1F), 62.50 – 61.76 (m, 4F).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3480 (vw), 3396 (vw), 1624 (m), 1608 (m), 1494 (w), 1460 (w), 1434 (vw), 1324 (w), 1312 (w), 1282 (w), 1126 (vw), 1094 (w), 906 (m), 826 (vs), 790 (vs), 772 (vs), 682 (m), 644 (s).
MS (EI, 70 eV): m/z (%) = 219 (100), 65 (37), 57 (14).
HRMS ($C_6H_6F_5NS$): calc.: 219.0141; found: 219.0118.

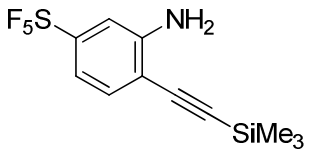
2-Bromo-5-(pentafluorosulfanyl)aniline (22)



N-Bromosuccinimide (2.67 g, 15.0 mmol) in 1,4-dioxane (15 mL) was added to a solution of 3-(pentafluorosulfanyl)aniline (3.15 g, 15.0 mmol) in 1,4-dioxane (60 mL). The resulting mixture was stirred for 14 h at 23 °C. Then, the solution was extracted 3 times with EtOAc and the combined extracts were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (isohexane:CH_2Cl_2 = 1:1, 2% NEt_3) to afford 2-bromo-5-(pentafluorosulfanyl)aniline (**22**) as colorless oil (3.36 g, 11.26 mmol, 75%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.50 – 7.43 (m, 1H), 7.12 (d, J = 2.5 Hz, 1H), 6.97 (dd, J = 8.9 Hz, J = 2.5 Hz, 1H), 4.27 (s_{br}, 2H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 154.2 – 153.2 (m), 144.3, 132.5, 116.4 – 116.0 (m), 112.8 – 112.4 (m), 111.9 – 111.8 (m).
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 85.52 – 83.12 (m, 1F), 63.28 – 62.35 (m, 4F).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3436 (vw), 3317 (w), 3205 (vw), 1621 (m), 1589 (w), 1481 (m), 1422 (m), 1312 (w), 1300 (w), 1256 (w), 1160 (vw), 1110 (w), 1026 (w), 919 (m), 866 (w), 830 (s), 800 (s), 785 (s), 658 (m).
MS (EI, 70 eV): m/z (%) = 299 (100), 297 (99), 191 (15), 189 (15), 172 (13), 170 (13), 110 (13), 90 (100) 63 (17), 52 (12).
HRMS ($C_6H_5F_5NSBr$): calc.: 296.9246; found: 296.9257.

5-(Pentafluorosulfanyl)-2-((trimethylsilyl)ethynyl)aniline (24)



2-Bromo-5-(pentafluorosulfanyl)aniline (**22**; 3.28 g, 11.0 mmol), $Pd(PPh_3)_2Cl_2$ (309 mg, 0.44 mmol, 4 mol%) and CuI (42 mg, 0.22 mmol, 2 mol%) were placed in an argon flushed *Schlenk*-flask. After addition of NEt_3 (35 mL) and THF (35 mL), (trimethylsilyl)acetylene (1.62 g, 16.5 mmol) was added. The mixture was stirred at 50 °C for 5 h. The reaction mixture was quenched with water (20 mL) and extracted 3 times with EtOAc. The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (isohexane:CH_2Cl_2 = 85:15, 1% NEt_3) to give 5-(pentafluorosulfanyl)-2-((trimethylsilyl)ethynyl)aniline (**24**) as yellow crystals (3.05 g, 9.66 mmol, 89%).

Mp.: 54-56 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.35 (d, J = 8.6 Hz, 1H), 7.09 (d, J = 2.2 Hz, 1H), 7.06 – 7.00 (m, 1H), 4.46 (s_{br}, 2H), 0.31 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 155.0 – 153.8 (m), 148.1, 132.1, 115.0 – 114.9 (m), 111.6 – 111.1 (m), 110.8, 102.9, 99.7, 0.15.

^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 85.88 – 83.47 (m, 1F), 62.78 – 61.87 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3493 (vw), 3390 (vw), 2965 (vw), 2906 (vw), 2153 (vw), 1739 (vw), 1612 (m), 1560 (vw), 1491 (w), 1430 (m), 1315 (vw), 1298 (vw), 1253 (m), 1232 (vw), 1212 (vw), 1149 (vw), 1107 (w), 1056 (vw), 933 (m), 834 (s), 804 (s), 763 (s), 703 (w).

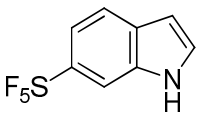
MS (EI, 70 eV): m/z (%) = 316 (12), 315 (73), 301 (18), 300 (100), 192 (11), 191 (11), 188 (21), 177 (28), 172 (13), 158 (18), 150 (32), 139 (16), 130 (68), 96 (21), 89 (24), 77 (66), 73 (21).

HRMS ($C_{11}H_{14}F_5NSSi$): calc.: 315.0536; found: 315.0542.

Purification of KH:

Potassium hydride (KH, 30% suspension in mineral oil) was transferred to a *Schlenk*-flask, evaporated and filled with argon. After the addition of dry hexane, the suspension was stirred for a short time before the solvent was removed again with a syringe. This process was repeated four times to give after evaporation *in vacuo* and refilling with argon, a white powder of KH.

6-(Pentafluorosulfanyl)-*1H*-indole (23)



KH (500 mg, 12.5 mmol) was suspended under argon in NMP (15 mL). A solution of 5-(pentafluorosulfanyl)-2-((trimethylsilyl)ethynyl)aniline (**24**; 2.1 g, 6.66 mmol) in NMP (10 mL) was added dropwise at room temperature and the reaction mixture was stirred for 3 h. The reaction mixture was quenched with water (20 mL) at 0 °C, then NH_4Cl (30 mL) was added. The mixture was extracted 3 times with EtOAc and dried over Na_2SO_4. The crude product was

purified by flash column chromatography on silica (isohexane:EtOAc = 5:1) to afford 6-(pentafluorosulfanyl)-*1H*-indole (**23**) as yellow crystals (1.35 g, 5.55 mmol, 83%).

Mp.: 97-99 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.38 (s_{br}, 1H), 7.90 – 7.84 (m, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.57 (dd, J = 8.8 Hz, J = 2.0 Hz, 1H), 7.40 (dd, J = 6.3 Hz, J = 3.2 Hz, 1H), 6.64 (ddd, J = 3.1 Hz, J = 2.0 Hz, J = 0.9 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 149.3 – 148.3 (m), 133.9, 129.8, 128.3 – 127.6 (m), 120.2, 117.6 – 116.9 (m), 110.1 – 109.4 (m), 102.9.

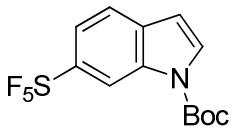
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 88.84 – 85.29 (m, 1F), 65.64 – 63.54 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2916 (w), 2850 (w), 1688 (w), 1588 (vw), 1454 (vw), 1416 (vw), 1380 (vw), 1144 (m), 1072 (m), 1038 (m), 1000 (m), 916 (m), 834 (s), 806 (vs), 782 (s), 710 (w), 660 (m), 638 (vw).

MS (EI, 70 eV): *m/z* (%) = 243 (97), 135 (50), 116 (44), 108 (21), 107 (11), 89 (20), 74 (66), 73 (12), 59 (100), 45 (73), 44 (40), 43 (33), 41 (21).

HRMS ($C_8H_6F_5NS$): calc.: 243.0141; found: 243.0145.

6-(Pentafluorosulfanyl)-1*H*-indole-1-carboxylic acid *tert*-butyl ester (25)



A solution of 6-(pentafluorosulfanyl)-*1H*-indole (**23**; 1.22 g, 5.0 mmol), di-*tert*-butyl dicarbonate (1.64 g, 7.5 mmol) and 4-dimethylaminopyridine (0.04 g, 0.35 mmol) in acetonitrile (15 mL) was stirred at 23 °C for 1 h. The reaction mixture was quenched with water and extracted 3 times with Et_2O. The extract was washed with sat. aqueous $NaHCO_3$-solution and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give the title compound **25** as colourless solid (1.48 g, 4.7 mmol, 94%).

Mp.: 89-91 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.66 (s_{br}, 1H), 7.76 (d, J = 3.5 Hz, 1H), 7.62 (d, J = 2.0 Hz, 1H), 7.60 (s, 1H), 6.61 (dd, J = 3.8 Hz, 0.7 Hz, 1H), 1.69 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 150.9 – 149.9 (m), 149.1, 133.6, 132.5, 129.3, 120.3, 120.3 – 120.1 (m), 114.2 – 113.7 (m), 106.7, 84.8, 28.1.

^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 86.96 – 85.12 (m, 1F), 65.59 – 64.44 (m, 4F).

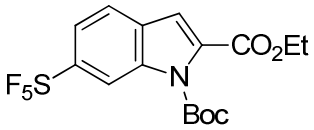
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1740 (m), 1469 (w), 1444 (w), 1396 (w), 1374 (w), 1365 (w), 1350 (m), 1270 (w), 1256 (m), 1216 (w), 1184 (w), 1162 (m), 1137 (m), 1099 (m), 1071 (w), 1041 (w), 1028 (w), 913 (w), 892 (w), 866 (w), 842 (s), 835 (s), 808 (vs), 782 (s), 764 (m), 756 (s), 726 (m), 655 (m), 633 (m), 586 (m), 568 (w).

MS (EI, 70 eV): *m/z* (%) = 343 (28), 287 (33), 270 (22), 135 (15), 134 (18), 83 (15), 57 (51).

HRMS ($C_{13}H_{14}F_5NO_2S$): calc.: 343.0665; found: 343.0661.

2.6 Functionalization of Position 2 and 3 of the Indole 23

6-(Pentafluorosulfanyl)-1*H*-indole-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-ethyl ester (26)



The title compound was prepared from 6-(pentafluorosulfanyl)-1*H*-indole-1-carboxylic acid *tert*-butyl ester (**25**; 630 mg, 2.0 mmol). The deprotonation was performed according to **TP6** using TMPMgCl·LiCl (**7**) (2.25 mL, 2.2 mmol, 0.98 M in THF) at 0 °C within 0.5 h. Ethyl cyanoformate (**14e**; 218 mg, 2.2 mmol) was added at -30 °C and the reaction mixture stirred for 1 h. The reaction mixture was quenched with sat. aqueous NH_4Cl-solution and extracted 3 times with Et_2O. The combined organic layers were dried over Na_2SO_4 and the solvent removed *in vacuo*. Flash column chromatographical purification (silica; isohexane:EtOAc = 19:1) afforded **26** as a white solid (729 mg, 1.9 mmol, 93%).

Mp.: 53-54 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.59 (d, J = 1.0 Hz, 1H), 7.67 – 7.59 (m, 2H), 7.05 (s, 1H), 4.39 (q, J = 7.2 Hz, 2H), 1.64 (s, 9H), 1.39 (t, J = 7.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 161.3, 152.6 – 151.5 (m), 148.4, 135.8, 134.2, 129.5, 121.7, 120.9 – 120.5 (m), 114.1 – 113.7 (m), 112.7, 85.8, 61.9, 27.8, 14.1.

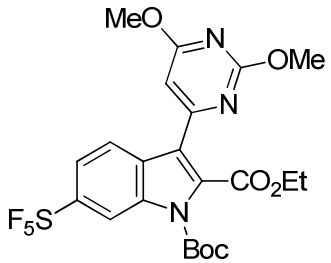
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 86.31 – 84.03 (m, 1F), 65.40 – 63.47 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2984 (w), 2361 (m), 2339 (m), 1745 (m), 1730 (m), 1554 (w), 1469 (w), 1433 (w), 1394 (w), 1370 (m), 1316 (s), 1294 (m), 1236 (s), 1201 (m), 1156 (m), 1135 (s), 1084 (m), 1060 (m), 1135 (s), 970 (w), 956 (vw), 926 (vw), 893 (w), 856 (m), 846 (w), 833 (s), 808 (vs), 766 (s), 755 (s), 743 (w), 667 (w), 645 (w), 636 (m), 621 (w).

MS (EI, 70 eV): *m/z* (%) = 415 (4), 315 (83), 269 (44), 57 (100).

HRMS ($C_{16}H_{18}F_5NO_4S$): calc.: 415.0877; found: 415.0869.

3-(2,6-Dimethoxy-pyrimidin-4-yl)-6-(pentafluorosulfanyl)-1*H*-indole-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-ethyl ester (27a)



The title compound was prepared from 6-(Pentafluorosulfanyl)-1*H*-indole-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-ethyl ester (**26**; 387 mg, 1.0 mmol). The deprotonation was performed according to **TP6** using TMPMgCl·LiCl (**7**) (1.12 mL, 1.1 mmol, 0.98 M in THF) at -40 °C within 2 h. A cross-coupling reaction was performed according to **TP7** using PEPPSI-*i*Pr (14 mg, 0.02 mmol) and 4-iodo-2,6-dimethoxypyrimidine (239 mg, 0.9 mmol) in 1 h at 23 °C. Flash

column chromatographical purification (silica; isohexane:EtOAc = 9:1) afforded **27a** as a yellow solid (310 mg, 0.6 mmol, 62%).

Mp.: 112-113 °C

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.65 (d, *J* = 1.9 Hz, 1H), 8.11 (d, *J* = 8.9 Hz, 1H), 7.69 (dd, *J* = 9.0 Hz, 2.1 Hz, 1H), 6.68 (s, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.00 (d, *J* = 6.6 Hz, 6H), 1.66 (s, 9H), 1.31 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 172.3, 165.4, 162.2, 159.4, 152.4 – 151.1 (m), 148.1, 133.8, 133.2, 128.7, 121.4, 121.3 – 121.2 (m), 118.8, 114.7 – 114.1 (m), 100.5, 86.9, 62.4, 54.9, 54.0, 27.8, 13.8.

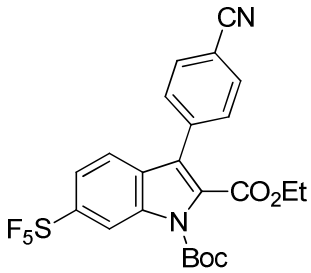
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 86.37 – 83.72 (m, 1F), 65.04 – 63.87 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2986 (vw), 903 (vw), 2361 (vw), 1757 (m), 1745 (m), 1600 (m), 1579 (w), 1542 (m), 1479 (m), 1458 (w), 1447 (w), 1436 (w), 1390 (w), 1362 (s), 1350 (m), 1318 (m), 1301 (m), 1257 (w), 1221 (m), 1181 (w), 1162 (m), 1140 (s), 1106 (s), 1064 (w), 1052 (m), 1028 (m), 995 (w), 970 (vw), 942 (w), 907 (w), 886 (w), 843 (vs), 824 (vs), 787 (m), 765 (s), 752 (m), 720 (w), 696 (w), 682 (m), 657 (m), 632 (m), 620 (w), 609 (m), 591 (s), 576 (m), 568 (m).

MS (EI, 70 eV): *m/z* (%) = 453 (37), 407 (29), 382 (16), 381 (100), 380 (40), 351 (17).

HRMS ($C_{22}H_{24}F_5N_3O_6S$): calc.: 553.1306; found: 553.1296.

3-(4-Cyano-phenyl)-6-(pentafluorosulfanyl)-1*H*-indole-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-ethyl ester (27b)



The title compound was prepared from 6-(pentafluorosulfanyl)-1*H*-indole-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-ethyl ester (**26**; 387 mg, 1.0 mmol). The deprotonation was performed according to **TP6** using TMPMgCl·LiCl (**7**) (1.12 mL, 1.1 mmol, 0.98 M in THF) at -40 °C within 2 h. A cross-coupling reaction was performed according to **TP7** using PEPPSI-*i*Pr (14 mg, 0.02 mmol) and 4-iodobenzonitrile (206 mg, 0.9 mmol) during 1 h at 23 °C. Flash column chromatographical purification (silica; isohexane:EtOAc = 9:1) afforded **27b** as a yellow liquid (305 mg, 0.59 mmol, 66%)

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.70 (d, *J* = 2.2 Hz, 1H), 7.79 – 7.75 (m, 2H), 7.69 (dd, *J* = 8.8 Hz, 2.2 Hz, 2H), 7.66 – 7.62 (m, 2H), 7.58 (d, *J* = 8.8 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.68 (s, 9H), 1.22 (t, *J* = 7.3 Hz, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 161.7, 152.6 – 151.8 (m), 148.2, 135.8, 134.1, 132.4, 131.0, 130.2, 129.4, 121.6, 121.4 – 121.2 (m), 120.0, 118.5, 114.6 – 114.4 (m), 112.1, 86.7, 62.3, 27.8, 13.8.

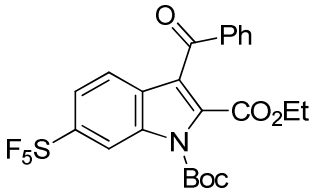
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 85.84 – 83.84 (m, 1F), 65.16 – 63.79 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2983 (vw), 2230 (vw), 1735 (m), 1612 (vw), 1472 (w), 1436 (w), 1396 (w), 1371 (m), 1356 (m), 1330 (m), 1247 (m), 1224 (s), 1188 (m), 1176 (m), 1155 (m), 1128 (s), 1090 (m), 1062 (w), 1018 (w), 980 (vw), 889 (w), 838 (vs), 822 (vs), 765 (m), 736 (m), 716 (w), 662 (w), 654 (w), 638 (w), 626 (w), 615 (w), 595 (m), 578 (vw), 571 (vw), 556 (w).

MS (EI, 70 eV): *m/z* (%) = 417 (16), 416 (100), 371 (22), 370 (30), 370 (48), 369 (24), 369 (24), 215 (44), 57 (22).

HRMS ($C_{23}H_{21}F_5N_2O_4S$): calc.: 516.1142; found: 516.1132.

3-Benzoyl-6-(pentafluorosulfanyl)-1*H*-indole-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-ethyl ester (27c)



The title compound was prepared from 6-(pentafluorosulfanyl)-1*H*-indole-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-ethyl ester (**26**; 387 mg, 1.0 mmol). The deprotonation was performed according to **TP6** using TMPMgCl·LiCl (**7**) (1.12 mL, 1.1 mmol, 0.98 M in THF) at -40 °C within 2 h. An acylation reaction was performed according to **TP4** using CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and benzoyl chloride (169 mg, 1.2 mmol) at -40 °C within 12 h. Flash column chromatographical purification (silica; isohexane:EtOAc = 9:1) afforded **27c** as a colorless oil (452 mg, 0.87 mmol, 87%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.72 (t, *J* = 1.2 Hz, 1H), 7.85 – 7.79 (m, 2H), 7.71 (d, *J* = 1.4 Hz, 2H), 7.68 – 7.59 (m, 1H), 7.54 – 7.46 (m, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 1.69 (s, 9H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 190.5, 160.9, 152.8 – 152.5 (m), 147.9, 138.3, 135.9, 134.1, 133.4, 129.2, 128.7, 128.6, 121.8, 121.7 – 121.5 (m), 120.7, 114.5 – 114.1 (m), 87.3, 62.5, 27.7, 13.5.

^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 85.98 – 83.51 (m, 1F), 64.96 – 63.95 (m, 4F).

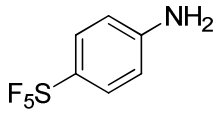
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2984 (vw), 1739 (m), 1655 (w), 1599 (vw), 1580 (vw), 1542 (w), 1473 (w), 1448 (w), 1434 (w), 1396 (w), 1370 (m), 1353 (m), 1337 (m), 1302 (m), 1268 (m), 1225 (s), 1210 (s), 1150 (s), 1107 (s), 1083 (m), 1042 (w), 1018 (m), 960 (w), 904 (vw), 837 (vs), 824 (vs), 807 (s), 765 (m), 751 (s), 716 (m), 695 (m), 667 (m), 642 (m), 633 (m), 611 (w), 595 (m), 576 (w), 570 (w).

MS (EI, 70 eV): *m/z* (%) = 420 (19), 419 (100), 374 (13), 373 (50), 342 (31), 265 (11), 190 (11), 105 (15).

HRMS ($C_{23}H_{22}F_5NO_5S$): calc.: 519.1139; found: 519.1136.

2.7 Synthesis of Benzothiophenes of Type 28

4-(Pentafluorosulfanyl)aniline

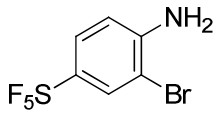


4-(Pentafluorosulfanyl)aniline was prepared according to a literature procedure.[5]

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.54 (d, J = 9.1 Hz, 2H), 6.63 (d, J = 8.6 Hz, 2H), 4.02 (s_{br}, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 149.0, 145.2 – 143.7 (m), 127.9 – 126.9 (m), 113.4.

2-Bromo-4-(pentafluorosulfanyl)aniline



4-(Pentafluorosulfanyl)aniline (4.38 g, 20 mmol) was dissolved in 1,4-dioxane (20 mL). NBS (3.6 g, 20 mmol) was added in several portions over a reaction time of 8 h at 23 °C. The reaction mixture was quenched with sat. aqueous NH_4Cl-solution and extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent removed *in vacuo*. Flash column chromatographical purification (silica; pentane:CH_2Cl_2:NEt_3 = 7:2.8:0.2) afforded 2-bromo-4-(pentafluorosulfanyl)aniline as a yellow solid (4.71 g, 15.8 mmol, 79%).

Mp.: 67-69 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.83 (d, J = 2.5 Hz, 1H), 7.51 (dd, J = 8.6 Hz, 2.5 Hz, 1H), 6.77 – 6.70 (m, 1H), 4.44 (s_{br}, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 146.7, 144.6 – 143.7 (m), 130.7 – 130.1 (m), 126.7 – 125.9 (m), 113.6, 106.9.

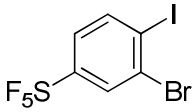
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 87.36 – 84.87 (m, 1F), 65.29 – 64.20 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3512 (w), 3408 (w), 1615 (m), 1496 (m), 1472 (w), 1414 (w), 1326 (m), 1172 (w), 1106 (m), 1067 (w), 1033 (w), 866 (m), 827 (s), 790 (vs), 692 (m), 662 (s), 611 (m), 586 (m), 574 (m).

MS (EI, 70 eV): *m/z* (%) = 299 (98), 297 (100), 191 (50), 189 (54), 172 (13), 170 (14), 110 (26), 91 (33), 90 (50), 83 (19), 63 (27).

HRMS ($C_6H_5BrF_5NS$): calc.: 296.9246; found: 296.9245.

2-Bromo-1-iodo-4-(pentafluorosulfanyl)benzene (29)



2-Bromo-4-(pentafluorosulfanyl)aniline (8.94 g, 30 mmol) was suspended in a mixture of H_2SO_4 (conc.; 15 mL) and water (30 mL) and cooled to 0 °C. A solution of $NaNO_2$ (2.14 g, 31 mmol, 6 M in water) was added dropwise over 1 h and the resulting mixture stirred further for 1 h at 0 °C. Then CuI (286 mg, 1.5 mmol) was added in one portion and following a solution of KI (5.31 g, 32 mmol, 6 M in water) was added dropwise over 1 h. The resulting sluggish reaction mixture was stirred over night while warming to room temperature. The solids were dissolved in

CH_2Cl_2, separated from the aqueous phase, then washed with NaOH (2 M) and aq. sat. $Na_2S_2O_3$-solution and dried over Na_2SO_4. After removal of the solvent *in vacuo*, the crude product was purified by flash column chromatography (silica; pentane) to afford **29** as a colorless solid (6.9 g, 16.9 mmol, 56%).

Mp.: 61-63 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.03 – 7.96 (m, 2H), 7.40 (dd, *J* = 8.6 Hz, 2.5 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 154.4 – 153.6 (m), 140.3, 130.2, 130.0 – 129.5 (m), 125.8 – 125.2 (m), 105.8.

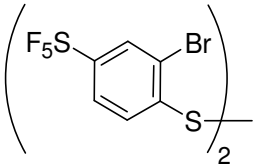
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 83.48 – 80.96 (m, 1F), 63.48 – 62.65 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3093 (w), 1919 (w), 1765 (w), 1642 (w), 1564 (w), 1451 (w), 1444 (w), 1402 (w), 1372 (m), 1268 (w), 1157 (w), 1130 (w), 1113 (w), 1097 (m), 1006 (w), 883 (m), 851 (m), 830 (vs), 810 (vs), 734 (s), 692 (m), 666 (s), 651 (m), 592 (s), 577 (m).

MS (EI, 70 eV): *m/z* (%) = 410 (58), 408 (76), 281 (12), 175 (21), 173 (29), 156 (27), 154 (19), 94 (44), 89 (30), 75 (100), 74 (56).

HRMS ($C_6H_3BrF_5IS$): calc.: 407.8104; found: 407.8109.

1,1´-Disulfanediylbis[2-bromo-4-(pentafluorosulfanyl)benzene] (30)



The aryl disulfide **30** was prepared according to a literature procedure[133] whereby the I/Mg-exchange was carried out with *i*PrMgCl·LiCl (**6**) (4.13 mL, 5.25 mmol, 1.27 M in THF) at -80 °C from **29** (2.04 g, 5.0 mmol) in THF (12 mL) and after transmetalation with $ZnCl_2$ (5.5 mL, 5.5 mmol, 1.0 M in THF), S_2Cl_2 (0.32 g, 2.4 mmol) was added. The reaction mixture was quenched with sat. aqueous NH_4Cl-solution and extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent removed *in vacuo*. Flash column chromatographical purification (silica; pentane) afforded **30** as a colorless solid (942 mg, 1.5 mmol, 60%).

Mp.: 116-118 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.96 (d, *J* = 1.9 Hz, 2H), 7.75 – 7.69 (m, 2H), 7.62 – 7.55 (m, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 153.1 – 152.0 (m), 135.1, 132.1, 131.9 – 131.6 (m), 130.4, 120.8.

^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 84.05 – 81.61 (m, 1F), 67.77 – 66.82 (m, 4F).

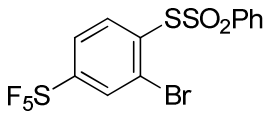
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3105 (vw), 1572 (vw), 1455 (m), 1445 (m), 1375 (w), 1264 (vw), 1247 (w), 1156 (w), 1114 (w), 1105 (w), 1089 (w), 1027 (m), 825 (vs), 811 (vs), 740 (vs), 698 (m), 671 (s), 649 (s).

MS (EI, 70 eV): *m/z* (%) = 631 (11), 630 (64), 628 (100), 626 (50), 207 (28), 205 (24), 188 (13), 126 (65), 107 (15), 89 (12).

[133] T. J. Korn, P. Knochel, *Synlett* **2005**, 1185-1187.

HRMS ($C_{12}H_6Br_2F_{10}S_4$): calc.: 625.7559; found: 625.7552.

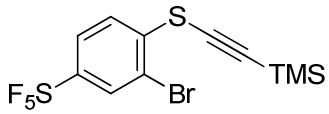
_S_-[2-Bromo-4-(pentafluorosulfanyl)phenyl] benzenesulfonothioate (31)



The sulfonothioate **31** was prepared according to a literature procedure.[134] To a mixture of sodium benzenesulfinate (2.36 g, 14.4 mmol) and disulfide **30** (2.38 g, 4.5 mmol) in CH_2Cl_2 (45 mL) was added I_2 (7.30 g, 28.8 mmol) in one portion. The resulting suspension was stirred until the disulfide was consumed (checked by TLC). Then CH_2Cl_2 (100 mL) was added and the crude reaction mixture was washed with aq. sat. $Na_2S_2O_3$-solution until the color of iodine disappeared. The organic layer was washed with water, dried over $MgSO_4$ and the solvent was evaporated. Flash column chromatographical purification (silica; pentane:Et_2O = 9:1) afforded **31** as a colorless solid (4.06 g, 8.9 mmol, 99%).

Mp.: 62-64 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.95 (d, *J* = 1.9 Hz, 1H), 7.91 – 7.84 (m, 1H), 7.74 (dd, *J* = 8.6 Hz, 1.9 Hz, 1H), 7.66 – 7.54 (m, 3H), 7.51 – 7.42 (m, 2H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 156.4 – 155.6 (m), 143.0, 141.1, 135.1, 134.4, 132.6 – 132.2 (m), 129.2, 127.3, 125.8, 124.2.
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 83.35 – 80.95 (m, 1F), 68.64 – 76.71(m, 4F).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3102 (w), 1448 (m), 1374 (w), 1327 (m), 1309 (m), 1294 (w), 1261 (w), 1173 (w), 1142 (s), 1104 (m), 1077 (m), 1056 (w), 1024 (w), 998 (w), 832 (vs), 750 (s), 715 (s), 681 (m), 666 (m), 629 (w), 608 (w).
MS (EI, 70 eV): *m/z* (%) = 456 (7), 454 (6), 141 (100), 126 (18), 125 (11), 77 (81).
HRMS ($C_{12}H_8BrF_5O_2S_3$): calc.: 453.8790; found: 453.8788.

[2-Bromo-4-(pentafluorosulfanyl)phenylsulfanylethynyl]-trimethylsilane (32)



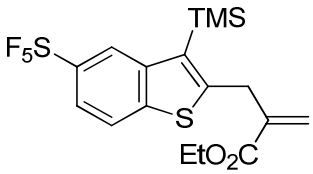
A dry and argon flushed *Schlenk*-flask, equipped with a septum and a magnetic stirring bar was charged with ethynyltrimethylsilane (1.32 g, 13.4 mmol) in THF (13 mL) and cooled to -30 °C. Then *i*PrMgCl·LiCl (**6**) (8.4 mL, 10.7 mmol, 1.27 M in THF) was added and the reaction was stirred for 30 min at this temperature before a solution of the sulfonothioate **31** (4.06 g, 8.9 mmol) in THF (9.0 mL) was added dropwise at -60 °C. The mixture was stirred for 15 min. The reaction mixture was quenched with saturated aqueous NH_4Cl-solution and extracted 3 times with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent removed *in vacuo*. Flash column chromatographical purification (silica; pentane) afforded **32** as a colorless solid (2.93 g, 7.0 mmol, 80%).

Mp.: 55-56 °C.

[134] K. Fujiki, N. Tanifuji, Y. Sasaki, T. Yokoyama, *Synthesis* **2002**, 343-348.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.94 (d, *J* = 1.9 Hz, 1H), 7.93 – 7.89 (m, 1H), 7.64 (dd, *J* = 8.9 Hz, 1.9 Hz, 1H), 0.29 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 152.2 – 150.8 (m), 134.8, 131.9 – 131.4 (m), 130.5, 126.5, 119.4, 110.9, 88.6 – 88.1 (m), -0.31.
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 83.69 – 81.30 (m, 1F), 66.17 – 65.13 (m, 4F).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2969 (w), 2361 (w), 2338 (w), 2103 (m), 1780 (w), 1576 (w), 1454 (m), 1411 (w), 1388 (w), 1377 (w), 1264 (vw), 1250 (m), 1199 (vw), 1167 (w), 1103 (m), 1024 (m), 877 (w), 829 (vs), 812 (s), 759 (s), 745 (s), 705 (w), 692 (w), 669 (m), 631 (m).
MS (EI, 70 eV): *m/z* (%) = 414 (14), 413 (17), 412 (100), 411 (18), 410 (87), 305 (12), 289 (36), 287 (29), 251 (16), 249 (13), 227 (39), 225 (34), 220 (26), 208 (16), 146 (25), 128 (18), 89 (28), 77 (50), 75 (15), 57 (20), 43 (24).
HRMS ($C_{11}H_{12}BrF_5S_2Si$): calc.: 409.9253; found: 409.9248.

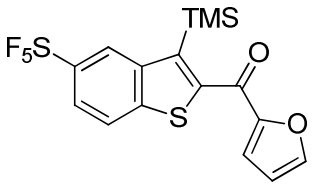
2-[5-(Pentafluorosulfanyl)-3-trimethylsilanyl-benzo[*b*]thiophen-2-ylmethyl]-acrylic acid ethyl ester (28a)



The title compound was prepared from the alkynyl(aryl)thioether **32** (617 mg, 1.5 mmol). A Br/Mg-exchange was performed according to **TP1** with *i*PrMgCl·LiCl (**6**) (1.3 mL, 1.27 M, 1.7 mmol) at 23 °C within 1 h. A mediated cyclization with CuCN·2LiCl (1.7 mL, 1.7 mmol, 1.0 M in THF) and a followed allylation reaction was performed according to **TP4** using 2-(bromomethyl)-acrylic acid ethyl ester (232 mg, 1.2 mmol) at 23°C within 12 h. Flash column chromatographical purification on silica gel (isohexane:Et_2O = 9:1) afforded **28a** as colorless oil (374 mg, 0.82 mmol, 70%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.83 – 7.77 (m, 1H), 7.72 – 7.66 (m, 1H), 7.56 (d, *J* = 2.5 Hz, 1H), 6.34 (d, *J* = 0.8 Hz, 1H), 5.43 (d, *J* = 0.8 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.69 (s, 2H), 1.30 (t, *J* = 7.2 Hz, 3H), 0.28 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.1, 152.6 – 151.2 (m), 137.4 – 127.3 (m), 136.9, 135.8, 127.4, 127.3 – 127.4 (m), 126.5, 125.4 – 124.7 (m), 108.7, 87.8, 61.1, 35.3, 14.1, -0.2.
^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 85.61 – 83.15 (m, 1F), 63.78 – 62.86 (m, 4F).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2963 (vw), 2100 (w), 1716 (m), 1634 (vw), 1469 (w), 1404 (w), 1370 (vw), 1301 (w), 1272 (w), 1251 (m), 1200 (w), 1134 (m), 1116 (w), 1048 (w), 1027 (w), 944 (vw), 904 (m), 877 (m), 836 (vs), 802 (vs), 759 (s), 741 (m), 702 (w), 679 (w), 662 (m), 630 (w).
MS (EI, 70 eV): *m/z* (%) = 444 (9), 415 (29), 401 (9), 171 (28), 88 (12), 86 (56), 84 (100), 75 (23), 73 (67), 71 (24), 57 (34), 56 (20), 49 (88), 47 (16), 44 (32), 43 (54).
HRMS ($C_{17}H_{21}F_5O_2S_2Si$): calc.: 444.0672; found: 444.0663.

Furan-2-yl-[5-(pentafluorosulfanyl)-3-trimethylsilanyl-benzo[*b*]thiophen-2-yl]-methanone (28b)



The title compound was prepared from the alkynyl(aryl)thioether **32** (617 mg, 1.5 mmol). A Br/Mg-exchange was performed according to **TP1** with *i*PrMgCl·LiCl (**6**) (1.3 mL, 1.27 M, 1.7 mmol) at 23°C within 1 h. A mediated cyclization with CuCN·2LiCl (1.7 mL, 1.7 mmol, 1.0 M in THF) and a followed allylation reaction was performed according to **TP4** using furan-2-carbonyl chloride (156 mg, 1.2 mmol) at 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:Et_2O = 9:1) afforded **28b** as yellow solid (325 mg, 0.76 mmol, 64%).

Mp.: 109-111 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.56 (d, *J* = 2.1 Hz, 1H), 8.00 (d, *J* = 9.1 Hz, 1H), 7.82 (dd, *J* = 8.9 Hz, 2.2 Hz, 1H), 7.77 (dd, *J* = 1.7 Hz, 0.6 Hz, 1H), 7.33 (dd, *J* = 3.7 Hz, 0.7 Hz, 1H), 6.66 (dd, *J* = 3.6, 1.7 Hz, 1H), 0.42 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 177.5, 152.5, 151.6 – 150.5 (m), 148.2, 147.5, 143.9, 143.3, 142.3, 124.6 – 123.9 (m), 122.8 – 122.5 (m), 122.4, 121.8, 112.8, 0.7.

^{19}F-NMR (280 MHz, $CDCl_3$): δ / ppm = 86.23 – 83.73 (m, 1F), 64.72 – 63.77 (m, 4F).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1627 (m), 1564 (w), 1467 (m), 1457 (w), 1407 (w), 1386 (w), 1285 (w), 1268 (m), 1246 (w), 1228 (w), 1158 (w), 1136 (w), 1100 (w), 1015 (w), 938 (w), 882 (w), 835 (s), 818 (vs), 794 (s), 757 (s), 752 (s), 744 (s), 719 (m), 674 (w), 662 (m), 644 (w), 628 (w), 611 (w).

MS (EI, 70 eV): *m/z* (%) = 426 (1), 412 (21), 411 (100), 284 (9), 74 (6), 59 (9).

HRMS ($C_{16}H_{15}F_5O_2S_2Si$): calc.: 426.0203; found: 426.0197.

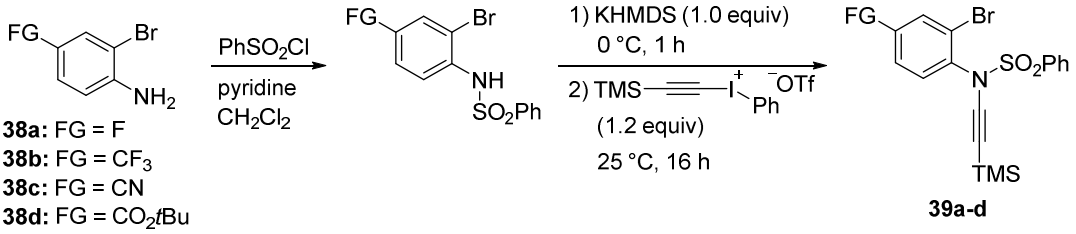
3. Preparation of Functionalized Indoles and Azaindolesvia an Intramolecular Copper-mediated Carbomagnesiation of Ynamides

3.1 Typical Procedures

Typical Procedure for the preparation of bromoanilines (38a-d):

Bromoanilines (**38a-d**) were prepared according to a literature procedure.[135]

Typical Procedure for the preparation of ynamides (39):



Scheme 57*:* Preparation of ynamides of type **39**.

Protection with $PhSO_2Cl$ (TP1):

N-(2-Bromophenyl)-benzenesulfonamides were prepared according to a literature procedure.[136] Benzenesulfonyl chloride (1.2 equiv) was added to a solution of **38** (1.0 equiv) and pyridine (3.0 equiv) in dichloromethane (1 M) at 0°C, and the reaction mixture was stirred at 0 °C for 1 h. The reaction solution was diluted with ether, washed with saturated aqueous $NaHCO_3$-solution and saturated aqueous NaCl-solution, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude residue was purified by flash column chromatography on silica gel.

Synthesis of ynamides of type 39, compounds 45, 52, 55, 58, 62 (TP2):

Phenyl((trimethylsilyl)ethynyl)iodonium triflate and the corresponding ynamides were prepared according to a literature procedure.[137]

1) A dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirrer and a septum was charged with $PhI(OAc)_2$ (13.86 g, 43 mmol) in CH_2Cl_2 (60 mL) and cooled to 0 °C. CF_3SO_3H (12.01 g, 7.1 mL, 80 mmol) was added dropwise using a glass pipette. After stirring at 0 °C for 0.5 h, bis(trimethylsilyl)acetylene (6.82 g, 40 mmol) was added. After stirring at 0 °C for 2 h, the resulting solution was concentrated in vacuo to give an oily residue. This oil was poured dropwise into stirred *n*-hexane (150 mL). The resulting solid was collected by filtration, washed with Et_2O, and dried in vacuo to give phenyl((trimethylsilyl)-ethynyl)iodonium triflate (1.35 g, 30 mmol, 75%).

Note: Although workup and crystallization procedures can be carried out in air, phenyl((trimethylsilyl)ethynyl)iodonium triflate should be stored under a dry inert atmosphere to avoid its decomposition.

2) Under argon, KHMDS (1.0 equiv) was added to a solution of *N*-(2-bromophenyl)-benzenesulfonamide (1.0 equiv) in toluene at 0 °C. After 1 h, phenyl((trimethylsilyl)-

[135]Y. Tobe, et al. *J. Am. Chem. Soc.* **2002**, *124*, 5350.
[136] H. Kunio, Y. Suzuki, I. Abe, Y. Hasegawa, K. Suzuki, *Tetrahedron: Asym.* **1998**, *9*, 3797.
[137] K. Tanaka, K. Takeishi, *Synthesis* **2007**, 2920.

ethynyl)iodonium triflate (1.2 equiv) was added in several portions. The resulting mixture was stirred for 16 h at 23 °C and filtered through a plug of silica gel. The crude residue was purified by flash column chromatography on silica gel.

Typical Procedure for Halogen/Magnesium-Exchange Reactions[138] (TP3):

A dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirrer and a septum was charged with the starting aryl bromide in THF (0.2-1.0 M solution) and cooled to the indicated temperature. Then *i*-PrMgCl·LiCl was added and the reaction mixture was stirred for the indicated time (the completion of the reaction was checked by HPLC analysis of reaction aliquots quenched with half concentrated aqueous NH_4Cl-solution).

Typical Procedure for the Copper-Mediated Cyclization Reaction (TP4):

After the completion of the halogen/magnesium-exchange (**TP3**), THF was added (0.05-0.2 M solution), CuCN·2LiCl solution (30-100 mol%, 1.0 M in THF) was added to the reaction mixture at the indicated temperature and stirred for the indicated time (the completion of the reaction was checked by HPLC analysis of reaction aliquots quenched with sat. aqueous NH_4Cl/NH_3-solution; typically two peaks with slightly differing retention time could be detected, corresponding to the open-chain and cyclized form).

Typical Procedure for Microwave-Assisted Reactions (TP5):

Microwave assisted reactions were carried out using a Biotage Initiator 2.5 system. The reaction mixture was therefore transferred into a dry and argon flushed microwave vial equipped with a stirring bar and septum pressure-cap. The reaction parameters (temperature, time, max. irradiation) are given for the respective substance.

Typical Procedure for Allylation or Acylation Reactions (TP6):

To the freshly prepared magnesium reagent was added CuCN·2LiCl (20-100 mol%, 1.0 M in THF) and the reaction mixture was stirred for 15 min at the indicated temperature unless copper was already present in the mixture from the cyclization step. The respective allyl bromide or acyl chloride was added and the reaction mixture was stirred for the indicated time at the indicated temperature. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1), extracted three times with EtOAc, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel.

Typical Procedure for the Conversion of the TMS-Group to Iodide (TP7):

To the respective TMS-substituted compound (approx. 0.2 M in CH_2Cl_2) was added iodine monochloride (ICl, 1.1 equiv) at 0 °C and the mixture was stirred for 5 min. The reaction mixture was quenched with sat. $Na_2S_2O_3$-solution, extracted three times with CH_2Cl_2, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel.

[138] a) A. Krasovskiy, P. Knochel, *Angew. Chem*.**2004**, *116*, 3396; *Angew. Chem. Int. Ed.***2004**,*43*, 3333; b) A. Krasovskiy, B. F. Straub, P. Knochel, *Angew. Chem.* **2006**, *118*, 165; *Angew. Chem. Int. Ed.* **2006**, *45*, 159.

Typical Procedure for Cross-coupling Reactions (TP8):

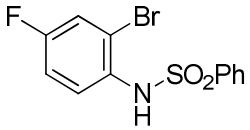
To the freshly prepared magnesium reagent was added $ZnCl_2$ (1.1 equiv, 1.0 M in THF) and the reaction mixture was stirred for 15 min at the indicated temperature. The catalytic system and the aryl halide (0.9-1.2 equiv) were added and the reaction mixture was warmed to 23 °C. After stirring for the indicated time, the reaction mixture was quenched with half concentrated aqueous NH_4Cl-solution, extracted three times with EtOAc, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel.

Typical Procedure for iodine/Magnesium exchange with MeMgCl (TP9):

A dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirrer and a septum was charged with the starting aryl iodine in THF (0.1 M solution) and cooled to -78 °C. Then MeMgCl (0.19 mL, 1.1 equiv, 0.55 mmol, 2.89 M in THF) was added and the reaction mixture was stirred for 0.5 h (the completion of the reaction was checked by HPLC analysis of reaction aliquots quenched with concentrated aqueous NH_4Cl-solution).

3.2 Synthesis of compounds of type 39

***N*-(2-Bromo-4-fluoro-phenyl)-benzenesulfonamide**



The title compound was prepared according to **TP1** from 2-bromo-4-fluoroaniline (**38a**) (5.0 mmol). Benzenesulfonyl chloride (1.06 g, 6.0 mmol) was added to a solution of 2-bromo-4-fluoroaniline (950 mg, 5.0 mmol) and pyridine (1.19 g, 1.21 mL, 15.0 mmol) in dichloromethane (5 mL) at 0 °C, and the reaction mixture was stirred at 0 °C for 1 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 7:3) afforded *N*-(2-bromo-4-fluoro-phenyl)-benzenesulfonamide (1.48 g, 4.8 mmol, 96%) as a brown powder.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.75 – 7.63 (m, 3H), 7.59 – 7.51 (m, 1H), 7.46 – 7.38 (m, 2H), 7.14 (dd, J = 7.7 Hz, J = 2.8 Hz, 1H), 7.07 – 6.98 (m, 1H), 6.79 (s_{br}, 1H).

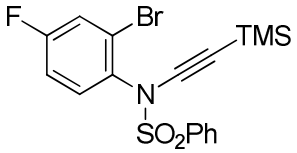
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 159.8 (d, J = 250.4 Hz), 138.6, 133.4, 130.9 (d, J = 3.4 Hz), 129.1, 127.3, 125.4 (d, J = 8.4 Hz), 119.7 (d, J = 25.5 Hz), 117.1 (d, J = 9.8 Hz), 115.7 (d, J = 22.2 Hz).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3256 (M), 1597 (W), 1486 (S), 1446 (M), 1421 (W), 1378 (M), 1337 (S), 1327 (M), 1309 (W), 1262 (M), 1249 (M), 1189 (W), 1167 (VS), 1129 (M), 1089 (M), 1069 (W), 1035 (M), 1026 (W), 1000 (W), 963 (W), 903 (M), 876 (S), 864 (S), 838 (S), 811 (W), 798 (M), 755 (M), 722 (VS), 700 (M), 684 (S), 672 (M).

MS (EI, 70 eV): m/z (%) = 332 (16), 331 (93), 329 (89), 191 (18), 190 (100), 188 (97), 185 (39), 109 (31), 77 (38).

HRMS ($C_{12}H_9BrFNO_2S$): calc.: 328.9521; found: 328.9502.

***N*-(2-Bromo-4-fluoro-phenyl)-*N*-trimethylsilanylethynyl-benzenesulfonamide (39a)**



The title compound was prepared according to **TP2** from *N*-(2-bromo-4-fluoro-phenyl)-benzenesulfonamide (13.0 mmol). Under argon, KHMDS (18.6 mL, 13.0 mmol, 0.7 M in toluene) was added to a solution of *N*-(2-bromo-4-fluoro-phenyl)-benzenesulfonamide (4.29 g, 13.0 mmol) in toluene (130 mL) at 0 °C. After 1 h, phenyl((trimethylsilyl)-ethynyl)iodonium triflate (6.97 g, 15.5 mmol) was added in several portions. The resulting mixture was stirred for 16 h at 23 °C. Flash column chromatographical purification on silica gel (isohexane:Et_2O:CH_2Cl_2 = 8:2:0.2) afforded *N*-(2-bromo-4-fluoro-phenyl)-*N*-trimethylsilanylethynyl-benzenesulfonamide (**39a**; 4.21 g, 9.9 mmol, 76%) as an orange oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.89 – 7.83 (m, 2H), 7.73 – 7.65 (m, 1H), 7.59 – 7.52 (m, 2H), 7.34 (dd, *J* = 8.0 Hz, *J* = 2.8 Hz, 1H), 7.24 – 7.18 (m, 1H), 7.06 – 6.98 (m, 1H), 0.14 (s, 9H).

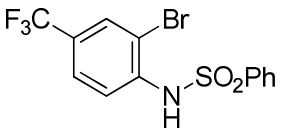
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 162.2 (d, *J* = 250.4 Hz), 136.9, 134.1, 133.3 (d, *J* = 3.7 Hz), 131.5 (d, *J* = 9.3 Hz), 128.9, 128.6, 124.3 (d, *J* = 10.1 Hz), 121.3 (d, *J* = 25.5 Hz), 115.4 (d, *J* = 22.7 Hz), 93.6, 73.8, -0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2968 (VW), 2961 (VW), 2162 (W), 2137 (VW),1592 (W), 1584 (W), 1483 (M), 1448 (W), 1392 (VW), 1373 (M), 1357 (W), 1335 (W), 1311 (VW), 1286 (VW), 1257 (M), 1245 (M), 1205 (M), 1176 (S), 1143 (W), 1125 (W), 1097 (VW), 1088 (M), 1071 (VW), 1034 (W), 1021 (VW), 999 VW912 (W), 863 (S), 843 (VS), 798 (W), 794 (W), 784 (W), 755 (S), 729 (S), 720 (S), 699 (W), 685 (S), 675 (M), 663 (S).

MS (EI, 70 eV): m/z (%) = 428 (27), 427 (100), 426 (26), 425 (89), 412 (63), 284 (54), 271 (16), 205 (97), 204 (30), 190 (20), 183 (30), 162 (35), 139 (21), 137 (21), 135 (98).

HRMS ($C_{17}H_{17}BrFNO_2SSi$): calc.: 424.9917; found: 424.9901.

***N*-(2-Bromo-4-trifluoromethyl-phenyl)-benzenesulfonamide**

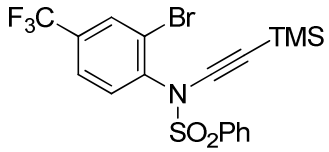


The title compound was prepared according to **TP1** from 2-bromo-4-(trifluoromethyl)aniline (**38b**) (40.0 mmol). Benzenesulfonyl chloride (8.48 g, 48.0 mmol) was added to a solution of 2-bromo-4-(trifluoromethyl)aniline (9.60 g, 40.0 mmol) and pyridine (9.49 g, 9.7 mL, 120.0 mmol) in dichloromethane (40 mL) at 0 °C, and the reaction mixture was stirred at 23 °C for 4 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded *N*-(2-bromo-4-trifluoromethyl-phenyl)-benzenesulfonamide (14.32 g, 38.0 mmol, 95%) as a colorless powder.

Mp.: 84-86 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.86 – 7.80 (m, 2H), 7.76 (dd, *J* = 8.7 Hz, 0.7 Hz, 1H), 7.70 (d, *J* = 1.9 Hz, 1H), 7.63 – 7.56 (m, 1H), 7.55 – 7.45 (m, 3H), 7.21 (s_{br}, 1H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 138.7, 137.9, 133.7, 129.8 (q, *J* = 3.7 Hz), 129.3, 127.8 (q, *J* = 33.7 Hz), 127.2, 125.7 (q, *J* = 3.9 Hz), 120.8, 114.4.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3265 (W), 3250 (W), 1608 (W), 1499 (W), 1449 (M), 1421 (M), 1384 (M), 1362 (W), 1346 (M), 1317 (VS), 1272 (M), 1231 (W), 1167 (S), 1138 (S), 1119 (VS), 1091 (M), 1080 (VS), 1045 (M), 1023 (W), 998 (W), 962 (W), 956 (W), 930 (W), 905 (S), 892 (S), 845 (M), 820 (M), 809 (W), 783 (W), 756 (M), 719 (S), 703 (M), 693 (M), 684 (VS), 653 (S).
MS (EI, 70 eV): m/z (%) = 381 (24), 379 (23), 235 (13), 78 (18), 77 (100), 64 (32).
HRMS ($C_{13}H_9BrF_3NO_2S$): calc.: 378.9489; found: 378.9480.

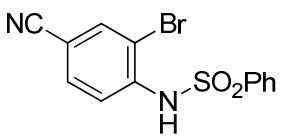
***N*-(2-Bromo-4-trifluoromethyl-phenyl)-*N*-trimethylsilanylethynyl-benzenesulfonamide (39b)**



The title compound was prepared according to **TP2** from *N*-(2-bromo-4-trifluoromethyl-phenyl)-benzenesulfonamide (5.0 mmol). Under argon, KHMDS (10 mL, 5.0 mmol, 0.5 M in toluene) was added to a solution of *N*-(2-bromo-4-trifluoromethyl-phenyl)-benzenesulfonamide (1.90 g, 5.0 mmol) in toluene (50 mL) at 0 °C. After 1 h, phenyl((trimethylsilyl)ethynyl)iodonium triflate (2.70 g, 6.0 mmol) was added in several portions. The resulting mixture was stirred for 16 h at 23 °C. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded *N*-(2-bromo-4-trifluoromethyl-phenyl)-*N*-trimethylsilanylethynyl-benzenesulfonamide (**39b**; 1.89 g, 4.0 mmol, 79%) as a yellow solid.

Mp.: 91-93 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.90 – 7.84 (m, 3H), 7.75 – 7.68 (m, 1H), 7.60 – 7.53 (m, 3H), 7.38 (d, *J* = 7.7 Hz, 1H), 0.14 (s. 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 140.1, 136.8, 134.3, 132.5 (q, *J* = 33.7 Hz), 131.4 (q, *J* = 3.7 Hz), 130.9, 129.0, 128.6, 125.2 (q, *J* = 3.7 Hz), 123.9, 122.6 (q, *J* = 273.3 Hz), 92.9, 74.7, -0.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2960 (VW), 2165 (M), 1606 (W), 1449 (M), 1380 (M), 1319 (VS), 1250 (M), 1172 (S), 1130 (VS), 1088 (M), 1077 (S), 1047 (M), 1005 (VW), 999 (W), 923 (W), 890 (M), 839 (VS), 807 (M), 756 (S), 724 (VS), 705 (S), 684 (S), 674 (S), 654 (M).
MS (EI, 70 eV): m/z (%) = 477 (18), 475 (16), 463 (16), 462 (65), 460 (57), 255 (22), 135 (100).
HRMS ($C_{18}H_{17}BrF_3NO_2SSi$): calc.: 474.9885; found: 474.9890.

***N*-(2-Bromo-4-cyano-phenyl)-benzenesulfonamide**



The title compound was prepared according to **TP1** from 4-amino-3-bromo-benzonitrile (**38d**) (20.0 mmol). Benzenesulfonyl chloride (4.24 g, 24.0 mmol) was added to a solution of 4-amino-3-bromo-benzonitrile (3.94 g, 20.0 mmol) and pyridine (4.75 g, 4.85 mL, 60.0 mmol) in dichloromethane (20 mL) at 0 °C, and the reaction mixture was stirred at 23 °C for 48 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2→1:1) afforded *N*-(2-bromo-4-cyano-phenyl)-benzenesulfonamide (3.13 g, 9.0 mmol, 46%) as a colorless solid.

^{1}H-NMR (600 MHz, $CDCl_3$): δ / ppm =7.91 (d, *J* = 1.9 Hz, 1H), 7.86 – 7.82 (m, 2H), 7.73 – 7.70 (m, 1H), 7.63 – 7.59 (m, 2H), 7.54 (dd, *J* = 8.6 Hz, *J* = 1.8 Hz, 1H), 7.33 (s_{br}, 1H), 7.23 (d, *J* = 8.0 Hz, 1H).

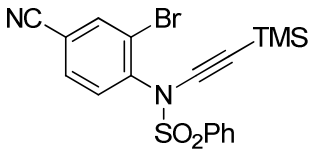
^{13}C-NMR (150 MHz, $CDCl_3$): δ / ppm = 138.9, 138.9, 138.4, 138.3, 137.5, 134.4, 131.4, 128.2, 116.9, 116.3, 114.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3192 (W), 2236 (W), 1600 (W), 1552 (VW), 1493 (M), 1475 (M), 1449 (M), 1421 (M), 1384 (S), 1363 (M), 1346 (M), 1340 (M), 1314 (W), 1285 (W), 1263 (W), 1238 (W), 1229 (W), 1173 V(S), 1152 (M), 1087 (S), 1074 (W), 1051 (W), 1046 (M), 1022 (W), 998 (W), 973 (W), 934 (M), 899 V(S), 886 (S), 866 (W), 852 (M), 842 (M), 823 (M), 757 V(S), 721 (S), 708 (M), 683 V(S), 675 (M).

MS (EI, 70 eV): m/z (%) = 336 (38), 192 (20), 77 (100).

HRMS ($C_{13}H_9BrN_2O_2S$): calc.: 335.9568; found: 335.9564.

***N*-(2-Bromo-4-cyano-phenyl)-*N*-trimethylsilanylethynyl-benzenesulfonamide (39d)**



The title compound was prepared according to **TP2** from *N*-(2-bromo-4-cyano-phenyl)-benzenesulfonamide (16.0 mmol). Under argon, KHMDS (22.9 mL, 16.0 mmol, 0.7 M in toluene) was added to a solution of *N*-(2-bromo-4-cyano-phenyl)-benzenesulfonamide (5.40 g, 16.0 mmol) in toluene (160 mL) at 0 °C. After 1 h, phenyl((trimethylsilyl)-ethynyl)iodonium triflate (8.56 g, 19.0 mmol) was added in several portions. The resulting mixture was stirred for 16 h at 23 °C. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded *N*-(2-bromo-4-cyano-phenyl)-*N*-trimethylsilanyl-ethynyl-benzenesulfonamide (**39d**; 3.12 g, 7.2 mmol, 45%) as a yellow oil.

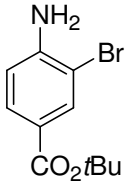
^{1}H-NMR (600 MHz, $CDCl_3$): δ / ppm = 7.90 (d, *J* = 1.9 Hz, 1H), 7.85 (dd, *J* = 8.5 Hz, *J* = 1.4 Hz, 2H), 7.74 – 7.70 (m, 1H), 7.61 (dd, *J* = 8.2 Hz, *J* = 1.9 Hz, 1H), 7.59 – 7.55 (m, 2H), 7.38 (d, *J* = 8.5 Hz, 1H), 0.14 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 141.1, 137.6, 136.6, 134.5, 131.8, 131.2, 129.1, 128.6, 124.1, 116.4, 114.5, 94.5, 75.2, -0.13.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (VW), 2233 (W), 2163 (M), 1476 (W), 1448 (W), 1381 (M), 1247 (M), 1183 (M), 1170 (S), 1156 (W), 1086 (M), 1045 (W), 919 (W), 882 (W), 842 (VS), 817 (M), 758 (M), 722 (S), 685 (S), 661 (M).

MS (EI, 70 eV): m/z (%) = 434 (44), 432 (39), 416 (76), 279 (34), 277 (32), 212 (22), 199 (21), 183 (15), 137 (18), 135 (100), 77 (41).
HRMS ($C_{18}H_{17}BrN_2O_2SSi$): calc.: 431.9963; found: 431.9968.

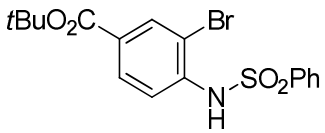
4-Amino-3-bromo-benzoic acid *tert*-butyl ester (38c)



4-Aminobenzoic acid (6.86 g, 50 mmol) was suspended in $SOCl_2$ (60 mL, 11.71 g, 98.4 mmol) at 23 °C. The suspension was refluxed for 2 h. $SOCl_2$ was removed under reduced pressure, the last traces by azeotrope with CH_2Cl_2 (3x50 mL). The resulting acid chloride was dissolved in CH_2Cl_2 (60 mL) and a solution of *t*-butanol (20 mL) in CH_2Cl_2 (20 mL) was added to the stirred solution, which was cooled to 0 °C. A solid white precipitate was formed - the hydrochloride salt of the title compound. This salt was isolated by evaporation of the solvent (CH_2Cl_2), followed by suspension of the solid in EtOAc (100 mL) and filtration. The material was suspended in 10% aqueous $NaHCO_3$-solution (100 mL) and extracted into CH_2Cl_2 (3 x 100 mL) to give 4-amino-benzoic acid *tert*-butyl ester (5.56 g, 58%) as a yellow oil. An additional bromination with NBS (5.59 g, 31.4 mmol, 1.0 equiv) according to a literature procedure starting from 4-amino-benzoic acid *tert*-butyl ester (6.07 g, 31.4 mmol) afforded 4-amino-3-bromo-benzoic acid *tert*-butyl ester (**38c**; 8.38 g, 30.8 mmol, 98%) as a brown oil.[139]

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.03 (d, J = 1.8 Hz, 1H), 7.73 (dd, J = 8.4 Hz, J = 1.9 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 4.44 (s_{br}, 2H), 1.55 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 164.7, 147.7, 134.3, 130.0, 122.8, 114.2, 107.8, 80.6, 28.2.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3479 (W), 3474 (W), 3361 (W), 3211 (VW), 2976 (W), 2931 (W), 1775 (W), 1689 (S), 1614 (S), 1595 (S), 1555 (W), 1504 (M), 1473 (W), 1455 (W), 1410 (W), 1392 (M), 1367 (M), 1294 V(S), 1247 V(S), 1167 V(S), 1151 V(S), 112(S), 1033 (M), 904 (M), 890 (M), 849 (M), 827 (M), 765 (S), 731 (M), 706 (M), 692 (S), 677 (S).
MS (EI, 70 eV): m/z (%) = 295 (5), 273 (15), 271 (15), 215 (100), 200 (47), 198 (49), 91 (15), 90 (22).
HRMS ($C_{11}H_{14}BrNO_2$): calc.: 271.0208; found: 271.0203.

4-Benzenesulfonylamino-3-bromo-benzoic acid *tert*-butyl ester



The title compound was prepared according to **TP1** from 4-amino-3-bromo-benzoic acid *tert*-butyl ester (**38c**) (31.0 mmol). Benzenesulfonyl chloride (6.54 g, 37.0 mmol) was added to a solution of 4-amino-3-bromo-benzoic acid *tert*-butyl ester (8.44 g, 31.0 mmol) and pyridine

[139] Y. Tobe, et al. *J. Am. Chem. Soc.* **2002**, *124*, 5350.

(7.36 g, 7.5 mL, 93.0 mmol) in dichloromethane (31 mL) at 0 °C, and the reaction mixture was stirred at 23 °C for 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2, 5% NEt_3) afforded 4-benzenesulfonylamino-3-bromo-benzoic acid *tert*-butyl ester (11.56 g, 28.0 mmol, 90%) as a colorless solid.

Mp.: 121-123 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.02 (d, J = 1.9 Hz, 1H), 7.85 (dd, J = 8.6 Hz, J = 1.9 Hz, 1H), 7.82 – 7.77 (m, 2H), 7.67 (d, J = 8.6 Hz, 1H), 7.58 – 7.51 (m, 1H), 7.48 – 7.40 (m, 2H), 7.24 (s_{br}, 1H), 1.54 (s, 9H).

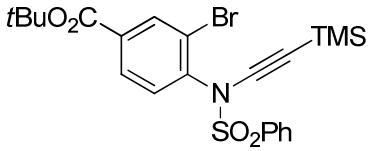
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 163.7, 138.6, 138.1, 133.8, 133.6, 129.8, 129.4, 129.2, 127.2, 120.2, 114.1, 81.8, 28.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1717 (M), 1477 (W), 1448 (M), 1382 (S), 1363 (M), 1341 (W), 1296 (M), 1276 (M), 1253 (M), 1169 (S), 1160 (S), 1121 (M), 1086 (M), 1043 (M), 970 (W), 915 (S), 901 (S), 878 (M), 847 (M), 830 (M), 774 (W), 762 (M), 755 (S), 736 (M), 721 (VS), 699 (M), 690 (M), 684 (S).

MS (EI, 70 eV): m/z (%) = 413 (26), 411 (26), 357 (81), 355 (76), 340 (23), 338 (22), 199 (49), 197 (51), 141 (79), 125 (22).

HRMS ($C_{17}H_{18}BrNO_4S$): calc.: 411.0140; found: 411.0138.

4-Benzenesulfonyl-trimethylsilanylethynyl-amino)-3-bromo-benzoic acid *tert*-butyl ester (39c)



The title compound was prepared according to **TP2** from 4-benzenesulfonylamino-3-bromo-benzoic acid *tert*-butyl ester (10.0 mmol). Under argon, KHMDS (14.3 mL, 10.0 mmol, 0.7 M in toluene) was added to a solution of 4-benzenesulfonylamino-3-bromo-benzoic acid *tert*-butyl ester (4.12 g, 10.0 mmol) in toluene (100 mL) at 0 °C. After 1 h, phenyl((trimethylsilyl)ethynyl)iodonium triflate (5.4 g, 12.0 mmol) was added in several portions. The resulting mixture was stirred for 16 h at 23 °C. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2, 5% NEt_3) afforded 4-benzenesulfonyl-trimethylsilanylethynyl-amino)-3-bromo-benzoic acid *tert*-butyl ester (**39c**; 3.5 g, 6.9 mmol, 69%) as an orange solid.

Mp.: 111-113 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.19 (d, J = 1.7 Hz, 1H), 7.90 (dd, J = 8.3 Hz, J = 1.9 Hz, 1H), 7.87 – 7.82 (m, 2H), 7.72 – 7.66 (m, 1H), 7.59 – 7.51 (m, 2H), 7.27 (d, J = 8.3 Hz, 1H), 1.57 (s, 9H), 0.13 (s, 9H).

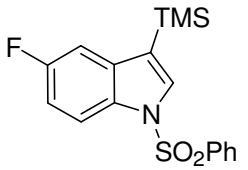
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 163.4, 140.2, 136.9, 135.1, 134.2, 134.1, 130.1, 129.1, 129.0, 128.6, 123.2, 93.3, 82.3, 74.3, 28.1, -0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2961 (VW), 2165 (M), 1719 (S), 1592 (W), 1561 (VW), 1478 (W), 1452 (W), 1395 (W), 1378 (M), 1367 (M), 1297 (S), 1247 (M), 1184 (M), 1172 (S),

1140 (M), 1112 (S), 1088 (M), 1041 (M), 905 (W), 842 (VS), 779 (M), 754 (S), 737 (W), 722 (S), 713 (M), 686 (S), 668 (S).
MS (EI, 70 eV): m/z (%) = 509 (30), 507 (27), 438 (44), 436 (55), 312 (67), 310 (66), 295 (25), 293 (22), 231 (37), 199 (33), 167 (23), 137 (21).
HRMS ($C_{22}H_{26}BrNO_4SSi$): calc.: 507.0535; found: 507.0548.

3.3 Synthesis of compounds of type 41

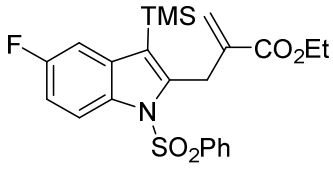
1-Benzenesulfonyl-5-fluoro-3-trimethylsilanyl-1*H*-indole (41a)



The title compound was prepared from the ynamide **39a** (468 mg, 1.1 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.39 M, 1.21 mmol, 1.1 equiv) at -10 °C within 0.5 h (1.0 M). After addition of THF (1 mL), a CuCN·2LiCl (0.33 mL, 30 mol%) mediated cyclization was performed according to **TP4** at 23 °C in 24 h. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1), extracted three times with EtOAc, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 95:5) afforded the indole **41a** (356 mg, 1.02 mmol, 93%) as a white solid.

Mp.: 103-105 °C.
^{1}H-NMR (600 MHz, $CDCl_3$): δ / ppm = 7.93 – 7.88 (m, 3H), 7.59 – 7.55 (m, 2H), 7.50 – 7.46 (m, 2H), 7.23 (dd, J = 9.1 Hz, J = 2.5 Hz, 1H), 7.04 (td, J = 9.1 Hz, J = 2.3 Hz, 1H), 0.35 (s, 9H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ / ppm = 159.4 (d, J = 239.5 Hz), 138.2, 135.6 (d, J = 9.8 Hz), 133.9, 133.0, 132.3 (d, J = 1.1 Hz), 129.3, 126.7, 118.4 (d, J = 4.2 Hz), 114.3 (d, J = 9.5 Hz), 112.2 (d, J = 25.5 Hz), 107.8 (d, J = 23.6 Hz), -0.9.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (W), 2926 (W), 2922 (W), 1705 (W), 1582 (W), 1515 (W), 1483 (W), 1475 (W), 1458 (M), 1447 (M), 1370 (M), 1349 (W), 1338 (W), 1313 (W), 1289 (W), 1258 (M), 1250 (M), 1235 (W), 1214 (W), 1195 (M), 1176 (S), 1164 (M), 1155 (S), 1144 (S), 1111 (M), 1091 (S), 1070 (M), 1055 (M), 1045 (M), 1034 (M), 1018 (M), 998 (M), 975 (M), 951 (W), 930 (W), 891 (W), 868 (S), 852 (S), 835 (S), 828 (S), 817 (S), 810 (VS), 771 (M), 756 (S), 740 (M), 723 (VS), 696 (M), 684 (S), 659 (M).
MS (EI, 70 eV): m/z (%) = 349 (11), 348 (27), 347 (100), 333 (21), 332 (90), 134 (9), 77 (14).
HRMS ($C_{17}H_{18}FNO_2SSi$): calc.: 347.0812; found: 347.0810.

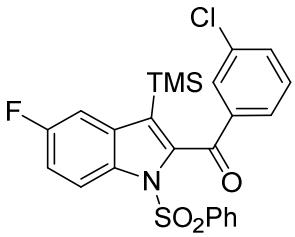
2-(1-Benzenesulfonyl-5-fluoro-3-trimethylsilanyl-1*H*-indol-2-ylmethyl)acrylic acid ethyl ester (41b)



The title compound was prepared from the ynamide **39a** (1.28 g, 3.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (2.6 mL, 1.27 M, 3.3 mmol, 1.1 equiv) at -10 °C within 0.5 h (1.0 M). After addition of THF (12 mL), a CuCN·2LiCl (1.0 mL, 30 mol%) mediated cyclization according to **TP4** at 23 °C in 24 h and a subsequent allylation reaction was performed according to **TP6** using ethyl 2-(bromomethyl)acrylate (521 mg, 2.7 mmol) at 0 °C within 2 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the indole **41b** (1.14 g, 2.48 mmol, 92%) as a yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ / ppm = 8.17 (dd, J = 9.3 Hz, J = 4.7 Hz, 1H), 7.76 – 7.72 (m, 2H), 7.54 – 7.50 (m, 1H), 7.43 – 7.39 (m, 2H), 7.27 (dd, J = 9.4 Hz, J = 2.6 Hz, 1H), 7.01 (dt,J = 9.0 Hz, J = 2.6 Hz, 1H), 6.18 – 6.16 (m, 1H), 5.03 – 5.02 (m, 1H), 4.09 (s_{br}, 2H), 4.29 (q, J = 7.2 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H), 0.32 (s, 9H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ / ppm = 166.4, 159.4 (d, J = 239.5 Hz), 143.6, 139.1, 138.9, 134.8 (d, J = 9.5 Hz), 133.9 (d, J = 1.1 Hz), 133.8, 129.2, 126.4, 125.1, 118.2 (d, J = 3.9 Hz), 115.7 (d, J = 9.3 Hz), 111.7 (d, J = 25.0 Hz), 107.2 (d, J = 23.5 Hz), 61.0, 30.4, 14.2, 0.4.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2956 (W), 1711 (M), 1635 (W), 1610 (W), 1584 (W), 1536 (W), 1462 (M), 1447 (M), 1407 (W), 1368 (S), 1349 (W), 1334 (W), 1310 (W), 1278 (M), 1251 (S), 1214 (M), 1189 (S), 1170 (M), 1145 (S), 1135 (S), 1118 (M), 1092 (S), 1024 (M), 999 (W), 987 (M), 933 (M), 913 (M), 852 (VS), 838 (S), 813 (S), 756 (M), 747 (M), 724 (VS), 685 (S), 659 (M).
MS (EI, 70 eV): m/z (%) = 459 (10), 445 (20), 444 (63), 370 (43), 319 (26), 318 (100), 275 (25), 258 (20), 230 (15), 226 (33), 200 (45), 172 (30).
HRMS ($C_{23}H_{26}FNO_4SSi$): calc.: 459.1336; found: 459.1328.

(1-Benzenesulfonyl-5-fluoro-3-trimethylsilanyl-1*H*-indol-2-yl)-(3-chloro-phenyl)-methanone (41c)



The title compound was prepared from the ynamide **39a** (1.28 g, 3.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (2.6 mL, 1.27 M, 3.3 mmol, 1.1 equiv) at -10 °C within 0.5 h (1.0 M). After addition of THF (12 mL), a CuCN·2LiCl (1.0 mL, 30 mol%) mediated cyclization according to **TP4** at 23 °C in 24 h and a subsequent acylation reaction was performed according to **TP6** using 3-chlorobenzoyl chloride (473 mg, 2.7 mmol) at 0 °C within 2 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the indole **41c** (1.2 g, 2.47 mmol, 92%) as a yellow solid.

Mp.: 138-140 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.06 – 8.00 (m, 1H), 7.89 (t, *J* = 1.8 Hz, 1H), 7.88 – 7.84 (m, 2H), 7.73 -7.68 (m, 1H), 7.58 – 7.50 (m, 2H), 7.47 – 7.37 (m, 3H), 7.33 – 7.28 (m, 1H), 7.12 (dt, *J* = 8.9 Hz, *J* = 2.5 Hz, 1H), 0.18 (s, 9H).

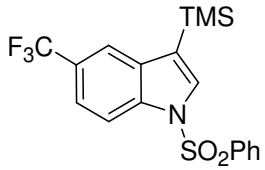
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 189.9, 159.8 (d, *J* = 241.6 Hz) 142.0, 139.8, 136.7, 135.2, 135.1, 134.2, 133.7, 132.4 (d, *J* = 1.1 Hz), 130.0, 129.1, 129.0, 127.9, 127.3, 121.0 (d, *J* = 4.1 Hz), 115.7 (d, *J* = 9.3 Hz), 113.7 (d, *J* = 25.4 Hz), 108.7 (d, *J* = 24.0 Hz), -0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1670 (M), 1586 (W), 1517 (W), 1458 (M), 1447 (M), 1425 (M), 1375 (S), 1307 (M), 1252 (S), 1218 (M), 1192 (VS), 1175 (S), 1148 (S), 1114 (M), 1090 (M), 1075 (M), 1072 (M), 991 (M), 871 (S), 863 (S), 844 (VS), 812 (S), 805 (S), 768 (S), 754 (S), 746 (S), 723 (VS), 698 (S), 687 (S), 675 (M), 667 (M).

MS (EI, 70 eV): m/z (%) = 487 (13), 485 (27), 472 (30), 471 (20), 470 (66), 344 (19), 331 (46), 330 (42), 329 (100), 314 (15), 235 (21).

HRMS ($C_{24}H_{21}ClFNO_3SSi$): calc.: 485.0684; found: 485.0681.

1-Benzenesulfonyl-5-trifluoromethyl-3-trimethylsilanyl-1*H*-indole (41d)



The title compound was prepared from the ynamide **39b** (476 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -20 °C within 0.25 h (0.5 M). After addition of THF (4 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 12 h. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1), extracted three times with EtOAc, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the indole **41d** (303 mg, 0.76 mmol, 76%) as a white solid.

Mp.: 70-72 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.08 – 8.03 (m, 1H), 7.94 – 7.89 (m, 2H), 7.83 – 7.80 (m, 1H), 7.61 – 7.60 (m, 1H), 7.59 – 7.45 (m, 4H), 0.36 (s, 9H).

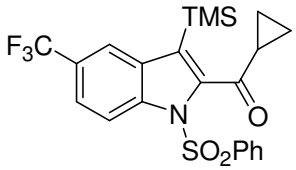
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 138.1, 137.5, 134.3, 134.2, 132.9, 129.5, 126.8, 125.6 (q, *J* = 32.6 Hz), 124.5 (q, *J* = 272.1 Hz), 122.7, 121.2 (q, *J* = 3.6 Hz), 119.5 (q, *J* = 4.1 Hz), 119.1, 118.7, 113.7, -0.8.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1519 (W), 1466 (W), 1448 (W), 1436 (W), 1371 (M), 1364 (M), 1339 (W), 1329 (S), 1313 (M), 1285 (M), 1275 (W), 1264 (W), 1253 (M), 1174 (S), 1167 (S), 1132 (M), 1117 (VS), 1089 (M), 1073 (W), 1062 (M), 1043 (M), 1026 (W), 1021 (W), 999 (W), 956 (M), 893 (M), 840 (S), 820 (S), 798 (M), 773 (M), 764 (M), 751 (S), 728 (S), 703 (S), 686 (S), 675 (W), 668 (M).

MS (EI, 70 eV): m/z (%) = 398 (11), 397 (62), 383 (24), 382 (100), 242 (19), 241 (14), 183 (16), 180 (11), 178 (13), 135 (13), 109 (10), 77 (46).

HRMS ($C_{18}H_{18}F_3NO_2SSi$): calc.: 397.0780; found: 397.0778.

(1-Benzenesulfonyl-5-trifluoromethyl-3-trimethylsilanyl-1*H*-indol-2-yl)-cyclopropyl-methanone (41e)



The title compound was prepared from the ynamide **39b** (476 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -20 °C within 0.25 h (0.5 M). After addition of THF (4 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 8 h and a subsequent acylation reaction was performed according to **TP6** using cyclopropanecarbonyl chloride (94 mg, 0.9 mmol) at -30 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the indole **41e** (396 mg, 0.85 mmol, 85%) as a white solid.

Mp.: 126-128 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 819 – 8.14 (m, 1H), 7.88 – 7.85 (m, 1H), 7.80 – 7.75 (m, 2H); 7.61 – 7.54 (m, 1H), 7.53 – 7.46 (m, 1H), 7.42 – 7.34 (m, 2H), 2.53 – 2.43 (m, 1H), 1.49 – 1.41 (m, 2H), 1.30 – 1.21 (m, 2H), 0.33 (s, 9H).

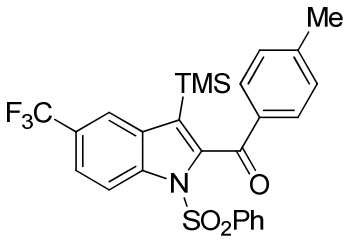
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 200.5, 146.1, 138.3, 136.3, 134.3, 134.2, 129.0, 127.2, 126.5 (q, J = 32.3 Hz), 124.3 (q, J = 272.2 Hz), 122.3 (q, J = 3.4 Hz), 120.4 (q, J = 4.2 Hz), 120.4, 115.4, 25.1, 15.1, 0.2.

IR (Diamond-ATR, neat): $\tilde{V}$ / cm^{-1} = 2961 (VW), 2168 (W), 1695 (M), 1613 (W), 1583 (VW), 1523 (W), 1477 (VW), 1448 (M), 1369 (S), 1357 (W), 1342 (W), 1327 (S), 1296 (W), 1265 (M), 1252 (M), 1238 (M), 1174 (S), 1153 (S), 1134 (S), 1118 (VS), 1090 (S), 1064 (S), 1049 (W), 1037 (M), 1003 (S), 982 (W), 958 (M), 888 (M), 878 (M), 841 (VS), 829 (VS), 786 (M), 773 (M), 764 (M), 752 (S), 725 (S), 702 (M), 688 (S), 677 (S), 654 (M).

MS (EI, 70 eV): m/z (%) = 465 (12), 452 (13), 451 (30), 450 (100), 310 (43), 309 (55), 294 (26), 77 (21).

HRMS ($C_{22}H_{22}F_3NO_3SSi$): calc.: 465.1042; found: 465.1038.

(1-Benzenesulfonyl-5-trifluoromethyl-3-trimethylsilanyl-1*H*-indol-2-yl)-*p*-tolyl-methanone (41f)



The title compound was prepared from the ynamide **39b** (476 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -20 °C within 0.25 h (0.5 M). After addition of THF (4 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 8 h and a subsequent acylation reaction was

performed according to **TP6** using 4-methylbenzoyl chloride (139 mg, 0.9 mmol) at -20 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the indole **41f** (401 mg, 0.78 mmol, 78%) as an orange solid.

Mp.:152-154 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.21 – 8.15 (m, 1H), 7.99 – 7.91 (m, 3H), 7.80 – 7.74 (m, 2H), 7.64 – 7.59 (m, 1H), 7.57 – 7.52 (m, 1H), 7.50 – 7.42 (m, 2H), 7.30 – 7.25 (m, 2H), 2.43 (s, 3H), 0.19 (s, 9H).

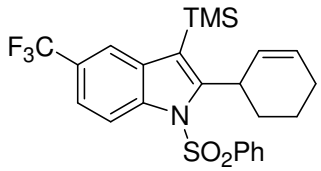
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 190.7, 145.1, 142.7, 137.5, 137.1, 135.8, 134.3, 133.8, 129.7, 129.5, 129.3, 127.4, 126.2 (q, J = 32.5 Hz), 124.4 (q, J = 272.3 Hz), 122.0 (q, J = 3.4 Hz), 120.0 (q, J = 3.9 Hz), 119.0, 114.7, 21.8, -0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2956 (W), 1669 (M), 1599 (M), 1569 (W), 1526 (W), 1448 (M), 1367 (M), 1333 (M), 1313 (S), 1264 (M), 1250 (M), 1228 (M), 1190 (M), 1167 (VS), 1133 (S), 1116 (VS), 1095 (S), 1063 (S), 1017 (M), 996 (M), 965 (M), 957 (M), 887 (M), 840 (S), 826 (S), 790 (M), 781 (S), 772 (M), 753 (S), 725 (VS), 702 (M), 684 (S), 658 (M).

MS (EI, 70 eV): m/z (%) = 516 (8), 515 (23), 501 (22), 500 (58), 374 (17), 361 (16), 360 (52), 359 (100), 344 (22), 285 (12), 119 (30), 91 (22), 77 (22).

HRMS ($C_{26}H_{24}F_3NO_3SSi$): calc.: 515.1198; found: 515.1191.

1-Benzenesulfonyl-2-cyclohex-2-enyl-5-trifluoromethyl-3-trimethylsilanyl-1*H*-indole (41g)



The title compound was prepared from the ynamide **39b** (476 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -20 °C within 0.25 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 8 h and a subsequent allylation reaction was performed according to **TP6** using 3-bromocyclohexene (94 mg, 0.9 mmol) at -30 °C.The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 95:5) afforded the indole **41g** (312 mg, 0.65 mmol, 65%) as a yellow oil.

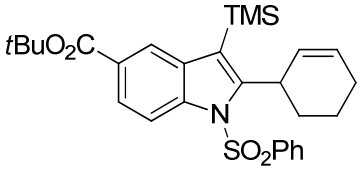
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.27 (d, J = 8.8 Hz, 1H), 7.95 – 7.92 (m, 1H), 7.73 – 7.67 (m, 2H), 7.59 -7.52 (m, 1H), 7.49 -7.40 (m, 3H), 5.77 – 5.70 (m, 1H), 5.49 -5.42 (m, 1H), 4.39 – 4.31 (m, 1H), 2.26 – 2.13 (m, 2H), 2.12 – 2.03 (m, 1H), 19.6 – 1.84 (m, 2H), 1.75 – 1.62 (m, 1H), 0.42 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 152.8, 139.7, 139.5, 133.8, 133.8, 129.3, 128.7, 127.9, 126.3, 125.1 (q, J = 31.9 Hz), 124.7 (q, J = 271.7 Hz), 120.3 (q, J = 3.5 Hz), 118.9 (q, J = 4.2 Hz), 116.7, 115.2, 38.0, 29.5, 24.2, 23.2, 2.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2950 (W), 1612 (W), 1518 (W), 1448 (M), 1374 (M), 1328 (VS), 1285 (M), 1253 (M), 1167 (S), 1117 (VS), 1090 (S), 1069 (S), 1046 (M), 994 (M), 958 (M), 890 (S), 838 (VS), 751 (S), 723 (VS), 698 (M), 684 (VS), 655 (M).

MS (EI, 70 eV): m/z (%) = 478 (25), 477 (74), 336 (27), 335 (40), 321 (40), 320 (100), 262 (14), 244 (22), 242 (17), 177 (25), 161 (18), 135 (33), 77 (29).
HRMS ($C_{24}H_{26}F_3NO_2SSi$): calc.: 477.1406; found: 477.1398.

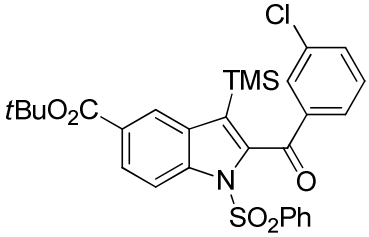
1-Benzenesulfonyl-2-cyclohex-2-enyl-3-trimethylsilanyl-1*H*-indole-5-carboxylic acid *tert*-butyl ester (41h)



The title compound was prepared from the ynamide **39c** (433 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -20 °C within 1.0 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP5** at 50 °C in 0.75 h and a subsequent allylation reaction was performed according to **TP6** using 3-bromocyclohexene (145 mg, 0.9 mmol) at -30 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 98:2) afforded the indole **41h** (282 mg, 0.56 mmol, 62%) as a white solid.

Mp.:132-134 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.37 (d, J = 1.7 Hz, 1H), 8.16 (d, J = 9.0 Hz, 1H), 7.86 (dd, J = 8.9 Hz, J = 1.6 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.55 – 7.48 (m, 1H), 7.44 – 7.36 (m, 2H), 5.77 – 5.66 (m, 1H), 5.47 (d, J = 10.1 Hz, 1H), 4.39 – 4.27 (m, 1H), 2.31 – 2.00 (m, 3H), 1.97 – 1.84 (m, 2H), 1.76 – 1.62 (m, 1H), 1.59 (s, 9H), 0.42 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.0, 152.3, 140.4, 139.8, 133.8, 133.6, 129.2, 128.9, 127.6, 126.7, 126.3, 124.7, 123.8, 117.3, 114.5, 80.7, 38.1, 29.5, 28.2, 24.3, 23.2, 2.0.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2950 (W), 1703 (S), 1601 (W), 1526 (W), 1455 (W), 1448 (M), 1364 (S), 1301 (S), 1279 (M), 1248 (M), 1222 (M), 1166 (S), 1128 (VS), 1102 (M), 1091 (S), 1046 (M), 1000 (M), 923 (M), 892 (S), 869 (M), 841 (VS), 830 (S), 752 (VS), 729 (S), 718 (S), 699 (M), 687 (S), 658 (W).
MS (EI, 70 eV): m/z (%) = 509 (32), 312 (32), 311 (25), 296 (37), 238 (16), 135 (13), 77 (35).
HRMS ($C_{28}H_{35}NO_4SSi$): calc.: 509.2056; found: 509.2059.

1-Benzenesulfonyl-2-(3-chloro-benzoyl)-3-trimethylsilanyl-1*H*-indole-5-carboxylic acid *tert*-butyl ester (41i)



The title compound was prepared from the ynamide **39c** (433 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at

-20 °C within 1.0 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP5** at 50 °C in 0.75 h and a subsequent acylation reaction was performed according to **TP6** using 3-chlorobenzoyl chloride (158 mg, 0.9 mmol) at -30 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the indole **41i** (476 mg, 0.84 mmol, 93%) as a yellow solid.

Mp.: 154-156 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.35 (dd, J = 1.7 Hz, J = 0.7 Hz, 1H), 8.06 (ddd, J = 10.4 Hz, J = 8.8 Hz, J = 1.1 Hz, 2H), 7.90 – 7.85 (m, 3H), 7.71 – 7.68 (m, 1H), 7.58 – 7.50 (m, 2H), 7.46 – 7.38 (m, 3H), 1.59 (s, 9H), 0.29 (s, 9H).

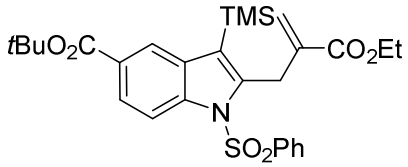
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 190.0, 165.5, 141.3, 139.8, 138.5, 136.7, 135.1, 134.4, 133.8, 133.7, 130.0, 129.2, 129.0, 128.0, 127.9, 127.3, 126.7, 125.0, 121.4, 114.0, 81.2, 28.2, 0.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1712 (M), 1669 (M), 1447 (M), 1369 (M), 1294 (M), 1252 (S), 1188 (S), 1170 (S), 1161 (S), 1137 (S), 1090 (S), 1033 (M), 1016 (M), 990 (S), 968 (M), 910 (M), 881 (M), 843 (VS), 774 (S), 765 (VS), 753 (S), 744 (S), 724 (VS), 684 (S), 675 (S).

MS (EI, 70 eV): m/z (%) = 569 (22), 568 (18), 567 (51), 554 (15), 552 (32), 498 (36), 497 (27), 496 (82), 412 (34), 370 (41), 358 (76).

HRMS ($C_{29}H_{30}ClNO_5SSi$): calc.: 567.1302; found: 567.1292.

1-Benzenesulfonyl-2-(2-ethoxycarbonyl-allyl)-3-trimethylsilanyl-1*H*-indole-5-carboxylic acid *tert*-butyl ester (41j)



The title compound was prepared from the ynamide **39c** (433 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -20 °C within 1.0 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP5** at 50 °C in 0.75 h and a subsequent allylation reaction was performed according to **TP6** using ethyl 2-(bromomethyl)acrylate (154 mg, 0.8 mmol) at -30 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc:Net_3 = 85:15:5) afforded the indole **41j** (208 mg, 0.56 mmol, 48%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.32 (dd,J = 1.6 Hz, J = 0.7 Hz, 1H), 8.23 (dd,J = 8.8 Hz, J = 0.6 Hz, 1H), 7.93 (dd,J = 8.8 Hz, J = 1.8 Hz, 1H), 7.77 – 7.72 (m, 2H), 7.56 – 7.49 (m, 1H), 6.17 – 6.15 (m, 1H), 7.43 – 7.37 (m, 2H), 5.01 – 4.98 (m, 1H), 4.28 (q,J = 7.2 Hz, 2H), 4.09 (s_{br}, 2H), 1.59 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H), 0.34 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.4, 165.9, 143.0, 140.2, 139.1, 138.9, 133.9, 133.4, 129.3, 127.1, 126.5, 125.2, 125.1, 123.5, 118.9, 114.3, 80.8, 61.0, 30.3, 28.2, 14.2, 0.6.

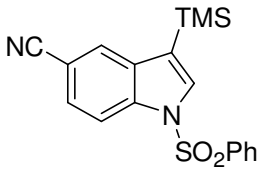
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2976 (W), 1707 (S), 1635 (W), 1604 (W), 1539 (W), 1447 (M), 1433 (W), 1367 (S), 1302 (S), 1252 (S), 1215 (M), 1188 (S), 1159 (VS), 1129 (VS),

1090 (S), 1024 (M), 980 (M), 932 (M), 915 (M), 867 (M), 837 (VS), 765 (S), 728 (VS), 705 (M), 685 (S).

MS (EI, 70 eV): m/z (%) = 565 (9), 564 (34), 559 (44), 486 (100), 396 (2), 223 (4).

HRMS ($C_{28}H_{39}N_2O_6SSi$): calc.: 559.2298; found: 559.2293 $[M+NH_4]^+$.

1-Benzenesulfonyl-3-trimethylsilanyl-1*H*-indole-5-carbonitrile (41k)



The title compound was prepared from the ynamide **39d** (433 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -5 °C within 0.5 h (0.5 M). After addition of THF (18 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 12 h. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1), extracted three times with EtOAc, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the indole **41k** (235 mg, 0.66 mmol, 66%) as an orange solid.

Mp.: 153-155 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.06 – 8.01 (m, 1H), 7.94 – 7.87 (m, 3H), 7.64 – 7.47 (m, 5H), 0.35 (s, 9H).

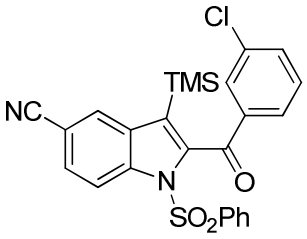
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 137.8, 134.6, 134.4, 133.3, 129.6, 127.4, 127.1, 127.0, 126.9, 119.5, 118.5, 114.2, 106.7, -0.8.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2960 (W), 2950 (W), 2223 (M), 1723 (M), 1710 (W), 1705 (W), 1512 (M), 1455 (M), 1447 (M), 1373 (S), 1296 (M), 1291 (M), 1274 (M), 1267 (M), 1248 (S), 1178 (S), 1144 (S), 1125 (S), 1091 (S), 1071 (M), 1047 (M), 1022 (W), 969 (S), 894 (M), 855 (S), 844 (S), 836 (VS), 809 (VS), 754 (S), 747 (S), 723 (VS), 685 (S).

MS (EI, 70 eV): m/z (%) = 354 (23), 339 (41), 214 (22), 200 (19), 199 (100), 85 (15), 77 (20), 71 (21).

HRMS ($C_{18}H_{18}N_2O_2SSi$):calc.: 354.0858; found: 354.0855.

1-Benzenesulfonyl-2-(3-chloro-benzoyl)-3-trimethylsilanyl-1*H*-indole-5-carbonitrile (41l)



The title compound was prepared from the ynamide **39d** (433 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -5 °C within 0.5 h (0.5 M). After addition of THF (18 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP5** at 50 °C in 1 h and a subsequent acylation reaction was

performed according to **TP6** using 3-chlorobenzoyl chloride (158 mg, 0.9 mmol) at 0 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1→8:2) afforded the indole **41l** (333 mg, 0.68 mmol, 68%) as an orange solid.

Mp.: 193-195 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.17 (d, J = 8.6 Hz, 1H), 8.00 – 7.96 (m, 1H), 7.93 – 7,85 (m, 3H), 7.69 (d, J = 7.7 Hz, 1H), 7.64 (dd, J = 8.7 Hz, J = 1.5 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.52 – 7.38 (m, 3H), 0.19 (s, 9H).

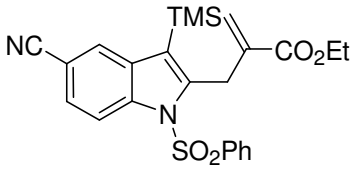
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 189.6, 142.0, 139.5, 137.9, 136.7, 135.3, 134.7, 134.0, 134.0, 130.1, 129.4, 129.1, 128.4, 127.9, 127.7, 127.4, 119.6, 119.1, 115.3, 107.7, 0.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2230 (W), 1671 (M), 1530 (W), 1458 (W), 1449 (M), 1430 (W), 1375 (S), 1307 (W), 1251 (S), 1231 (M), 1191 (S), 1173 (VS), 1148 (M), 1133 (M), 1090 (M), 1073 (W), 1000 (W), 991 (M), 966 (W), 889 (M), 840 (VS), 821 (S), 789 (M), 766 (M), 760 (M), 751 (S), 742 (S), 722 (VS), 689 (S), 678 (M), 667 (M).

MS (EI, 70 eV): m/z (%) = 494 (10), 492 (19), 479 (27), 478 (18), 477 (58), 339 (14), 338 (30), 337 (36), 336 (61), 275 (12), 242 (11).

HRMS ($C_{25}H_{21}ClN_2O_3SSi$): calc.: 492.0731; found: 492.0725.

2-(1-Benzenesulfonyl-5-cyano-3-trimethylsilanyl-1*H*-indol-2-ylmethyl)-acrylic acid ethyl ester (41m)



The title compound was prepared from the ynamide **39d** (433 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -5 °C within 0.5 h (0.5 M). After addition of THF (18 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP5** at 50 °C in 1 h and a subsequent allylation reaction was performed according to **TP6** using ethyl 2-(bromomethyl)acrylate (174 mg, 0.9 mmol) at 0 °C.The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1→8:2) afforded the indole **41m** (333 mg, 0.68 mmol, 42%) as white solid.

Mp.: 132-134 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.32 (dd, J = 8.7 Hz,J = 0.7 Hz, 1H), 7.93 (dd, J = 1.7 Hz,J = 0.8 Hz, 1H), 7.79 – 7.73 (m, 2H), 7,61 – 7.52 (m, 2H), 7.48 – 7.41 (m, 2H), 6.16 – 6.12 (m, 1H), 4.96 – 4.93 (m, 1H), 4.28 (q, J = 7.1 Hz, 2H), 4.12 – 4.07 (m, 2H), 1.34 (t, J = 7.1 Hz, 3H), 0.33 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.2, 144.2, 139.7, 138.8, 138.6, 134.3, 133.8, 129.5 (2C), 127.1, 126.6 (2C), 126.2, 125.1, 119.6, 118.0, 115.6, 106.7, 61.1, 30.2, 14.2, 0.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2225 (W), 1712 (M), 1458 (M), 1450 (M), 1378 (M), 1295 (M), 1275 (M), 1252 (M), 1221 (W), 1189 (M), 1178 (M), 1167 (S), 1149 (S), 1090 (M),

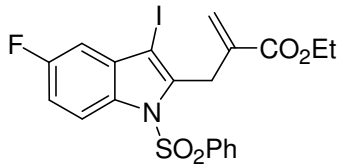
1069 (W), 1020 (W), 978 (W), 950 (W), 928 (M), 913 (M), 886 (M), 849 (S), 837 (VS), 829 (VS), 795 (M), 769 (W), 752 (M), 724 (S), 688 (S), 660 (W).

MS (EI, 70 eV): m/z (%) = 466 (3), 452 (12), 451 (34), 377 (13), 325 (44), 280 (30), 266 (23), 265 (100), 207 (16).

HRMS ($C_{24}H_{26}N_2O_4SSi$):calc.: 466.1383; found: 466.1374.

3.4 Synthesis of compounds of type 10

2-(1-Benzenesulfonyl-5-fluoro-3-iodo-1*H*-indol-2-ylmethyl)-acrylic acid ethyl ester (42)



The title compound was prepared according to **TP7** from **41b** (506 mg, 1.1 mmol) and iodine monochloride (196 mg, 1.21 mmol). Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded **42** (516 mg, 0.99 mmol, 90%) as a yellow solid.

Mp.: 83-85 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ / ppm = 8.18 (dd, J = 9.1 Hz, J = 4.3 Hz, 1H), 7.78 – 7.75 (m, 2H), 7.60 – 7.56 (m, 1H), 7.47 – 7.43 (m, 2H), 7.14 – 7.07 (m, 2H), 6.19 – 6.18 (m, 1H), 5.04 – 5.03 (m, 1H), 4.32 (q, J = 7.1 Hz, 2H), 4.15 (t, J = 1.8 Hz, 2H), 1.38 (t, J = 7.1 Hz, 3H).

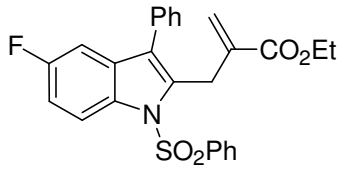
^{13}C-NMR (150 MHz, $CDCl_3$): δ / ppm = 166.3, 160.2 (d, J = 242.6 Hz), 139.5, 138.3, 136.2, 134.2, 132.9 (d, J = 10.4 Hz), 132.8 (d, J = 1.4 Hz), 129.4, 126.5, 125.2, 116.3 (d, J = 9.3 Hz), 113.7 (d, J = 25.4 Hz), 107.5 (d, J = 25.0 Hz), 75.2, 61.1, 31.2, 14.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1711 (S), 1631 (W), 1612 (W), 1471 (M), 1463 (M), 1447 (S), 1430 (M), 1367 (S), 1339 (M), 1260 (S), 1215 (M), 1174 (S), 1158 (VS), 1151 (VS), 1119 (M), 1088 (S), 1064 (S), 1024 (S), 981 (M), 956 (M), 927 (S), 914 (M), 852 (S), 809 (S), 801 (S), 752 (S), 724 (VS), 683 (VS), 658 (S).

MS (EI, 70 eV): m/z (%) = 513 (20), 373 (17), 372 (100), 245 (35), 216 (25), 173 (17), 172 (43), 128 (75), 127 (48).

HRMS ($C_{20}H_{17}FINO_4S$): calc.: 512.9907; found: 512.9910.

2-(1-Benzenesulfonyl-5-fluoro-3-phenyl-1*H*-indol-2-ylmethyl)-acrylic acid ethyl ester (43a)



The title compound was prepared according to **TP8** from PhMgCl·LiCl (0.23 mL, 1.76 M, 0.4 mmol), **42** (180 mg, 0.35 mmol) and PEPPSI-iPr (10 mg, 3 mol%) at 23 °C in 0.5 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1→8:2) afforded **43a** (143 mg, 0.31 mmol,89%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.23 (dd, J = 9.8 Hz, J = 4.5 Hz, 1H), 7.78 – 7.75 (m, 2H), 7.58 – 7.52 (m, 1H), 7.46 – 7.35 (m, 5H), 7.31 – 7.27 (m, 2H), 7.11 – 7.04 (m, 2H), 6.26 – 6.22 (m, 1H), 5.25 – 5.22 (m, 1H), 4.25 (q, J = 7.1 Hz, 2H), 4.02 (t, J = 1.8 Hz, 2H), 1.32 (t, J = 7.1 Hz, 3H).

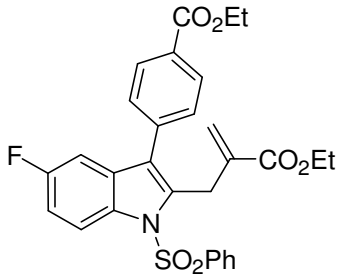
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.4, 160.0 (d, J = 242.6 Hz), 138.8, 138.6, 134.8, 133.9, 132.9(d, J = 1.3 Hz), 131.9, 131.1(d, J = 9.8 Hz), 129.3, 129.1, 128.8, 128.0, 126.4, 125.3, 125.2 (d, J = 4.0 Hz), 116.2 (d, J = 9.0 Hz), 112.7 (d, J = 25.0 Hz), 105.4 (d, J = 24.4 Hz), 61.0, 28.7, 14.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2981 (VW), 1710 (S), 1634 (W), 1607 (W), 1593 (W), 1466 (S), 1447 (M), 1365 (M), 1338 (M), 1263 (S), 1211 (M), 1186 (S), 1160 (S), 1133 (S), 1089 (S), 1047 (S), 1022 (S), 986 (M), 934 (M), 911 (M), 862 (M), 837 (S), 807 (M), 773 (M), 752 (M), 725 (VS), 702 (S), 684 (S).

MS (EI, 70 eV): m/z (%) = 463 (13), 323 (31), 322 (73), 277 (38), 276 (56), 249 (44), 248 (100), 246 (16), 222 (58), 216 (16), 172 (13).

HRMS ($C_{26}H_{22}FNO_4S$): calc.: 463.1254; found: 463.1249.

4-[1-Benzenesulfonyl-2-(2-ethoxycarbonyl-allyl)-5-fluoro-1*H*-indol-3-yl]-benzoic acid ethyl ester (43b)



(4-(Ethoxycarbonyl)phenyl)magnesium chloride/lithium chloride was prepared according to **TP3** from ethyl-4-bromobenzoate (166 mg, 0.6 mmol). The title compound was prepared according to **TP8** from (4-(ethoxycarbonyl)phenyl)magnesium chloride/lithium chloride, (**42**; 257 mg, 0.5 mmol) and PEPPSI-*iPr* (10 mg, 3 mol%) at 23 °C in 2 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the indole **43b** (198 mg, 0.37 mmol, 74%) as a yellow oil.

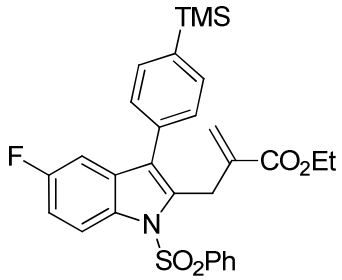
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.27 – 8.21 (m, 1H), 8.13 – 8.07 (m, 2H), 7.82 – 7.76 (m, 2H), 7.60 – 7.52 (m, 1H), 7.48 – 7.35 (m, 4H), 7.14 – 7.03 (m, 2H), 6.25 – 621 (m, 1H), 5.24 – 5.20 (m, 1H), 4.39 (q, J = 7.2 Hz, 2H), 4.25 (q, J = 7.0 Hz, 2H), 4.02 (t, J = 1.7 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.2(d, J = 2.0 Hz), 161.5 (d, J = 241.5 Hz), 158.5, 138.6, 138.5, 136.7, 135.2, 134.1, 132.9 (d, J = 0.8 Hz), 130.5 (d, J = 9.5 Hz), 130.1, 130.0, 129.4, 129.1, 126.5, 125.3, 124.1 (d, J = 3.9 Hz), 116.3 (d, J = 9.3 Hz), 113.0 (d, J = 25.3 Hz), 105.2 (d, J = 24.4 Hz), 61.1, 61.0, 28.7, 14.3, 14.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2981 (W), 1710 (VS), 1634 (W), 1611 (M), 1594 (W), 1466 (S), 1447 (S), 1405 (M), 1366 (S), 1338 (W), 1268 (VS), 1211 (M), 1162 (S), 1133 (VS), 1100 (VS), 1088 (VS), 1041 (S), 1017 (VS), 987 (S), 933 (M), 919 (M), 854 (M), 833 (S), 808 (M), 776 (S), 752 (S), 726 (VS), 708 (S), 685 (VS).

MS (EI, 70 eV): m/z (%) = 535 (11), 395 (39), 394 (70), 350 (20), 349 (66), 348 (100), 321 (26), 320 (33), 294 (36), 292 (37), 249 (20), 248 (58), 247 (22), 246 (23), 222 (18), 77 (27).
HRMS ($C_{29}H_{26}FNO_6S$): calc.: 535.1465; found: 535.1462.

2-[1-Benzenesulfonyl-5-fluoro-3-(4-trimethylsilanyl-phenyl)-1*H*-indol-2-ylmethyl]-acrylic acid ethyl ester (43c)



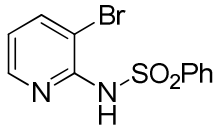
(4-(trimethylsilyl)phenyl)magnesium chloride/lithium chloride was prepared from (4-bromophenyl)trimethylsilane (138 mg, 0.6 mmol) by magnesium insertion.[140] Magnesium turnings (36 mg, 1.5 mmol) and LiCl (32 mg, 0.75 mmol) were placed in a *Schlenk*-flask, equipped with a magnestic stirrer and a septum, dried for 5 min at 250 °C in high vacuum and then dissolved in dry THF (1.2 mL). (4-Bromophenyl)trimethylsilane (138 mg, 0.6 mmol) was added and the reaction mixture was stirred until GC analysis of a quenched reaction aliquot showed complete conversion. Then, $ZnCl_2$ (0.66 mL, 0.66 mmol, 1.0 M in THF) was added and stirred for 5 min. The title compound was subsequently prepared according to **TP8** from (4-(trimethylsilyl)phenyl)zinc chloride/lithium chloride, **42** (257 mg, 0.5 mmol) and PEPPSI-*iPr* (10 mg, 3 mol%) at 23 °C in 2 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded **43c** (168 mg, 0.31 mmol, 63%) as a brown solid.

Mp.: 127-128 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.25 (dd, J = 8.9 Hz, J = 4.4 Hz, 1H), 7.82 – 7.76 (m, 2H), 7.62 – 7.53 (m, 3H), 7.48 – 7.41 (m, 2H), 7.33 – 7.28 (m, 2H), 7.16 – 7.05 (m, 2H), 6.28 – 6.25 (m, 1H), 5.28 – 5.24 (m, 1H), 4.28 (q, J = 7.0 Hz, 2H), 4.05 (t, J = 1.7 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H), 0.31 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.4, 160.2 (d, J = 241.3 Hz), 140.3, 138.9, 138.6, 134.8, 133.9, 133.8, 133.0 (d, J = 0.9 Hz), 132.3, 131.1 (d, J = 9.5 Hz), 129.3, 128.3, 126.5, 125.3, 125.2 (d, J = 4.0 Hz), 116.2 (d, J = 9.3 Hz), 112.7 (d, J = 25.1 Hz), 105.5 (d, J = 24.3 Hz), 61.0, 28.7, 14.2, -1.2.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1719 (S), 1462 (M), 1446 (M), 1378 (M), 1362 (M), 1248 (S), 1183 (M), 1160 (S), 1148 (S), 1123 (M), 1090 (M), 1035 (S), 1017 (M), 987 (M), 965 (M), 876 (S), 855 (S), 841 (S), 825 (VS), 818 (VS),757 (S), 745 (M), 724 (VS), 683 (VS).
MS (EI, 70 eV): m/z (%) = 535 (12), 396 (11), 395 (43), 394 (91), 350 (14), 349 (28), 348 (34), 334 (24), 320 (36), 302 (31), 294 (29), 276 (52), 248 (39).
HRMS ($C_{29}H_{30}FNO_4SSi$): calc.: 535.1649; found: 535.1646.

[140] a) F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem.* **2008**, *120*, 6907; *Angew. Chem. Int. Ed.* **2008**, *47*, 6802; b) F. M. Piller, A. Metzger, M. A. Schade, B. A. Haag, A. Gavryushin, P. Knochel, *Chem Eur. J.* **2009**, *15*, 7192.

3.5 Synthesis of compounds 45, 52, 55, 58, 62

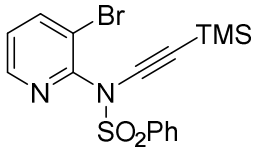
***N*-(3-Bromopyridin-2-ylbenzenesulfonamide**



The title compound was prepared according to **TP1** from 2-amino-3-bromopyridine (**44**) (5.0 mmol). Benzenesulfonyl chloride (1.06 g, 6.0 mmol) was added to a solution of 2-amino-3-bromopyridine (865 mg, 5.0 mmol) and pyridine (1.19 g, 1.2 mL, 15.0 mmol) in dichloromethane (5 mL) at 23 °C, and the reaction mixture was stirred at 23 °C for 72 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2→1:9) afforded *N*-(3-bromopyridin-2-ylbenzenesulfonamide (1.25 g, 4.0 mmol, 80%) as a white solid.

Mp.: 148-150 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.20 – 8.05 (m, 3H), 7.76 (dd, *J* = 7.9 Hz, *J* = 1.2 Hz, 1H), 7.62 – 7.46 (m, 3H), 6.78 (dd, *J* = 7.6 Hz, *J* = 4.8 Hz, 1H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm =141.1, 139.8, 134.1, 133.2, 129.3, 128.6, 128.3, 126.7, 123.5.
MS (EI, 70 eV): m/z (%) = 312 (1), 249 (100), 168 (8), 77 (29).
HRMS ($C_{16}H_{17}BrN_2O_2SSi$): calc.: 311.9568; found: 311.9566.

***N*-(3-Bromo-pyridin-2-yl)-*N*-trimethylsilanylethynyl-benzenesulfonamide(45)**

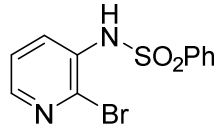


The title compound was prepared according to **TP2** from *N*-(3-bromopyridin-2-yl)benzenesulfonylamide (5.0 mmol). Under argon, KHMDS (10 mL, 5.0 mmol, 0.5 M in toluene) was added to a solution of *N*-(3-bromopyridin-2-yl)benzenesulfonylamide (1.57 g, 5.0 mmol) in toluene (50 mL) at 0 °C. After 1 h, phenyl((trimethylsilyl)ethynyl)iodonium triflate (2.7 g, 6.0 mmol) was added in several portions. The resulting mixture was stirred for 16 h at 23 °C. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 7:3) afforded *N*-(3-bromo-pyridin-2-yl)-*N*-trimethylsilanylethynyl-benzenesulfonamide (**45**; 1.68 g, 4.1 mmol, 82%) as a brown solid.

Mp.: 115-117 °C.
^{1}H-NMR (600 MHz, $CDCl_3$): δ / ppm = 8.40 (dd, *J* = 4.5 Hz, *J* = 1.8 Hz, 1H), 8.04 – 8.00 (m, 3H), 7.70 – 7.66 (m, 1H), 7.59 – 7.55 (m, 2H), 7.22 (dd, *J* = 7.9 Hz, *J* = 4.6 Hz, 1H), 0.11 (s, 9H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ / ppm = 149.5, 147.8, 143.1, 137.3, 134.0, 129.1, 128.7, 125.5, 120.5, 92.4, 75.1, -0.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2163 (M), 1448 (M), 1416 (M), 1377 (S), 1249 (M), 1245 (M), 1183 (S), 1170 (S), 1089 (M), 1063 (M), 1028 (S), 933 (M), 839 (VS), 814 (S), 774 (M), 760 (S), 751 (S), 737 (VS), 715 (S), 681 (VS), 665 (S).

MS (EI, 70 eV): m/z (%) = 411 (10), 410 (41), 408 (41), 395 (27), 395 (25), 346 (31), 345 (29), 344 (32), 343 (20), 331 (51), 329 (52), 239 (17), 167 (34), 139 (29), 135 (100).
HRMS ($C_{16}H_{17}BrN_2O_2SSi$):calc.: 407.9963; found: 407.9977.

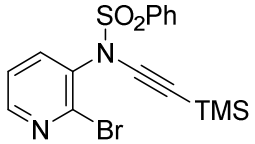
***N*-(2-Bromopyridin-3-yl)benzenesulfonamide**



The title compound was prepared according to **TP1** from 3-amino-2-bromopyridine (**51**) (5.0 mmol). Benzenesulfonyl chloride (1.06 g, 6.0 mmol) was added to a solution of 3-amino-2-bromopyridine (865 mg, 5.0 mmol) and pyridine (1.19 g, 1.2 mL, 15.0 mmol) in dichloromethane (5 mL) at 0 °C, and the reaction mixture was stirred at 23 °C for 1 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2→7:3) afforded *N*-(2-bromopyridin-3-yl)benzenesulfonamide (1.19 g, 3.8 mmol, 76%) as a brown solid.

Mp.: 113-115 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.11 (dd, J = 4.7 Hz, J = 1.7 Hz, 1H), 7.98 (dd, J = 8.2 Hz, J = 1.8 Hz, 1H), 7.81 – 7.76 (m, 2H), 7.63 – 7.56 (m, 1H), 7.52 – 7.44 (m, 2H), 7.26 (dd, J = 8.0 Hz, J = 4.7 Hz, 1H), 7.03 (s_{br}, 1H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 146.0, 138.5, 135.6, 133.7, 132.6, 129.9, 129.3, 127.2, 123.6.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3062 (W), 1564 (W), 1447 (M), 1438 (S), 1376 (W), 1328 (S), 1307 (W), 1293 (W), 1276 (W), 1234 (W), 1202 (W), 1192 (W), 1163 (S), 1122 (M), 1090 (M), 1072 (M), 1057 (M), 1022 (W), 976 (W), 949 (W), 897 (M), 835 (W), 791 (M), 752 (M), 735 (VS), 719 (S), 686 (VS).
MS (EI, 70 eV): m/z (%) = 314 (28), 312 (22), 168 (18), 92 (14), 78 (11), 77 (73), 61 (15), 45 (14).
HRMS ($C_{11}H_9BrN_2O_2S$): calc.:311.9568; found: 311.9564.

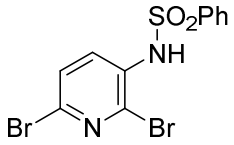
***N*-(2-Bromo-pyridin-3-yl)-*N*-((trimethylsilyl)ethynyl)-benzenesulfonamide (52)**



The title compound was prepared according to **TP2** from *N*-(2-bromopyridin-3-yl)benzenesulfonamide (14.1 mmol). Under argon, KHMDS (28.2 mL, 14.1 mmol, 0.5 M in toluene) was added to a solution of *N*-(2-bromopyridin-3-yl)benzenesulfonamide (4.44 g, 14.1 mmol) in toluene (140 mL) at 0 °C. After 1 h, phenyl((trimethylsilyl)ethynyl)iodonium triflate (6.98 g, 15.5 mmol) was added in several portions. The resulting mixture was stirred for 16 h at 23 °C. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2→7:3) afforded *N*-(2-bromo-pyridin-3-yl)-*N*-((trimethylsilyl)-ethynyl)-benzenesulfonamide (**52**; 4.27 g, 10.4 mmol, 74%) as an orange solid.
Mp.: 93-95 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.39 (dd, *J* = 4.7 Hz, *J* = 1.9 Hz, 1H), 7.91 – 7.85 (m, 2H), 7.76 – 7.67 (m, 2H), 7.62 – 7.54 (m, 2H), 7.37 -7.32 (m, 1H), 0.17 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 150.1, 142.3, 139.0, 136.8, 134.6, 134.4, 129.9, 128.6, 123.2, 92.6, 74.8, -0.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2952 (VW), 2164 (M), 1561 (W), 1445 (M), 1400 (M), 1372 (M), 1330 (W), 1306 (W), 1297 (W), 1263 (W), 1253 (M), 1188 (M), 1174 (S), 1157 (M), 1117 (W), 1087 (M), 1059 (M), 1018 (W), 916 (W), 841 (VS), 810 (S), 758 (M), 732 (VS), 713 (S), 685 (S), 666 (S).
MS (EI, 70 eV): m/z (%) = 410 (24), 408 (22), 396 (15), 395 (58), 392 (55), 199 (21), 187 (17), 145 (18), 139 (49), 137 (48), 135 (100), 77 (44).
HRMS ($C_{16}H_{17}BrN_2O_2SSi$): calc.:407.9963; found: 407.9957.

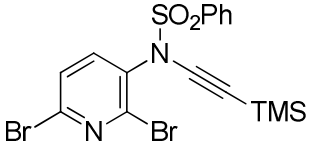
***N*-(2,6-Dibromopyridin-3-yl)benzenesulfonamide**



The title compound was prepared according to **TP1** from 3-amino-2,6-dibromopyridine (**56**) (2.3 mmol). Benzenesulfonyl chloride (495 mg, 2.8 mmol) was added to a solution of 3-amino-2,6-dibromopyridine (581 mg, 2.3 mmol) and pyridine (546 mg, 0.56 mL, 6.9 mmol) in dichloromethane (2.3 mL) at 0 °C, and the reaction mixture was stirred at 23 °C for 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 7:3) afforded *N*-(2,6-dibromopyridin-3-yl)benzenesulfonamide (616 mg, 1.5 mmol, 65%) as a brown solid.

Mp.: 122-124 °C.
^{1}H-NMR (300 MHz, CD_3OD): δ / ppm = 7.86 (d, *J* = 8.6 Hz, 1H), 7.81 – 7.74 (m, 2H), 7.64 – 7.58 (m, 1H), 7.55 – 7.47 (m, 2H), 7.42 (d, *J* = 7.7 Hz, 1H), 6.94 (s_{br}, 1H).
^{13}C-NMR (75 MHz, CD_3OD): δ / ppm = 138.3, 135.4, 134.0, 132.3, 131.9, 129.5, 129.1, 128.0, 127.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3263 (W), 1543 (W), 1534 (W), 1448 (M), 1438 (S), 1415 (M), 1378 (M), 1363 (M), 1337 (W), 1313 (M), 1268 (M), 1248 (W), 1226 (M), 1168 (S), 1149 (S), 1117 (M), 1089 (S), 1063 (M), 1050 (S), 1023 (M), 1000 (W), 970 (W), 890 (S), 834 (S), 821 (M), 773 (M), 750 (S), 725 (S), 720 (VS), 710 (S), 682 (VS).
MS (EI, 70 eV): m/z (%) = 394 (30), 392 (57), 389 (27), 253 (16), 251 (38), 249 (18), 77 (100).
HRMS ($C_{11}H_8Br_2N_2O_2S$): calc.: 389.8673; found: 389.8668.

***N*-(2,6-Dibromopyridin-3-yl)-*N*-((trimethylsilyl)ethynyl)-benzenesulfonamide (55)**

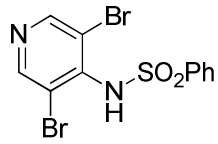


The title compound was prepared according to **TP2** from *N*-(2,6-dibromopyridin-3-yl)benzenesulfonamide (2.5 mmol). Under argon, KHMDS (3.57 mL, 2.5 mmol, 0.7 M in toluene) was added to a solution of *N*-(2,6-dibromopyridin-3-yl)benzenesulfonamide (980 mg,

2.5 mmol) in toluene (25 mL) at 0 °C. After 1 h, phenyl((trimethylsilyl)ethynyl)iodonium triflate (1.35 g, 3.0 mmol) was added in several portions. The resulting mixture was stirred for 16 h at 23 °C. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the pyridine **55** (760 mg, 1.56 mmol, 62%) as a yellow solid.

Mp.: 115-117 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.86 – 7.83 (m, 2H), 7.73 – 7.69 (m, 1H), 7.59 – 7.55 (m, 2H), 7.53 – 7.48 (m, 2H), 0.14 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 141.1, 140.6, 140.6, 136.6, 134.6, 134.2, 129.2, 128.5, 127.8, 92.0, 75.1, -0.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2169 (M), 1536 (W), 1447 (W), 1415 (S), 1377 (S), 1337 (M), 1250 (M), 1168 (S), 1116 (W), 1087 (M), 1054 (M), 914 (W), 840 (VS), 777 (M), 755 (S), 737 (S), 721 (VS), 686 (S), 671 (S).
MS (EI, 70 eV): m/z (%) = 488 (9), 475 (15), 473 (26), 333 (25), 199 (21), 139 (32), 137 (33), 135 (100), 77 (41), 73 (43).
HRMS ($C_{16}H_{16}Br_2N_2O_2SSi$): calc.: 485.9069; found: 485.9058.

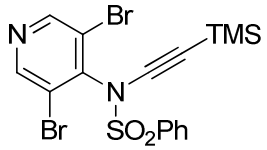
***N*-(3,5-Dibromo-pyridin-4-yl)-benzenesulfonamide**



4-Amino-3,5-dibromopyridine (1.26 g, 5.0 mmol) was dissolved in THF (10 mL) and cooled to 0 °C. NaH (400 mg, 10.0 mmol, 60% in mineral oil) was added and the reaction mixture was stirred at 0 °C for 0.5 h. Benzenesulfonyl chloride (883 mg, 5.0 mmol) was added and the reaction mixture was allowed to warm slowly to 23 °C within 2 h. The reaction mixture was quenched with concentrated aqueous NH_4Cl-solution, extracted three times with EtOAc, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2→1:1) afforded *N*-(2,6-dibromopyridin-3-yl)benzenesulfonamide (1.2 g, 3.06 mmol, 51%) as a yellow solid.

Mp.: 37-40 °C.
^{1}H-NMR (400 MHz, DMSO-d_6): δ / ppm = 10.60 (s_{br}, 1H), 8.74 (s, 2H), 7.83 – 7.73 (m, 2H), 7.72 – 7.63 (m, 1H), 7.63 – 7.54 (m, 2H).
^{13}C-NMR (100 MHz, DMSO-d_6): δ / ppm = 152.1, 142.6, 142.3, 133.5, 129.7, 127.1, 123.6.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3404 (VW), 3074 (W), 2924 (W), 2849 (W), 2814 (W), 2716 (W), 2631 (W), 2257 (W), 1729 (W), 1583 (W), 1568 (W), 1549 (W), 1527 (W), 1478 (W), 1447 (M), 1395 (M), 1368 (W), 1344 (S), 1316 (M), 1311 (M), 1295 (W), 1259 (M), 1225 (M), 1213 (M), 1180 (M), 1166 (S), 1160 (S), 1147 (S), 1093 (S), 1075 (M), 1065 (M), 1051 (M), 1024 (M), 1005 (M), 996 (M), 971 (M), 920 (S), 885 (S), 856 (W), 821 (M), 763 (S), 751 (S), 726 (S), 691 V(S).
MS (EI, 70 eV): m/z (%) = 392 (11), 390 (5), 313 (18), 311 (16), 142 (6), 77 (100).
HRMS ($C_{11}H_8Br_2N_2O_2S$): calc.: 389.8673; found: 389.8663.

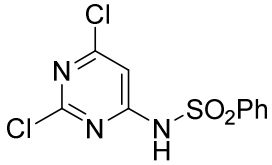
***N*-(3,5-Dibromo-pyridin-4-yl)-*N*-trimethylsilanylethynyl-benzenesulfonamide (58)**



The title compound was prepared according to **TP2** from *N*-(3,5-dibromo-pyridin-4-yl)-benzenesulfonamide (3.0 mmol). Under argon, KHMDS (4.3 mL, 3.0 mmol, 0.7 M in toluene) was added to a solution of *N*-(3,5-dibromo-pyridin-4-yl)-benzenesulfonamide (1.18 g, 3.0 mmol) in toluene (30 mL) at 0 °C. After 1 h, phenyl((trimethylsilyl)ethynyl)iodonium triflate (1.58 g, 3.5 mmol) was added in several portions. The resulting mixture was stirred for 16 h at 23 °C. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1→8:2) afforded the pyridine **58** (497 mg, 1.0 mmol, 34%) as a yellow solid.

Mp.: 78-80 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.70 (s, 2H), 8.00 – 7.93 (m, 2H), 7.75 – 7.66 (m, 1H), 7.61 – 7.52 (m, 2H), 0.16 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 152.3, 143.5, 137.6, 134.5, 129.0, 128.8, 123.0, 91.0, 75.7, -0.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (VW), 2164 (M), 1583 (VW), 1551 (VW), 1524 (VW), 1479 (VW), 1449 (M), 1440 (M), 1394 (W), 1386 (M), 1372 (S), 1356 (W), 1336 (W), 1314 (W), 1289 (VW), 1248 (M), 1226 (W), 1217 (W), 1198 (W), 1187 (M), 1171 (M), 1129 (W), 1088 (M), 1073 (W), 1063 (W), 1022 (VW), 999 (W), 930 (W), 919 (W), 888 (W), 881 (W), 841 V(S), 760 (S), 751 (S), 730 (S), 725 (S), 694 (S), 683 (S), 652 (M).
MS (EI, 70 eV): m/z (%) = 490 (11), 488 (20), 486 (10), 476 (13), 475 (52), 474 (20), 473 (100), 471 (48), 333 (11), 139 (26), 137 (25), 135 (76), 77 (56), 73 (37).
HRMS ($C_{16}H_{16}Br_2N_2O_2SSi$): calc.: 485.9069; found: 485.9064.

***N*-(2,6-dichloropyrimidin-4-yl)benzenesulfonamide**



4-Amine-2,6-dichloropyrimidine (1.64 g, 10.0 mmol) was dissolved in THF (10 mL) and cooled to 0 °C. NaH (800 mg, 20.0 mmol, 60% in mineral oil) was added in one portion and the reaction mixture was stirred at 0 °C for 1 h. Benzenesulfonyl chloride (1.766 g, 10.0 mmol) was added and the reaction mixture was allowed to warm slowly to room temperature and stirred for 1 h. The reaction mixture was quenched with concentrated aqueous NaCl-solution. The organic layer was separated and aqueous phase extracted three times with EtOAc. Organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (gradient from isohexane:EtOAc:DCM:NEt_3 = 3:6.5:0.3:0.2 -> 0:9.5:0.3:0.2) afforded *N*-(2,6-dichloropyrimidin-4-yl)benzenesulfonamide (2.43 g, 8.0 mmol, 80%) as a white solid.

Mp.: 78-80 °C.

^{1}H-NMR (400 MHz, DMSO-d$_6$): δ / ppm = 7.96 – 7.89 (m, 2H), 7.65 – 7.53 (m, 3H), 6.82 (s, 1H).

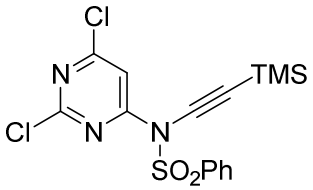
^{13}C-NMR (100 MHz, DMSO-d$_6$): δ / ppm = 163.2, 159.6, 158.8, 141.4, 133.1, 129.3, 127.6, 106.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2988 (W), 2674 (W), 2628 (W), 2484 (W), 1556 (S), 1503 (M), 1492 (M), 1484 (M), 1475 (M), 1456 (M), 1443 (M), 1424 (M), 1416 (M), 1397 (M), 1360 (M), 1354 (M), 1347 (S), 1317 (W), 1302 (W), 1291 (M), 1273 (S), 1201 (M), 1172 (W), 1138 (S), 1119 (S), 1099 (W), 1085 (VS), 1069 (M), 1033 (VS), 998 (W), 991 (W), 968 (M), 924 (W), 849 (VS), 836 (M), 825 (VS), 820 (S), 795 (M), 754 (M), 748 (M), 714 (S), 692 (S), 667 (W), 657 (W).

MS (EI, 70 eV): m/z (%) = 303 (1), 249 (12), 247 (11), 246 (61), 244 (91), 206 (8), 141 (10), 77 (100).

HRMS ($C_{10}H_7Cl_2N_3O_2S$): calc.: 302.9636; found: 302.9623.

***N*-(2,6-dichloropyrimidin-4-yl)-*N*-((trimethylsilyl)ethynyl)benzenesulfonamide (62)**



To a solution of *N*-(2,6-dichloropyrimidin-4-yl)benzenesulfonamide (1.52 g, 5.0 mmol) in toluene (50 mL) at 0 °C under an argon atmosphere was slowly added KHMDS (7.86 mL, 5.5 mmol, 0.7 M solution in toluene). After 1 h, phenyl[(trimethylsilyl)ethynyl]iodoniumtriflate[141] (2.7 g, 6.0 mmol) was added in several portions. The resulting mixture was allowed to warm up to 23 °C and stirred for further 16 h. The reaction mixture was filtered through a plug of silica gel and washed with EtOAc. The crude residue was purified by flash column chromatography on silica gel (isohexane:EtOAc = 9:1) to afford the ynamide **62** (1.0 g , 2.5 mmol, 25%) as an colorless solid.

M.p.: 52-54 °C.

^{1}H-NMR (300 MHz, CDCl$_3$): δ / ppm = 8.30 – 8.25 (m, 2H), 7.73 – 7.66 (m, 1H), 7.68 (s, 1H), 7.63 – 7.56 (m, 2H), 0.41 (s, 9H).

^{13}C-NMR (75 MHz, CDCl$_3$): δ / ppm = 162.7, 160.5, 137.4, 135.1, 133.9, 129.7, 128.9, 107.1, 87.8, 83.3, -0.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3066 (W), 2957 (W), 2922 (W), 2916 (W), 2850 (W), 1748 (M), 1625 (M), 1605 (W), 1583 (W), 1549 (S), 1529 (S), 1448 (M), 1412 (M), 1371 (M), 1333 (M), 1280 (M), 1250 (S), 1219 (M), 1209 (M), 1182 (S), 1169 (S), 1124 (S), 1085 (S), 1071 (M), 1034 (M), 1016 (M), 1001 (M), 995 (S), 983 (S), 975 (S), 836 (VS), 811 (S), 753 (S), 727 (S), 719 (S), 683 (S), 670 (M), 660 (M).

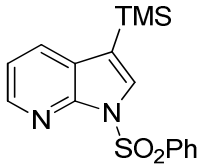
MS (EI, 70 eV): m/z (%) = 399 (3), 384 (15), 364 (5), 320 (10), 167 (9), 135 (19), 95 (10), 77 (57).

HRMS ($C_{15}H_{15}Cl_2N_3O_2SSi$):calc.: 399.0031; found: 399.0031.

[141]Prepared according to literature procedure: K. Tanaka, K. Takeishi, *Synthesis* **2007**, 2920.

3.6 Synthesis of compounds of type 47

1-Benzenesulfonyl-3-trimethylsilanyl-1*H*-pyrrolo[2,3-*b*]pyridine (47a)



The title compound was prepared from the ynamide **45** (409 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -45 °C within 1.0 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP5** at 50 °C in 1 h was performed. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1), extracted three times with EtOAc, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 7-azaindole **47a** (263 mg, 0.79 mmol, 79%) as a colorless solid.

Mp.: 128-130 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ / ppm = 8.39 (dd, *J* = 4.8 Hz, *J* = 1.5 Hz, 1H), 8.24 – 8.21 (m, 2H), 7.86 (dd, *J* = 7.8 Hz, *J* = 1.5 Hz, 1H), 7.66 (s, 1H), 7.58 – 7.54 (m, 1H), 7.50 – 7.46 (m, 2H), 7.15 (dd, *J* = 7.8 Hz, *J* = 4.8 Hz, 1H), 0.33 (s, 9H).

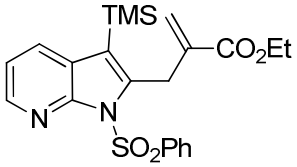
^{13}C-NMR (150 MHz, $CDCl_3$): δ / ppm = 148.7, 144.5, 138.5, 133.9, 131.3, 130.2, 128.9, 128.1, 126.7, 118.6, 115.0, -0.8.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3142 (VW), 2955 (VW), 1584 (W), 1570 (W), 1502 (M), 1469 (W), 1448 (W), 1392 (M), 1364 (S), 1350 (M), 1314 (W), 1281 (M), 1248 (M), 1191 (M), 1173 (S), 1166 (S), 1154 (S), 1093 (M), 1072 (W), 1057 (W), 1024 (VW), 947 (S), 838 (VS), 816 (M), 797 (S), 769 (M), 755 (VS), 730 (VS), 707 (M), 688 (VS).

MS (EI, 70 eV): m/z (%) = 331 (23), 330 (43), 315 (91), 251 (43), 199 (20), 175 (56), 147 (15), 110 (20), 85 (19), 78 (21), 77 (37), 69 (19), 58 (22).

HRMS ($C_{16}H_{18}N_2O_2SSi$): calc.: 330.0858; found: 330.0862.

2-(1-Benzenesulfonyl-3-trimethylsilanyl-1*H*-pyrrolo[2,3-*b*]pyridine-2-ylmethyl)-acrylic acid ethyl ester (47b)

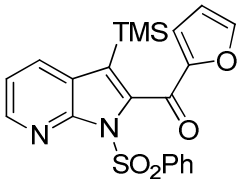


The title compound was prepared from the ynamide **45** (409 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -45 °C within 1.0 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP5** at 50 °C in 1 h and a subsequent allylation reaction was performed according to **TP6** using ethyl 2-(bromomethyl)acrylate (173 mg, 0.9 mmol) at -20 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column

chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 7-azaindole **47b** (337 mg, 0.76 mmol, 84%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.37 (dd, *J* = 4.7 Hz, *J* = 1.7 Hz, 1H), 8.24 – 8.19 (m, 2H), 7.90 (dd, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H), 7.59 – 7.52 (m, 1H), 7.49 – 7.42 (m, 2H), 7.14 (dd, *J* = 8.0 Hz, *J* = 4.7 Hz, 1H), 6.27 – 6.25 (m, 1H), 5.10 – 5.07 (m, 1H), 4.34 (q, *J* = 7.0 Hz,2H), 4.26 (s_{br}, 2H), 1.39 (t, *J* = 7.0 Hz,3H), 0.36 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.5, 149.7, 143.6, 143.1, 139.7, 139.2, 133.7, 129.3, 128.6, 128.4, 125.5, 125.0, 118.6, 114.6, 61.0, 30.8, 14.2, 0.7.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1712 (M), 1447 (M), 1401 (M), 1368 (S), 1249 (M), 1191 (S), 1165 (S), 1132 (S), 1087 (M), 949 (M), 927 (S), 913 (M), 836 (VS), 797 (S), 771 (S), 756 (S), 730 (VS), 704 (S), 682 (VS).
MS (EI, 70 eV): m/z (%) = 442 (8), 428 (11), 427 (37), 353 (16), 302 (28), 301 (100), 256 (37), 255 (22), 241 (77), 199 (13), 183 (29), 155 (16), 73 (39).
HRMS ($C_{22}H_{26}N_2O_4SSi$): calc.: 442.1383; found: 442.1379.

1-Benzenesulfonyl-3-trimethylsilanyl-1*H*-pyrrolo[2,3-*b*]pyridine-2-yl)-furan-2-yl-methanone (47c)

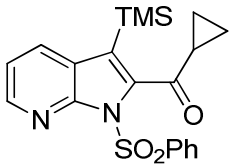


The title compound was prepared from the ynamide **45** (409 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -45 °C within 1.0 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP5** at 50 °C in 1 h and a subsequent acylation reaction was performed according to **TP6** using furoyl chloride (130 mg, 0.9 mmol) at 0 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 7-azaindole **47c** (263 mg, 0.62 mmol, 69%) as an orange solid.

Mp.: 188-190 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.51 (dd, *J* = 4.8 Hz, *J* = 1.5 Hz, 1H), 8.43 – 8.25 (m, 2H), 7.98 (dd, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H), 7.70 (dd, *J* = 1.7 Hz, *J* = 0.6 Hz, 1H), 7.60 – 7.53 (m, 1H), 7.52 – 7.45 (m, 2H), 7.22 (dd, *J* = 8.0 Hz, *J* = 4.7 Hz, 1H), 7.17 (dd, *J* = 3.6 Hz, *J* = 0.6 Hz, 1H), 6.62 (dd, *J* = 3.6 Hz, *J* = 1.9 Hz, 1H), 0.21 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 177.7, 153.7, 148.7, 147.7, 145.7, 139.8, 137.9, 134.1, 131.1, 128.8, 128.5, 125.7, 120.6, 119.2, 116.5, 112.8, 0.0.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1650 (S), 1572 (W), 1563 (W), 1499 (W), 1464 (M), 1449 (W), 1389 (M), 1366 (S), 1327 (M), 1281 (W), 1246 (S), 1188 (S), 1174 (S), 1158 (M), 1122 (W), 1095 (M), 1083 (W), 1075 (W), 1048 (W), 1021 (M), 975 (S), 949 (M), 909 (M), 883 (W), 835 (VS), 794 (S), 778 (S), 774 (VS), 754 (VS), 728 (VS), 683 (S).

MS (EI, 70 eV): m/z (%) = 424 (5), 409 (17), 270 (24), 269 (100), 268 (18), 215 (24), 212 (93), 155 (15), 144 (44), 135 (36), 117 (21), 116 (23), 77 (26).
HRMS ($C_{21}H_{20}N_2O_4SSi$): calc.: 424.0913; found: 424.0909.

1-Benzenesulfonyl-3-trimethylsilanyl-1*H*-pyrrolo[2,3-*b*]pyridine-2-yl)-cyclopropyl-methanone (47d)

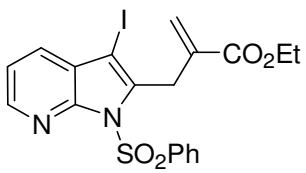


The title compound was prepared from the ynamide **45** (409 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -45 °C within 1.0 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP5** at 50 °C in 1 h and a subsequent acylation reaction was performed according to **TP6** using cyclopropanecarbonyl chloride (105 mg, 0.9 mmol) at 0 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 7-azaindole **47d** (303 mg, 0.76 mmol, 84%) as an colorless solid.

Mp.: 123-125 °C.
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.45 (dd, J = 4.8 Hz, J = 1.7 Hz, 1H), 8.11 – 8.05 (m, 2H), 7.94 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.45 – 7.38 (m, 2H), 7.16 (dd, J = 8.0 Hz, J = 4.7 Hz, 1H), 2.52 – 2.44 (m, 1H), 1.50 – 1.44 (m, 2H), 1.30 – 1.23 (m, 2H), 0.34 (s, 9H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 200.1, 149.2, 145.7, 144.2, 137.5, 134.0, 131.4, 128.7, 128.2, 126.1, 119.3, 116.6, 24.9, 15.0, 0.3.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2163 (W), 1677 (W), 1447 (W), 1416 (M), 1377 (S), 1250 (M), 1182 (S), 1170 (S), 1123 (W), 1089 (M), 1064 (W), 1046 (W), 1028 (M), 1007 (M), 951 (W), 933 (W), 839 (VS), 814 (S), 798 (M), 774 (M), 757 (S), 751 (S), 737 (S), 727 (M), 715 (M), 698 (M), 682 (S), 666 (M).
MS (EI, 70 eV): m/z (%) = 399 (3), 398 (9), 385 (13), 384 (31), 383 (100), 319 (18), 243 (25), 242 (56), 241 (15), 227 (41), 77 (15).
HRMS ($C_{20}H_{22}N_2O_3SSi$): calc.: 398.1120; found: 398.1117.

3.7 Synthesis of compounds of type 48

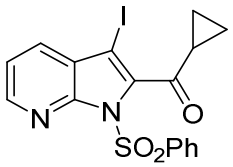
2-(1-Benzenesulfonyl-3-iodo-1*H*-pyrrolo[2,3-*b*]pyridine-2-ylmethyl)-acrylic acid ethyl ester (48a)



The title compound was prepared according to **TP7** from **47b** (1.1 g, 2.5 mmol) and iodine monochloride (447 mg, 2.75 mmol). Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 7-azaindole **48a** (942 mg, 1.90 mmol, 76%) as a yellow solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.45 (dd, *J* = 4.8 Hz, *J* = 1.7 Hz, 1H), 8.22 – 8.18 (m, 2H), 7.66 (dd, *J* = 7.8 Hz, *J* = 1.7 Hz, 1H), 7.60 – 7.55 (m, 1H), 7.50 – 7.44 (m, 2H), 7.26 (dd, *J* = 7.9 Hz, *J* = 4.8 Hz, 1H), 6.28 – 6.25 (m, 1H), 5.10 – 5.08 (m, 1H), 4.34 (q, *J* = 7.2 Hz, 2H), 4.30 (t, *J* = 1.8 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.4, 148.2, 145.5, 138.7, 138.5, 136.9, 134.1, 129.6, 128.8, 128.4, 125.0, 124.1, 119.8, 70.9, 61.2, 31.5, 14.3.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2981 (W), 1711 (S), 1689 (M), 1673 (W), 1638 (W), 1604 (W), 1574 (W), 1544 (W), 1471 (W), 1449 (M), 1408 (M), 1391 (M), 1377 (S), 1363 (M), 1294 (S), 1261 (S), 1189 (S), 1169 (S), 1144 (S), 1116 (M), 1089 (S), 1061 (S), 1042 (M), 998 (W), 976 (W), 957 (M), 946 (M), 926 (M), 840 (M), 817 (W), 793 (M), 766 (S), 760 (S), 726 (VS), 695 (S), 687 (S).
MS (EI, 70 eV): m/z (%) = 496 (6), 356 (19), 355 (100), 229 (19), 228 (59), 100 (17), 199 (31), 156 (21), 155 (50).
HRMS ($C_{19}H_{17}IN_2O_4S$): calc.: 495.9954; found:495.9946.

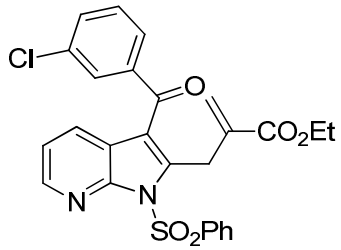
(1-Benzenesulfonyl-3-iodo-1*H*-pyrrolo[2,3-*b*]pyridin-2-yl)-cyclopropyl-methanone (48b)



The title compound was prepared according to **TP7** from **47d** (833 mg, 2.09 mmol) and iodine monochloride (373 mg, 2.3 mmol). Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 7-azaindole **48b** (670 mg, 1.5 mmol, 72%) as a yellow solid.

Mp.: 148-150 °C.
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.51 (dd, *J* = 4.8 Hz, *J* = 1.6 Hz, 1H), 8.23 – 8.15 (m, 2H), 7.71 (dd, *J* = 7.9 Hz, *J* = 1.6 Hz, 1H), 7.60 – 7.54 (m, 1H), 7.51 – 7.45 (m, 2H), 7.28 (dd, *J* = 7.9Hz, *J* = 4.9 Hz, 1H), 2.61 – 2.53 (m, 1H), 1.55 – 1.49 (m, 2H), 1.31 – 1.24 (m, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 197.2, 147.5, 139.9, 137.5, 134.4, 131.4, 130.1, 128.9, 128.5, 128.3, 124.6, 120.4, 24.1, 14.4.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1678 (M), 1568 (M), 1446 (M), 1377 (S), 1361 (M), 1281 (M), 1269 (M), 1186 (S), 1171 (S), 1122 (M), 1105 (M), 1087 (S), 1077 (S), 1039 (M), 1031 (S), 1001 (S), 995 (S), 868 (M), 800 (S), 755 (S), 727 (VS), 706 (M), 695 (M), 683 (VS), 655 (M).
MS (EI, 70 eV): m/z (%) = 452 (40), 358 (30),356 (22), 312 (18), 271 (10), 254 (11), 91 (11), 77 (60).
HRMS ($C_{17}H_{13}IN_2O_3S$): calc.: 451.9692; found: 451.9677.

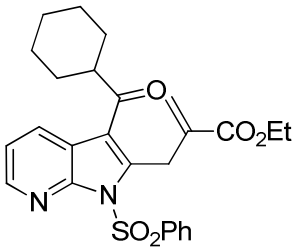
2-(1-Benzenesulfonyl-3-cyclohexanecarbonyl-1*H*-pyrrolo[2,3-*b*]pyridin-2-ylmethyl)-acrylic acid ethyl ester (50a)



A I/Mg-exchange was performed according to **TP9** with MeMgCl. After addition of $ZnCl_2$ (0.6 mL, 0.6 mmol, 1.1 equiv, 1.0 M in THF), the reaction mixture was stirred for 10 min. A subsequent acylation reaction was performed according to **TP6** using 3-chlorobenzoyl chloride (78 mg, 0.45 mmol) at -45 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 7:3→1:1) afforded the 7-azaindole **50a** (mg, 0.35 mmol, 85%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ / ppm = 8.45 (dd, J = 4.7 Hz, J = 1.9 Hz, 1H), 8.19 – 8.15 (m, 2H), 7.78 (dd, J = 7.8 Hz, J = 1.8 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.57 (t, J = 8.0 Hz, 2H), 7.40 (t, J = 1.9 Hz, 1H), 7.28 – 7.22 (m, 4H), 7.07 (t, J = 8.0 Hz, 1H), 6.42 – 6.39 (m, 1H), 6.08 – 6.05 (m, 1H), 4.26 (q, J = 7.1 Hz, 2H), 3.46 – 3.44 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ / ppm = 167.4, 165.8, 151.3, 148.2, 141.6, 139.2, 135.7, 134.4, 133.9, 131.4, 129.7, 129.1, 128.6, 128.5, 126.9, 126.2, 124.1, 122.4, 95.7, 78.2, 61.1, 29.7, 22.5, 14.2.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (W), 2920 (M), 2850 (M), 1705 (M), 1700 (M), 1589 (W), 1583 (W), 1558 (W), 1515 (W), 1476 (W), 1451 (M), 1414 (M), 1396 (M), 1364 (VS), 1348 (M), 1331 (M), 1308 (M), 1302 (M), 1279 (M), 1243 (S), 1185 (S), 1174 (S), 1164 (S), 1135 (S), 1110 (VS), 1086 (S), 1071 (S), 1052 (M), 1021 (M), 1000 (M), 988 (M), 976 (M), 950 (S), 925 (W), 842 (S), 827 (S), 796 (S), 787 (S), 766 (S), 754 (S), 731 (VS), 708 (S), 685 (VS).
MS (EI, 70 eV): m/z (%) = 508 (1), 463 (3), 446 (9), 444 (23), 415 (9), 371 (7), 367 (19), 339 (10), 139 (100), 111 (39).
HRMS ($C_{26}H_{21}ClN_2O_5S$): calc.: 508.0860; found: 508.0852.

Ethyl 2-((3-(cyclohexanecarbonyl)-1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine-2-yl)methyl)acryliate(50b)

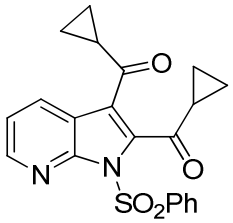


A I/Mg-exchange was performed according to **TP9** with MeMgCl. After addition of $ZnCl_2$ (0.6 mL, 0.6 mmol, 1.1 equiv, 1.0 M in THF), the reaction mixture was stirred for 10 min. A subsequent acylation reaction was performed according to **TP6** using cyclohexanecarbonyl chloride (66 mg, 0.45 mmol) at -40 °C. The reaction mixture was allowed to warm slowly to

23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2→1:1) afforded the 7-azaindole **50b** (180 mg, 0.35 mmol, 85%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.58 (dd, *J* = 4.8 Hz, *J* = 1.8 Hz, 1H), 8.23 – 8.19 (m, 2H), 7.97 (dd, *J* = 7.7 Hz, *J* = 1.8 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.57 – 7.51 (m, 2H), 7.43 (dd, *J* = 7.8 Hz, *J* = 4.9 Hz, 1H), 6.38 (q, *J* = 1.6 Hz,1H), 6.10 (td, *J* = 1.9 Hz, *J* = 0.8 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.50 (t, *J* = 1.5 Hz, 2H), 1.90 – 1.80 (m, 1H), 1.73 -1.57 (m, 4H), 1.54 – 1.47 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.28 – 1.24 (m, 1H), 1.10 -1.02 (m, 1H), 0.96 – 0.80 (m, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 175.1, 165.9, 150.9, 148.3, 141.6, 139.8, 134.4, 133.5, 129.2, 128.6, 126.9, 124.4, 122.7, 95.4, 78.2, 61.1, 44.4, 28.7, 25.3, 25.2, 22.5, 14.2.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2929 (M), 2856 (W), 1709 (S), 1638 (W), 1583 (W), 1556 (W), 1448 (M), 1416 (S), 1361 (S), 1296 (M), 1267 (M), 1246 (S), 1155 (VS), 1126 (VS), 1086 (S), 1024 (S), 980 (M), 917 (M), 883 (M), 845 (M), 810 (M), 756 (S), 729 (S), 684 (S).
MS (EI, 70 eV): m/z (%) = 480 (1), 371 (19), 305 (30), 230 (12), 229 (33), 83 (13), 77 (18), 71 (17), 57 (24), 43 (100).
HRMS ($C_{26}H_{28}N_2O_5S$): calc.: 480.1719; found: 480.1735.

(1-Benzenesulfonyl-3-cyclopropanecarbonyl-1*H*-pyrrolo[2,3-*b*]pyridin-2-yl)-cyclopropyl-methanone (50c)



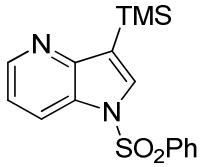
A I/Mg-exchange was performed according to **TP9** with MeMgCl. After addition of $ZnCl_2$ (0.6 mL, 0.6 mmol, 1.1 equiv, 1.0 M in THF) the reaction mixture was stirred for 10 min. A subsequent acylation reaction was performed according to **TP6** using cyclopropanecarbonyl chloride (47 mg, 0.45 mmol) at -40 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2→1:9) afforded the 7-azaindole **50c** (132 mg, 0.34 mmol, 74%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ / ppm = 8.54 – 8.51 (m, 1H), 8.38 (d, *J* = 7.7 Hz, 1H), 8.27 (d, *J* = 8.2 Hz, 2H), 7.63 – 7.59 (m, 1H), 7.52 (t, *J* = 7.7 Hz, 2H), 7.34 – 7.29 (m, 1H), 2.59 – 2.53 (m, 1H), 2.42 – 2.36 (m, 1H), 1.61 – 1.56 (m, 2H), 1.38 – 1.33 (m, 2H), 1.33 – 1.29 (m, 2H), 1.08 – 1.03 (m, 2H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ / ppm = 199.7, 195.9, 146.9, 146.6, 140.7, 137.3, 134.6, 131.2, 129.0, 128.8, 120.6, 119.3, 117.9, 25.2, 21.1, 15.2, 12.3.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1565 (W), 1447 (S), 1438 (S), 1401 (W), 1377 (W), 1329 (S), 1308 (W), 1293 (W), 1277 (W), 1234 (W), 1202 (W), 1163 (S), 1122 (M), 1090 (M), 1072 (S), 1057 (M), 1022 (W), 976 (W), 894 (M), 835 (W), 791 (M), 752 (M), 735 (VS), 720 (S), 686 (VS).
MS (EI, 70 eV): m/z (%) = 394 (5), 253 (25), 226 (86), 225 (23), 213 (18), 198 (33), 197 (29), 185 (48), 169 (47), 157 (33), 145 (32), 77 (64), 69 (38), 57 (31), 43 (100).

HRMS ($C_{21}H_{18}N_2O_4S$): calc.: 394.0987; found: 394.0980.

3.8 Synthesis of compounds of type 53, 54

1-(Phenylsulfonyl)-3-(trimethylsilyl)-1*H*-pyrrolo[3,2-*b*]pyridine (53a)



The title compound was prepared from the ynamide **52** (409 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -45 °C within 24 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 16 h was performed. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1). Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 4-azaindole **53a** (173 mg, 0.52 mmol, 52%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.55 (dd, J = 4.8 Hz, J = 1.5 Hz, 1H), 8.21 (dd, J = 8.3 Hz, J = 1.7 Hz, 1H), 7.93 – 7.88 (m, 2H), 7.71 (s, 1H), 7.62 – 7.55 (m, 1H), 7.52 – 7.45 (m, 2H), 7.20 (dd, J = 8.3 Hz, J = 4.4 Hz, 1H), 0.39 (s, 9H).

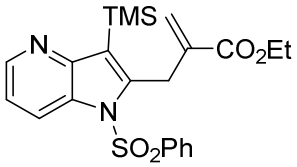
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3119 (VW), 2953 (W), 1652 (VW), 1588 (W), 1558 (W), 1514 (M), 1477 (W), 1451 (M), 1395 (M), 1364 (S), 1347 (W), 1330 (W), 1308 (W), 1302 (W), 1291 (W), 1278 (W), 1264 (W), 1243 (S), 1206 (VW), 1184 (S), 1174 (S), 1163 (M), 1132 (S), 1109 (S), 1088 (M), 1070 (W), 1051 (M), 1031 (W), 1021 (W), 1000 (W), 981 (VW), 973 (VW), 949 (M), 925 (VW), 839 (VS), 827 (S), 796 (S), 786 (S), 766 (M), 752 (S), 730 (S), 706 (S), 684 (S).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 153.2, 145.9, 138.2, 134.1, 133.7, 129.4, 129.2, 126.8, 120.3, 120.2, 118.6, -1.0.

MS (EI, 70 eV): m/z (%) = 331 (7), 330 (33).316 (25), 315 (100), 131 (22), 97 (13), 77 (15).

HRMS ($C_{16}H_{18}N_2O_2SSi$): calc.:330.0858; found: 330.0863.

2-(1-Benzenesulfonyl-3-trimethylsilanyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-acrylic acid ethyl ester (53b)

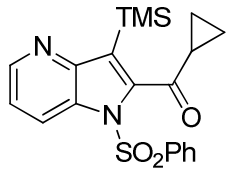


The title compound was prepared from the ynamide **52** (409 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -45 °C within 24 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 16 h was performed and a subsequent allylation reaction was performed according to **TP6** using ethyl 2-(bromomethyl)acrylate (174 mg, 0.9 mmol) at 0 °C.The reaction mixture was allowed to warm slowly to 23 °C within

12 h. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1). Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the 4-azaindole **53b** (141 mg, 0.32 mmol, 36%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.52 (dd, J = 4.7 Hz, J = 1.4 Hz, 1H), 8.42 (dd, J = 8.4 Hz, J = 1.5 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.59 – 7.52 (m, 1H), 7.47 – 7.39 (m, 2H), 7.18 (dd, J = 8.3 Hz, J = 4.7 Hz, 1H), 6.16 – 6.14 (m, 1H), 5.03 – 5.00 (m, 1H), 4.29 (q, J = 7.2 Hz, 2H), 4.12 – 4.09 (m, 2H), 1.36 (t, J = 7.1 Hz, 3H), 0.35 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.3, 152.5, 145.7, 144.5, 139.0, 138.8, 134.0, 130.9, 129.4, 126.6, 125.1, 121.4, 120.2, 118.5, 61.0, 29.7, 14.2, 0.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2925 (W), 1712 (M), 1634 (W), 1586 (W), 1544 (W), 1447 (M), 1405 (M), 1368 (S), 1297 (M), 1273 (M), 1245 (S), 1202 (M), 1188 (S), 1152 (S), 1134 (S), 1090 (S), 1071 (M), 1024 (M), 962 (W), 930 (S), 913 (M), 837 (VS), 784 (S), 755 (M), 730 (VS), 704 (S), 684 (S).
MS (EI, 70 eV): m/z (%) = 442 (4), 428 (36), 427 (100), 305 (34), 302 (28), 301 (50), 285 (42), 257 (26), 243 (22), 229 (36).
HRMS ($C_{22}H_{26}N_2O_4SSi$): calc.:442.1383; found: 442.1377.

(1-Benzenesulfonyl-3-trimethylsilanyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-yl)-cyclopropyl-methanone (53c)

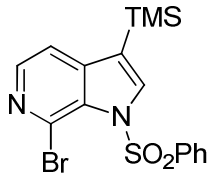


The title compound was prepared from the ynamide **52** (409 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -45 °C within 24 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 16 h was performed and a subsequent allylation reaction was performed according to **TP6** using cyclopropanecarbonyl chloride (94 mg, 0.9 mmol) at 0 °C.The reaction mixture was allowed to warm slowly to 23 °C within 12 h. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1). Flash column chromatographical purification on silica gel (isohexane:EtOAc = 85:15) afforded the 4-azaindole **53c** (160 mg, 0.4 mmol, 45%) as a yellow solid.

Mp.: 91-93 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.50 (dd, J = 4.7 Hz,J = 1.4 Hz, 1H), 8.27 (dd, J = 8.3 Hz,J = 1.4 Hz, 1H), 7.81 – 7.76 (m, 2H), 7.52 – 7.45 (m, 1H), 7.42 – 7.34 (m, 2H), 7.20 (dd, J = 8.3 Hz,J = 4.7 Hz, 1H), 2.53 – 2.44 (m, 1H), 1.49 – 1.42 (m, 2H), 1.29 – 1.25 (m, 2H), 0.34 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 200.8, 153.1, 146.6, 146.5, 136.5, 134.2, 129.7, 129.0, 127.2, 121.9, 121.5, 119.6, 25.1, 15.0, -0.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (W), 2921 (M), 2852 (W), 1688 (M), 1528 (W), 1448 (M), 1408 (W), 1372 (S), 1296 (W), 1261 (W), 1230 (S), 1190 (M), 1171 (S), 1123 (M), 1092 (M), 1050 (M), 1038 (M), 1004 (S), 952 (M), 881 (M), 840 (VS), 798 (M), 778 (S), 754 (S), 728 (VS), 699 (S), 683 (S).
MS (EI, 70 eV): m/z (%) = 398 (2), 384 (22), 383 (74), 258 (27), 257 (100), 243 (24), 242 (61), 227 (64).
HRMS ($C_{20}H_{22}N_2O_3SSi$): calc.: 398.1120; found: 398.1113.

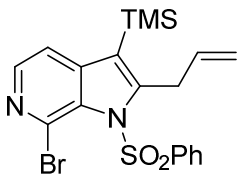
7-Bromo-1-(phenylsulfonyl)-3-(trimethylsilyl)-1*H*-pyrrolo[2,3-*c*]pyridine (54a)



The title compound was prepared from the ynamide **52** (409 mg, 1.0 mmol, 0.2 M). $MgCl_2$ (2.8 mL, 1.4 mmol, 0.5 M in THF) was added to **52** at 23 °C and the reaction mixture stirred for 10 min. After cooling down to -78 °C, TMPLi (**12**) (1.9 mL, 1.2 mmol, 0.63 M) was added dropwise and the reaction mixture stirred for 30 min. CuCN·2LiCl (1.2 mL, 100 mol%) was added and the mediated cyclization according to **TP4** at 23 °C in 48 h was performed. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1), extracted three times with EtOAc, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 6-azaindole **54a** (248 mg, 0.60 mmol, 60%) as a white solid.

Mp.: 131-130 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.15 (d, J = 5.3 Hz, 1H), 8.01 (s, 1H), 7.89 – 7.82 (m, 2H), 7.69 – 7.61 (m, 1H), 7.57 – 7.49 (m, 3H), 0.41 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 144.4, 142.1, 139.9, 138.6, 133.9, 133.0, 129.2, 127.2, 125.4, 116.4, 116.0, -0.8.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (W), 2921 (M), 2850 (W), 1704 (M), 1588 (W), 1583 (W), 1570 (W), 1558 (W), 1515 (W), 1476 (W), 1450 (M), 1414 (M), 1396 (M), 1364 (S), 1348 (M), 1331 (M), 1308 (M), 1302 (M), 1279 (M), 1243 (S), 1185 (S), 1174 (S), 1167 (S), 1135 (S), 1110 (S), 1085 (S), 1052 (M), 1022 (M), 1000 (M), 976 (M), 950 (S), 925 (M), 865 (M), 842 (S), 827 (M), 797 (S), 787 (S), 766 (M), 754 (S), 730 (VS), 708 (S), 684 (VS), 658 (M).
MS (EI, 70 eV): m/z (%) = 412 (7), 410 (87), 408 (82), 395 (83), 393 (76), 313 (22), 254 (11), 185 (21), 183 (34), 173 (35), 135 (29).
HRMS ($C_{16}H_{17}BrN_2O_2SSi$): calc.: 407.9963; found: 407.9958.

2-Allyl-7-bromo-1-(phenylsulfonyl)-3-(trimethylsilyl)-1H-pyrrolo[2,3-c]pyridine (54b)

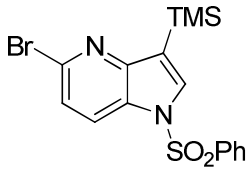


The title compound was prepared from the ynamide **52** (409 mg, 1.0 mmol, 0.2 M). $MgCl_2$ (3.25 mL, 1.3 mmol, 0.4 M in THF) was added to **52** at 23 °C and the reaction mixture stirred for 10 min. After cooling down to -78 °C, TMPLi (**12**) (1.9 mL, 1.2 mmol, 0.63 M) was added dropwise and the reaction mixture stirred for 30 min. CuCN·2LiCl (1.2 mL, 100 mol%) was added and the mediated cyclization according to **TP4** at 23 °C in 48 h was performed and a subsequent allylation reaction was performed according to **TP6** using allyl bromide (96 mg, 0.8 mmol) at 0 °C.The reaction mixture was allowed to warm slowly to 23 °C within 1 h. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1), extracted three times with EtOAc, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1→8:2) afforded the 6-azaindole **54b** (240 mg, 0.53 mmol, 67%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.18 (d, J = 5.1 Hz, 1H), 7.81 – 7.72 (m, 2H), 7.66 – 7.54 (m, 1H), 7.51 – 7.37 (m, 3H), 5.94 – 5.72 (m, 1H), 5.09 – 4.81 (m, 2H), 3.87 (dd, J = 5.9 Hz, 3.3 Hz, 1H), 0.33 (s, 9H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ / ppm = 153.4, 146.0, 143.4, 139.2, 136.8, 135.0, 133.7, 129.2, 128.8, 126.7, 120.6, 117.2, 115.4, 33.5, 0.4.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3411 (VW), 3003 (VW), 2957 (VW), 2921 (VW), 2360 (VW), 2339 (W), 1747 (W), 1711 (VS), 1675 (W), 1576 (W), 1548 (W), 1539 (VW), 1446 (W), 1436 (W), 1423 (W), 1419 (W), 1399 (W), 1359 (S), 1253 (W), 1220 (S), 1181 (W), 1157 (VW), 1091 (W), 972 (VW), 901 (W), 845 (W), 782 (VW), 759 (VW), 727 (W), 688 (W), 686 (W), 668 (W).
MS (ESI, 70 eV): m/z (%) = 449 (30), 409 (32), 407 (34), 308 (19), 307 (21), 155 (10), 141 (100).
HRMS ($C_{19}H_{22}BrN_2O_2SSi$): calc.: 449,0349; found: 449.0355 [M+H$^+$].

3.9 Synthesis of compounds of type 57

1-Benzenesulfonyl-5-bromo-3-trimethylsilanyl-1*H*-pyrrolo[3,2-*b*]pyridine (57a)

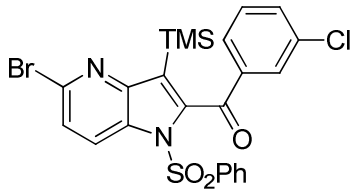


The title compound was prepared from the ynamide **55** (488 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -40 °C within 3 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 48 h was performed. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1). Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 4-azaindole **57a** (227 mg, 0.55 mmol, 55%) as a colorless solid.

Mp.: 127-129 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ / ppm = 8.05 (d, J = 8.8 Hz,1H), 7.90 – 7.85 (m, 2H), 7.67 (s, 1H), 7.65 – 7.58 (m, 1H), 7.55 – 7.47 (m, 2H), 7.34 (d, J = 8.6 Hz,1H), 0.37 (s, 9H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ / ppm = 153.6, 137.9, 137.2, 134.3, 134.3, 129.6, 128.2, 126.7, 122.5, 122.4, 119.9,-1.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3114 (VW), 2954 (W), 2925 (W), 2922 (W), 2852 (VW), 2169 (W), 1585 (W), 1539 (W), 1510 (M), 1452 (M), 1417 (M), 1391 (M), 1375 V(S), 1337 (W), 1317 (W), 1289 (W), 1273 (W), 1246 (S), 1187 (S), 1174 (S), 1145 (S), 1119 (S), 1089 (S), 1055 (M), 1022 (W), 999 (W), 951 (M), 841 V(S), 834 V(S), 818 V(S), 782 (M), 772 (S), 747 V(S), 722 (S), 682 V(S), 671 (M).
MS (EI, 70 eV): m/z (%) = 410 (22), 408 (21), 396 (23), 395 (100), 394 (93), 135 (18), 77 (20).
HRMS ($C_{16}H_{17}BrN_2O_2SSi$): calc.: 407.9963; found: 407.9952.

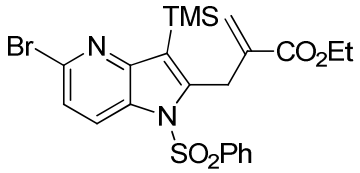
(1-Benzenesulfonyl-5-bromo-3-trimethylsilanyl-1*H*-pyrrolo[3,2-*b*]pyridine-2-yl)-(3-chloro-phenyl)-methanone (57b)



The title compound was prepared from the ynamide **55** (488 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -40 °C within 3 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 48 h and a subsequent acylation reaction was performed according to **TP6** using 3-chlorobenzoyl chloride (158 mg, 0.9 mmol) at 0 °C. The reaction mixture was allowed to warm slowly to 23 °C within 3 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the 4-azaindole **57b** (362 mg, 0.66 mmol, 73%) as a yellow crystals.

Mp.: 57-59 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.19 – 8.17 (m, 1H), 7.93 – 7.87 (m, 3H), 7.75 – 7.70 (m, 1H), 7.65 – 7.58 (m, 2H), 7.54 – 7.41 (m, 4H), 0. 21 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 189.6, 152.8, 142.8, 139.3, 137.9, 136.8, 135.2, 134.7, 134.0, 130.1, 129.4, 129.2, 128.3, 127.9, 127.4, 123.7, 123.7, 121.2, -0.5.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3064 (VW), 2953 (VW), 1667 (W), 1574 (W), 1543 (W), 1517 (W), 1477 (VW), 1465 (VW), 1448 (W), 1423 (W), 1398 (M), 1371 (S), 1343 (W), 1317 (M), 1295 (W), 1276 (W), 1248 (M), 1235 (M), 1183 (S), 1169 (S), 1164 (S), 1123 (M), 1090 (M), 1073 (W), 991 (M), 954 (W), 913 (W), 846 V(S), 811 (S), 776 (S), 755 (S), 742 (S), 733 V(S), 719 (S), 685 (S), 673 (M), 652 (W).
MS (EI, 70 eV): m/z (%) = 545 (2), 535 (30), 534 (27), 533 (85), 526 (61), 409 (30), 408 (24), 407 (100), 406 (23), 391 (81), 390 (61), 377 (19), 375 (14), 336 (13), 311 (18), 139 (24), 111 (24), 77 (44).
HRMS ($C_{23}H_{20}BrClN_2O_3SSi$): calc.: 545.9836; found: 545.9840.

Ethyl 2-((5-bromo-1-(phenylsulfonyl)-3-(trimethylsilanyl)-1*H*-pyrrolo[3,2-*b*]pyridine-2-yl)-methyl)acrylate (57c)



The title compound was prepared from the ynamide **55** (488 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -40 °C within 3 h (0.5 M). After addition of THF (8 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 48 h and a subsequent allylation reaction was performed according to **TP6** using ethyl 2-(bromomethyl)acrylate (173 mg, 0.9 mmol) at 0 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the 4-azaindole **57c** (298 mg, 0.57 mmol, 63%) as a white solid.

Mp.: 91-93 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.30 (d, J = 8.8 Hz,1H), 7.78 – 7.71 (m, 2H), 7.64 – 7.56 (m, 1H), 7.51 – 7.43 (m, 2H), 7.34 (d, J = 8.6 Hz,1H), 6.18 – 6.13 (m, 1H), 4.99 – 4.95 (m, 1H), 4.31 (q, J = 7.2 Hz,2H), 4.09 (t, J = 1.8 Hz,2H), 1.37 (t, J = 7.2 Hz,3H), 0.35 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.2, 152.9, 145.6, 138.7, 138.5, 136.9, 134.3, 129.9, 129.5, 126.6, 125.2, 123.8, 122.2, 119.7, 61.1, 30.1, 14.2, -0.1.

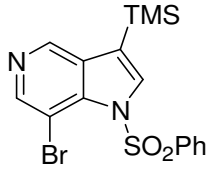
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (W), 2922 (M), 2851 (W), 1708 (M), 1633 (W), 1586 (W), 1542 (M), 1463 (W), 1447 (M), 1423 (W), 1400 (M), 1375 (S), 1350 (M), 1331 (W), 1313 (W), 1299 (M), 1275 (M), 1256 (M), 1245 (M), 1225 (M), 1190 (M), 1161 (M), 1135 (S), 1125 (S), 1105 (M), 1087 (S), 1077 (M), 1020 (M), 999 (W), 967 (M), 935 (M), 915 (M), 844 (VS), 806 (S), 782 (M), 754 (M), 740 (S), 717 (S), 680 (S), 661 (M).

MS (EI, 70 eV): m/z (%) = 520 (1), 508 (28), 507 (100), 506 (27), 505 (82), 477 (13), 381 (28), 379 (27), 335 (16).

HRMS ($C_{22}H_{25}BrN_2O_4SSi$): calc.: 520.0488; found: 520.0480.

3.10 Synthesis of compounds of type 60

1-Benzenesulfonyl-7-bromo-3-trimethylsilanyl-1*H*-pyrrolo[3,2-*c*]pyridine (60a)

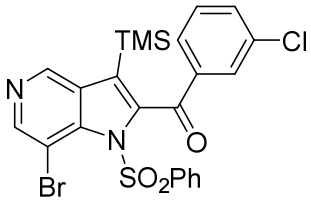


The title compound was prepared from the ynamide **58** (488 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -80 °C within 0.5 h (0.25 M). After addition of THF (6 mL), a CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 48 h was performed. The reaction mixture was quenched with concentrated aqueous NH_4Cl/NH_3-solution (19:1). Flash column

chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 5-azaindole **60a** (214 mg, 0.52 mmol, 52%) as a white solid.

Mp.: 113-115 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.83 (s, 1H), 8.49 (s, 1H), 7.84 (s, 1H), 7.85 – 7.79 (m, 2H), 7.66 – 7.58 (m, 1H), 7.55 – 7.47 (m, 2H), 0.41 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 147.7, 143.4, 139.8, 138.9, 135.8, 134.2, 134.1, 129.3, 127.2, 115.8, 103.9, -0.7.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3144 (VW), 2955 (W), 1638 (VW), 1580 (W), 1536 (VW), 1521 (W), 1478 (W), 1448 (M), 1429 (M), 1403 (M), 1362 (S), 1312 (W), 1288 (M), 1248 (M), 1182 (S), 1169 (M), 1157 (S), 1144 (M), 1115 (S), 1088 (M), 1075 (M), 1045 (W), 1025 (W), 1000 (W), 955 (S), 909 (M), 885 (M), 857 (M), 830 (S), 820 (S), 758 (S), 745 (S), 727 V(S), 689 (S).
MS (EI, 70 eV): m/z (%) = 412 (11), 411 (24), 410 (98), 409 (24), 408 (100), 396 (15), 395 (64), 386 (62), 254 (15), 185 (26), 183 (25), 173 (17), 145 (13), 135 (39).
HRMS ($C_{16}H_{17}BrN_2O_2SSi$): calc.: 407.9963; found: 407.9961.

(7-Bromo-1-(phenylsulfonyl)-3-(trimethylsilyl)-1*H*-pyrrolo[3,2-*c*]pyridine-2-yl)(3-chlorophenyl)methanone (60b)

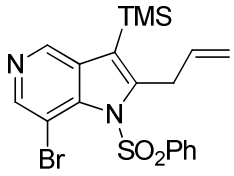


The title compound was prepared from the ynamide **58** (488 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -80 °C within 0.5 h (0.2 M). A CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 48 h and a subsequent allylation reaction was performed according to **TP6** using 3-chlorobenzoyl chloride (158 mg, 0.9 mmol) at 0 °C. The reaction mixture was allowed to warm slowly to 23 °C within 3 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 5-azaindole **60b** (351 mg, 0.64 mmol, 71%) as a yellow solid.

Mp.: 68-70 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.96 (s, 1H), 8.65 (s, 1H), 8.10 – 8.04 (m, 2H), 7.99 (t, J = 1.8 Hz, 1H), 7.85 (dt, J = 7.7 Hz, J = 1.2 Hz, 1H), 7.67 – 7.58 (m, 2H), 7.57 – 7.43 (m, 3H), 0.22 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 188.4, 148.8, 144.5, 143.9, 141.0, 139.4, 138.3, 135.1, 134.3, 133.9, 133.6, 130.0, 129.6, 129.1, 128.2, 127.7, 126.0, 120.3, 0.3.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3064 (VW), 2950 (VW), 1672 (W), 1570 (W), 1520 (VW), 1448 (W), 1423 (W), 1401 (W), 1369 (M), 1306 (W), 1280 (W), 1249 (M), 1179 (S), 1140 (M), 1122 (M), 1088 (M), 1074 (W), 1033 (W), 1015 (W), 990 (M), 980 (M), 952 (M), 879 (W), 840 V(S), 775 (M), 749 V(S), 726 (S), 685 (S), 672 (M).

MS (EI, 70 eV): m/z (%) = 546 (10), 535 (13), 533 (35), 528 (21), 408 (29), 407 (27), 396 (24), 395 (100), 392 (71), 336 (47), 334 (33), 225 (23), 215 (21), 139 (56).
HRMS ($C_{23}H_{20}BrClN_2O_3SSi$): calc.: 545.9836; found: 545.9837.

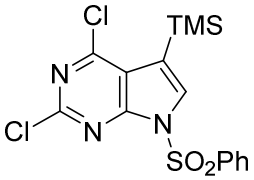
2-Allyl-7-bromo-1-(phenylsulfonyl)-3-(trimethylsilyl)-1*H*-pyrrolo[3,2-*c*]pyridine (60c)



The title compound was prepared from the ynamide **58** (488 mg, 1.0 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (0.87 mL, 1.27 M, 1.1 mmol, 1.1 equiv) at -80 °C within 0.5 h (0.2 M). A CuCN·2LiCl (1.0 mL, 100 mol%) mediated cyclization according to **TP4** at 23 °C in 48 h and a subsequent allylation reaction was performed according to **TP6** using allyl bromide (108 mg, 0.9 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded the 5-azaindole **60c** (280 mg, 0.62 mmol, 69%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.81 (s, 1H), 8.55 (s, 1H), 7.82 – 7.75 (m, 2H), 7.65 – 7.57 (m, 1H), 7.52 – 7.43 (m, 2H), 5.90 – 5.75 (m, 1H), 5.04 – 4.98 (m, 1H), 4.91 – 4.82 (m, 1H), 3.90 (dt, J = 5.7 Hz, J = 1.7 Hz, 2H), 0.39 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 149.5, 148.1, 143.3, 142.3, 139.9, 135.4, 134.7, 133.7, 128.9, 126.6, 118.6, 117.0, 107.3, 33.1, 0.7.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3061 (VW), 2953 (W), 2167 (VW), 1638 (VW), 1571 (W), 1478 (VW), 1447 (M), 1429 (M), 1403 (M), 1364 (M), 1310 (W), 1291 (W), 1251 (M), 1180 (S), 1159 (M), 1139 (M), 1121 (W), 1088 (M), 1045 (W), 1034 (W), 996 (W), 962 (M), 910 (M), 894 (M), 880 (M), 837 V(S), 750 (S), 725 V(S), 707 (M), 684 (S).
MS (EI, 70 eV): m/z (%) = 450 (27), 448 (18), 310 (42), 309 (60), 308 (60), 307 (51), 294 (28), 293 (100), 291 (26), 279 (13), 277 (16), 265 (16), 135 (33), 125 (20), 77 (61), 73 (68), 59 (23).
HRMS ($C_{19}H_{21}BrN_2O_2SSi$): calc.: 448.0276; found: 448.0269.

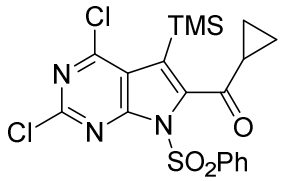
2,4-Dichloro-7-(phenylsulfonyl)-5-(trimethylsilyl)-7H-pyrrolo[2,3-*d*]pyrimidine (63a)



The title compound was prepared from ynamide **62** (200 mg, 0.5 mmol) according to **TP5**. After addition of CuCN·2LiCl solution (0.5 mL, 0.5 mmol) at -78 ºC, the copper-mediated cyclization was carried out according to **TP2.** The mixture was allowed to warm to 23 °C and stirred for further 72 h. After completion, the reaction was quenched with concentrated aqueous NH_4Cl/NH_3-solution (2:1), extracted three times with EtOAc and CH_2Cl_2, the organic layers dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded the azaindole **63a** (134 mg, 0.33 mmol, 67%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.30 – 8.25 (m, 2H), 7.73 – 7.66 (m, 1H), 7.68 (s, 1H), 7.63 – 7.56 (m, 2H), 0.41 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 154.2, 153.9, 153.5, 136.9, 135.1, 129.3, 128.9, 122.0, 114.2, -0.2.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3121 (VW), 3067 (VW), 2957 (W), 2924 (W), 2852 (W), 2360 (W), 2358 (W), 2176 (W), 1749 (W), 1627 (W), 1548 (S), 1538 (S), 1449 (M), 1413 (M), 1376 (M), 1331 (M), 1282 (M), 1251 (M), 1220 (M), 1208 (M), 1187 (S), 1170 (S), 1125 (M), 1112 (M), 1085 (S), 1035 (M), 1016 (M), 1001 (M), 995 (M), 984 (M), 973 (S), 837 (VS), 751 (S), 720 (S), 682 (S), 668 (S)
MS (EI, 70 eV): m/z (%) = 399 (3), 388 (4), 384 (22), 320 (15), 246 (16), 135 (36), 94 (17), 77 (100).
HRMS ($C_{15}H_{15}Cl_2N_3O_2SSi$): calc.: 399.0031; found: 399.0027.

Cyclopropyl(2,4-dichloro-7-(phenylsulfonyl)-5-(trimethylsilyl)-7H-pyrrolo[2,3-*d*]pyrimidin-6-yl)methanone (63b)

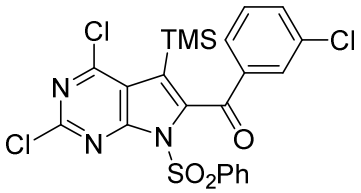


The title compound was prepared from ynamide **62** (200 mg, 0.5 mmol) according to **TP5**. After addition of CuCN·2LiCl solution (0.5 mL, 0.5 mmol) at -78 ºC, the copper-mediated cyclization was carried out according to **TP2.** The mixture was allowed to warm 23 °C and stirred for further 72 h. After completion, a subsequent acylation was performed using cyclopropanecarbonyl chloride (47 mg, 0.45 mmol) at 23 °C for 12 h. The reaction was quenched with concentrated aqueous NH_4Cl/NH_3-solution (2:1), extracted three times with EtOAc and CH_2Cl_2, the organic layers dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 95:5 -> 9:1) afforded the azaindole **63b** (146 mg, 0.31 mmol, 69%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.28 – 8.18 (m, 2H), 7.71 – 7.64 (m, 1H), 7.61 – 7.53 (m, 2H), 2.46 – 2.36 (m, 1H), 1.62 – 1.53 (m, 2H), 1.45 – 1.36 (m, 2H), 0.41 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 200.1, 154.5, 154.2, 153.8, 144.2, 136.6, 135.2, 129.3, 129.2, 121.1, 111.6, 25.9, 16.7, 1.5.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2960 (W), 2366 (W), 2362 (W), 2360 (W), 2358 (W), 2357 (W), 2338 (W), 1699 (M), 1559 (M), 1522 (M), 1507 (W), 1450 (M), 1400 (M), 1389 (M), 1377 (M), 1354 (S), 1346 (M), 1315 (W), 1283 (W), 1259 (M), 1253 (M), 1237 (M), 1218 (W), 1192 (S), 1172 (S), 1160 (M), 1155 (M), 1131 (W), 1123 (W), 1122 (W), 1104 (M), 1093 (S), 1083 (M), 1079 (M), 1054 (VS), 1027 (M), 1023 (M), 1002 (W), 1000 (W), 995 (W), 984 (S), 896 (W), 878 (S), 866 (S), 843 (VS), 824 (M), 822 (M), 815 (S), 805 (M), 799 (S), 770 (M), 754 (S), 729 (VS), 717 (M), 707 (M), 703 (M), 701 (M), 697 (M), 681 (VS), 668 (M), 661 (W), 653 (S),
MS (EI, 70 eV): m/z (%) = 467 (3), 456 (14), 455 (13), 454 (57), 452 (67), 314 (65), 312 (100), 311 (30), 135 (10), 77 (66).

HRMS ($C_{19}H_{19}Cl_2N_3O_3SSi$): calc.: 467.0293; found: 467.0284.

(3-Chlorophenyl)(2,4-dichloro-7-(phenylsulfonyl)-5-(trimethylsilyl)-7H-pyrrolo[2,3-*d*]pyrimidin-6-yl)methanone (63c)



The title compound was prepared from ynamide **62** (200 mg, 0.5 mmol) according to **TP5**. After addition of CuCN·2LiCl solution (0.5 mL, 0.5 mmol) at -78 ºC, the copper-mediated cyclization was carried out according to **TP2.** The mixture was allowed to warm to 23 °C and stirred for further 72 h. After completion, a subsequent acylation was performed using 3-chlorobenzoyl chloride (79 mg, 0.45 mmol) at 23 °C for 12 h. The reaction was quenched with concentrated aqueous NH_4Cl/NH_3-solution (2:1), extracted three times with EtOAc and CH_2Cl_2, the organic layers dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 95:5 -> 9:1) afforded the azaindole **63c** (146 mg, 0.31 mmol, 69%) as a white solid.

Mp.:170-172 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.18 – 8.13 (m, 2H), 7.92 (s_{br}, 1H), 7.77 (s_{br}, 1H), 7.73 – 7.63 (m, 2H), 7.62 – 7.55 (m, 2H), 7.49 (t, J = 7.9 Hz, 1H), 0.23 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 188.7, 154.7, 154.2, 154.1, 140.8, 139.3, 136.3, 135.5, 135.4, 134.3, 130.4, 129.3 (2C), 129.0, 127.7, 121.1, 113.6, 1.3.

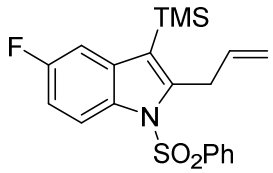
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3064 (W), 2956 (W), 2359 (W), 2336 (W), 1698 (M), 1674 (M), 1651 (W), 1567 (M), 1520 (M), 1485 (W), 1480 (W), 1471 (W), 1450 (M), 1411 (M), 1389 (M), 1373 (M), 1354 (M), 1348 (M), 1307 (M), 1245 (S), 1205 (S), 1192 (S), 1179 (S), 1170 (S), 1158 (S), 1126 (M), 1091 (S), 1074 (M), 1032 (S), 1016 (M), 996 (M), 949 (S), 927 (M), 897 (M), 879 (M), 841 (VS), 815 (S), 784 (M), 769 (S), 765 (S), 749 (VS), 723 (VS), 700 (M), 689 (M), 685 (M), 679 (S), 674 (S), 668 (VS), 653 (M).

MS (EI, 70 eV): m/z (%) = 539 (9), 537 (7), 527 (12), 526 (42), 524 (100), 522 (92), 386 (28),385 (28), 384 (84), 383 (54), 382 (81), 381 (35), 348 (16), 346 (22), 141 (38), 139 (37), 111 (32).

HRMS ($C_{22}H_{18}Cl_3N_3O_3SSi$):calc.: 536.9904; found: 536.9901.

3.11 Scaleable Preparation of Functionalized Indoles and Azaindoles *via* an Intramolecular Copper-mediated Carbomagnesiation of Ynamides

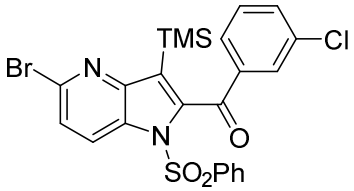
2-Allyl-5-fluoro-1-(phenylsulfonyl)-3-(trimethylsilyl)-1H-indole (41n)



The title compound was prepared from the ynamide **39a** (21.3 g, 50 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (45.8 mL, 1.2 M, 55 mmol, 1.1 equiv) at -10 °C within 0.5 h (1.0 M). After addition of THF (450 mL), a CuCN·2LiCl (50 mL, 50 mmol) mediated cyclization according to **TP4** at 23 °C in 30 h and a subsequent allylation reaction was performed according to **TP6** using allylbromide (6.1 g, 50 mmol) at 0 °C within 16 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc:NEt_3 = 98:1:1) afforded the indole **41n** (17.2 g, 44.4 mmol, 99%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.11 (dd, *J* = 9.2, 4.7 Hz, 1H), 7.76 – 7.70 (m, 2H), 7.56 – 7.49 (m, 1H), 7.46 – 7.37 (m, 2H) 7.25 (dd, *J* = 9.5, 2.6 Hz, 1H), 6.98 (ddd, *J* = 9.1, 2.6 Hz, 1H), 6.06 – 5.91 (m, 2H), 5.07 – 5.01 (m, 1H), 4.93 – 4.84 (m, 1H), 3.90 (dt, *J* = 5.3, 1.8 Hz, 2H), 0.37 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 159.5 (d, *J* = 239.5 Hz), 145.8, 139.1, 136.0, 135.2 (d, *J* = 9.6 Hz), 134.0 (d, *J* = 1.2 Hz), 133.8, 129.2, 126.5, 117.2 (d, *J* = 3.9 Hz), 116.3, 115.9 (d, *J* = 9.3 Hz), 111.5 (d, *J* = 24.9 Hz), 107.3 (d, *J* = 23.8 Hz), 32.1, 0.8.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2954 (W), 2168 (W), 1638 (W), 1584 (M), 1502 (W), 1459 (S), 1447 (M), 1368 (S), 1312 (W), 1295 (W), 1251 (M), 1214 (M), 1189 (S), 1171 (S), 1144 (S), 1118 (M), 1089 (S), 1070 (M), 1024 (W), 984 (M), 909 (M), 851 (VS), 837 (VS), 811 (S), 753 (S), 723 (VS), 984 (VS).
MS (EI, 70 eV): m/z (%) = 388 (29), 387 (100), 372 (17), 247 (19), 246 (75), 232 (21), 231 (85), 230 (85), 216 (53), 173 (81), 172 (33), 154 (20), 153 (34), 135 (47), 77 (28).
HRMS ($C_{22}H_{18}Cl_3N_3O_3SSi$): calc.: 387.1125; found: 387.1112.

(1-Benzenesulfonyl-5-bromo-3-trimethylsilanyl-1*H*-pyrrolo[3,2-*b*]pyridine-2-yl)-(3-chloro-phenyl)-methanone (57b)

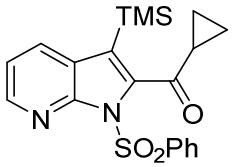


The title compound was prepared from the ynamide **55** (22.0 g, 45 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (41.3 mL, 1.2 M, 49.5 mmol, 1.1 equiv) at -40 °C within 3 h (0.5 M). After addition of THF (360 mL), a CuCN·2LiCl (45 mL, 45 mmol) mediated cyclization according to **TP4** at 23 °C in 24 h and a subsequent acylation reaction was

performed according to **TP6** using 3-chlorobenzoyl chloride (7.96 g, 41.0 mmol) at 0 °C. The reaction mixture was allowed to warm slowly to 23 °C within 3 h. Recrystallization in *i*Hex/EtOAc afforded the 4-azaindole **57b** (15.9 g, 29.1 mmol, 71%) as yellow crystals.

Mp.: 57-59 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.19 – 8.17 (m, 1H), 7.93 – 7.87 (m, 3H), 7.75 – 7.70 (m, 1H), 7.65 – 7.58 (m, 2H), 7.54 – 7.41 (m, 4H), 0. 21 (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 189.6, 152.8, 142.8, 139.3, 137.9, 136.8, 135.2, 134.7, 134.0, 130.1, 129.4, 129.2, 128.3, 127.9, 127.4, 123.7, 123.7, 121.2, -0.5.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3064 (VW), 2953 (VW), 1667 (W), 1574 (W), 1543 (W), 1517 (W), 1477 (VW), 1465 (VW), 1448 (W), 1423 (W), 1398 (M), 1371 (S), 1343 (W), 1317 (M), 1295 (W), 1276 (W), 1248 (M), 1235 (M), 1183 (S), 1169 (S), 1164 (S), 1123 (M), 1090 (M), 1073 (W), 991 (M), 954 (W), 913 (W), 846 V(S), 811 (S), 776 (S), 755 (S), 742 (S), 733 V(S), 719 (S), 685 (S), 673 (M), 652 (W).
MS (EI, 70 eV): m/z (%) = 545 (2), 535 (30), 534 (27), 533 (85), 526 (61), 409 (30), 408 (24), 407 (100), 406 (23), 391 (81), 390 (61), 377 (19), 375 (14), 336 (13), 311 (18), 139 (24), 111 (24), 77 (44).
HRMS ($C_{23}H_{20}BrClN_2O_3SSi$): calc.: 545.9836; found: 545.9840.

1-Benzenesulfonyl-3-trimethylsilanyl-1*H*-pyrrolo[2,3-*b*]pyridine-2-yl)-cyclopropyl-methanone (47d)



The title compound was prepared from the ynamide **45** (20.4 g, 50 mmol). A Br/Mg-exchange was performed according to **TP3** with *i*-PrMgCl·LiCl (43 mL, 1.28 M, 55 mmol, 1.1 equiv) at -45 °C within 1 h (0.5 M). After addition of THF (400 mL), a CuCN·2LiCl (50 mL, 50 mmol) mediated cyclization according to **TP4** at 23 °C in 36 h and a subsequent acylation reaction was performed according to **TP6** using cyclopropanecarbonyl chloride (4.7 g, 45 mmol) at 0 °C. The reaction mixture was allowed to warm slowly to 23 °C within 12 h. Flash column chromatographical purification on silica gel (isohexane:EtOAc:NEt_3 = 9:1:0.2 -> 8:2:0.2) afforded the 7-azaindole **47d** (14.1 g, 35.4 mmol, 79%) as an colorless solid.

Mp.:123-125 °C.
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.45 (dd, J = 4.8 Hz, J = 1.7 Hz, 1H), 8.11 – 8.05 (m, 2H), 7.94 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.45 – 7.38 (m, 2H), 7.16 (dd, J = 8.0 Hz, J = 4.7 Hz, 1H), 2.52 – 2.44 (m, 1H), 1.50 – 1.44 (m, 2H), 1.30 – 1.23 (m, 2H), 0.34 (s, 9H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 200.1, 149.2, 145.7, 144.2, 137.5, 134.0, 131.4, 128.7, 128.2, 126.1, 119.3, 116.6, 24.9, 15.0, 0.3.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2163 (W), 1677 (W), 1447 (W), 1416 (M), 1377 (S), 1250 (M), 1182 (S), 1170 (S), 1123 (W), 1089 (M), 1064 (W), 1046 (W), 1028 (M), 1007 (M),

951 (W), 933 (W), 839 (VS), 814 (S), 798 (M), 774 (M), 757 (S), 751 (S), 737 (S), 727 (M), 715 (M), 698 (M), 682 (S), 666 (M).

MS (EI, 70 eV): m/z (%) = 399 (3), 398 (9), 385 (13), 384 (31), 383 (100), 319 (18), 243 (25), 242 (56), 241 (15), 227 (41), 77 (15).

HRMS ($C_{20}H_{22}N_2O_3SSi$): calc.: 398.1120; found: 398.1117.

4. Unprecedented Regioselectivities in Metalations of Functionalized Arenes and Heteroarenes with TMPLi in the Presence of $ZnCl_2$ and other Metal Salts (in situ Trapping Method)

4.1 Typical Procedures

Typical Procedure for metalation/transmetalation with $MgCl_2 \cdot 2LiCl$ (TP1):

A dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirrer and a septum was charged with the starting aromatic compound in THF (0.2-0.25 M solution) and cooled to -78 ºC. Then, magnesium chloride (1.1 equiv) and LiCl (2.2 equiv) solutions were added, prior to the addition of TMPLi (**12**) (1.5 equiv). The corresponding electrophile was added (0.9 - 1.0 equiv) afterwards and the reaction mixture was stirred for the indicated time and at the indicated temperature. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with concentrated aqueous NH_4Cl-, H_2O or $Na_2S_2O_3$-solutions and using undecane as an internal standard.

Typical Procedure for metalation/transmetalation with $MgCl_2$ (TP1'):

TP1 was performed without addition of LiCl solution.

Typical Procedure for metalation/transmetalation with $ZnCl_2 \cdot 2LiCl$ (TP2):

A dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirrer and a septum was charged with the starting aromatic compound in THF (0.2-0.25 M solution) and cooled to -78 ºC. Then, $ZnCl_2$ (1.1 equiv) and LiCl (2.2 equiv) solutions were added, prior to the addition of TMPLi (**12**) (1.5 equiv). The corresponding electrophile was added (0.9 - 1.0 equiv) afterwards and the reaction mixture was stirred for the indicated timeand at the indicated temperature. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with concentrated aqueous NH_4Cl- or $Na_2S_2O_3$-solutions and using undecane as an internal standard.

Typical Procedure for metalation/transmetalation with $ZnCl_2$ (TP2'):

TP2 was performed without addition of LiCl solution.

Typical Procedure for metalation/transmetalation with $CuCN \cdot 2LiCl$ (TP3):

A dry and argon flushed *Schlenk*-flask, equipped with a magnetic stirrer and a septum was charged with the starting aromatic compound in THF (0.2-0.25 M solution) and cooled to -78 ºC. Then, $CuCN \cdot 2LiCl$ (1.1 equiv) solution was added, prior to the addition of TMPLi (**12**) (1.5 equiv). The corresponding electrophile was added (0.8 - 1.0 equiv) afterwards and the reaction mixture was stirred for the indicated time and at the indicated temperature. The completion of the reaction was checked by GC analysis of reaction aliquots quenched with concentrated aqueous NH_4Cl/NH_3 (2:1)-solution and using undecane as an internal standard.

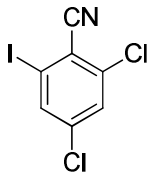
Typical Procedure for Cross-coupling Reactions (TP4):

To the freshly prepared zinc reagent, $Pd(dba)_2$ (2 mol%), tfp (4 mol%) and the aryl iodide (0.7 – 1.0 equiv) were added and the reaction mixture stirred at 23 °C for the indicated time. The reaction mixture was quenched with half concentrated aqueous NH_4Cl-solution, extracted three

times with EtOAc, the organic layers dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel.

4.2 Synthesis of compounds of type 72

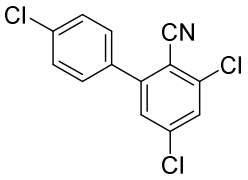
2,4-Dichloro-6-iodobenzonitrile (72a)[142]



The title compound was prepared according to **TP2** from 2,4-dichlorobenzonitrile (**69a**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of 2,4-dichlorobenzonitrile (172 mg, 1.0 mmol), $ZnCl_2$ (1.1 mL, 1.0 M, 1.1 mmol) and LiCl (3.14 mL, 0.7 M, 2.2 mmol) in THF (2.5 mL) at -78 °C. An excess of iodine was added and stirred for 5 min at -78 °C prior to quench with sat. $Na_2S_2O_3$-solution. Before chromatographic separation, the crude regioselectivity was 95:5. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 95:5) afforded 2,4-dichloro-6-iodobenzonitrile (**72a**) (219 mg, 0.74 mmol, 74%) as white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.85 (d, J = 2.0 Hz, 1H), 7.53 (d, J = 1.7 Hz, 1H).

3,4`,5-Trichloro-[1,1`-biphenyl]-2-carbonitrile (72b)



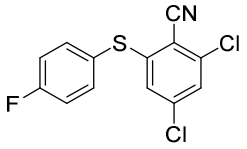
The title compound was prepared according to **TP2** from 2,4-dichlorobenzonitrile (**69a**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of 2,4-dichlorobenzonitrile (172 mg, 1.0 mmol), $ZnCl_2$ (1.1 mL, 1.0 M, 1.1 mmol) and LiCl (3.14 mL, 0.7 M, 2.2 mmol) in THF (2 mL) at -78 °C. According to **TP4** the corresponding zinc reagent was reacted with 1-chloro-4-iodobenzene (215 mg, 0.9 mmol) at that temperature for 5 min and additional 2 h at 23 °C prior to quench with sat. NH_4Cl-solution. Before chromatographic separation, the crude regioselectivity was 97:3. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 95:5) afforded 3,4`,5-trichloro-[1,1`-biphenyl]-2-carbonitrile (**72b**) (172 mg, 0.61 mmol, 68%) as white solid.

M.p.: 160-163 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.55 (d, J = 2.0 Hz, 1H), 7.53 – 7.43 (m, 4H), 7.39(d, J = 1.7 Hz, 1H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 147.5, 139.5, 139.0, 136.1, 134.6, 129.9, 129.2, 128.8, 128.5, 114.8, 110.9.

[142] Spectral data in full accordance to those reported in the literature: S.D. Kuduk, M.R. Wood, M.G. Bock, PCT Int. Appl. **2004**, WO2004019868.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3073 (w), 2231 (w), 1596 (m), 1580 (m), 1568 (w), 1543 (m), 1494 (m), 1435 (m), 1408 (m), 1387 (m), 1291 (w), 1195 (w), 1106 (m), 1093 (s), 1073 (w), 1065 (w), 1057 (m), 1014 (m), 910 (w), 868 (w), 858 (m), 850 (m), 828 (vs), 744 (w), 720 (m), 707 (w), 656 (m).
MS (EI, 70 eV): m/z (%) = 285 (30), 283 (95), 281 (100), 248 (17), 246 (25), 211 (40).
HRMS ($C_{13}H_6Cl_3N$): calc.: 280.9566; found: 280.9571.

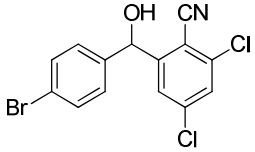
2,4-Dichloro-6-[(4-fluorophenyl)thio]benzonitrile (72c)



The title compound was prepared according to **TP1** from 2,4-dichlorobenzonitrile (**69a**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of 2,4-dichlorobenzonitrile (172 mg, 1.0 mmol), $MgCl_2$ (2.2 mL, 0.5 M, 1.1 mmol) and LiCl (3.14 mL, 0.7 M, 2.2 mmol) in THF (2 mL) at -78 °C. S-(4-fluorophenyl) benzenesulfonothioate (242 mg, 0.9 mmol) was added afterwards and stirred at that temperature for 0.5 h prior to quench with sat. NH_4Cl-solution. Before chromatographic separation the crude regioselectivity was 88:12. Flash column chromatographical purification on silica gel (toluene:CH_2Cl_2 = 7:3) afforded 2,4-dichloro-6-((4-fluorophenyl)thio)benzonitrile (**72c**) (200 mg, 0.67 mmol, 75%) as white solid.

M.p.: 128-130 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.62 – 7.52 (m, 2H), 7.30 – 7.15 (m, 3H), 6.70 (d, J = 1.9 Hz, 1H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 164.0 (d, J = 252.6 Hz), 148.0 (d, J = 1.7 Hz), 139.8, 138.8, 137.5 (d, J = 8.7 Hz), 126.5, 125.3, 124.0 (d, J = 3.5 Hz), 117.7 (d, J = 22.3 Hz), 113.3, 109.6.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3074 (w), 2229 (w), 1590 (m), 1565 (m), 1556 (m), 1538 (m), 1489 (s), 1461 (w), 1432 (w), 1417 (m), 1399 (w), 1381 (m), 1372 (m), 1346 (w), 1291 (w), 1240 (s), 1226 (m), 1190 (m), 1158 (m), 1138 (m), 1094 (m), 1078 (m), 1052 (w), 1012 (w), 938 (w), 872 (m), 844 (s), 832 (vs), 817 (s), 799 (s), 714 (w), 687 (w), 674 (w), 660 (m).
MS (EI, 70 eV): m/z (%) = 300 (15), 299 (77), 297 (100), 270 (21), 227 (31).
HRMS ($C_{13}H_6Cl_2FNS$): calc.: 296.9582; found: 296.9568.

2-((4-Bromophenyl)(hydroxy)methyl)-4,6-dichlorobenzonitrile (72d)

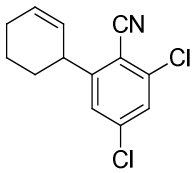


The title compound was prepared according to **TP1** from 2,4-dichlorobenzonitrile (**69a**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of 2,4-dichlorobenzonitrile (172 mg, 1.0 mmol), $MgCl_2$ (2.2 mL, 0.5 M, 1.1 mmol) and LiCl (3.14 mL, 0.7 M, 2.2 mmol) in THF (2 mL) at -78 °C. 4-Bromobenzaldehyde (167 mg, 0.9 mmol) was added afterwards and stirred at that temperature for 1 h prior to quench with sat. NH_4Cl-solution.

Flash column chromatographical purification on silica gel (DCM) afforded 2-((4-bromophenyl)(hydroxy)methyl)-4,6-dichlorobenzonitrile **72e** (165 mg, 0.46 mmol, 51%) as white solid.

Mp.: 135.3-137.0 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.61 – 7.47 (m, 3H), 7.22 – 7.06 (m, 3H), 6.27 (s, 1H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.1, 152.5, 141.6, 134.3, 134.3, 132.5, 131.2, 128.5, 124.0, 121.7, 120.7, 80.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3074 (w), 2962 (w), 1777 (s), 1727 (w), 1704 (w), 1698 (w), 1694 (w), 1682 (w), 1593 (m), 1583 (m), 1487 (m), 1447 (m), 1417 (w), 1399 (m), 1328 (w), 1314 (w), 1282 (m), 1261 (m), 1212 (m), 1180 (w), 1101 (m), 1086 (s), 1070 (m), 1054 (s), 1035 (m), 1022 (s), 1006 (vs), 951 (m), 942 (m), 902 (w), 884 (w), 872 (m), 850 (s), 823 (m), 807 (s), 791 (s), 759 (s), 718 (m), 690 (m), 676 (s), 656 (s).
MS (EI, 70 eV): m/z (%) = 357 (17), 355 (14), 281 (32), 281 (24), 277 (40), 221 (29), 208 (28), 207 (100), 185 (27), 183 (21), 169 (19).
HRMS ($C_{14}H_8BrCl_2NO$): calc.: 354.9166; found: 354.9162.

3,5-Dichloro-1`,2`,3`,4`-tetrahydro-[1,1`-biphenyl]-2-carbonitrile(72e)

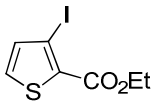


The title compound was prepared according to **TP3** from 2,4-dichlorobenzonitrile (**69a**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of 2,4-dichlorobenzonitrile (172 mg, 1.0 mmol), and CuCN·2LiCl (1.1 mL, 1 M, 1.1 mmol) in THF (3 mL) at -78 °C. 3-Bromocyclohex-1-ene (145 mg, 0.9 mmol) was added afterwards and stirred at that temperature for 30 min prior to quench with sat. NH_4Cl/NH_3-solution. Before chromatographic separation the crude regioselectivity was 97:3. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 95:5) afforded 3,5-dichloro-1`,2`,3`,4`-tetrahydro-[1,1`-biphenyl]-2-carbonitrile (**72d**) (202 mg, 0.8 mmol, 89%) as white solid.

M.p.: 57-59 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.31 (d, J = 2.0 Hz, 1H), 7.21 – 7.17 (m, 1H), 6.03 – 5.93 (m, 1H), 5.59 – 5.45 (m, 1H), 3.84 – 3.72 (m, 1H), 2.15 – 2.00 (m, 3H), 1.71 – 1.36 (m, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 154.1, 139.6, 138.0, 131.3, 127.7, 127.1, 126.6, 114.4, 111.7, 40.4, 31.2, 24.7, 20.6.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3070 (w), 3024 (w), 2932 (m), 2863 (w), 2834 (w), 2230 (m), 1576 (s), 1551 (s), 1447 (m), 1434 (m), 1398 (s), 1371 (w), 1354 (w), 1342 (w), 1306 (w), 1260 (w), 1238 (w), 1222 (w), 1197 (w), 1158 (m), 1137 (w), 1088 (m), 1042 (m), 999 (w), 969 (w), 938 (w), 922 (w), 897 (m), 884 (m), 872 (s), 862 (m), 838 (s), 806 (m), 752 (w), 743 (m), 728 (m), 717 (m), 676 (w), 654 (vs).
MS (EI, 70 eV): m/z (%) = 253 (29), 251 (100), 236 (38), 223 (29), 197 (24), 190 (31), 188 (51), 175 (20), 162 (26), 153 (23).

HRMS ($C_{13}H_{11}Cl_2N$): calc.: 251.0269; found: 251.0256.

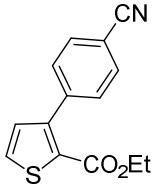
Ethyl 3-iodothiophene-2-carboxylate (72f)



The title compound was prepared according to **TP2`** from ethyl thiophene-2-carboxylate (**69b**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of ethyl thiophene-2-carboxylate (156 mg, 1.0 mmol) and $ZnCl_2$ (1.1 mL, 1.0 M, 1.1 mmol) in THF (2.5 mL) at -78 °C. An excess of iodine was added and stirred for 5 min at -78 °C prior to quench with sat. $Na_2S_2O_3$-solution. Before chromatographic separation, the crude regioselectivity was 75:25. Flash column chromatographical purification on silica gel (isohexane:EtOAc:CH_2Cl_2 = 7:1:2) afforded a mixture of ethyl 3-iodothiophene-2-carboxylate (**72f**) and ethyl 5-iodothiophene-2-carboxylate (75:25) as yellow oil (242 mg, 0.86 mmol, 86%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.43 (d, J = 5.1 Hz, 1H), 7.43* (d, J = 3.7 Hz, 1H), 7.26* (d, J = 3.7 Hz, 1H), 7.22 (d, J = 5.1 Hz, 1H),4.38 (q, J = 7.3 Hz, 2H), 4.36*(q, J = 7.2 Hz, 2H),1.40 (t, J = 7.1 Hz, 3H), 1.37*(t, J = 7.1 Hz, 3H).
*shows the signals for ethyl 5-iodothiophene-2-carboxylate

Ethyl 3-(4-cyanophenyl)thiophene-2-carboxylate (72g)

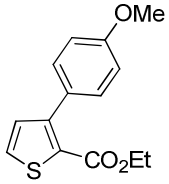


The title compound was prepared according to **TP2`** from ethyl thiophene-2-carboxylate (**69b**) (1.0 mmol). TMPLi (**12**) (2.19 mL, 0.64 M, 1.4 mmol) was added dropwise to a solution of ethyl thiophene-2-carboxylate (156 mg, 1.0 mmol) and $ZnCl_2$ (0.5 mL, 1.0 M, 0.5 mmol) in THF (2 mL) at -78 °C. According to **TP4**, the corresponding zinc reagent was reacted with 4-iodobenzonitrile (183 mg, 0.8 mmol) at that temperature for 5 min and additional 0.5 h at room temperature prior to quench with sat. NH_4Cl-solution. Before chromatographic separation, the crude regioselectivity was 75:25. Flash column chromatographical purification on silica gel (isohexane:CH_2Cl_2 = 9:1 + 2% NEt_3) afforded ethyl 3-(4-cyanophenyl)thiophene-2-carboxylate (**72g**) (156 mg, 0.61 mmol, 76%) as white solid.

M.p.: 96-98 °C.
^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.72 - 7.66 (m, 2H), 7.60 - 7.53 (m, 3H), 7.08 (d, J = 5.2 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 1.26 (t, J = 7.2 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 161.6, 146.0, 140.5, 131.5, 130.8, 130.8, 130.1, 128.7, 118.8, 111.5, 61.2, 14.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3097 (W), 3006 (W), 2987 (W), 2961 (W), 2937 (W), 2904 (W), 2837 (W), 2358 (W), 2342 (W), 2339 (W), 1703 (S), 1608 (M), 1576 (W), 1538 (W), 1500 (M), 1480 (M), 1467 (M), 1455 (M), 1450 (M), 1442 (M), 1419 (M), 1404 (M), 1392 (M),

1371 (W), 1360 (W), 1306 (W), 1290 (M), 1276 (S), 1245 (S), 1220 (S), 1188 (M), 1179 (S), 1154 (M), 1112 (S), 1103 (S), 1083 (S), 1067 (S), 1020 (S), 1014 (S), 952 (M), 940 (M), 906 (M), 896 (M), 869 (M), 842 (M), 824 (S), 778 (VS), 753 (M), 743 (S), 724 (S), 701 (W), 697 (W), 679 (S), 668 (M), 659 (S).
MS (EI, 70 eV): m/z (%) = 258 (9), 257 (52), 229 (22), 213 (16), 212 (100), 185 (15), 140 (41).
HRMS ($C_{14}H_{11}NO_2S$): calc.: 257.0510; found: 257.0505.

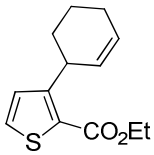
Ethyl 3-(4-methoxyphenyl)thiophene-2-carboxylate (72h)



The title compound was prepared according to **TP2** from ethyl thiophene-2-carboxylate (**69b**) (1.0 mmol). TMPLi (**12**) (2.19 mL, 0.64 M, 1.4 mmol) was added dropwise to a solution of ethyl thiophene-2-carboxylate (156 mg, 1.0 mmol) and $ZnCl_2$ (1.1 mL, 1.0 M, 1.1 mmol) in THF (2 mL) at -78 °C. According to **TP4**, the corresponding zinc reagent was reacted with 4-iodoanisole (187 mg, 0.8 mmol) at that temperature for 5 min and additional 0.5 h at room temperature prior to quench with sat. NH_4Cl-solution. Before chromatographic separation the crude regioselectivity was 75:25. Flash column chromatographical purification on silica gel (isohexane:CH_2Cl_2 = 9:1 + 2% NEt_3) afforded ethyl 3-(4-methoxyphenyl)thiophene-2-carboxylate (**72h**) (153 mg, 0.58 mmol, 73%) as colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.48 (d, J = 5.2 Hz, 1H), 7.46 - 7.40 (m, 2H), 7.08 (d, J = 5.0 Hz, 1H), 6.99 - 6.91 (m, 2H), 4.26 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 162.2, 159.4, 148.2, 131.5, 130.5, 129.9, 128.0, 126.7, 113.2, 60.8, 55.2, 14.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3104 (W), 3088 (VW), 2986 (W), 2358 (W), 2330 (W), 2229 (M), 1705 (S), 1652 (W), 1635 (W), 1605 (W), 1558 (W), 1534 (W), 1498 (M), 1472 (W), 1457 (W), 1422 (M), 1405 (W), 1388 (W), 1377 (W), 1369 (W), 1360 (W), 1285 (M), 1275 (S), 1251 (W), 1231 (S), 1177 (M), 1156 (W), 1133 (W), 1133 (W), 1121 (M), 1115 (M), 1110 (M), 1086 (M), 1075 (S), 1025 (M), 1019 (M), 968 (W), 906 (M), 899 (W), 868 (M), 852 (VS), 839 (M), 822 (M), 807 (M), 777 (VS), 736 (M), 727 (S), 672 (S), 668 (M), 658 (M).
MS (EI, 70 eV): m/z (%) = 263 (16), 262 (100), 234 (25), 217 (52), 190 (14).
HRMS ($C_{14}H_{14}O_3S$): calc.: 262.0664; found: 262.0659.

Ethyl 3-(cyclohex-2-en-1-yl)thiophene-2-carboxylate (72i)



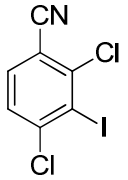
The title compound was prepared according to **TP3** from ethyl thiophene-2-carboxylate (**69b**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of ethyl

thiophene-2-carboxylate (156 mg, 1.0 mmol), and CuCN·2LiCl (2.0 mL, 1 M, 2.0 mmol) in THF (3 mL) at -78 °C. 3-Bromocyclohex-1-ene (113 mg, 0.7 mmol) was added afterwards and stirred at that temperature for 30 min prior to quench with sat. NH_4Cl/NH_3-solution.Before chromatographic separation the crude regioselectivity was 87:13. Flash column chromatographical purification on silica gel (isohexane:CH_2Cl_2 = 95:5 + 2% NEt_3) afforded ethyl 3-(cyclohex-2-en-1-yl)thiophene-2-carboxylate (**72i**) (115 mg, 0.49 mmol, 70%) as colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.39 (d, *J* = 4.9 Hz, 1H), 7.03 (d, *J* = 5.2 Hz, 1H), 5.88 – 5.84 (m, 1H), 5.69 – 5.65 (m, 1H), 4.46 – 4.41 (m, 1H), 4.37 – 4.39 (m, 2H), 2.11 – 2.05 (m, 3H), 1.78 – 164 (m, 2H), 1.57 – 1.49 (m, 1H), 1.38 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm =162.5, 154.9, 129.9, 129.8, 129.5, 128.0, 126.3, 60.7, 35.5, 30.8, 25.0, 21.4, 14.3.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3102 (VW), 3019 (VW), 2980 (W), 2931 (W), 2858 (W), 2834 (VW), 2359 (W), 2339 (VW), 1702 (S), 1699 (S), 1653 (W), 1635 (W), 1528 (M), 1476 (W), 1473 (W), 1456 (W), 1445 (M), 1436 (W), 1417 (M), 1389 (M), 1380 (W), 1365 (M), 1338 (W), 1287 (S), 1269 (M), 1240 (VS), 1230 (VS), 1212 (S), 1188 (M), 1171 (M), 1135 (W), 1095 (S), 1071 (VS), 1019 (M), 958 (M), 924 (M), 888 (W), 882 (W), 863 (M), 846 (M), 824 (M), 811 (W), 777 (S), 759 (M), 749 (S), 724 (M), 707 (W), 701 (W), 697 (W), 694 (W), 692 (W), 686 (W), 668 (M), 661 (M).
MS (EI, 70 eV): m/z (%) = 236 (57), 190 (85), 189 (100), 171 (21), 161 (43), 125 (21), 128 (17).
HRMS ($C_{13}H_{16}O_2S$): calc.: 236.0871; found: 236.0876.

4.3 Synthesis of compound of type 73

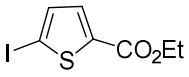
2,4-Dichloro-3-iodobenzonitrile (73a)



The title compound was prepared by reaction of 2,4-dichlorobenzonitrile (**1a**; 175 mg, 1.0 mmol) dissolved in anhydrous THF (1 mL) and TMPZnCl·LiCl (1.10 M, 1.0 mL, 1.1 mmol) at 60 °C for 12 h. Then, a solution of iodine (254 mg, 1.0 mmol) in THF (1 mL) was added and the reaction mixture was stirred at that temperature for 15 min before it was quenched with sat. $Na_2S_2O_3$-solution. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 95:5) afforded 2,4-dichloro-3-iodobenzonitrile (**73a**) (228 mg, 0.76 mmol, 78%) as a white powder.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.61 (d, *J* = 8.3 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 145.9, 143.2, 133.4, 127.5, 115.2, 111.7, 105.8.
MS (EI, 70 eV): m/z (%) = 297 (6), 153 (10), 131 (10), 113 (23), 97 (100), 83 (22).
HRMS ($C_7H_2Cl_2IN$): calc.: 296.8609; found: 296.8588.

Ethyl 5-iodothiophene-2-carboxylate (73b)[143]

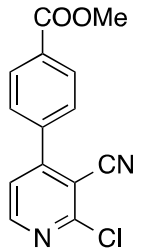


The title compound was prepared from ethyl thiophene-2-carboxylate (**69b**) (1.0 mmol). TMPMgCl·LiCl (0.94 mL, 1.17 M, 1.1 mmol) was added at 23 °C and the reaction mixture stirred for 3.5 h. Then, a solution of iodine (254 mg, 1.0 mmol) in THF (1 mL) was added and the reaction mixture was stirred at that temperature for 15 min before it was quenched with sat. $Na_2S_2O_3$-solution. Flash column chromatographical purification on silica gel (isohexane:EtOAc:DCM = 7:1:2) afforded Ethyl 5-iodothiophene-2-carboxylate (**73b**) (170 mg, 0.6 mmol, 60%) as yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.43 (d, J = 3.9 Hz, 1H), 7.26 (d, J = 3.9 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.2 Hz.

4.4 Synthesis of compounds of type 75

Methyl 4-(2-chloro-3-cyanopyridin-4-yl)benzoate (75a)



The title compound was prepared according to **TP2** from 2-chloro-3-cyanopyridine (**74a**) (1.0mmol). TMPLi (**12**) (2.38 mL, 0.64M, 1.5 mmol) was added dropwise to a solution of 2-chloro-3-cyanopyridine (142 mg, 1.0 mmol), $ZnCl_2$ (1.1 mL, 1M, 1.1 mmol) and LiCl (3.14 mL, 0.7M, 2.2 mmol) in THF (4 mL) at -78 °C. According to **TP4**, the corresponding zinc reagent was reacted with methyl 4-iodobenzoate (236mg, 0.9 mmol) at that temperature for 5 min and additional 2 h at room temperature prior to quench. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 7:3) afforded methyl 4-(2-chloro-3-cyanopyridin-4-yl)benzoate (**75a**) (247mg, 0.91 mmol, 90%) as a yellow powder.

M.p.:185-187 ºC.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.61 (d, J = 5.1 Hz, 1H), 8.20 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 5.1 Hz, 1H), 3.96 (s, 3H).

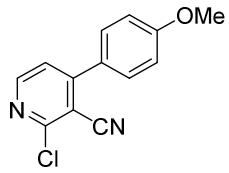
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.0, 155.0, 154.4, 152.1, 139.0, 132.1, 130.4, 128.6, 122.6, 114.3, 109.3, 52.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1713 (S), 1700 (M), 1695 (M), 1571 (S), 1558 (M), 1532 (M), 1456 (M), 1432 (S), 1405 (M), 1363 (M), 1307 (M), 1290 (S), 1274 (S), 1254 (M), 1239 (M), 1234 (M), 1210 (M), 1187 (M), 1179 (M), 1115 (S), 1106 (S), 1103 (S), 1059 (S), 1015

[143] Spectral data in full accordance to those reported in the literature: T.T. Nguyen, N. Marquise, F. Chevallier, F. Mongin, *Chem. Eur. J. 17* **2011**, 10405.

(M), 966 (M), 878 (M), 854 (S), 837 (M), 809 (M), 794 (M), 784 (M), 778 (S), 756 (VS), 743 (M), 704 (VS), 683 (S), 677 (M), 675 (M), 673 (M).
MS (EI, 70 eV): m/z (%) = 272 (46), 243 (39), 241 (100), 213 (9), 177 (33), 151 (18).
HRMS ($C_{14}H_9N_2O_2Cl$): calc.: 272.0353; found: 272.0358.

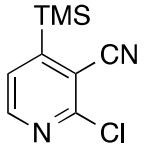
2-Chloro-4-(4-methoxyphenyl)-3-cyanopyridine 75b



The title compound was prepared according to **TP2** from 2-chloro-3-cyanopyridine (**74a**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of 2-chloro-3-cyanopyridine (138 mg, 1.0 mmol), $ZnCl_2$ (1.1 mL, 1.0 M, 1.1 mmol) and LiCl (3.14 mL, 0.7M, 2.2 mmol) in THF (2 mL) at -78 °C. According to **TP4**, the corresponding zinc reagent was reacted with 4-iodoanisole (234 mg, 1.0 mmol) at that temperature for 5 min and additional 2 h at room temperature prior to quench with sat. NH_4Cl-solution. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 1:1) afforded 2-chloro-4-(4-methoxyphenyl)-3-cyanopyridine (**75b**) (176 mg, 0.72 mmol, 72%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.53 (d, J = 5.4 Hz, 1H), 7.62 – 7.57 (m, 2H), 7.38 (d, J = 5.1 Hz, 1H), 7.09 – 7.03 (m, 2H), 3.89 (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 161.7, 155.7, 154.4, 151.6, 130.0, 127.0, 122.3, 114.7, 108.6, 55.5.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3010 (w), 2946 (w), 2847 (w), 2227 (w), 1606 (m), 1573 (m), 1538 (w), 1524 (m), 1513 (s), 1464 (w), 1454 (m), 1442 (m), 1418 (w), 1369 (m), 1310 (m), 1294 (m), 1259 (s), 1236 (m), 1202 (m), 1182 (s), 1156 (m), 1116(m), 1077 (w), 1062 (s), 1022 (s), 973 (m), 960 (w), 851 (m), 828 (vs), 819 (vs), 799 (m), 761 (s), 725 (w), 686 (w).
MS (EI, 70 eV): m/z (%) = 246 (31), 245 (14), 244 (100), 201 (16), 166 (10), 165 (22).
HRMS ($C_{12}H_9ClN_2O$): calc.: 244.0403; found: 244.0396.

2-Chloro-3-cyano-4-(trimethylsilyl)pyridine (75c)



The title compound was prepared according to **TP1** from 2-chloro-3-cyanopyridine (**74a**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of 2-chloro-3-cyanopyridine (142 mg, 1.0 mmol), $MgCl_2$ (2.2 mL, 0.5M, 1.1 mmol) and LiCl (3.14 mL, 0.7 M, 2.2 mmol) in THF (2.5 mL) at -78 °C. Trimethylsilylchloride (127 µL, 1.0 mmol) was added afterwards and stirred at that temperature for 10 min and additional 5 min at 23 °C prior to quench. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded 2-chloro-3-cyano-4-(trimethylsilyl)pyridine (**75c**) (210 mg, 0.99 mmol, 99%) as a white powder.

M.p.: 128-130 ºC.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.50 (d, *J* = 4.8 Hz, 1H), 7.43 (d, *J* = 4.8 Hz, 1H), 0.47 (s, 9H).

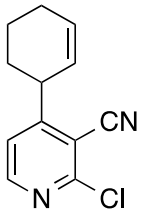
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 159.3, 153.5, 151.0, 126.9, 115.7, 114.8, -2.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2961 (VW), 2229 (W), 1564 (W), 1558 (W), 1539 (VW), 1533 (VW), 1509 (W), 1496 (VW), 1489 (VW), 1436 (W), 1432 (W), 1424 (VW), 1419 (VW), 1413 (VW), 1357 (M), 1270 (W), 1256 (M), 1246 (M), 1223 (W), 1199 (W), 1178 (VW), 1159 (VW), 1141 (W), 1121 (M), 1087 (W), 881 (VW), 845 (VS), 801 (M), 784 (W), 773 (M), 743 (S), 720 (W), 717 (W), 712 (W), 702 (W), 698 (W), 683 (W), 680 (W), 677 (W), 672 (W), 667 (W), 665 (VW), 661 (VW), 657 (VW), 655 (VW), 653 (VW), 651 (VW).

MS (EI, 70 eV): m/z (%) = 212 (2), 210 (5), 197 (37), 195 (100), 73 (21), 72 (7).

HRMS ($C_9H_{11}N_2ClSi$): calc.: 210.0380; found: 210.0383.

2-Chloro-4-(cyclohex-2-en-1-yl)-3-cyanopyridine(75d)



The title compound was prepared according to **TP3** from2-chloro-3-cyanopyridine (**74a**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of 2-chloro-3-cyanopyridine (142 mg, 1.0 mmol) and CuCN·2LiCl (1.1 mL, 1 M, 1.1 mmol) in THF (4 mL) at -78 °C. 3-bromocyclohex-1-ene(115 µL, 1.0 mmol) was added afterwards and stirred at that temperature for 10 min and additional 1 h at 0 ºC prior to quench. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded 2-chloro-4-(cyclohex-2-en-1-yl)-3-cyanopyridine (**75d**) (210mg, 0.96 mmol, 96%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.39 (d, *J* = 5.2 Hz, 1H), 7.22 (d, *J* = 5.2 Hz, 1H), 6.00 – 5.98 (m, 1H), 5.53 – 5.49 (m, 1H), 3.76 (td, *J* = 5.6, 2.8 Hz, 1H), 2.10 – 2.03 (m, 3H), 1.63 – 1 56 (m, 2H), 1.49 - 1.41 (m, 1H).

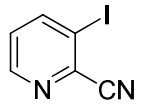
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 162.7, 153.0, 151.8, 131.5, 125.3, 121.4, 113.6, 110.2, 40.1, 30.4, 24.4, 20.3.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3024 (W), 2933 (W), 2894 (W), 2881 (W), 2862 (W), 2860 (W), 2836 (W), 2229 (W), 1575 (VS), 1560 (W), 1554 (W), 1541 (S), 1450 (M), 1436 (W), 1432 (W), 1393 (M), 1370 (VS), 1306 (W), 1258 (W), 1239 (W), 1204 (W), 1192 (W), 1175 (W), 1161 (M), 1152 (W), 1135 (W), 1076 (W), 1060 (W), 1045 (M), 939 (W), 909 (M), 902 (M), 890 (M), 841 (S), 805 (M), 796 (W), 766 (W), 751 (M), 731 (S), 716 (S), 697 (M), 686 (W), 684 (W), 683 (W), 677 (W), 675 (W), 668 (W).

MS (EI, 70 eV): m/z (%) =218 (66), 217 (100), 203 (30), 189 (15), 181 (14), 166 (16), 155 (18), 54 (12).

HRMS ($C_{12}H_{11}N_2Cl$): calc.: 218.0611; found: 218.027.

3-Iodopicolinonitrile



The title compound was prepared according to **TP1`** from picolinonitrile (**74b**) (1.0 mmol). TMPLi (**12**) (1.72 mL, 0.64 M, 1.1 mmol) was added dropwise to a solution of picolinonitrile (104 mg, 1.0 mmol), $MgCl_2$ (2.6 mL, 0.5 M, 1.3 mmol) in THF (3.0 mL) at -78 °C. A solution of iodine in THF (in excess) was added afterwards and stirred at that temperature for 10 min and additional 5 min at room temperature prior to quench with sat. $Na_2S_2O_3$-solution. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2 -> 6:4) afforded 3-iodopicolinonitrile (165 mg, 0.72 mmol, 72%) as a white powder.

Mp.: 108-110 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.68 (dd, *J* = 4.6, 1.5 Hz, 1H), 8.25 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.30 – 7.23 (m, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 149.4, 146.7, 139.5, 127.4, 117.4, 97.6.

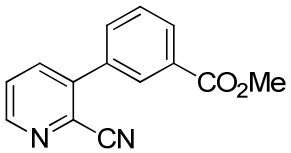
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3056 (w), 3048 (w), 2238 (w), 1549 (m), 1434 (w), 1420 (w), 1409 (s), 1259 (m), 1246 (w), 1234 (w), 1192 (w), 1181 (w), 1129 (w), 1104 (w), 1060 (s), 1013 (s), 990 (m), 951 (w), 924 (w), 880 (w), 817 (w), 796 (vs), 752 (w), 744 (s), 686 (w), 668 (w).

MS (EI, 70 eV): m/z (%) = 231 (8), 230 (100), 127 (12), 103 (66), 76 (24), 69 (11).

HRMS ($C_6H_3IN_2$): calc.: 229.9341; found: 229.9326.

NMR-data: G. Bentabed-Ababsa, S. C: S. Ely, S. Hesse, E. Nassar, F. Chevallier, T. T: Nguyen, A. Derdour, F. Mongin, *J. Org. Chem.* **2010**, *75*, 839.

Methyl 3-(2-cyanopyridin-3-yl)benzoate (75e)



The title compound was prepared according to **TP2** from picolinonitrile (**74b**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of picolinonitrile (104 mg, 1.0 mmol), $ZnCl_2$ (1.1 mL, 1.0 M, 1.1 mmol) in THF (2 mL) at -78 °C. According to **TP4** the corresponding zinc reagent was reacted with methyl 3-iodobenzoate (236 mg, 0.9 mmol) at that temperature for 5 min and additional 15 min at room temperature prior to quench with sat. NH_4Cl-solution. Flash column chromatographical purification on silica gel (CH_2Cl_2→CH_2Cl_2:EtOAc = 9:1) afforded methyl 3-(2-cyanopyridin-3-yl)benzoate (**75e**) (180 mg, 0.76 mmol, 84%) as a brown powder.

M.p.: 215-218 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.75 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.08 – 8.25 (m, 2H), 7.91 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.82 (ddd, *J* = 7.7, 1.9, 1.1 Hz, 1H), 7.77 – 7.67 (m, 2H), 3.96 (s, 3H).

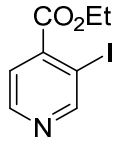
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.3, 149.8, 141.1, 137.6, 135.6, 133.0, 132.2, 131.1, 130.5, 129.9, 129.2, 126.7, 116.6, 52.4.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3049 (w), 2964 (w), 2232 (w), 1722 (s), 1587 (w), 1556 (w), 1470 (w), 1454 (w), 1447 (w), 1427 (m), 1404 (w), 1322 (w), 1310 (m), 1284 (w), 1266 (vs), 1230 (m), 1186 (m), 1124 (w), 1110 (m), 1090 (s), 1070 (w), 1028 (w), 1000 (w), 964 (m), 919 (w), 824 (w), 810 (m), 774 (m), 750 (s), 731 (m), 696 (s), 665 (w).

MS (EI, 70 eV): m/z (%) = 239 (14), 238 (15), 230 (16), 207 (29), 179 (15), 149 (15), 126 (13), 104 (14), 88 (15), 86 (62), 84 (100), 51 (20).

HRMS ($C_{14}H_{10}N_2O_2$): calc.: 238.0742; found: 238.0729.

Ethyl 3-iodoisonicotinate



The title compound was prepared according to **TP2`** from ethyl isonicotinate (**74c**)[144] (1.0 mmol). TMPLi (**12**) (1.72 mL, 0.64 M, 1.1 mmol) was added dropwise to a solution of ethyl isonicotinate (151 mg, 1.0 mmol), $ZnCl_2$ (1.3 mL, 1.0 M, 1.3 mmol) in THF (5.0 mL) at -78 °C. A solution of iodine in THF (in excess) was added afterwards and stirred at that temperature for 10 min and additional 5 min at 23 °C prior to quench with sat. $Na_2S_2O_3$-solution. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded ethyl 3-iodoisonicotinate[145] (180 mg, 0.65 mmol, 65%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 9.09 (s, 1H), 8.61 (d, J = 4.9, 0.7 Hz, 1H), 7.63 (dd, J = 5.0, 0.7 Hz, 1H), 4.42 (q, J = 7.2 Hz, 2H), 1.41 (t, J = 7.2 Hz, 3H).

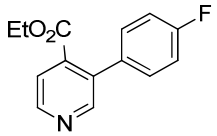
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 164.9, 159.4, 149.0, 142.5, 124.4, 92.4, 62.4, 14.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3040 (w), 2981 (w), 1727 (s), 1574 (w), 1528 (w), 1465 (w), 1445 (w), 1394 (m), 1366 (m), 1298 (s), 1261 (vs), 1209 (m), 1178 (s), 1112 (s), 1078 (s), 1010 (s), 872 (m), 842 (m), 776 (s), 700 (s), 663 (s).

MS (EI, 70 eV): m/z (%) = 278 (8), 277 (100), 249 (43), 232 (58), 204 (18), 177 (15), 122 (10).

HRMS ($C_8H_8INO_2$): calc.: 276.9600; found: 276.9585.

Ethyl 3-(4-fluorophenyl)isonicotinate (75f)



The title compound was prepared according to **TP2** from ethyl isonicotinate (**74c**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of ethyl isonicotinate (151 mg, 1.0 mmol), $ZnCl_2$ (1.1 mL, 1.0 M, 1.1 mmol) in THF (2 mL) at -78 °C. According to

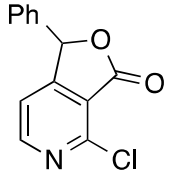
[144]Alternatively, a metalation with $TMP_2Mg{\cdot}2LiCl$ at -40 °C over 12 h is possible. See: G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem.* **2007**, *119*, 7825; *Angew. Chem. Int. Ed.***2007**, *46*, 7681.

[145] G. Bentabed-Ababsa, S. C: S. Ely, S. Hesse, E. Nassar, F. Chevallier, T. T: Nguyen, A. Derdour, F. Mongin, *J. Org. Chem.***2010**, *75*, 839.

TP4 the corresponding zinc reagent was treated with 1-fluoro-4-iodobenzene (178 mg, 0.8 mmol) at that temperature for 5 min and additional 2 h at room temperature prior to quench with sat. NH_4Cl-solution. Flash column chromatographical purification on silica gel (CH_2Cl_2) afforded ethyl 3-(4-fluorophenyl)isonicotinate (**75f**) (155 mg, 0.63 mmol, 79%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.71 (d, *J* = 5.0 Hz, 1H), 8.67 (s, 1H), 7.65 (dd, *J* = 5.1, 0.7 Hz, 1H), 7.35 – 7.27 (m, 2H), 7.19 – 7.09 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.10(t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.7, 162.7 (d, *J* = 248.0 Hz), 151.3, 149.1, 138.1, 135.1, 133.4 (d, *J* = 3.4 Hz), 130.4 (d, *J* = 8.1 Hz), 122.6, 115.3 (d, *J* = 21.6 Hz), 61.7, 13.7.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} =3039 (VW), 2981 (W), 2935 (VW), 2360 (W), 2358 (W), 2354 (VW), 2341 (VW), 2338 (VW), 2334 (VW), 2332 (VW), 1721 (S), 1607 (M), 1596 (W), 1583 (W), 1558 (W), 1550 (W), 1542 (VW), 1539 (VW), 1512 (S), 1498 (W), 1479 (M), 1457 (W), 1445 (W), 1437 (W), 1414 (M), 1396 (M), 1366 (M), 1313 (M), 1285 (S), 1280 (S), 1245 (S), 1222 (S), 1178 (S), 1160 (S), 1095 (S), 1075 (M), 1015 (M), 1004 (M), 876 (W), 835 (VS), 820 (S), 791 (S), 739 (M), 734 (M), 714 (S), 672 (S), 653 (W).
MS (EI, 70 eV): m/z (%) = 246 (16), 245 (86), 238 (12), 217 (28), 201 (22), 200 (100), 172 (44).
HRMS ($C_{14}H_{12}FNO_2$): calc.: 245.0852; found: 245.0852.

4-Chloro-1-phenylfuro[3,4-*c*]pyridin-3(1*H*)-one (75g)[146]



The title compound was prepared according to **TP1'** from ethyl 2-chloronicotinate (**74d**)[147] (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of ethyl 2-chloronicotinate (168 µL, 1.0 mmol) and magnesium chloride (2.2 mL, 0.5 M, 1.1 mmol) in THF (4 mL) at -78 °C. Benzaldehyde (102 µL, 1.0 mmol) was added afterwards and stirred at that temperature for 10 min and additional 2 h at room temperature prior to quench. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 6:4 to 2:8) afforded 4-chloro-1-phenylfuro[3,4-*c*]pyridin-3(1*H*)-one (**75g**) (231mg, 0.94 mmol, 94%) as a light orange solid.

M.p.:100-102 ºC.
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.55 (d, *J* = 5.1 Hz, 1H), 7.40 - 7.35 (m, 3H), 7.29 (d, *J* = 5.1 Hz, 1H), 7.26 - 7.21 (m, 2H), 6.39 (s, 1H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 165.7, 161.1, 153.5, 149.3, 134.0, 129.8, 129.1, 126.6, 119.1, 117.1, 80.9.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1769 (S), 1718 (M), 1700 (W), 1695 (W), 1671 (M), 1669 (M), 1653 (M), 1635 (W), 1628 (W), 1616 (W), 1594 (M), 1586 (M), 1576 (M), 1560 (M), 1542 (W), 1533 (W), 1496 (W), 1448 (M), 1404 (M), 1347 (W), 1303 (M), 1279 (M), 1252 (M),

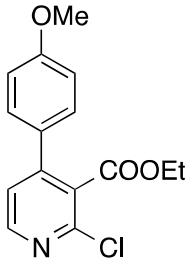
[146] Spectral data in full accordance to those reported in the literature: M. Abarbri, J. Thibonnet, L. Berillon, F. Dehmel, M. Rottlaender, P. Knochel, *J. Org. Chem.* **2000**, *65*, 4618.
[147] Alternatively, a metalation with $TMP_2Zn{\cdot}2MgCl_2$ 2LiCl at 23 °C over 5 h is possible. See: G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem.* **2007**, *119*, 7825; *Angew. Chem. Int. Ed.***2007**, *46*, 7681.

1218 (M), 1202 (M), 1174 (M), 1172 (M), 1124 (M), 1089 (M), 1061 (M), 1038 (M), 1029 (M), 997 (M), 991 (M), 948 (S), 915 (M), 876 (W), 862 (M), 824 (M), 821 (M), 787 (M), 761 (S), 730 (S), 696 (VS), 667 (M), 665 (M), 663 (M), 660 (M), 653 (M).

MS (EI, 70 eV): m/z (%) = 332 (16), 331 (93), 329 (89), 191 (18), 190 (100), 188 (97), 185 (39), 109 (31), 77 (38).

HRMS ($C_{13}H_8NO_2Cl$): calc.: 245.0244; found: 245.0243.

Ethyl 2-chloro-4-(4-methoxyphenyl)nicotinate (75h)



The title compound was prepared according to **TP2** from ethyl 2-chloronicotinate (**74d**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of ethyl 2-chloronicotinate (168 µL, 1.0 mmol), $ZnCl_2$ (1.1 mL, 1 M, 1.1 mmol) and LiCl (3.14 mL, 0.7 M, 2.2 mmol) in THF (4 mL) at -78 °C. According to **TP4** the corresponding zinc reagent was reacted with 1-iodo-4-methoxybenzene (234 mg, 1.0 mmol) at that temperature for 5 min and additional 3 h at room temperature prior to quench. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 85:15 to 3:1) afforded ethyl 2-chloro-4-(4-methoxyphenyl)nicotinate (**75h**) (251mg, 0.86 mmol, 86%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.39 (d, J = 5.2 Hz, 1H), 7.34 (d, J = 8.8 Hz, 2H), 7.23 (d, J = 5.2 Hz, 1H), 6.94 (d, J = 8.8 Hz, 2H), 4.23 (q, J = 7.1 Hz, 2H), 3.82 (s, 3H), 1.15 (t, J = 7.1 Hz, 3H).

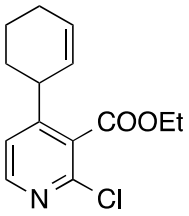
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 166.0, 160.6, 150.0, 149.6, 147.9, 129.4, 129.1, 128.9, 123.0, 114.3, 62.1, 55.4, 13.8.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2981 (W), 2936 (VW), 2934 (VW), 2903 (VW), 2838 (VW), 1729 (S), 1700 (W), 1696 (W), 1684 (VW), 1653 (VW), 1635 (VW), 1608 (M), 1575 (S), 1554 (W), 1534 (M), 1514 (S), 1487 (W), 1453 (M), 1442 (M), 1416 (W), 1378 (M), 1362 (M), 1266 (S), 1250 (VS), 1214 (M), 1196 (M), 1179 (S), 1130 (S), 1113 (M), 1094 (W), 1063 (S), 1055 (VS), 1026 (S), 853 (M), 827 (VS), 794 (M), 781 (M), 775 (M), 742 (S), 726 (W), 702 (W), 690 (W), 686 (W), 684 (W), 683 (W), 677 (W), 674 (W), 668 (W), 665 (W), 663 (W), 660 (W), 657 (W), 655 (W).

MS (EI, 70 eV): m/z (%) = 293 (35), 291 (100), 263 (13), 248 (27), 246 (75), 210 (63), 140 (17).

HRMS ($C_{15}H_{14}NO_3Cl$): calc.: 291.0662; found: 291.0655.

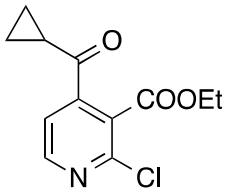
Ethyl 2-chloro-4-(cyclohex-2-en-1-yl)nicotinate (75i)



The title compound was prepared according to **TP3** from ethyl 2-chloronicotinate (**74d**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of ethyl 2-chloronicotinate (168 µL, 1.0 mmol) andCuCN·2LiCl (1.1 mL, 1 M, 1.1 mmol) in THF (4 mL) at -78 °C. 3-bromocyclohex-1-ene(115 µL, 1.0 mmol) was added afterwards and stirred at that temperature for 10 min and additional 2 h at 0 ºC prior to quench. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded ethyl 2-chloro-4-(cyclohex-2-en-1-yl)nicotinate (**75i**) (228mg, 0.86 mmol, 86%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.28 (d, *J* = 5.2 Hz, 1H), 7.14 (d, *J* = 5.2 Hz, 1H), 5.96 – 5.91 (m, 1H), 5.54 – 5.50 (m, 1H), 4.47 – 4.31 (m, 2H), 3.42 – 3.38 (m, 1H), 2.10 - 1.99 (m, 3H), 1.77 - 1.63 (m, 1H), 1.62 - 1.41 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 165.9, 155.6, 149.7, 147.3, 130.5, 129.8, 127.1, 121.8, 62.1, 39.2, 31.1, 24.6, 20.8, 14.0.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3024 (VW), 3023 (VW), 2984 (W), 2980 (W), 2933 (W), 2931 (W), 2928 (W), 2865 (W), 2860 (W), 2837 (W), 1729 (VS), 1700 (W), 1696 (W), 1685 (W), 1675 (VW), 1653 (VW), 1579 (S), 1546 (M), 1456 (M), 1447 (M), 1436 (W), 1432 (W), 1419 (W), 1393 (M), 1379 (M), 1363 (M), 1309 (M), 1270 (S), 1227 (M), 1216 (M), 1180 (S), 1119 (S), 1095 (M), 1061 (VS), 1044 (M), 1012 (M), 939 (W), 937 (W), 911 (M), 902 (W), 890 (M), 853 (M), 841 (M), 804 (W), 797 (W), 780 (W), 775 (W), 737 (S), 725 (S), 694 (M), 685 (W), 667 (W), 661 (W), 658 (W), 655 (W), 651 (W).
MS (EI, 70 eV): m/z (%) =265 (36), 236 (44), 219 (100), 200 (40), 182 (82), 166 (45), 154 (44), 128 (31), 77 (40).
HRMS ($C_{14}H_{16}NO_2Cl$): calc.: 265.0870; found: 265.0861.

Ethyl 2-chloro-4-(cyclopropanecarbonyl)nicotinate (75j)



The title compound was prepared according to **TP3** from ethyl 2-chloronicotinate (**74d**) (1.0 mmol). TMPLi (**12**) (3.26 mL, 0.46 M, 1.5 mmol) was added dropwise to a solution of ethyl 2-chloronicotinate (168 µL, 1.0 mmol) and CuCN·2LiCl (1.1 mL, 1 M, 1.1 mmol) in THF (4 mL) at -78 °C. Cyclopropanecarbonyl chloride (73 µL, 0.8 mmol) was added afterwards and stirred at that temperature for 10 min and additional 1.5 h at 0 ºC prior to quench. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2 to 1:1) afforded ethyl 2-chloro-4-(cyclopropanecarbonyl)nicotinate (**75j**) (190mg, 0.75 mmol, 94%) as a clear oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.57 (d, *J* = 5.0 Hz, 1H), 7.64 (d, *J* = 5.0 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.43 (tt, *J* = 7.8, 4.5 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.30 - 1.25 (m, 2H), 1.17 - 1.11 (m, 2H).

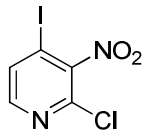
^{13}C-NMR (100 MHz, $CDCl_3$): δ / ppm = 199.2, 165.2, 150.7, 149.1, 146.2, 127.5, 120.2, 62.4, 19.3, 13.8, 13.4.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3010 (VW), 3006 (VW), 2983 (W), 1768 (VW), 1732 (S), 1683 (S), 1663 (W), 1653 (W), 1646 (VW), 1635 (VW), 1574 (M), 1557 (W), 1545 (M), 1521 (VW), 1506 (VW), 1464 (W), 1456 (M), 1447 (M), 1419 (W), 1383 (VS), 1363 (M), 1340 (VW), 1262 (VS), 1235 (VS), 1198 (S), 1190 (S), 1127 (VS), 1081 (W), 1063 (S), 1046 (M), 1016 (S), 918 (VW), 913 (VW), 883 (S), 854 (S), 842 (S), 812 (M), 780 (M), 778 (M), 739 (M), 731 (S), 724 (M), 702 (W), 689 (W), 686 (W), 683 (VW), 664 (S).

MS (EI, 70 eV): m/z (%) = 253 (10), 225 (19), 208 (70), 197 (81), 184 (100), 144 (21), 116 (29), 69 (74).

HRMS ($C_{12}H_{12}NO_3Cl$): calc.: 253.0506; found: 253.0515.

2-Chloro-4-iodo-3-nitropyridine



The title compound was prepared according to **TP2** from 2-chloro-3-nitropyridine (0.5 mmol). TMPLi (**12**) (1.19 mL, 0.64 M, 0.75 mmol) was added dropwiseto a solution of 2-chloro-3-nitropyridine (79 mg, 0.5 mmol), zinc chloride (0.55 mL, 1.0 M, 0.55 mmol) and LiCl (1.57 mL, 0.7 M, 1.1 mmol) in THF (2.5 mL) at -78 °C. A solution of iodine in THF (in excess) was added afterwards and stirred at that temperature for 10 min and additional 5 min at room temperature prior to quench with sat. $Na_2S_2O_3$-solution. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 85:15) afforded 2-chloro-4-iodo-3-nitropyridine (77 mg, 0.27 mmol, 54%) as a yellow solid.

Mp.:130-132 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.17 – 8.11 (m, 1H), 7.85 – 7.78 (m, 1H).

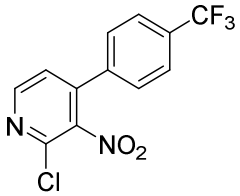
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 152.3, 149.9, 141.6, 133.8, 98.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1536 (vs), 1527 (vs), 1488 (m), 1456 (w), 1434 (m), 1380 (m), 1351 (s), 1338 (s), 1267 (w), 1234 (w), 1220 (w), 1208 (m), 1175 (w), 1096 (m), 1060 (m), 967 (w), 854 (s), 826 (s), 776 (vs), 747 (w), 726 (m), 698 (s).

MS (EI, 70 eV): m/z (%) = 284 (9), 238 (2), 211 (2), 177 (2), 129 (2), 127 (8), 111 (12), 86 (30), 84 (88), 76 (42), 75 (34).

HRMS ($C_5H_2ClIN_2O_2$): calc.: 283.8849; found: 283.8866.

2-Chloro-3-nitro-4-(4-(trifluoromethyl)phenyl)pyridine (75k)



The title compound was prepared according to **TP2** from 2-chloro-3-nitropyridine (**74e**)[148] (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of 2-chloro-3-nitropyridine (159 mg, 1.0 mmol), $ZnCl_2$ (1.1 mL, 1.0 M, 1.1 mmol) and LiCl (3.14 mL, 0.7 M, 2.2 mmol) in THF (2 mL) at -78 °C. According to **TP4**, the corresponding zinc reagent was treated with 1-iodo-4-(trifluoromethyl)benzene (190 mg, 0.7 mmol) at that temperature for 5 min and additional 2 h at room temperature prior to quench with sat. NH_4Cl-solution. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 8:2) afforded 2-chloro-3-nitro-4-(4-(trifluoromethyl)phenyl)pyridine (**75k**) (170 mg, 0.56 mmol, 80%) as a white solid.

M.p.: 116-119 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.61 (d, J = 5.3 Hz, 1H), 7.76 (dd, J = 8.2, 0.7 Hz, 2H),7.53 (dd, J = 8.2, 0.7 Hz, 2H),7.39 (dd, J = 5.1, 0.7 Hz, 1H).

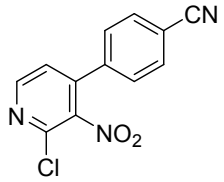
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 150.4, 144.9, 143.1, 142.5, 136.3, 132.5 (q, J = 33.1 Hz), 128.2, 126.3 (q, J = 3.8 Hz), 124.0, 123.5 (q, J = 272.6 Hz).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1589 (m), 1532 (vs), 1454 (w), 1407 (w), 1385 (w), 1353 (m), 1321 (vs), 1212 (w), 1166 (s), 1148 (w), 1116 (vs), 1075 (m), 1052 (s), 1019 (m), 963 (w), 858 (s), 842 (m), 828 (s), 770 (m), 745 (w), 731 (w), 719 (w), 658 (w).

MS (EI, 70 eV): m/z (%) = 302 (15), 285 (32), 283 (15), 276 (30), 274 (100), 256 (15), 236 (62), 221 (29), 220 (24), 210 (23), 194 (31), 193 (20), 183 (26), 175 (36).

HRMS ($C_{12}H_6ClF_3N_2O_2$): calc.: 302.0070; found: 302.0065.

4-(2-Chloro-3-nitropyridin-4-yl)benzonitrile (7l)



The title compound was prepared according to **TP2** from 2-chloro-3-nitropyridine (**74e**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of 2-chloro-3-nitropyridine (159 mg, 1.0 mmol), $ZnCl_2$ (1.1 mL, 1.0 M, 1.1 mmol) and LiCl (3.14 mL, 0.7 M, 2.2 mmol) in THF (2 mL) at -78 °C. According to **TP4**, the corresponding zinc reagent was reacted with 4-iodo-benzonitrile (160 mg, 0.7 mmol) at that temperature for 5 min and additional 2 h at room temperature prior to quench with sat. NH_4Cl-solution. Flash column chromatographical purification on silica gel (isohexane:CH_2Cl_2 = 1:1 ->CH_2Cl_2) afforded 4-(2-chloro-3-nitropyridin-4-yl)benzonitrile (**75l**) (127 mg, 0.49 mmol, 70%) as a brown solid.

[148]Alternatively, a metalation with $TMP_2Zn{\cdot}2MgCl_2$ 2LiCl at -40 °C over 1.5 h is possible. See: G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem.* **2007**, *119*, 7825; *Angew. Chem. Int. Ed.***2007**, *46*, 7681.

M.p.:149-152 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.63 (d, *J* = 5.0 Hz, 1H), 7.84 – 7.76 (m, 2H), 7.56 – 7.48 (m, 2H), 7.38 (d, *J* = 5.0 Hz, 1H).

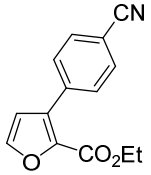
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 150.5, 144.7, 142.6, 142.5, 137.1, 133.0, 128.5, 123.7, 117.6, 114.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} =2234 (w), 1591 (m), 1530 (vs), 1504 (m), 1451 (m), 1402 (w), 1377 (w), 1351 (s), 1309 (w), 1299 (w), 1272 (w), 1230 (w), 1200 (m), 1180 (w), 1110 (w), 1066 (w), 1056 (m), 1018 (w), 856 (s), 841 (m), 828 (vs), 790 (w), 781 (w), 764 (m), 730 (m), 723 (w), 705 (m), 676 (w), 652 (w).

MS (EI, 70 eV): m/z (%) = 261 (19), 259 (52), 242 (22), 233 (18), 231 (52), 213 (28), 203 (32), 193 (69), 178 (61), 177 (144), 167 (46), 165 (39), 152 (46), 151 (100), 142 (41), 140 (40), 125 (42).

HRMS ($C_{12}H_6ClN_3O_2$): calc.: 259.0149; found: 259.0141.

Ethyl 3-(4-cyanophenyl)furan-2-carboxylate (75m)



The title compound was prepared according to **TP2** from ethyl furan-2-carboxylate (**74f**)[149](1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of ethyl furan-2-carboxylate (140 mg, 1.0 mmol), $ZnCl_2$ (0.5 mL, 1.0 M, 0.5 mmol) and LiCl (1.43 mL, 0.7 M, 1.0 mmol) in THF (2 mL) at -78 °C. According to **TP4**, the corresponding zinc reagent was reacted with 4-iodo-benzonitrile (206 mg, 0.9 mmol) at that temperature for 5 min and additional 2 h at 23 °C prior to quench with sat. NH_4Cl-solution. Before chromatographic separation the crude regioselectivity was 89:11. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 9:1 -> 8:2) afforded ethyl 3-(4-cyanophenyl)furan-2-carboxylate (**75m**) (153 mg, 0.63 mmol, 70%) as white solid.

M.p.: 97-98 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.70 (s, 4H), 7.63 (d, *J* = 2.0 Hz, 1H), 6.64 (d, *J* = 2.0 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H).

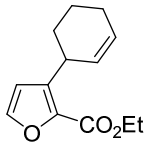
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 158.7, 145.4, 136.7, 132.7, 131.8, 130.1, 125.1, 118.7, 114.0, 111.9, 61.3, 14.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3149 (w), 3130 (w), 3109 (w), 2993 (w), 2912 (w), 2223 (m), 1716 (vs), 1610 (w), 1592 (w), 1556 (w), 1509 (w), 1484 (m), 1449 (w), 1419 (m), 1384 (m), 1360 (w), 1304 (s), 1285 (s), 1262 (s), 1218 (w), 1190 (s), 1184 (m), 1177 (m), 1150 (m), 1134 (m), 1121 (m), 1102 (s), 1074 (m), 1018 (s), 971 (m), 946 (w), 922 (w), 895 (m), 873 (w), 863 (w), 846 (s), 834 (m), 820 (m), 799 (s), 788 (vs), 762 (m), 730 (w), 679 (m), 664 (w).

[149]Alternatively, a metalation with TMPMg·LiCl at -40 °C over 2 h leads to 50% conversion and a regioselectivity of 82:18. After this time only slow decomposition of the magnesiated species was observed.

MS (EI, 70 eV): m/z (%) = 242 (14), 241 (76), 213 (53), 212 (23), 196 (100), 169 (55), 140 (47).
HRMS ($C_{14}H_{11}NO_3$): calc.: 241.0739; found: 241.0714.

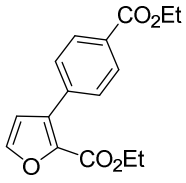
Ethyl 3-(cyclohex-2-en-1-yl)furan-2-carboxylate (4n)



The title compound was prepared according to **TP3** from ethyl furan-2-carboxylate (**74f**) (1.0 mmol). TMPLi (**12**) (2.03 mL, 0.64 M, 1.3 mmol) was added dropwise to a solution of ethyl furan-2-carboxylate (140 mg, 1.0 mmol), and CuCN·2LiCl (1.1 mL, 1 M, 1.1 mmol) in THF (3 mL) at -78 °C. 3-Bromocyclohex-1-ene (145 mg, 0.9 mmol) was added afterwards and stirred at that temperature for 30 min prior to quench with sat. NH_4Cl/NH_3-solution. Before chromatographic separation the crude regioselectivity was 91:9. Flash column chromatographical purification on silica gel (isohexane:EtOAc = 95:5) afforded ethyl 3-(cyclohex-2-en-1-yl)furan-2-carboxylate (**75n**) (160 mg, 0.73 mmol, 81%) as colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 7.44 (dd, *J* = 1.7, 0.6 Hz, 1H), 6.42 (d, *J* = 1.4 Hz, 1H), 5.90 – 5.80 (m, 1H), 5.65 – 5.57 (m, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 4.15 – 4.05 (m, 1H), 2.12 – 1.97 (m, 3H), 1.82 – 1.46 (m, 3H), 1.39 (t, *J* = 7.2 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 159.4, 144.7, 140.0, 139.2, 129.0, 128.4, 112.7, 60.6, 32.2, 30.2, 24.8, 21.2, 14.3.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2981 (W), 2932 (W), 2860 (W), 2358 (W), 1704 (VS), 1653 (W), 1635 (W), 1588 (M), 1517 (W), 1506 (W), 1487 (M), 1465 (W), 1456 (W), 1447 (M), 1436 (W), 1414 (M), 1389 (M), 1366 (M), 1307 (S), 1272 (S), 1261 (S), 1218 (M), 1176 (VS), 1120 (VS), 1093 (S), 1069 (VS), 1032 (S), 1015 (S), 979 (M), 963 (M), 957 (M), 929 (M), 899 (S), 872 (M), 864 (M), 841 (M), 824 (M), 785 (S), 761 (S), 724 (M), 682 (M), 679 (M), 668 (M).
MS (EI, 70 eV): m/z (%) = 227 (13), 220 (24), 191 (24), 173 (74), 145 (25), 117 (48), 115 (35), 91 (54), 85 (45).
HRMS ($C_{13}H_{16}O_3$): calc.:220.1099; found: 220.1091.

Ethyl 3-(4-(ethoxycarbonyl)phenyl)furan-2-carboxylate (75o)



The title compound was prepared according to **TP2** from ethyl furan-2-carboxylate (**74f**) (1.0 mmol). TMPLi (**12**) (2.38 mL, 0.64 M, 1.5 mmol) was added dropwise to a solution of ethyl furan-2-carboxylate (140 mg, 1.0 mmol), $ZnCl_2$ (0.5 mL, 1.0 M, 0.5 mmol) and LiCl (1.43 mL, 0.7 M, 1.0 mmol) in tetrahydrofurane (2 mL) at -78 °C. According to **TP4**, the corresponding zinc reagent was reacted with ethyl 4-iodobenzoate (248 mg, 0.9 mmol) at that temperature for 5 min and additional 2 h at room temperature prior to quench with sat. NH_4Cl-solution. Flash column

chromatographical purification on silica gel (isohexane:EtOAc = 9:1) afforded ethyl 3-(4-(ethoxycarbonyl)phenyl)furan-2-carboxylate (**75o**) (167 mg, 0.58 mmol, 64%) as white solid.

Mp.: 93.8-95.6 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ / ppm = 8.12 – 8.05 (m, 2H), 7.68 – 7.62 (m, 2H), 7.61 (dd, *J* = 1.7, 0.6 Hz, 1H), 6.65 (dd, *J* = 1.8, 0.7 Hz, 1H), 4.41 (q, *J* = 7.0 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ / ppm = 166.3, 158.8, 145.1, 139.5, 136.5, 133.4, 130.1, 129.3, 129.2, 114.2, 61.1, 61.0, 14.3, 14.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3126 (w), 3105 (w), 2994 (w), 2985 (w), 2943 (w), 2907 (w), 1708 (vs), 1662 (w), 1617 (w), 1591 (m), 1568 (w), 1513 (w), 1484 (m), 1443 (w), 1420 (m), 1407 (w), 1384 (m), 1365 (m), 1310 (m), 1283 (s), 1268 (vs), 1219 (m), 1178 (s), 1152 (m), 1126 (s), 1111 (s), 1099 (vs), 1072 (s), 1036 (m), 1020 (s), 980 (w), 970 (s), 922 (w), 892 (m), 870 (m), 858 (s), 838 (m), 829 (m), 800 (s), 771 (vs), 764 (vs), 712 (m), 701 (s), 680 (m).

MS (EI, 70 eV): m/z (%) = 289 (18), 288 (100), 244 (16), 243 (100), 216 (20), 215 (37), 188 (13), 171 (18).

HRMS ($C_{16}H_{16}O_5$): calc.: 288.0998; found: 288.1000.

4.5 Kinetic experiments

General Information:

First of all, the iodinated compounds of 2,4-dichlorobenzonitrile (**1a**) and benzothiazole were isolated. Stock solutions of the aryl or heteroaryl iodides (0.1 M) and of an internal standard (0.1 M) were prepared. As internal standard for all calibration curves *n*-undecane was used. For each iodinated compound GC-samples of different iodide/internal standard ratios were prepared and measured (at least 7 for each iodide) and these ratios were plotted against the area ratios of the corresponding GC-analysis to give a linear graph with a determined equation. With these equations the amount of iodinated substance could be calculated.

To show the presence of TMPZnCl·LiCl, benzothiazole was added at 23 °C to the reaction mixtures.

Procedures:

2-Iodobenzothiazole was prepared by reaction of benzothiazole (135 mg, 1.0 mmol) dissolved in anhydrous THF (1 mL) and TMPZnCl·LiCl (1.10 M, 1.0 mL, 1.1 mmol) at 23 °C for 20 min and quenched with a solution of iodine (254 mg, 1.0 mmol) in THF (1 mL).

TMPLi (**12**) (1.56 mL, 0.64 M, 1.0 mmol) was added dropwise to a solution of 2,4-dichlorobenzonitrile (**1a**) (172 mg, 1.0 mmol) and $ZnCl_2$ (0.5 mmol-2.0 mmol) in THF (2.0 mL) at -78 °C. After warming up to 23 °C, benzothiazole (135 mg, 1.0 mmol), dissolved in THF (0.66 mL, 1.5 M), was added. A part of the THF was removed (ca. 1.0 M) and the reaction mixture stirred for 30 min at 23 °C. An excess of iodine was added and stirred for 5 min at 23 °C prior to quench with $Na_2S_2O_3$-solution. The following yields are results of the calculation by GC-analysis of the iodinated substances.

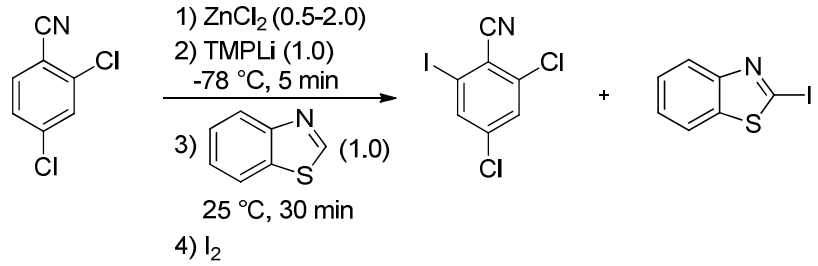
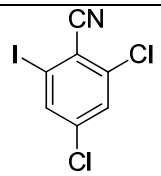
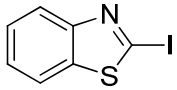
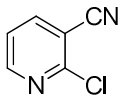


Table 8: Results of the metalation of 2,4-dichlorobenzonitrile with TMPLi (**12**) (1.0 equiv) in the presence of $ZnCl_2$ (0.5-2.0 equiv) at -78 °C, addition of benzothiazole (1.0 equiv) at 23 °C, and additional quenching with iodine.

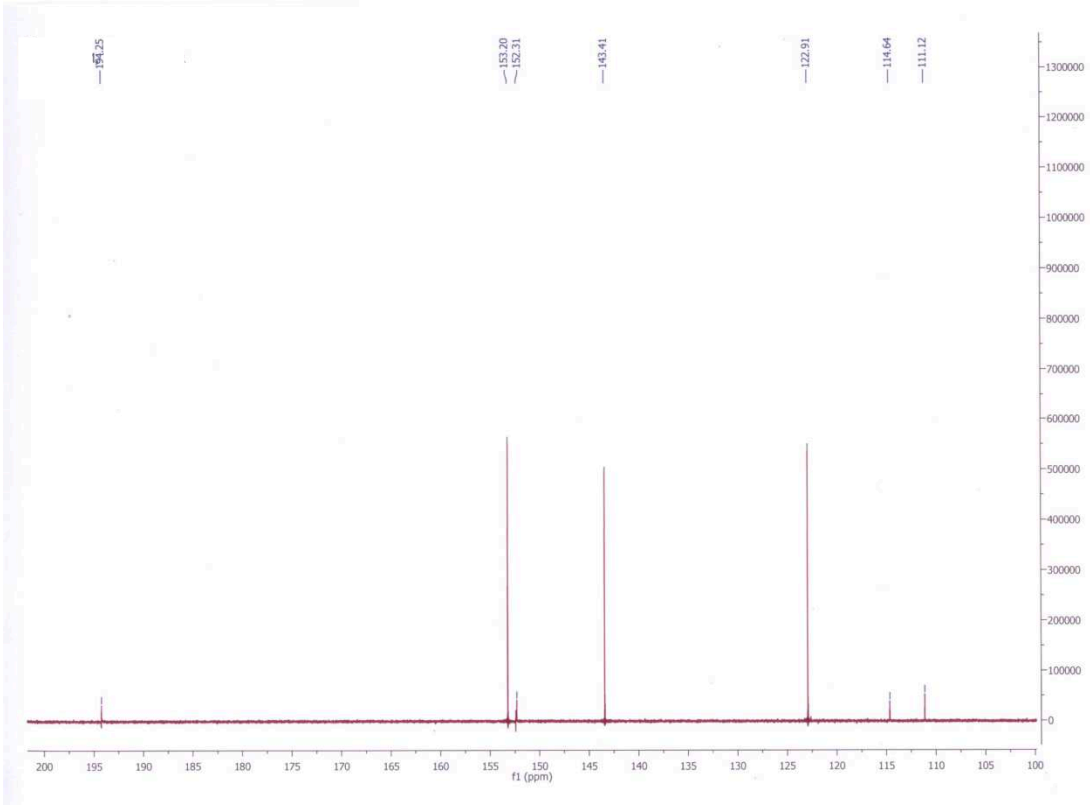
$ZnCl_2$ [equiv]		
0.5	82%	<1%
1.0	76%	6%
1.5	56%	14%
2.0	50%	16%

D: APPENDIX

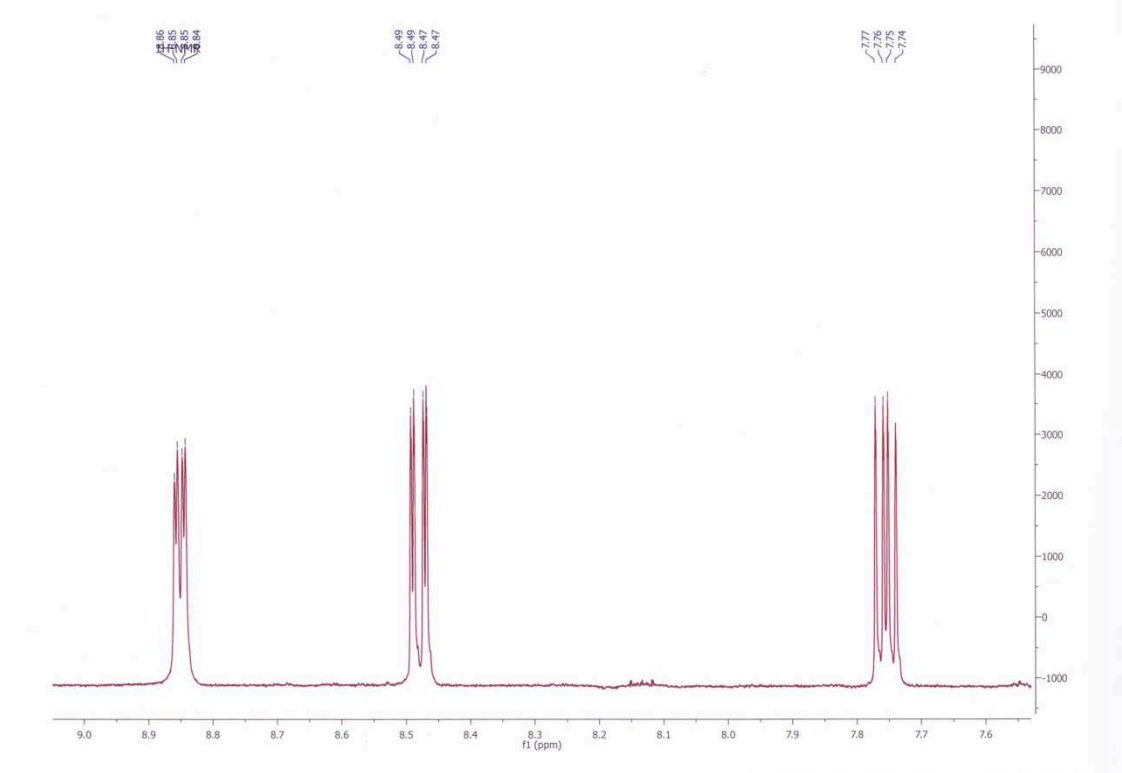


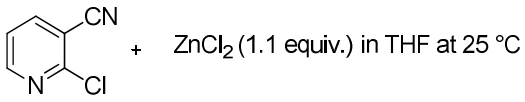
in THF at 25 °C

^{13}C NMR:

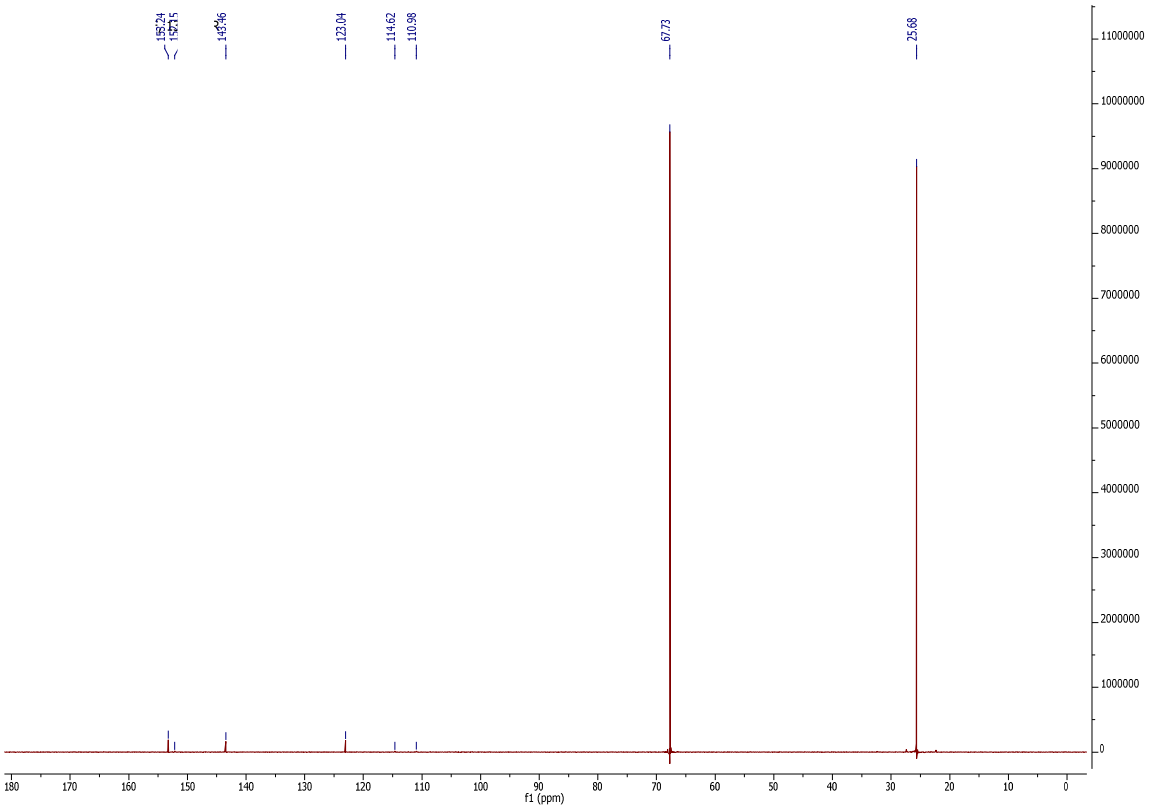


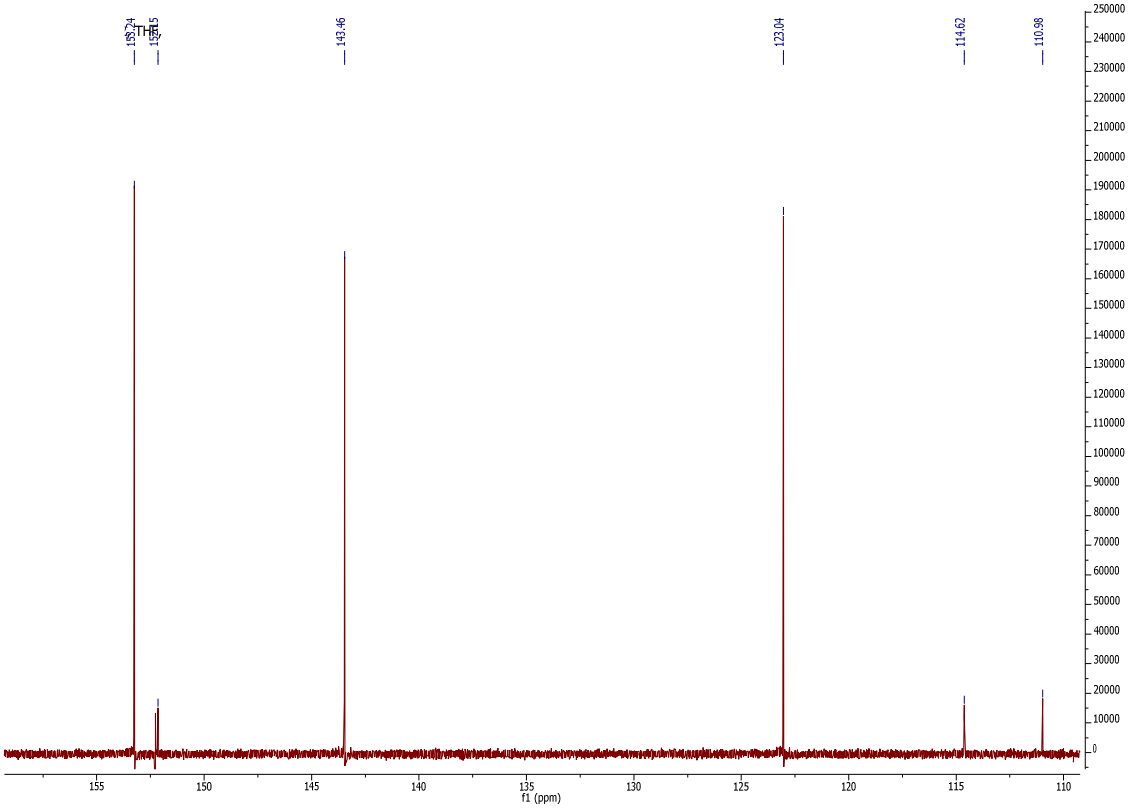
^{1}H NMR:



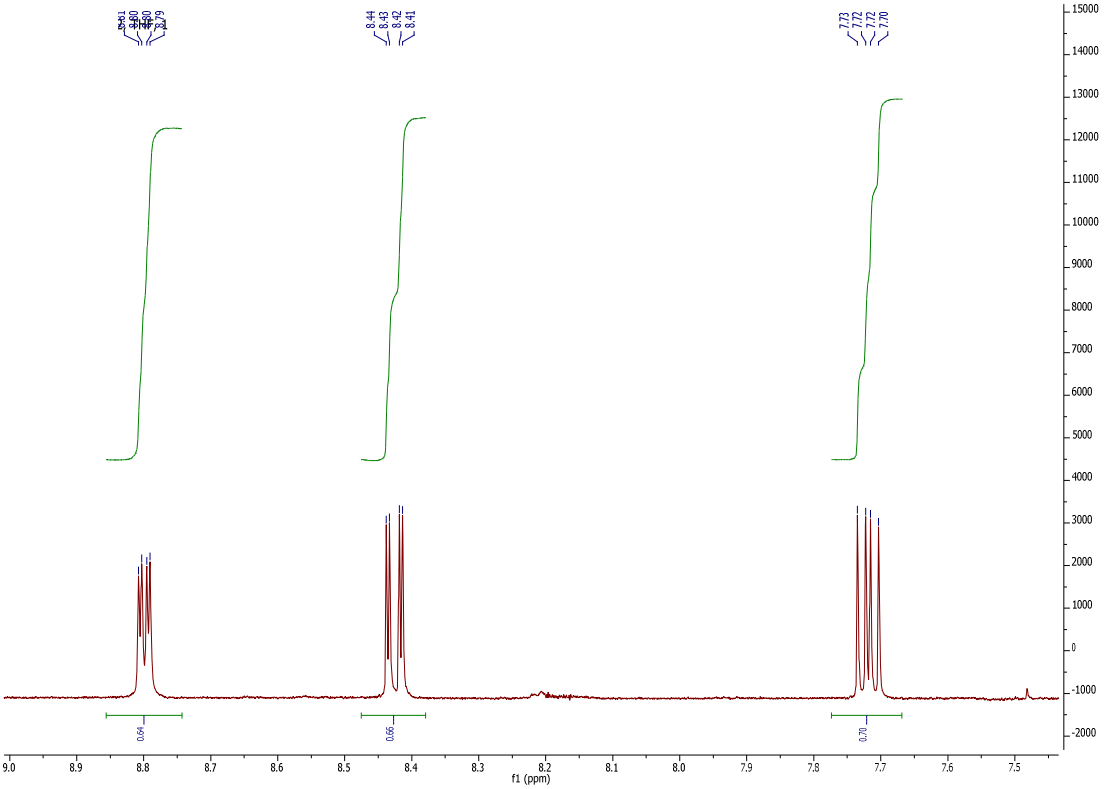


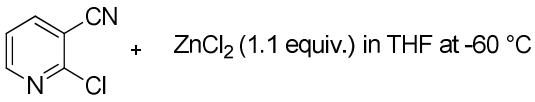
^{13}C NMR:



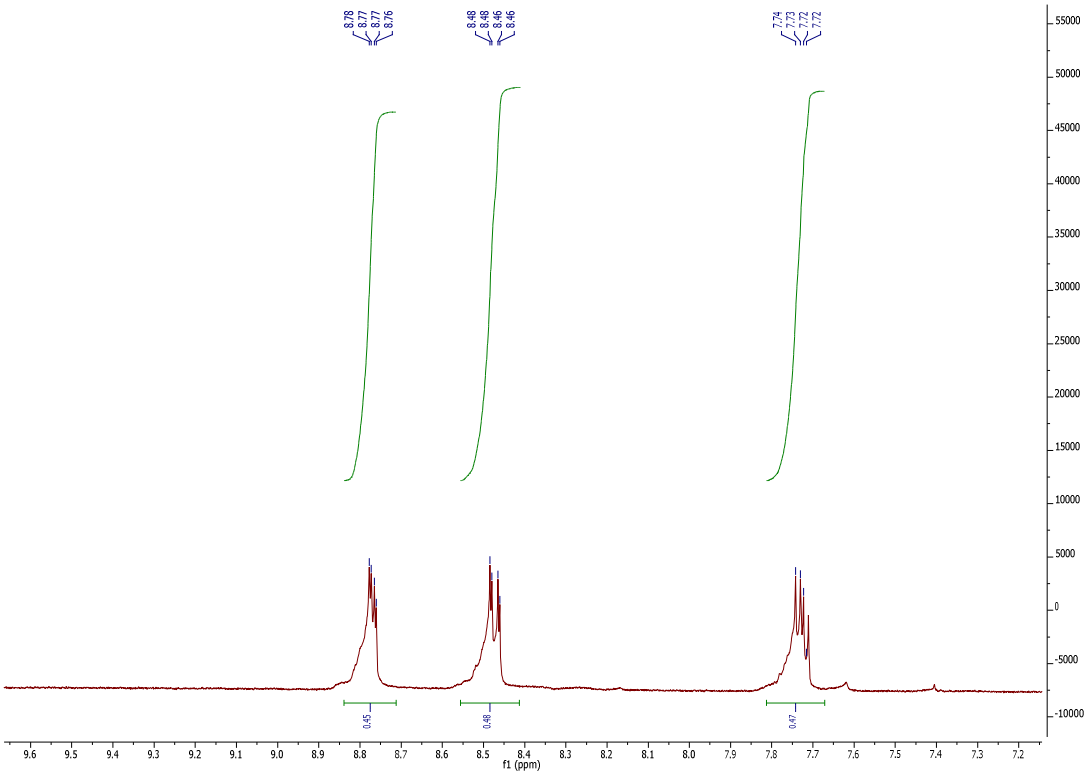


^{1}H NMR:

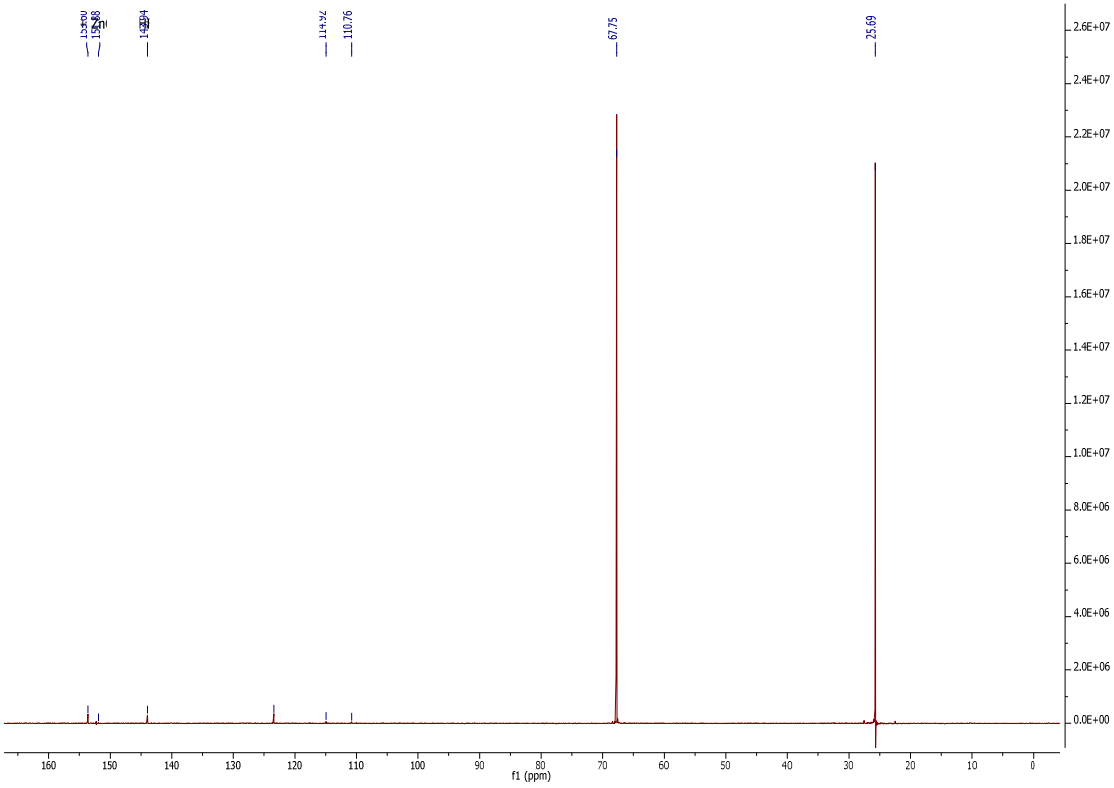

8.81
8.80
8.80
8.79
8.79
8.44
8.43
8.42
8.41
7.73
7.72
7.72
7.72
7.70
0.64
0.66
0.70
f1 (ppm)

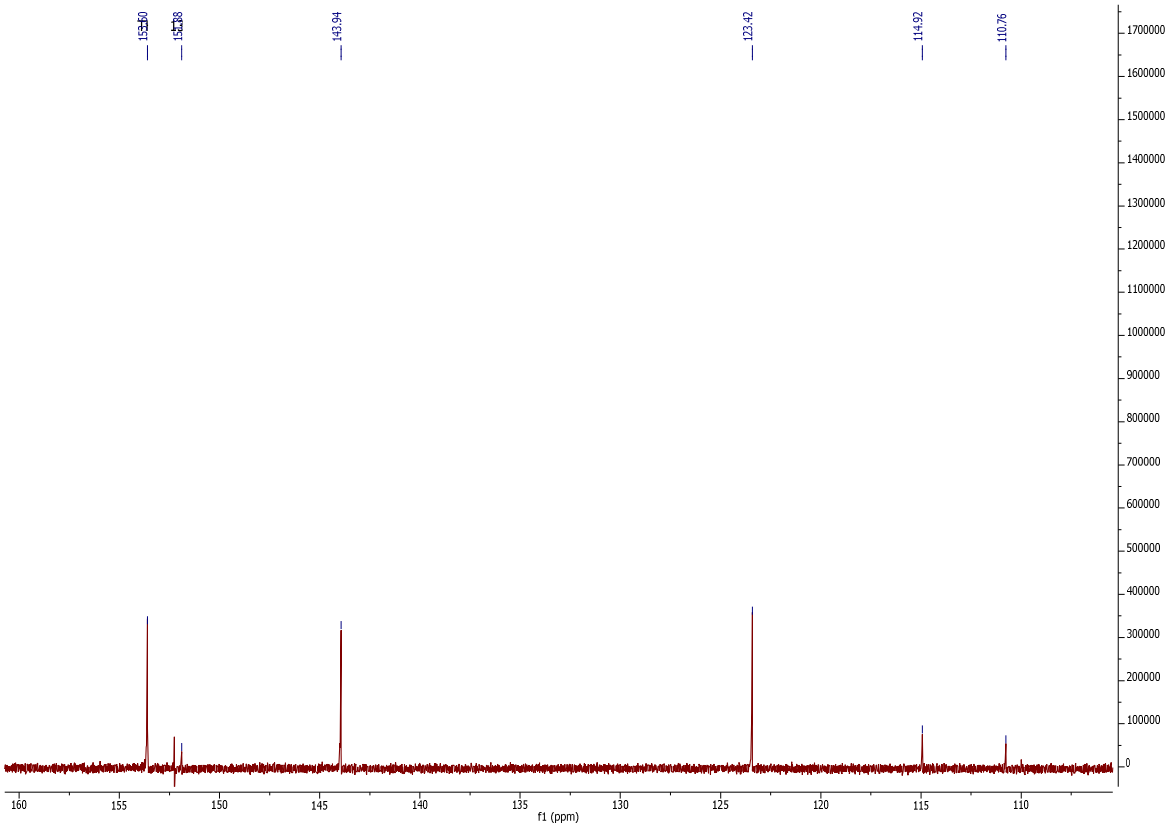


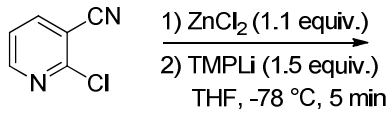
^{1}H NMR:



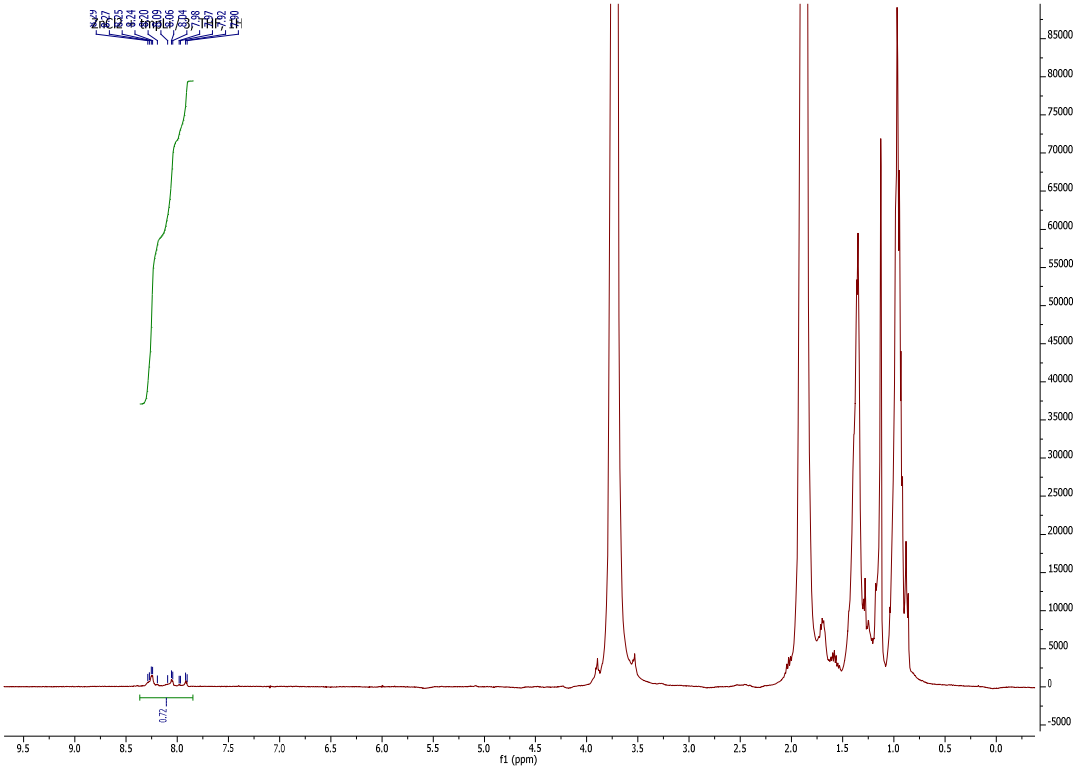
^{13}C NMR:

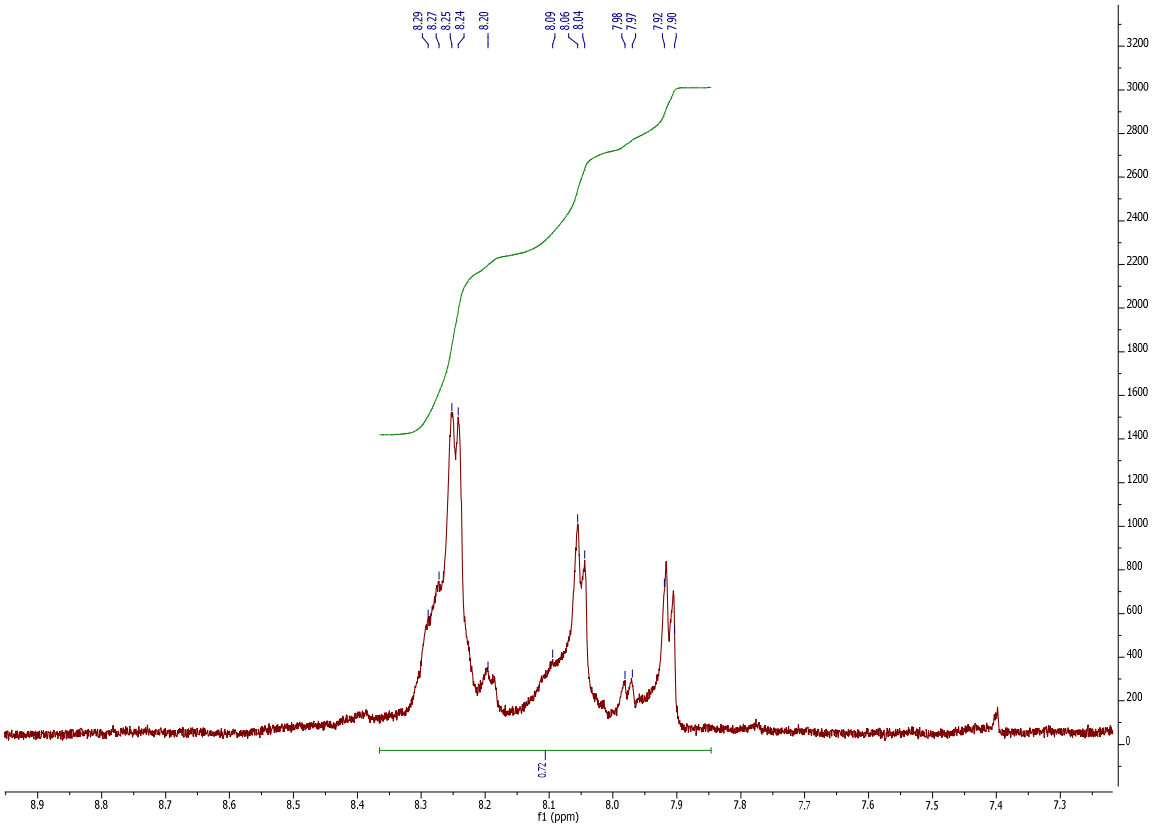



152.60
152.38
143.94
123.42
114.92
110.76
1700000
1600000
1500000
1400000
1300000
1200000
1100000
1000000
900000
800000
700000
600000
500000
400000
300000
200000
100000
0
160
155
150
145
140
135
130
125
120
115
110
f1 (ppm)

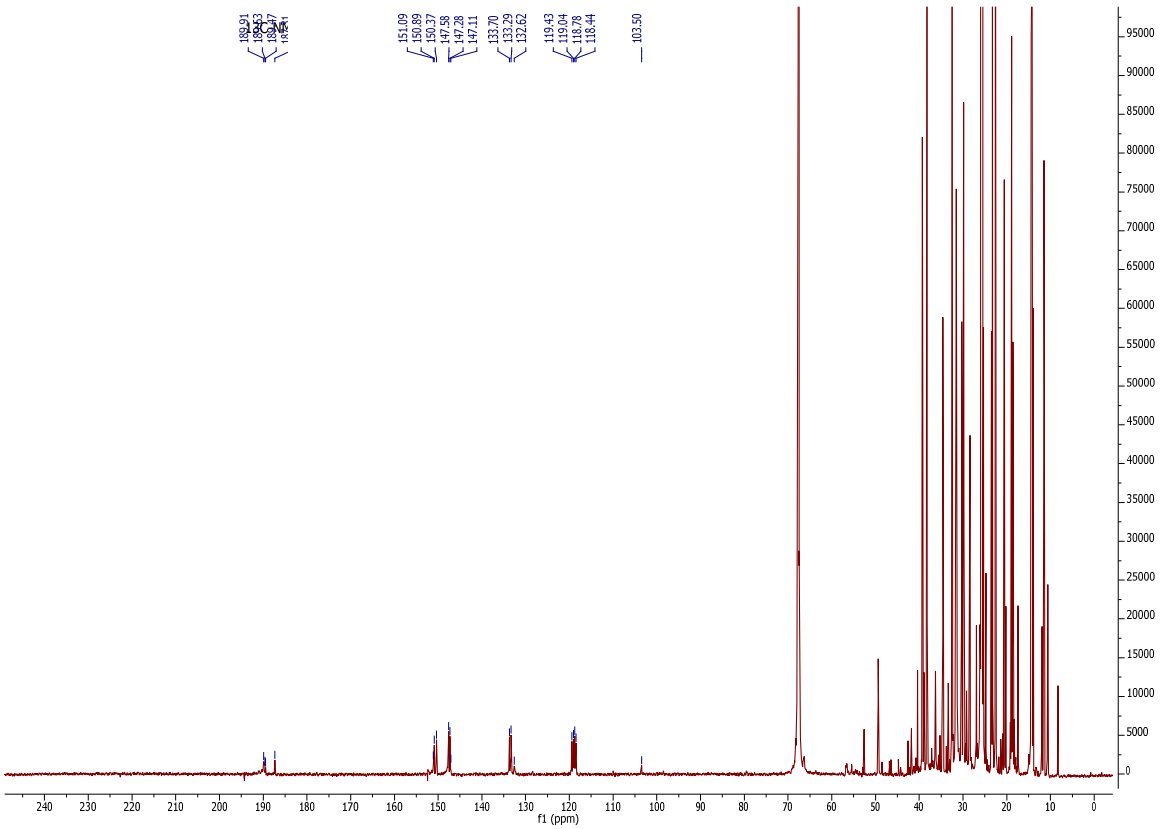


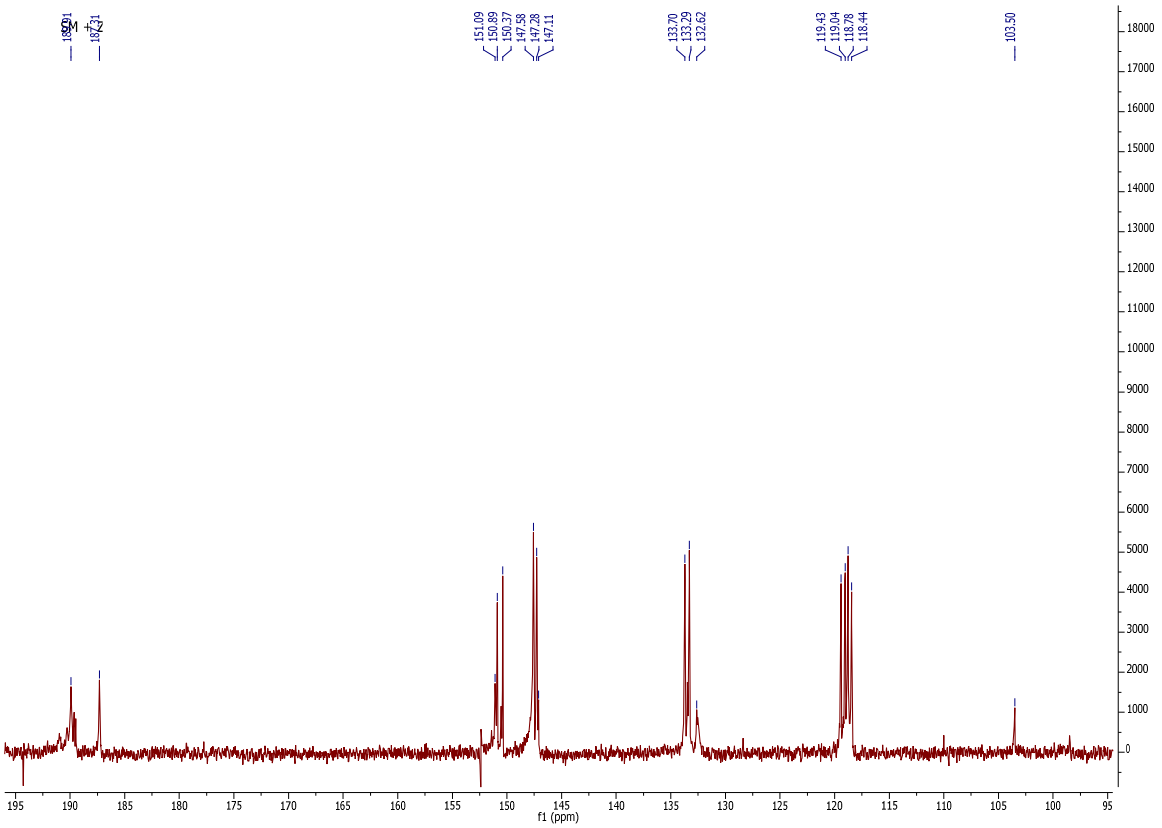
^{1}H NMR at -60 °C from the metalated intermediate:

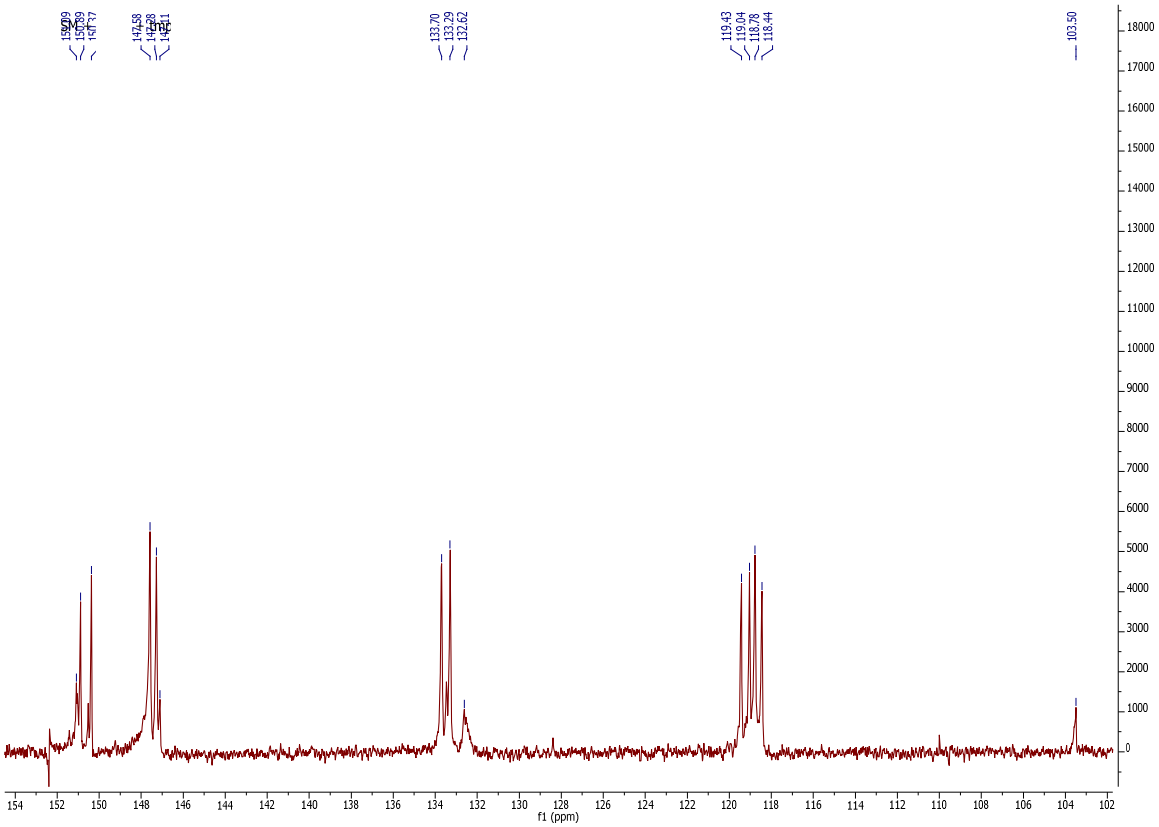


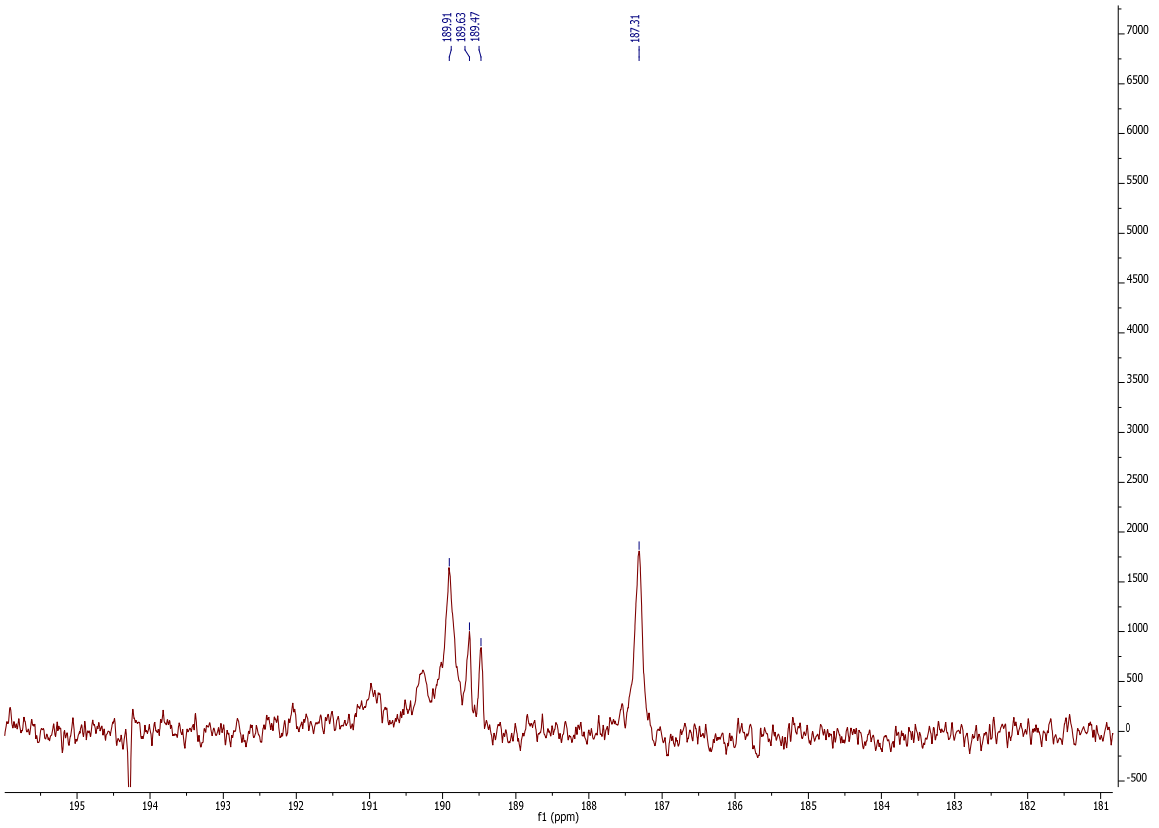


^{13}C NMR at -60 °C from the metalated intermediate:

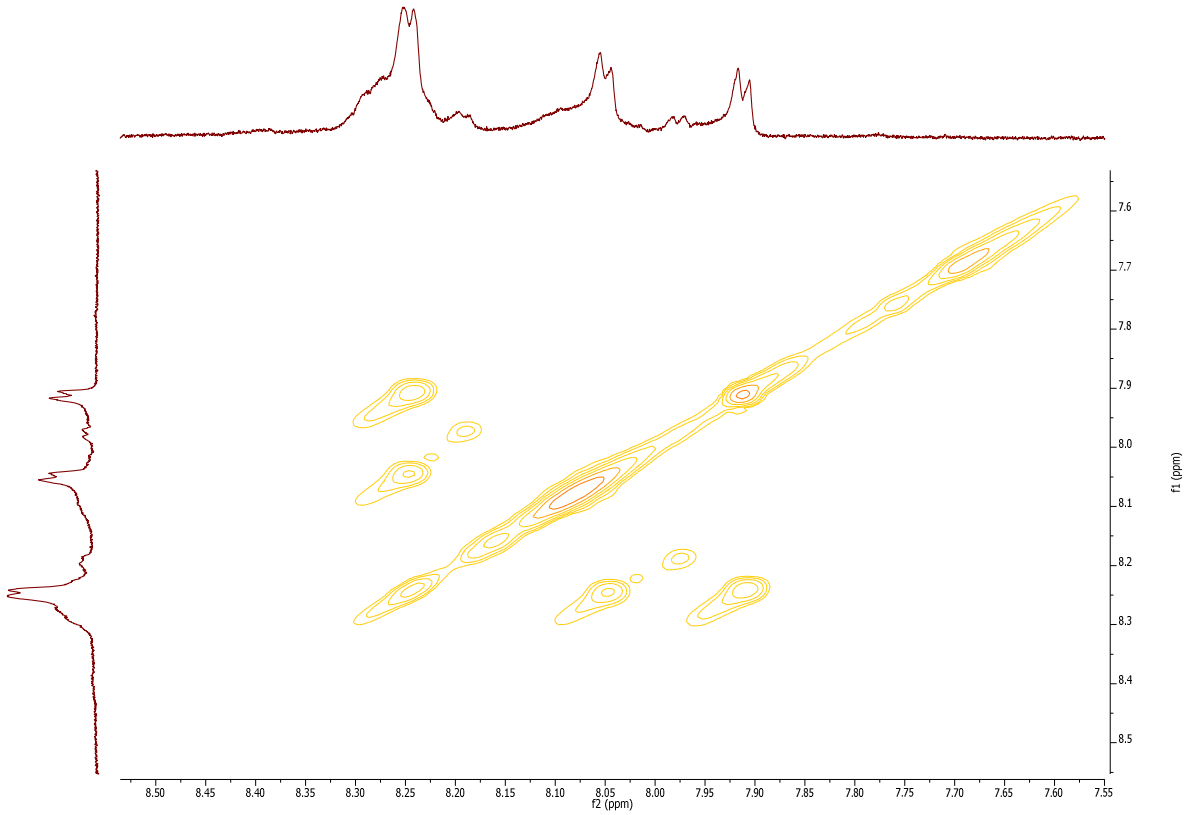

182.91
182.03
181.77
181.31
151.09
150.89
150.37
147.58
147.28
147.11
133.70
133.29
132.62
119.43
119.04
118.78
118.44
103.50
f1 (ppm)


182.91
181.77
151.09
150.89
150.37
147.58
147.28
147.11
133.70
133.29
132.62
119.43
119.04
118.78
118.44
103.50
f1 (ppm)

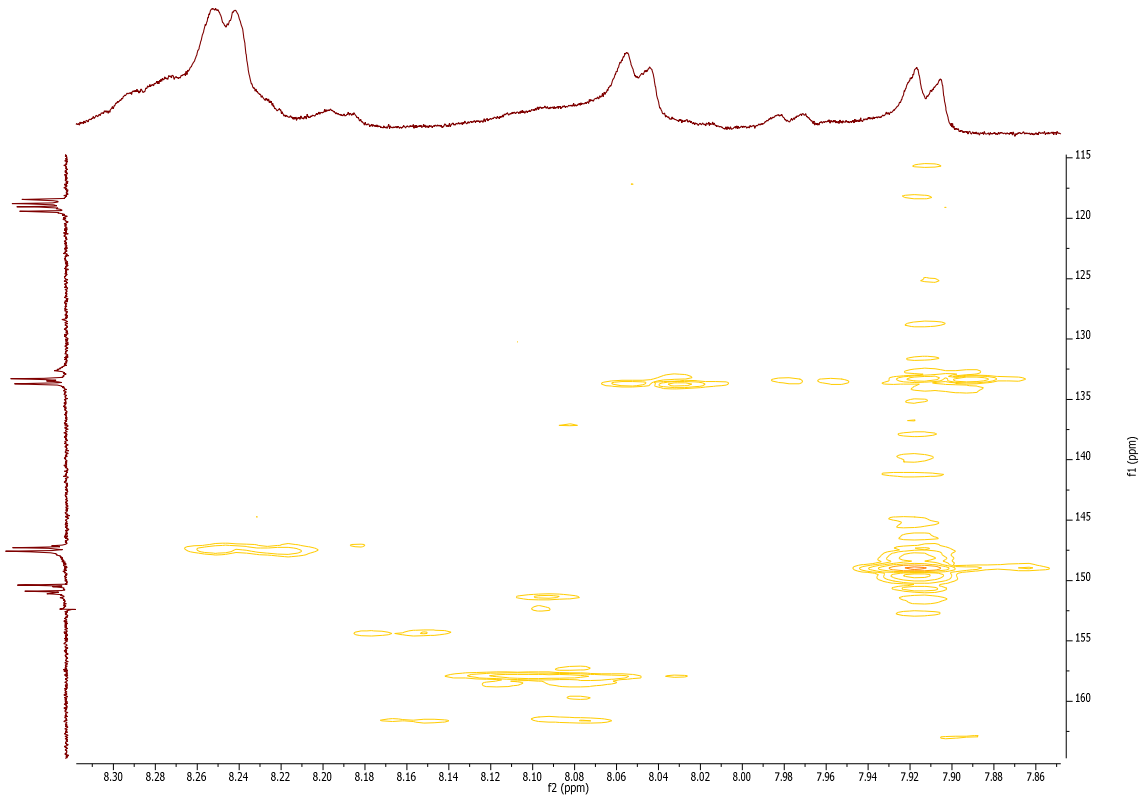

152.09
150.89
147.58
147.28
147.11
133.70
133.29
132.62
119.43
119.04
118.78
118.44
103.50
f1 (ppm)


189.91
189.63
189.47
187.31
f1 (ppm)

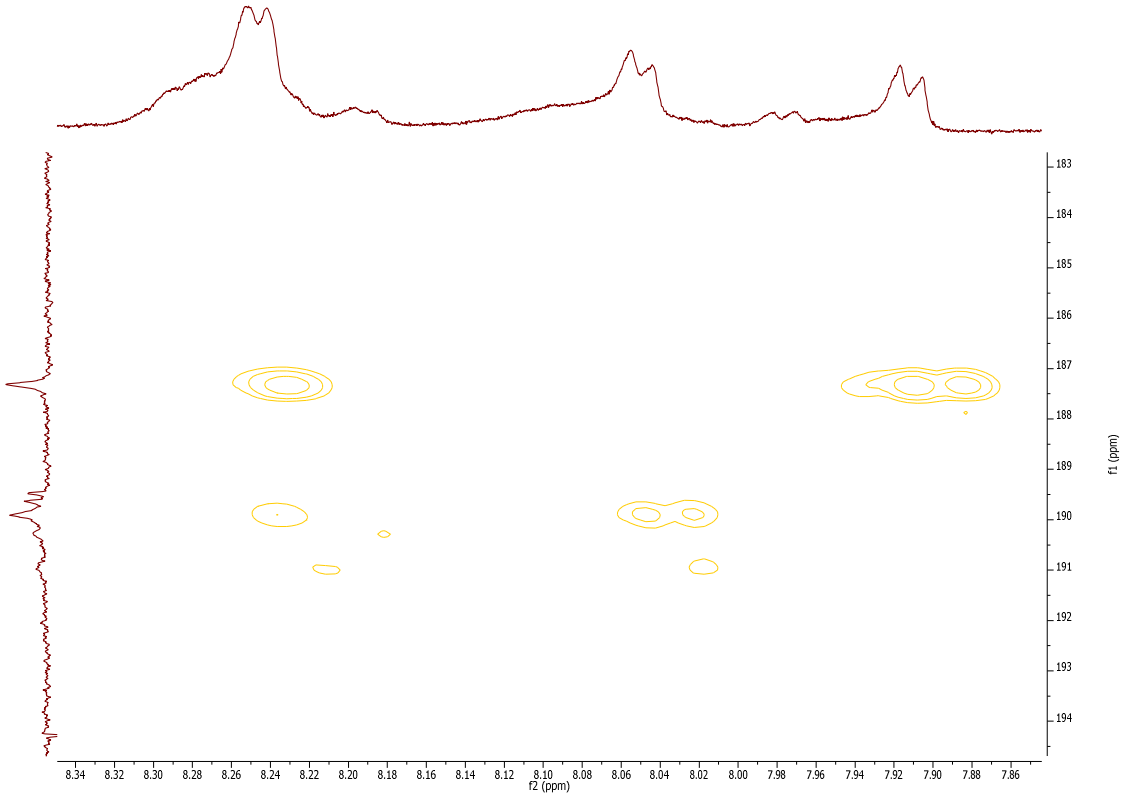
COSY, -60 °C:



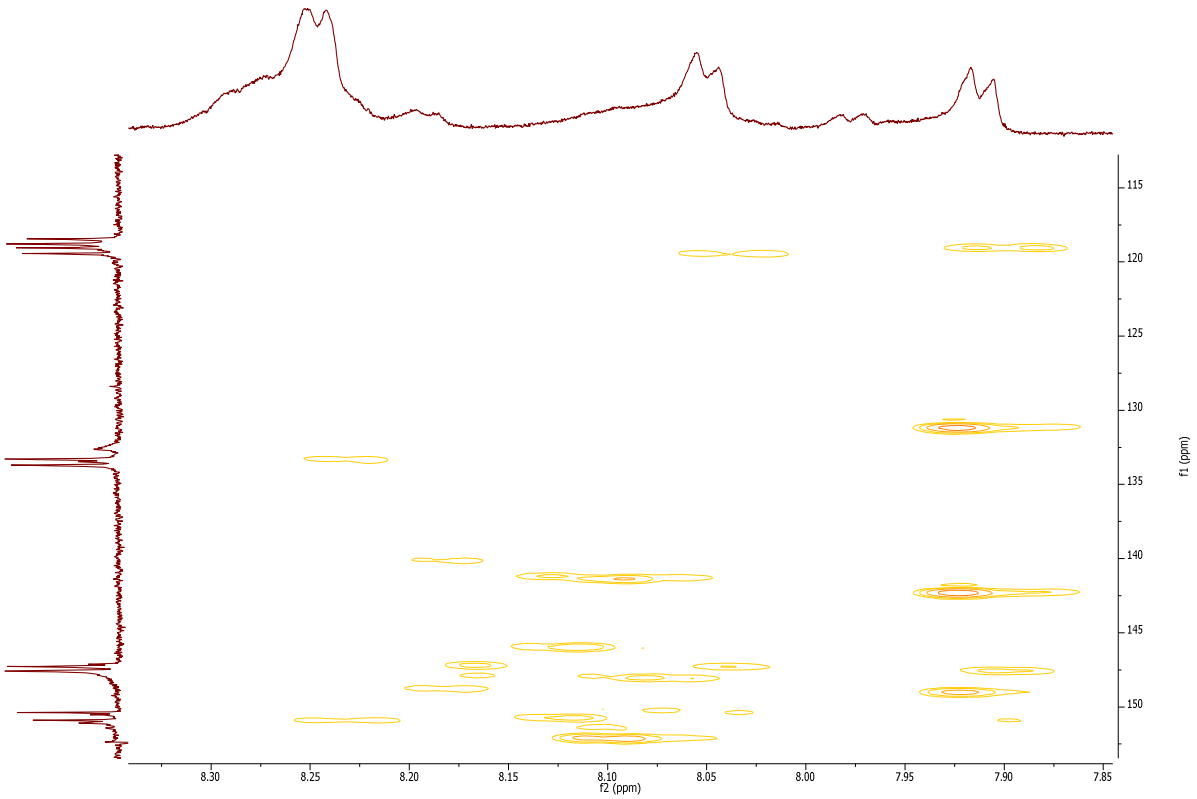
^{1}H, ^{13}C HMQC, -60 °C:

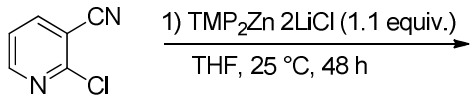


^{1}H, ^{13}C HMBC, -60 °C:

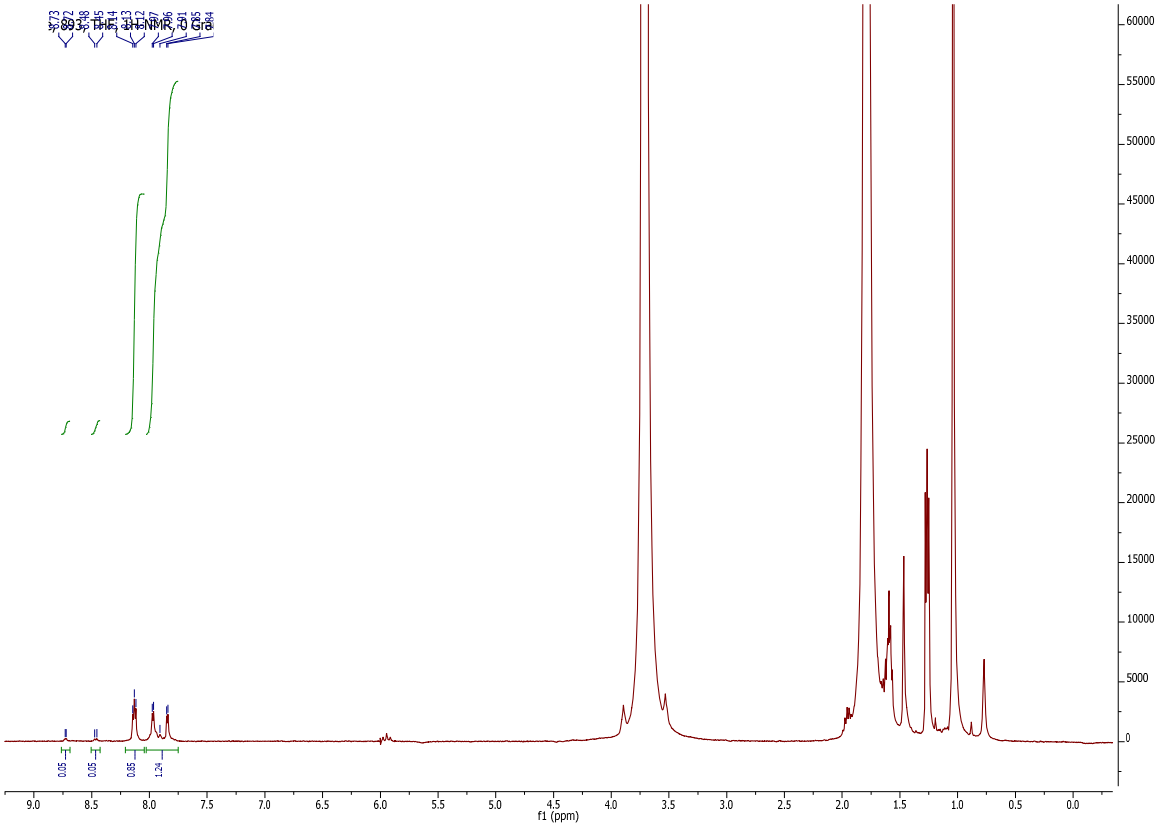


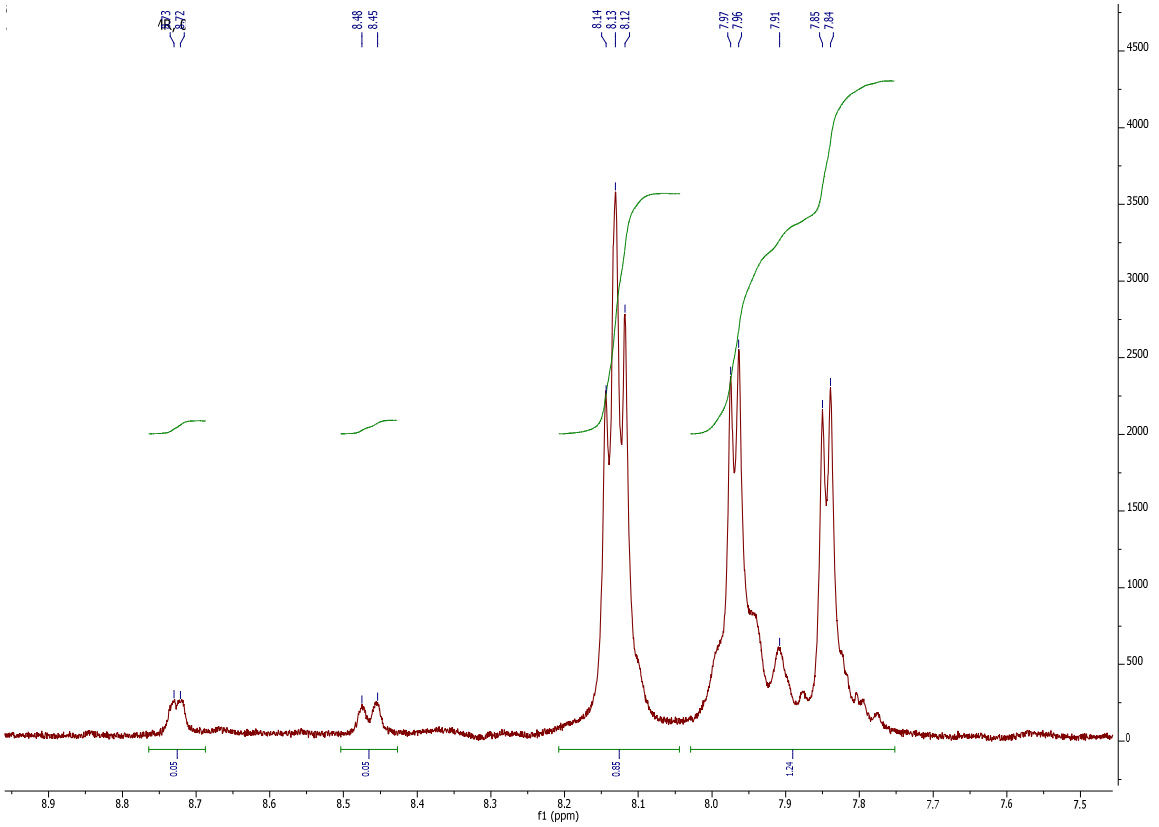
^{1}H, ^{13}C HMQC, -60 °C:



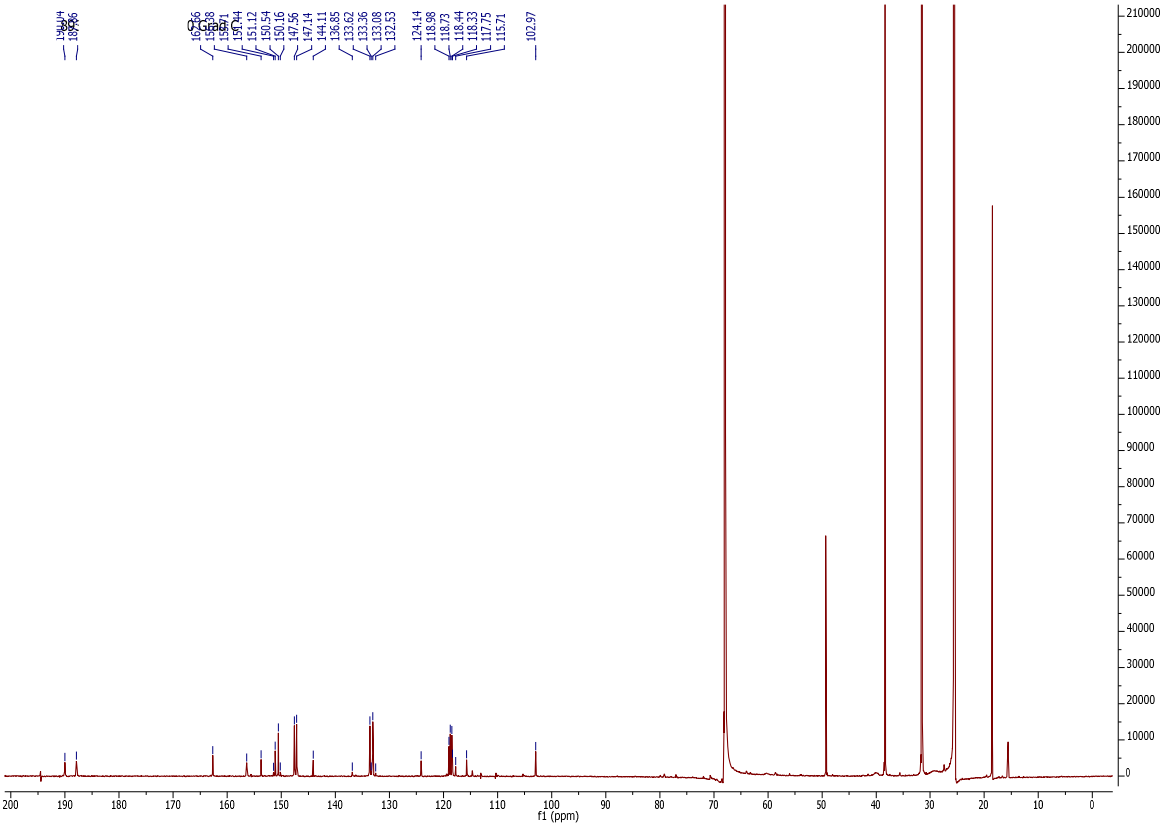


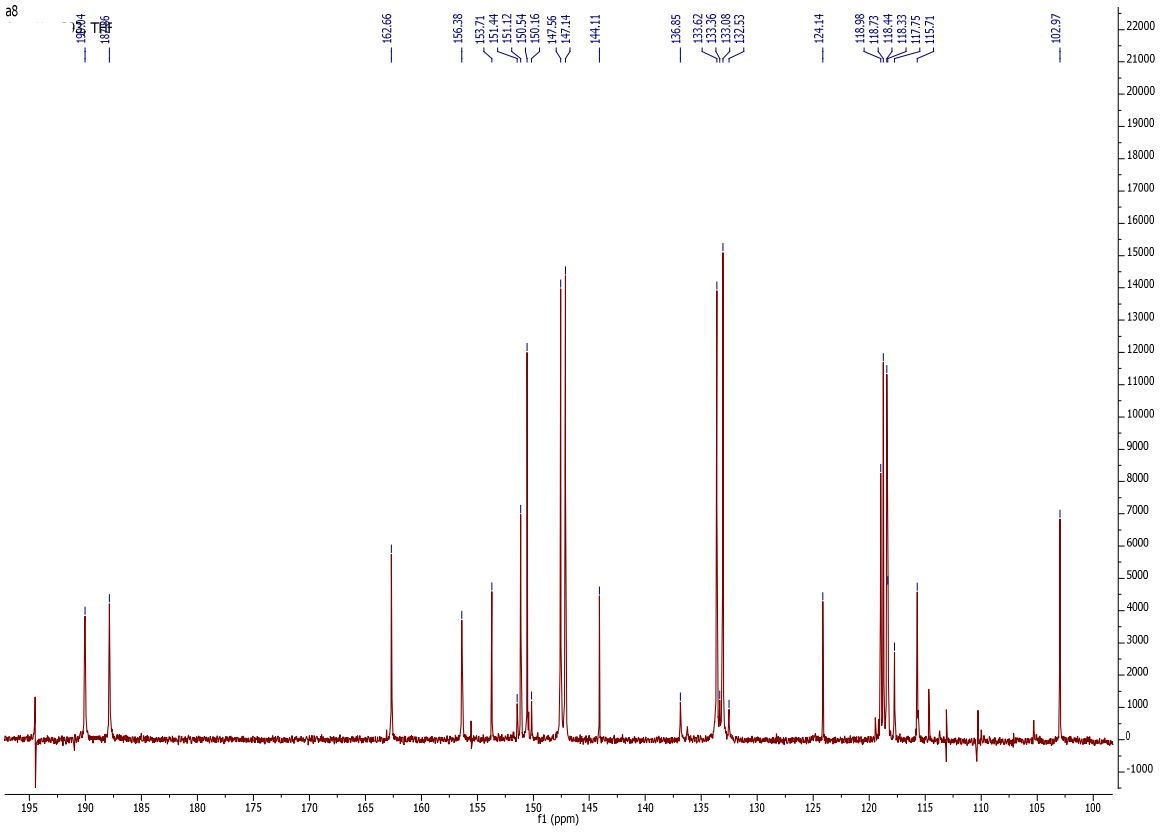
^{1}H NMR, 0 °C from the metalated intermediate:

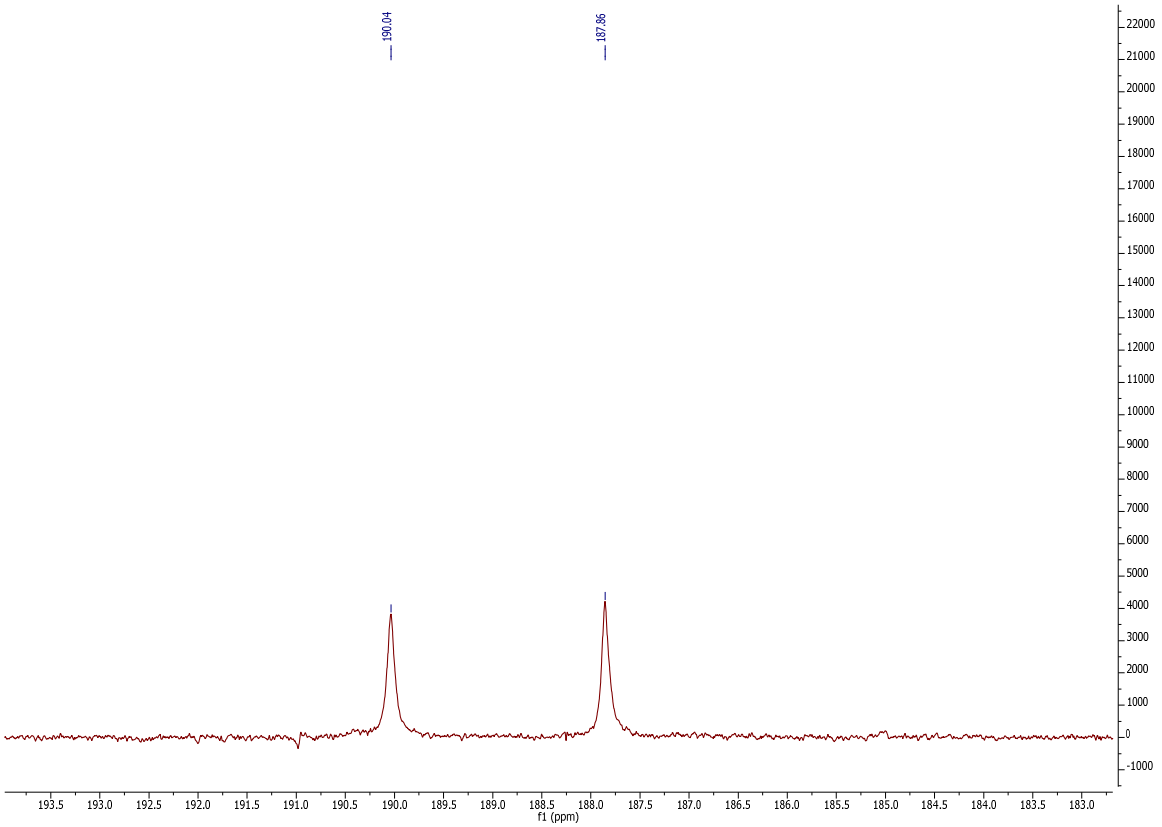




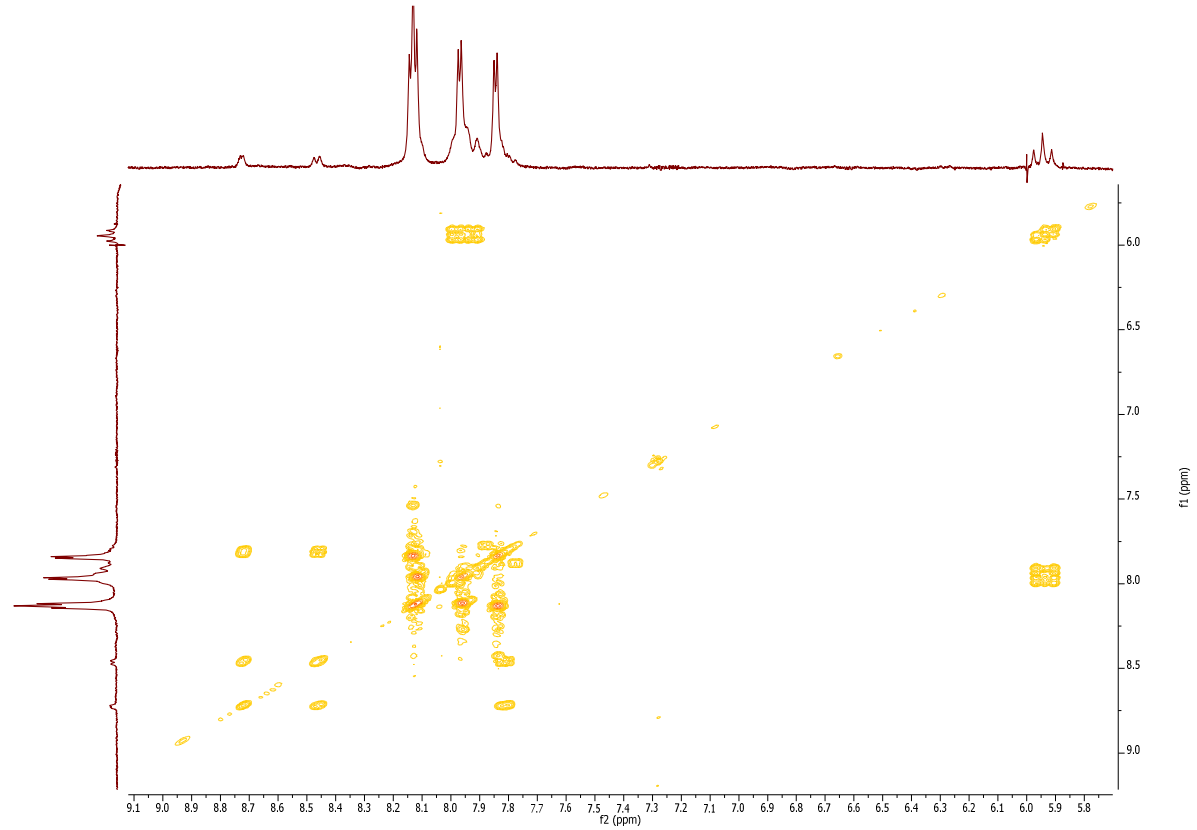
^{13}C NMR, 0 °C from the metalated intermediate:

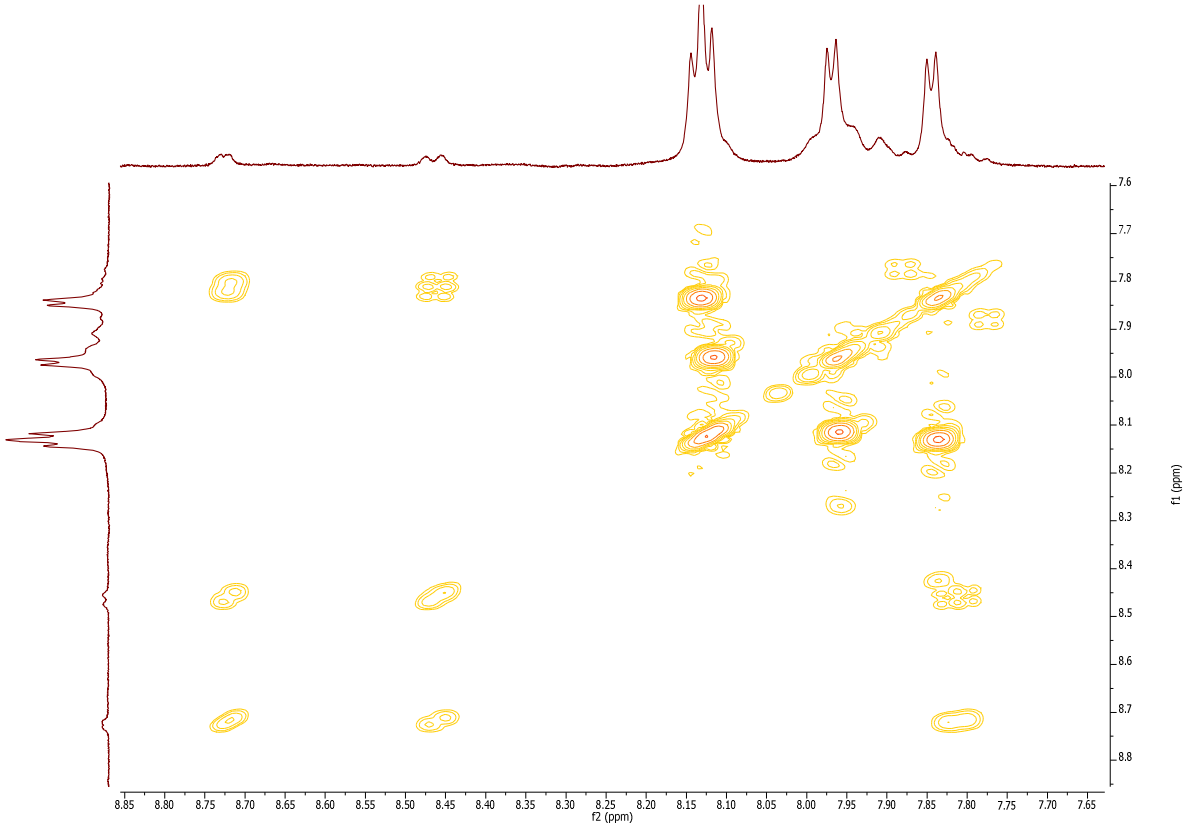




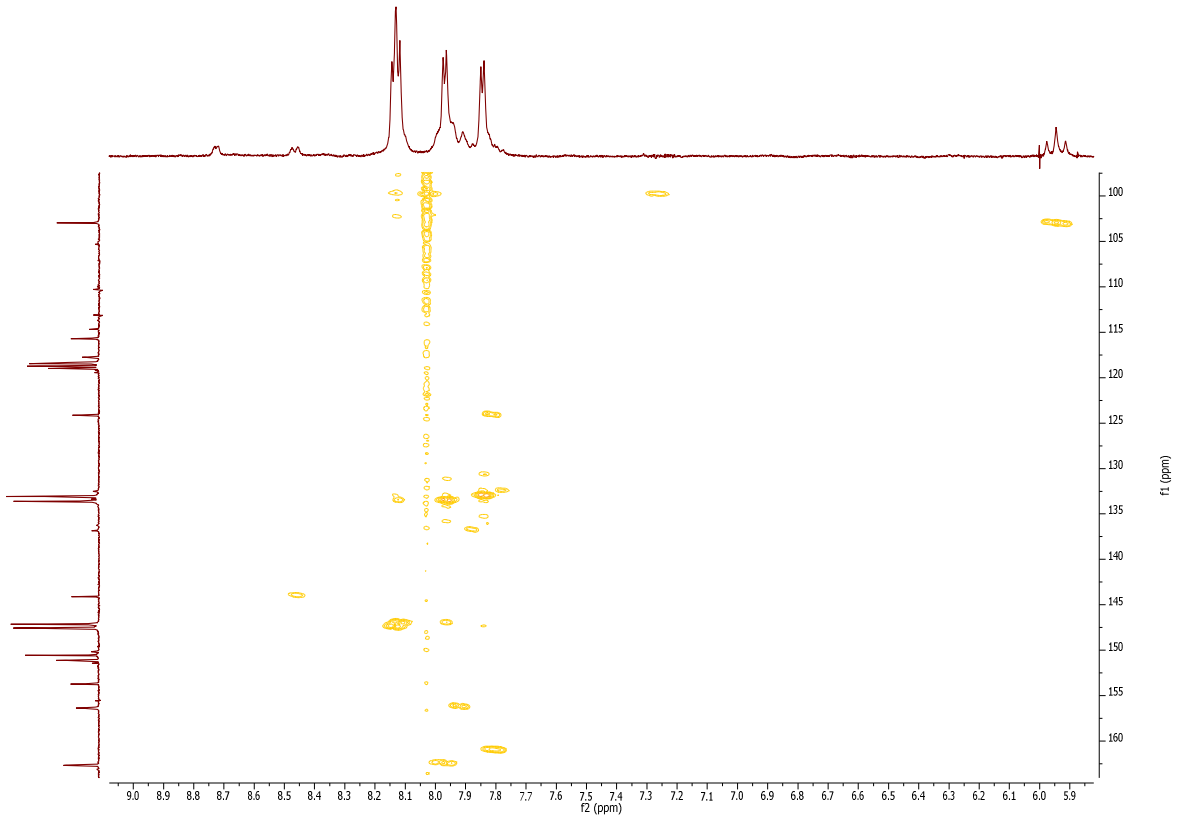


COSY, 0 °C:

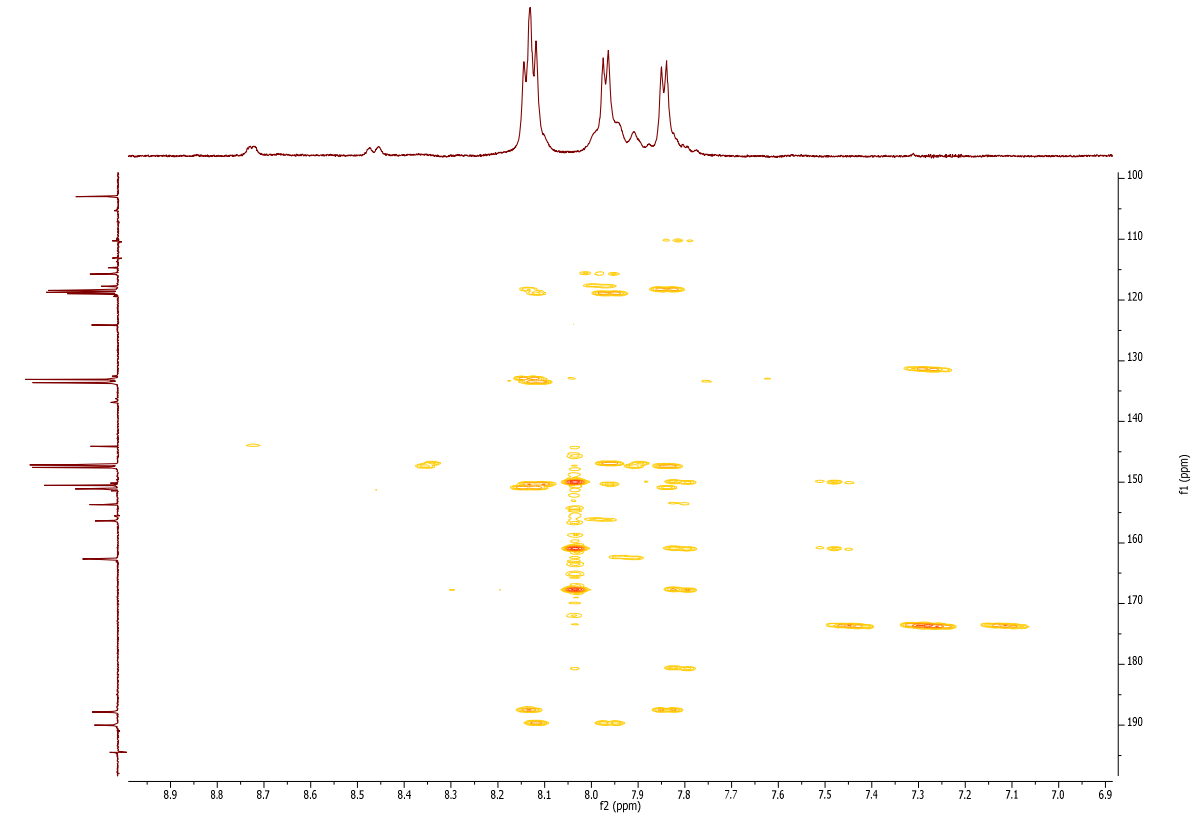


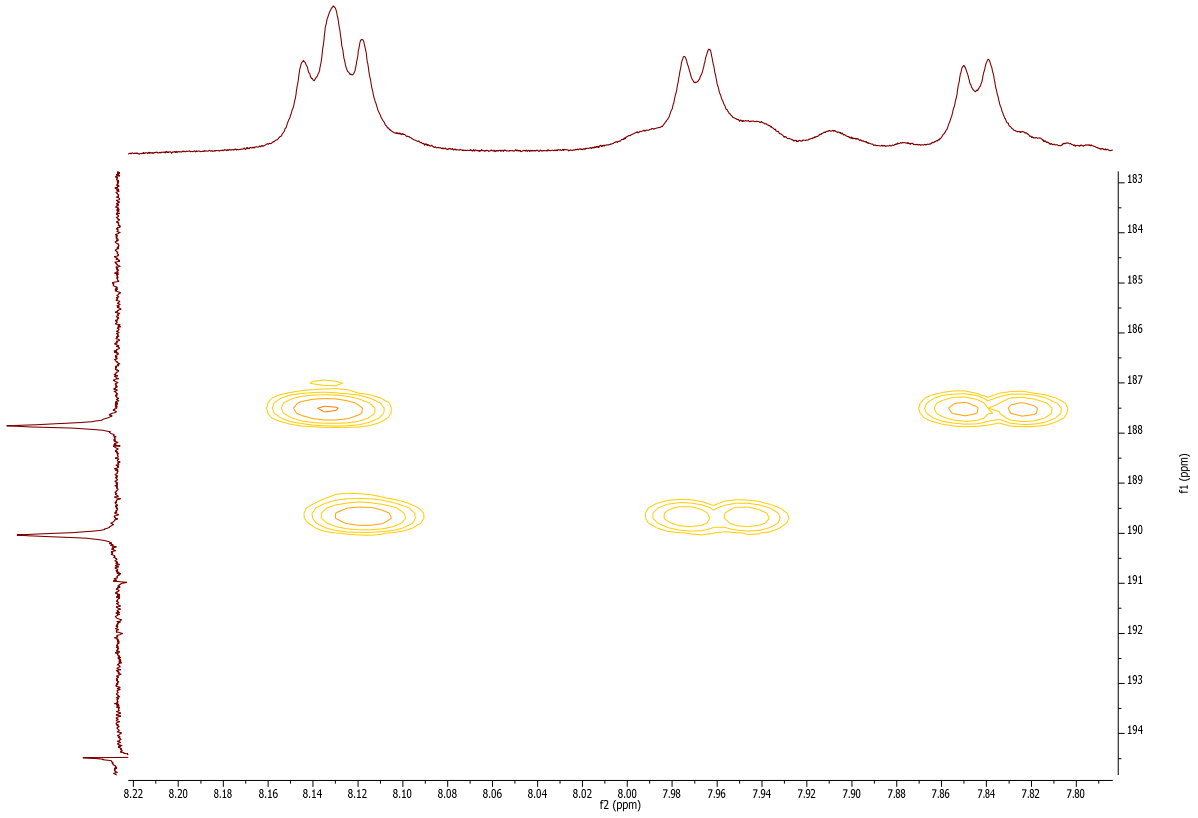


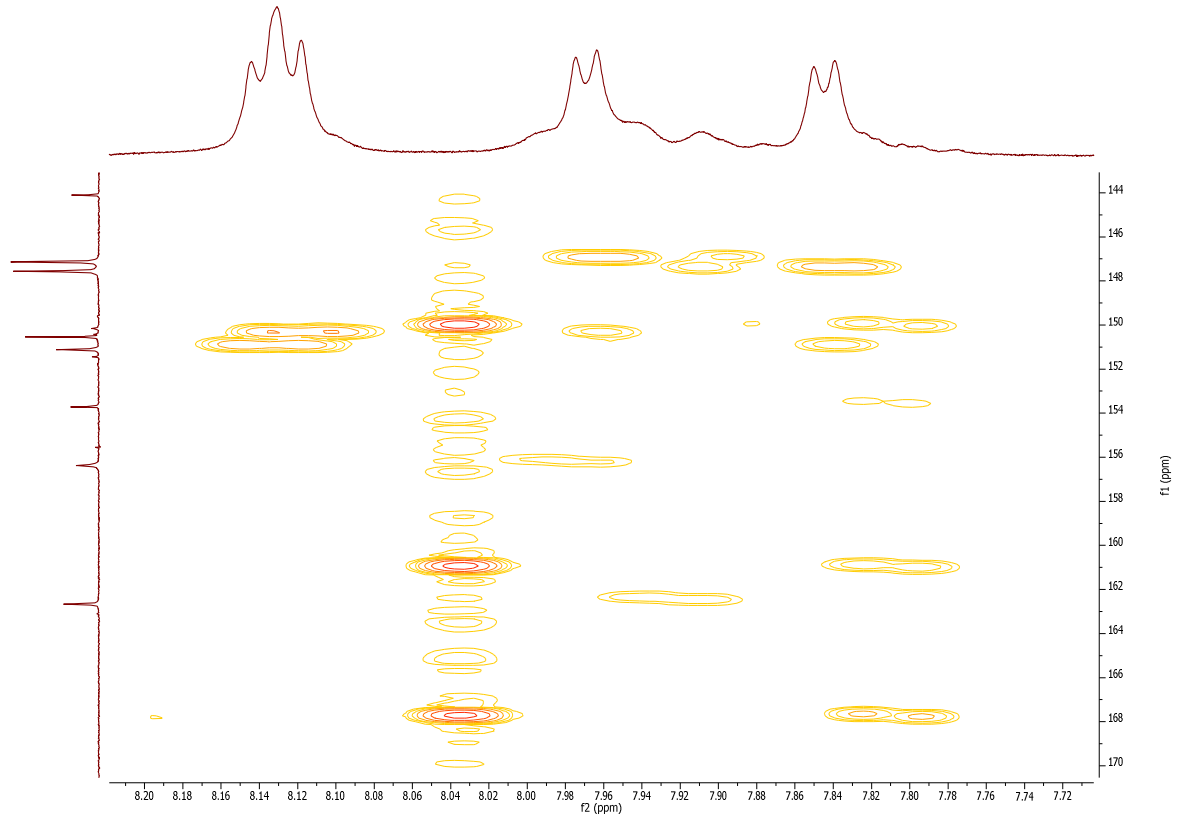
^{1}H, ^{13}C HMQC, 0 °C:

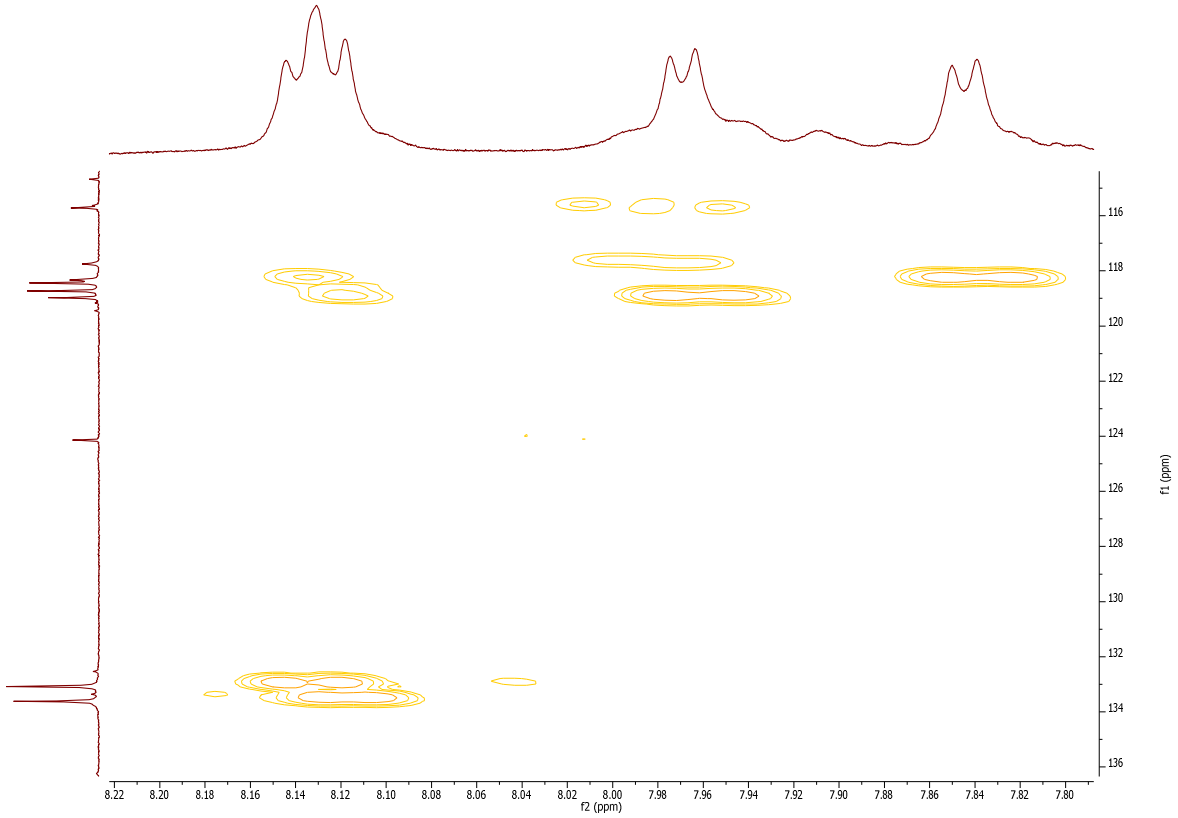


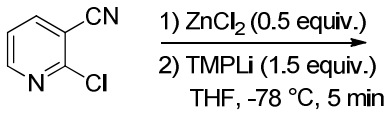
^{1}H, ^{13}C HMBC, 0 °C:



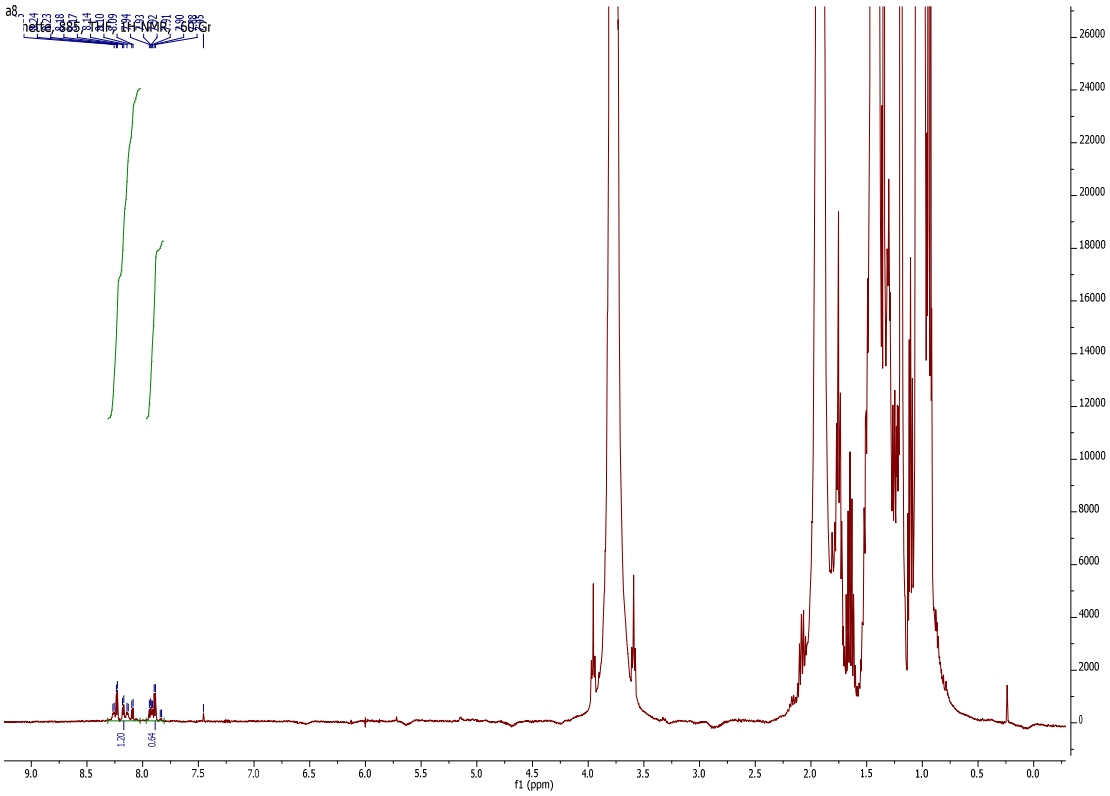


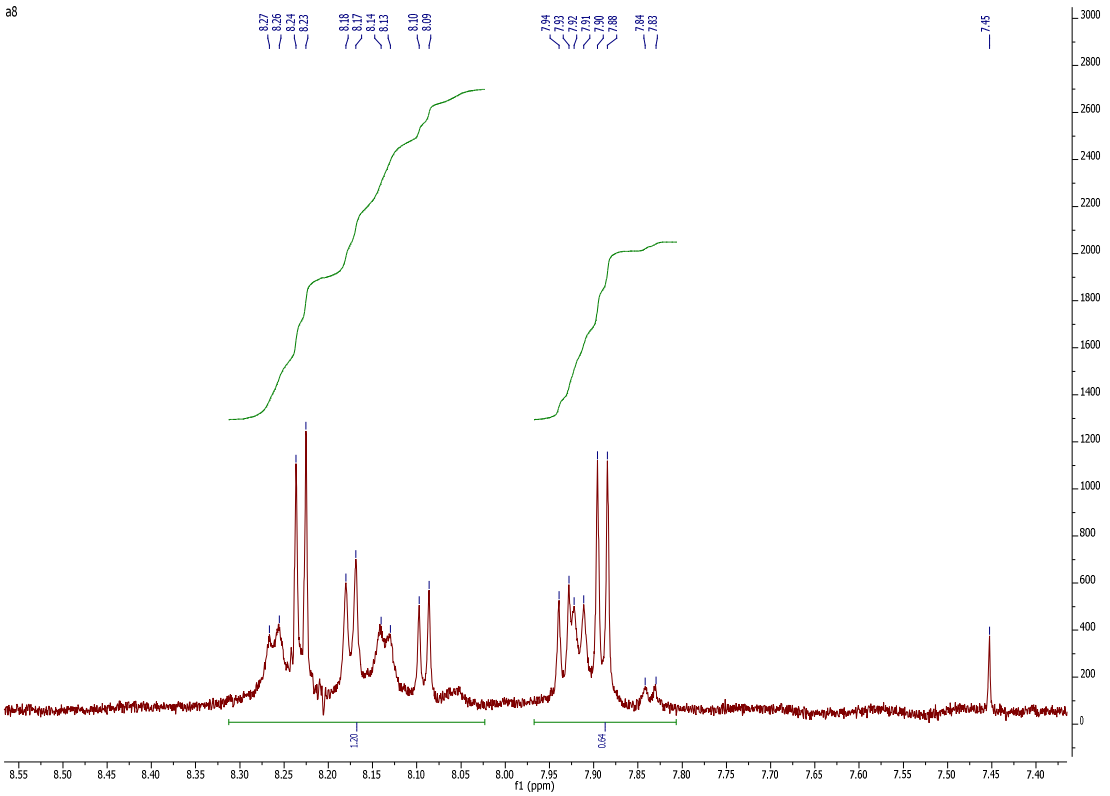

144
146
148
150
152
154
156
158
160
162
164
166
168
170
f1 (ppm)
8.20 8.18 8.16 8.14 8.12 8.10 8.08 8.06 8.04 8.02 8.00 7.98 7.96 7.94 7.92 7.90 7.88 7.86 7.84 7.82 7.80 7.78 7.76 7.74 7.72
f2 (ppm)


116
118
120
122
124
126
128
130
132
134
136
f1 (ppm)
8.22 8.20 8.18 8.16 8.14 8.12 8.10 8.08 8.06 8.04 8.02 8.00 7.98 7.96 7.94 7.92 7.90 7.88 7.86 7.84 7.82 7.80
f2 (ppm)

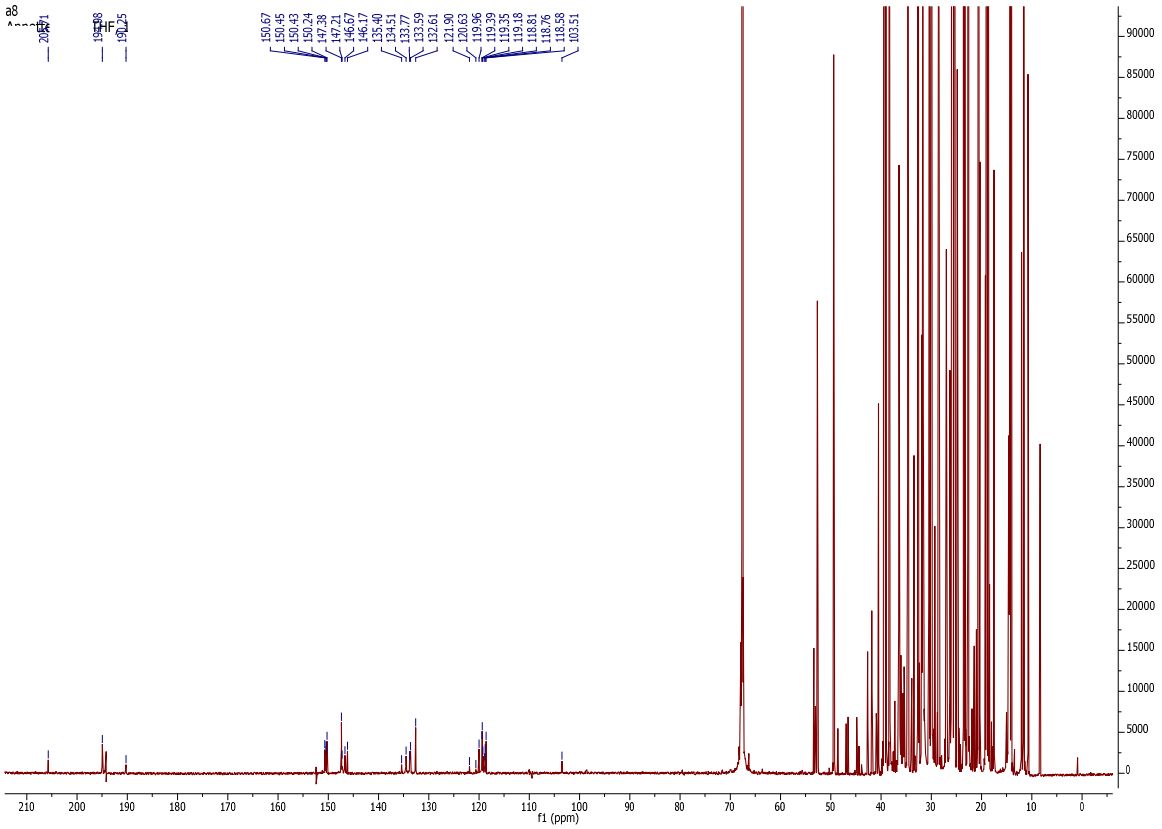

CN
N
Cl
1) ZnCl2 (0.5 equiv.)
2) TMPLi (1.5 equiv.)
THF, -78 °C, 5 min

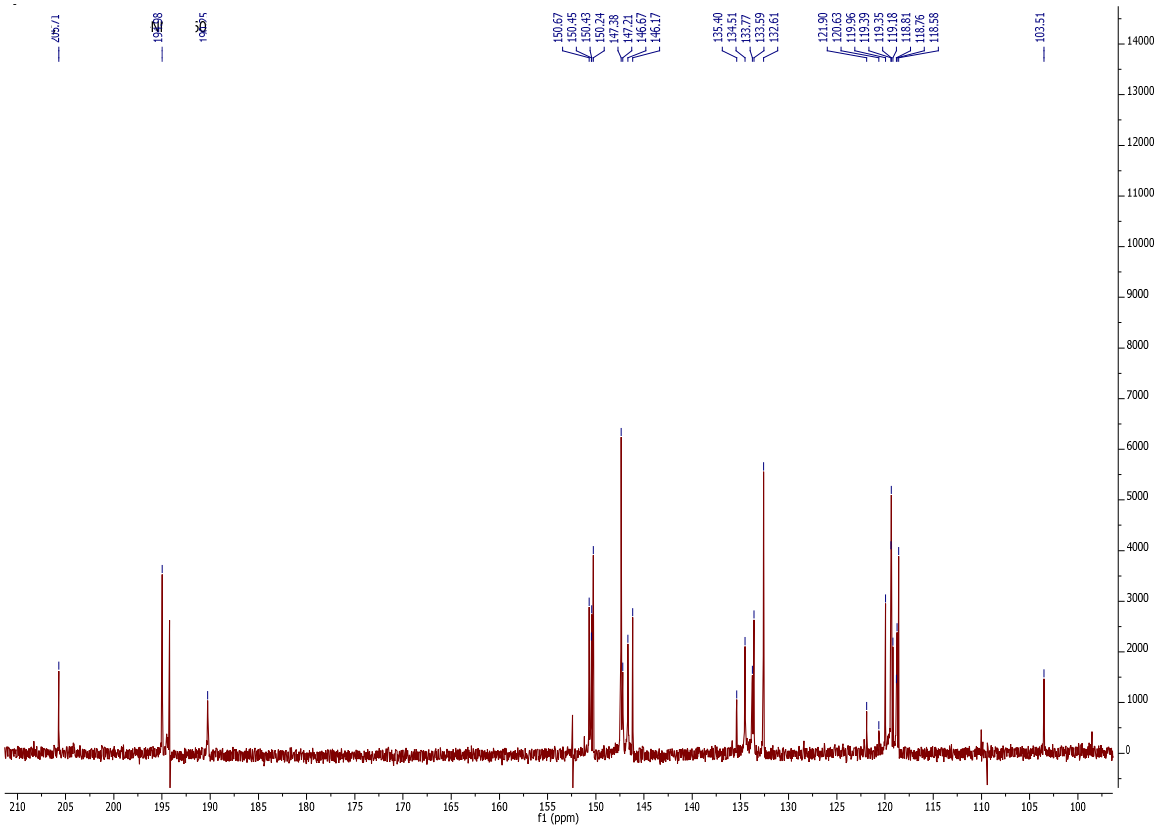
^{1}H NMR, -60 °C:

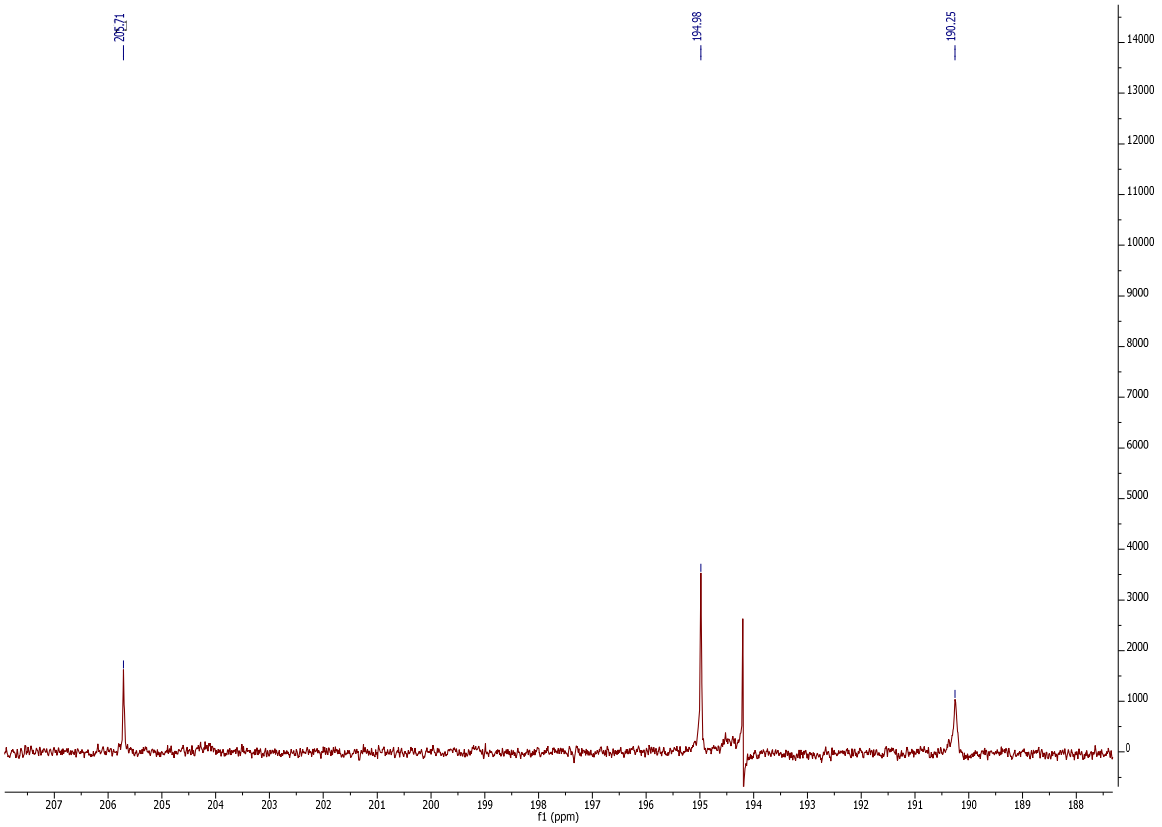

a8
f1 (ppm)


a8
8.27
8.26
8.24
8.23
8.18
8.17
8.14
8.13
8.10
8.09
7.94
7.93
7.92
7.91
7.90
7.88
7.84
7.83
7.45
1.20
0.64
f1 (ppm)

^{13}C NMR, -60 °C:


150.67
150.45
150.43
150.24
147.38
147.21
146.67
146.17
135.40
134.51
133.77
133.59
132.61
121.90
120.63
119.96
119.39
119.35
119.18
118.81
118.76
118.58
103.51
f1 (ppm)


150.67
150.45
150.43
150.24
147.38
147.21
146.67
146.17
135.40
134.51
133.77
133.59
132.61
121.90
120.63
119.96
119.39
119.35
119.18
118.81
118.76
118.58
103.51
f1 (ppm)


205.71
194.98
190.25
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
207
206
205
204
203
202
201
200
199
198
197
196
195
194
193
192
191
190
189
188
f1 (ppm)