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A new Pathway for the Total Functionalization of the Purine Scaffold and for the Preparation of new Materials Based on Benzo[*c*][1,2,5]thiadiazole *via* Mg and Zn Intermediates

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aus

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Erklärung

Diese Dissertation wurde im Sinne von § 13 Abs. 3 bzw. 4 der Promotionsordnung vom 29. Januar 1998 (in der Fassung der vierten Änderungssatzung vom 26. November 2004) von Herrn Prof. Dr. Paul Knochel betreut.

Ehrenwörtliche Versicherung

Diese Dissertation wurde selbständig, ohne unerlaubte Hilfe erarbeitet.

München, den 14.02.2011

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Silvia Daniela Zimdars

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To Steffen and my family

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

Heinz Langhals, Paul Knochel, Andreas Esterbauer, Andreas Walter, Silvia Zimdars "**Benzothiadiazoloperylene-amorphe funktionale Materialien**" Patent application DE 10 2009 048 848.0.

Silvia Zimdars, Xavier Mollat du Jourdin, François Crestey, Thomas Carell and Paul Knochel "**Trifunctionalization of the Purine Scaffold using Mg and Zn Organometallic Intermediates**" *Org. Lett.* **2011**, *13*, 792.

Silvia Zimdars, Heinz Langhals and Paul Knochel "**Functionalization of the Benzo[*c*][1,2,5]thiadiazole Scaffold *via* Mg-, Zn- and Mn-Intermediates**" *Synthesis*, accepted for publication.

Abbreviations

Ac	acetyl
approx.	approximate
aq	aqueous
Ar	aryl
Bn	benzyl
BTD	benzo[*c*][1,2,5]thiadiazole
calc.	calculated
cat	catalytic
conc	concentrated
COF	covalent organic framework
Cy	cyclohexyl
dba	*trans,trans*-dibenzylideneacetone
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
equiv	equivalent
E	electrophile
Et	ethyl
FCC	flash column chromatography
FG	functional group
FRET	Förster type energy transfer
GC	gas chromatography
h	hour
HR-MS	high resolution mass spectroscopy
*i*Pr	isopropyl
IR	infra-red
J	coupling constant (NMR)
M	molar
m	*meta*
Me	methyl
min	minute
mp	melting point
Mbs	4-methoxybenzenesulfonyl
MOM	methoxymethyl
MS	mass spectroscopy
*n*Bu	butyl
NMR	nuclear magnetic resonance
NMP	*N*-methyl-2-pyrrolidine
o	*ortho*
OLED	organic light emitting diode
p	*para*
PIP	piperidyl
pK_a	acid dissociation constant
PG	protecting group
Ph	phenyl
R	organic substituent
Rf	ribofuranosyl
sat	saturated
SPhos	2-dicyclohexylphosphino-2’,6’-dimethoxybiphenyl
*t*Bu	*tert*-butyl
TLC	thin layer chromatography
THF	tetrahydrofuran
THP	2,2,3,3-tetrahydropyranyl
TMP	2,2,6,6-tetramethylpiperidyl
TMS	trimethylsilyl
Ts	4-toluenesulfonyl
TP	typical procedure

A. INTRODUCTION

1. Overview

Modern life is unthinkable without the epochal achievements that have been made in chemistry and especially in organic chemistry. In terms of synthetics, glues, fuel, fuel additives, dyes, pharmaceuticals, fertilizer and food additives chemistry is all-around. Still, there is a significant demand for fundamental research, as well as for the development of new and more efficient synthetic methods. Due to the higher complexity of the target molecules nowadays, the new processes should provide a high functional group tolerance, selectivity and atom efficiency. A wide sphere of novel syntheses was found in 1849 by Frankland[1] who synthesized diethylzinc as the first organometallic compound. Since that time, organometallic chemistry became an important and diverse part of the organic and inorganic chemistry and several nobel prizes have been awarded in this field of research. In the beginning, organolithium[2] and organomagnesium[3] derivatives were mainly investigated and they are still very important intermediates for carbon-carbon bond formation.[4] Organozinc reagents are more stable and easier to handle, but therefor less reactive. For this reason, the interest in organozinc compounds grew not before they were found to react nearly quantitative with acid chlorides[5] and their reactivity was found to be tunable by addition of lewis acids.[6] More recently, the discovery of transmetalation reactions with various transition metal salts[7,8] became the breakthrough in organozinc chemistry as these results have shown the diverse reactivity in addition to an excellent functional group tolerance.

[1] (a) Frankland, E. *Liebigs Ann. Chem.* **1848-49**, *71*, 171; (b) Frankland, E. *J. Chem. Soc.* **1848-49**, *2*, 263.

[2] (a) Schlenk, W.; Holtz, J. *Chem. Ber.* **1917**, *50*, 262; (b) Ziegler, K.; Colonius, H. *Liebigs Ann. Chem.* **1930**, *479*, 135.

[3] Grignard, V. *Compt. Rend.* **1900**, *130*, 1322.

[4] (a) Li, B.; Wu, Z.; Gu, Y.; Sun, C.; Wang, B.; Shi, Z. *Angew. Chem Int. Ed.* **2011**, *50*, 1109; (b) Shao, Z.; Peng, F. *Angew. Chem. Int. Ed.* **2010**, *49*, 9566; (c) Boyce, G.; Johnson, J. *Angew. Chem. Int. Ed.* **2010**, *49*, 8930.

[5] Klein, H.; Neff, H. *Angew. Chem.* **1956**, *68*, 681.

[6] Marx, B.; Henry-Basch, E.; Freon, P. *Compt. Rend.* **1967**, *264*, 527.

[7] Negishi, E.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821.

[8] (a) Knochel, P.; Yeh, M., Berk, S.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390; (b) Dübner, F.; Knochel, P. *Angew. Chem. Int. Ed.* **1999**, *38*, 379.

2. General preparation of functionalized organomagnesium and organozinc intermediates

2.1. Metal insertion into organic halides

2.1.1. Magnesium insertion

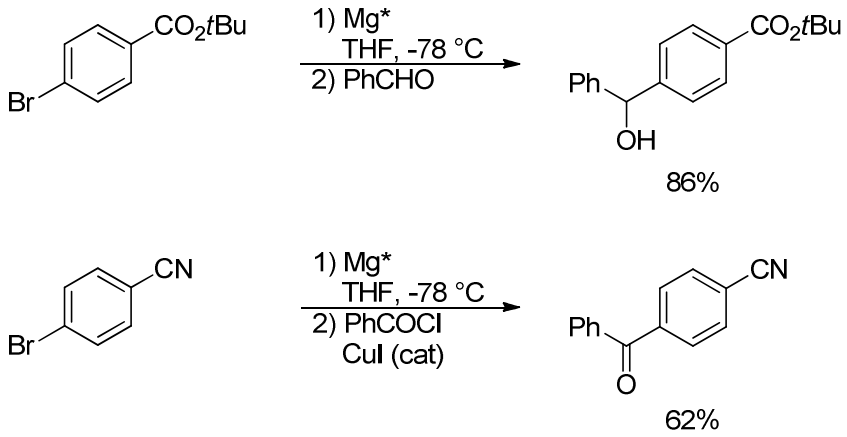
The initiation of the organomagnesium chemistry is strongly associated with the name Grignard who generated organomagnesium compounds *via* oxidative insertion of magnesium into organic halides in 1901.[9] The synthesis of those Grignard reagents is made in polar and aprotic solvents like THF or diethyl ether and is illustrated in Scheme 1.

Scheme 1: General reaction scheme for the generation of a Grignard reagent via oxidative insertion.

Due to the normally used reflux conditions, the functional group tolerance of this reaction is very low and can be improved by the use of activated Rieke magnesium (Mg*). Thereby, stable functional groups like *tert*-butylesters or nitriles are tolerated (Scheme 2).[10]

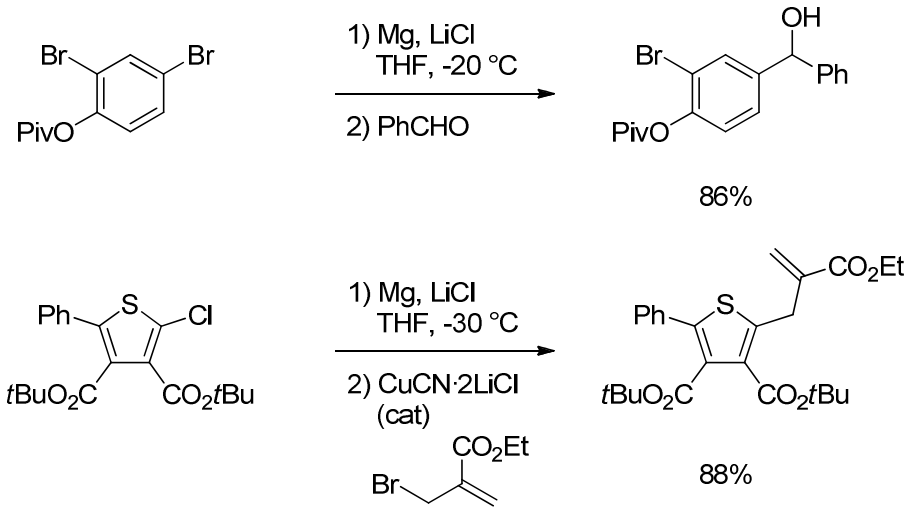
[9] Grignard, V. *Ann. Chim.* **1901**, *24*, 433.

[10] (a) Rieke, R.; Li, T.; Burns, T.; Uhm, S. *J. Org. Chem.* **1981**, *46*, 4323; (b) Burns, T.; Rieke, R. *J. Org. Chem.* **1987**, *52*, 3674; (c) Rieke, R. *Science* **1989**, *246*, 1260; (d) Rieke, R.; Sell, M.; Klein, W.; Chen, T.; Brown, J.; Hansan, M. *Active Metals* (Ed.: A. Fuerstner), Wiley-VCH, Weinheim, **1995**; (e) Lee, J.; Velarde-Ortiz, R.; Guijarro, A.; Wurst, J.; Rieke, R. *J. Org. Chem.* **2000**, *65*, 5428.



Scheme 2: Examples for the synthesis of Grignard reagents with Rieke magnesium (Mg*) and subsequent reaction with electrophiles.

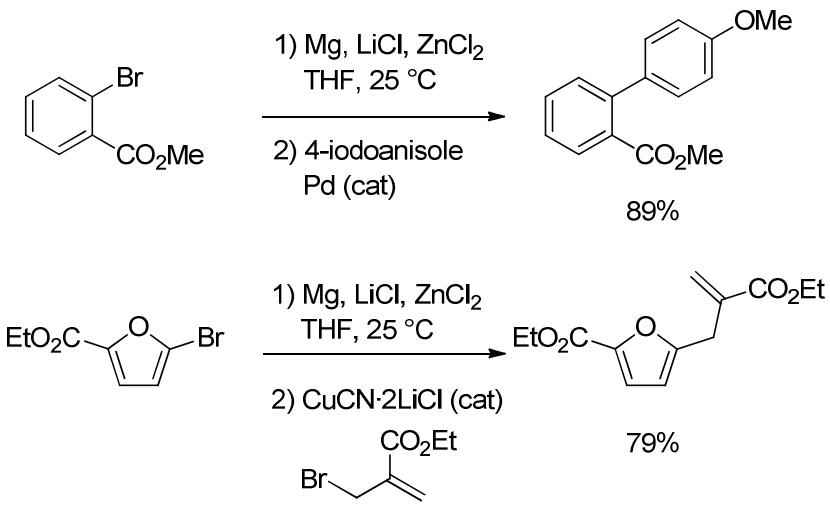
Even though the oxidative insertion provides a simple and atom efficient route to magnesium reagents, the functional group tolerance is still restricted and Rieke magnesium has to be freshly prepared by the treatment of $MgCl_2$ with lithium in the presence of 20 mol% naphthalene. Recently, Knochel and co-workers found the LiCl promoted insertion of magnesium into aromatic or heteroaromatic chlorides and bromides to be a very mild method for the generation of highly functionalized magnesium reagents (Scheme 3).[11]



Scheme 3: Examples for the generation of Grignard reagents in the presence of LiCl and subsequent reaction with electrophiles.

[11] Piller, F.; Appukkuttan, P.; Gavryushin, A.; Helm, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2008**, *47*, 6802.

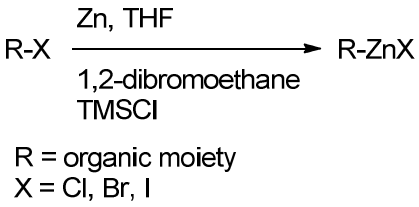
Even more sensitive functionalities are tolerated if the magnesium insertion is made in the presence of $ZnCl_2$ and the corresponding zinc reagent is formed *in situ* (Scheme 4).



Scheme 4: Examples for the generation of zinc reagents *via* magnesium insertion in the presence of LiCl and subsequent reaction with electrophiles.

2.1.2. Zinc insertion

The zinc insertion is proceeding similarly to the magnesium insertion (Scheme 5). One of the most important differences is the additional activation of the zinc metal with 1,2-dibromoethane and TMSCl, which is essential because of the passivated surface.[12] Generally, the reaction times of the zinc insertion are longer and almost all functional groups can be tolerated.[13]

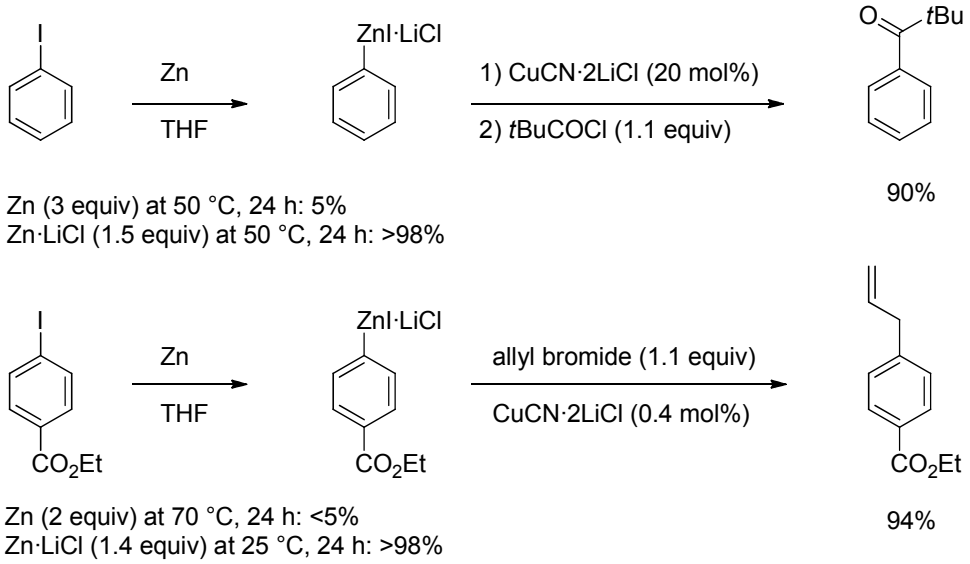


Scheme 5: General reaction scheme for the oxidative zinc insertion.

[12] (a) Gaudemar, M. *Bull. Soc. Chim. Fr.* **1962**, *5*, 974; (b) Erdik, E. *Tetrahedron* **1987**, *43*, 2203.

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

Even though this provides a general access to organozinc reagents it was almost exclusively limited to organic iodides in the beginning. Rieke developed highly activated zinc metal, which is freshly prepared in a reaction of $ZnCl_2$ with lithium naphthalenide and therefore much more reactive.[10] In 2006, Knochel found another possibility for speeding up the zinc insertion by addition of LiCl.[14] Thus, reaction times became shorter, reaction temperatures became lower and even the insertion into organic bromides became accessible (Scheme 6). Another important advantage is the influence of the LiCl on the solubility of the formed zinc reagents.



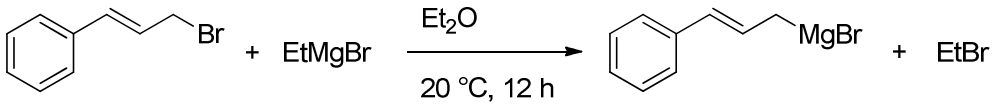
Scheme 6: Examples for the preparation of arylzinc halides in the absence and in the presence of stoichiometric amounts of LiCl.

2.2. Halogen/ magnesium exchange

Problems which occure due to the heterogeneous reaction conditions of metal insertion reactions can be avoided with the halogen/ magnesium exchange reaction that was first observed by Prévost in 1931 as shown in Scheme 7.[15]

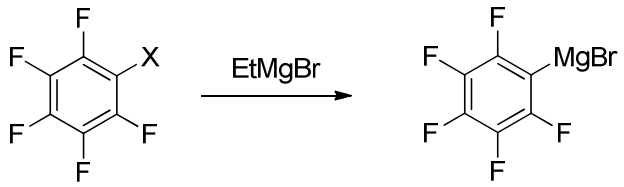
[14] (a) Boudet, N.; Sase, S.; Sinha, P.; Liu, C.; Krasovskiy, A.; Knochel, P. *J. Am. Chem. Soc.* **2007**, *129*, 12358; (b) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2006**, *45*, 6040.

[15] Prévost, C. *Bull. Soc. Chim. Fr.* **1931**, *49*, 1372.

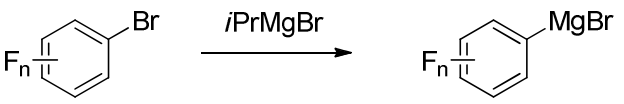


Scheme 7: Bromine/ magnesium exchange with cinnamylbromide by Prévost.

In 1971, Tamborski and Moore have shown that the halogen/ magnesium exchange highly depends on the halogen as well as on the nature of the organic compound that is used.[16] The higher the polarizability of the halogen and the lower the bond strength of the carbon-halogen bond, the higher is the reactivity as shown in Scheme 8. Therefore, the reaction with chlorines only occures on highly activated substrates like chloro pentafluorobenzene. The dependency of the reactivity on the number of electron withdrawing substituents like fluorine was shown by Knochel (Scheme 8).[17]



X	T	t
Cl	25 °C	1 h
Br	0 °C	1 min
I	0 °C	1 min



n	T	t
5	-78 °C	30 min
3	-10 °C	1 h
2	25 °C	2 h
1	25 °C	3 h

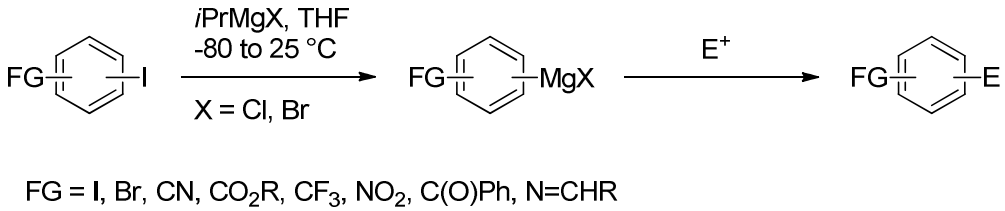
Scheme 8: Celerity of the halogen/ magnesium exchange reaction depending on the halogen and on the substrate.

The further development of the iodine/ magnesium exchange at low temperatures has shown an excellent functional group tolerance beside a good reactivity of the organometallic reagents (Scheme 9).[18]

[16] Tamborski, C.; Moore, G. *J. Organomet. Chem.* **1971**, *26*, 153.

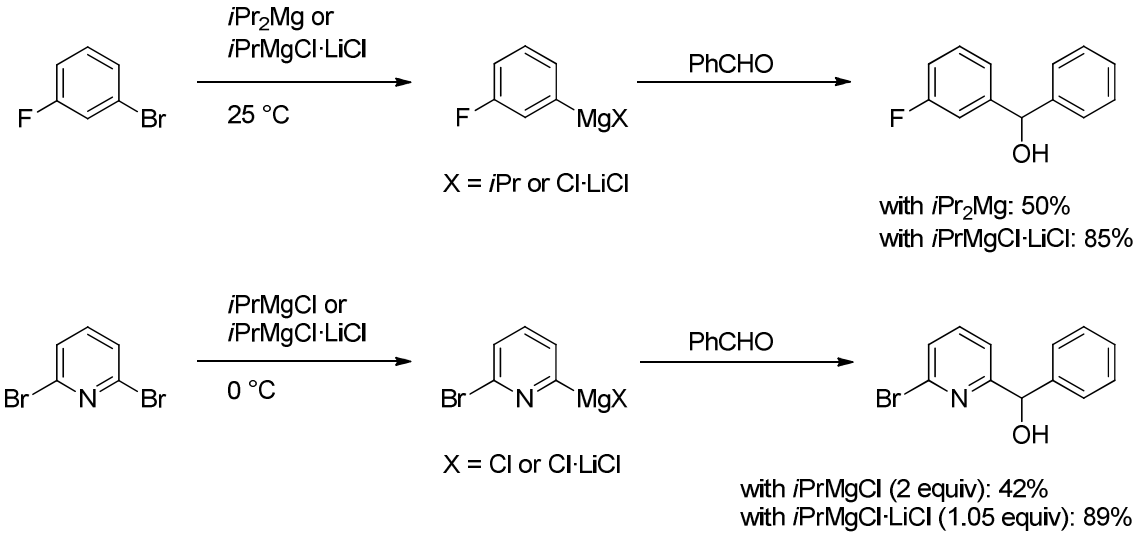
[17] Abarbri, M; Dehmel, F.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 7449.

[18] a) Boymond, L.; Rottländer, M.; Cahiez, G.; Knochel, P. *Angew. Chem. Int. Ed.* **1998**, *37*, 1701; b) Boudier, A.; Bromm, L.; Lotz, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2000**, *39*, 4415; c) Sapountzis, I.; Knochel, P.



Scheme 9: General reaction scheme for the iodine/ magnesium exchange pointing out the functional group tolerance.

At that time, the halogen/ magnesium exchange on non-activated substrates was restricted to iodinated aryl or heteroaryl[19] compounds which normally are more expensive and less stable than the corresponding brominated derivatives. In 2004, Knochel discovered a new method for speeding up the bromine/ magnesium exchange by the addition of LiCl which breaks the aggregated *i*PrMgCl (Scheme 10).[20]



Scheme 10: Celerity of the bromine/ magnesium exchange reaction by the addition of LiCl.

Angew. Chem. Int. Ed. **2002**, *41*, 1610; d) Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. *Angew. Chem. Int. Ed.* **2003**, *42*, 4302.

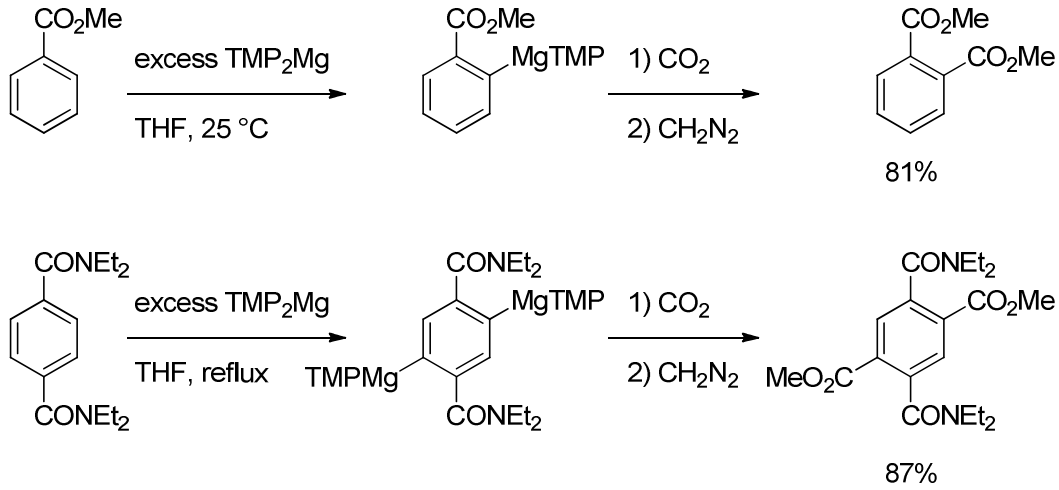
[19] a) Bérillon, L.; Leprêtre, A.; Turck, A.; Plé, N.; Quéguiner, G.; Cahiez, G.; Knochel, P. *Synlett* **1998**, 1359; b) Abarbri, M.; Dehmel, F.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 7449; c) Abarbri, M.; Thibonnet, J.; Bérillon, L.; Dehmel, F.; Rottländer, M.; Knochel, P. *J. Org. Chem.* **2000**, *65*, 4618.

[20] Krasovskiy, A.; Knochel, P. *Angew. Chem.* **2004**, *116*, 3369; *Angew. Chem. Int. Ed.* **2004**, *43*, 3333.

2.3. Directed metalation with amide-bases

2.3.1. Directed metalation with magnesium amides

The deprotonation of organic compounds is an elegant method for the metalation as no halogenated substrate is required. As organomagnesium reagents are kinetically weak bases this method is limited to coordinating substrates. Amides and coordinating functional groups are used to minimize the intrinsic barrier and to break up the aggregated organometallic reagents.[21] In 1989, Eaton reported *ortho*- and double-magnesiation on aromatics with Hauser bases (R_2NMgBr) and magnesium bisamides ($(R_2N)_2Mg$) (Scheme 11).[22]



Scheme 11: Examples for directed metalation with magnesium bisamides by Eaton.

In 1995, Mulzer developed the regioselective magnesiation of mono- and disubstituted pyridines with TMPMgCl,[23] but due to the low solubility and the required large quantity of base the scope was quite narrow. The directed magnesiation became more prevalent when Knochel reported mixed lithium-magnesium amide bases, which are readily soluble and are therefore used in stoichiometric amounts.[24] The preparation of the first synthesized bases and

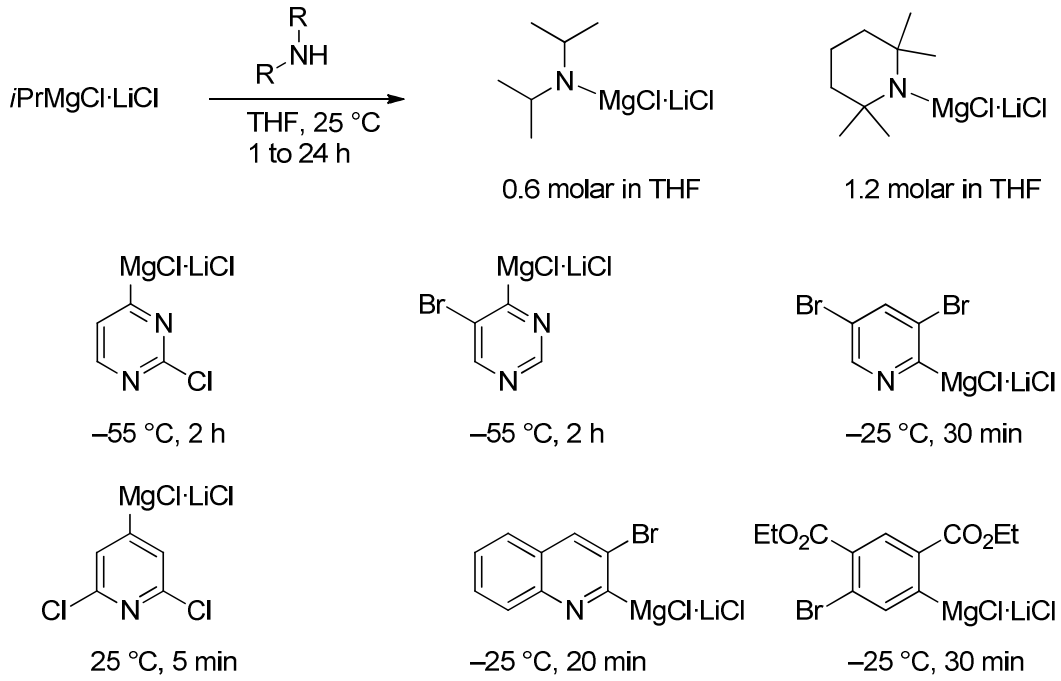
[21] Baron, O.; Dissertation, Ludwig-Maximilians-Universität München, 2006.

[22] Eaton, P.; Lee, C.; Xiong, Y. *J. Am. Chem. Soc.* **1989**, *111*, 8016.

[23] Schlecker, W.; Huth, A.; Ottow, E.; Mulzer, J. *J. Org. Chem.* **1995**, *60*, 8414.

[24] (a) Krasovskiy, A.; Krasovskaya, V.; Knochel, P. *Angew. Chem. Int. Ed.* **2006**, *45*, 2958; (b) Lin, W.; Baron, O.; Knochel, P. *Org. Lett.* **2006**, *8*, 5673.

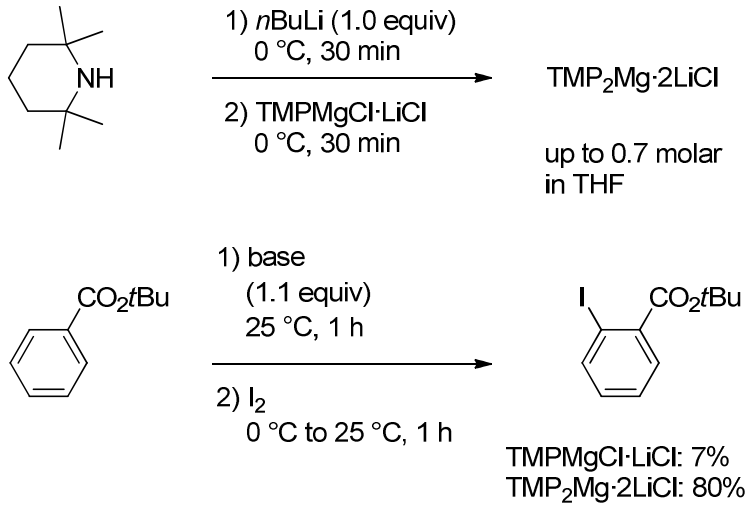
some examples for the deprotonation of aromatic or heteroaromatic substrates with TMPMgCl·LiCl are shown in Scheme 12.



Scheme 12: Preparation of mixed lithium-magnesium amide bases and some examples for the use of TMPMgCl·LiCl in deprotonation reactions.

In continuation to this work it was shown that the bisamide $TMP_2Mg·2LiCl$ has an improved kinetic basicity even though its solubility is lower (Scheme 13).[25]

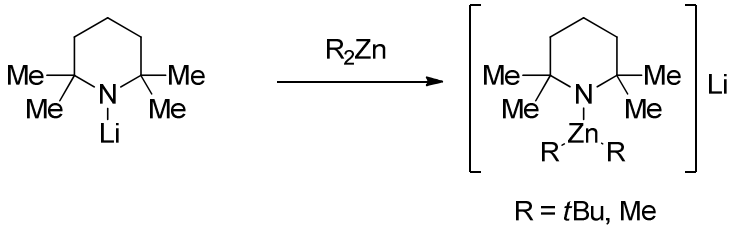
[25] (a) Clososki, G.; Rohbogner, C.; Knochel, P. *Angew. Chem.* **2007**, *119*, 7825; *Angew. Chem. Int. Ed.* **2007**, *46*, 7681; (b) Rohbogner, C.; Wagner, A.; Clososki, G.; Knochel, P. *Org. Synth.* **2009**, *86*, 374.



Scheme 13: Preparation of $TMP_2Mg \cdot 2LiCl$ and its reactivity compared to $TMPMgCl \cdot LiCl$.

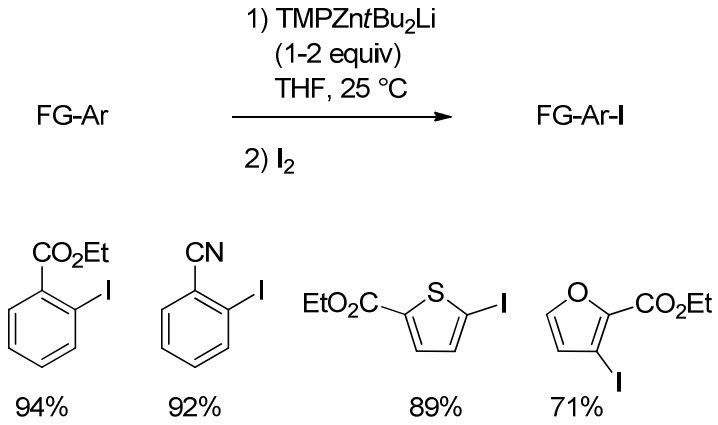
2.3.2. Directed metalation with zinc amides

The first directed metalation reactions with zincate bases were published by Kondo in 1999. The synthesis of $TMPZnR_2Li$ is shown in Scheme 14 and some examples for the deprotonation of aryls and heteroaryls with subsequent iodination in Scheme 15.[26]



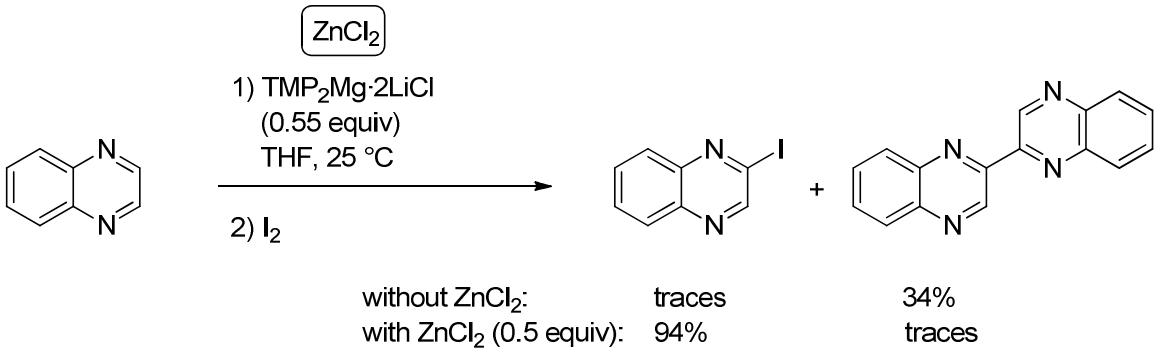
Scheme 14: Synthesis of zincate bases published by Kondo.

[26] (a) Kondo, Y.; Shilai, H; Uchiyama, M.; Sakamoto, T. *J. Am. Chem. Soc.* **1999**, *121*, 3539; (b) Imahori, T.; Uchiyama, M.; Kondo, Y. *Chem. Commun.* **2001**, 2450; (c) Uchiyama, M.; Miyoshi, T.; Kajihara, Y.; Sakamoto, T.; Otami, Y.; Ohwada, T.; Kondo, Y. *J. Am. Chem. Soc.* **2002**, *124*, 8514.



Scheme 15: First directed metalation reactions with a zincate base published by Kondo.

If the deprotonation occured *ortho* to a bromine atom the corresponding benzyne was formed at 25 to 66 °C.[27] Moreover, these highly reactive zincates were not compatible with very sensitive heterocycles like 1,3,4-oxadiazole derivatives and functional groups like aldehydes and nitro groups. To achieve the directed metalation in those cases Knochel and co-workers developed pathways using either an *in situ* method with $TMP_2Mg\cdot 2LiCl$ in the presence of $ZnCl_2$[28] (Scheme 16) or new bisamide zinc bases[29] (Scheme 17). These bases are even stable at higher temperatures and can therefore be used under microwave irradiation up to 120 °C.[30]



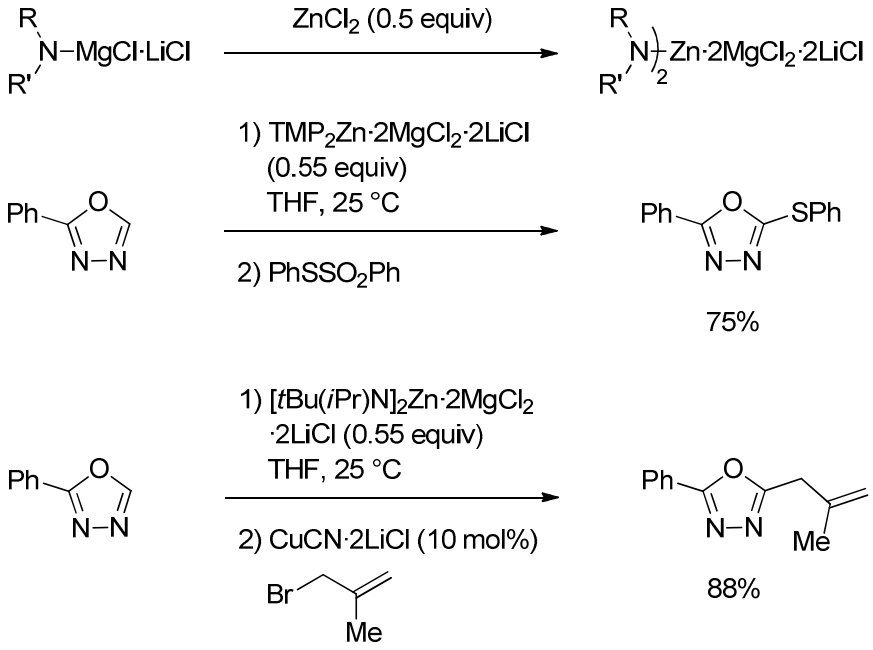
Scheme 16: *In situ* method with $TMP_2Mg\cdot 2LiCl$ in the presence of $ZnCl_2$ by Knochel.

[27] Uchiyama, M.; Kobayashi, Y.; Furuyama, T.; Nakamura, S.; Kajihara, Y.; Miyoshi, T.; Sakamoto, T.; Kondo, Y.; Morokuma, K. *J. Am. Chem. Soc.* **2008**, *130*, 472.

[28] Dong, Z.; Clososki, G.; Wunderlich, S.; Unsinn, A.; Li, J.; Knochel, P. *Chem. Eur. J.* **2009**, *15*, 457.

[29] (a) Wunderlich, S.; Knochel, P. *Angew. Chem. Int. Ed.* **2007**, *46*, 7685; (b) Rohbogner, C.; Wunderlich, S.; Clososki, G.; Knochel, P. *Eur. J. Org. Chem.* **2009**, 1781.

[30] Wunderlich, S.; Knochel, P. *Org. Lett.* **2008**, *10*, 4705.

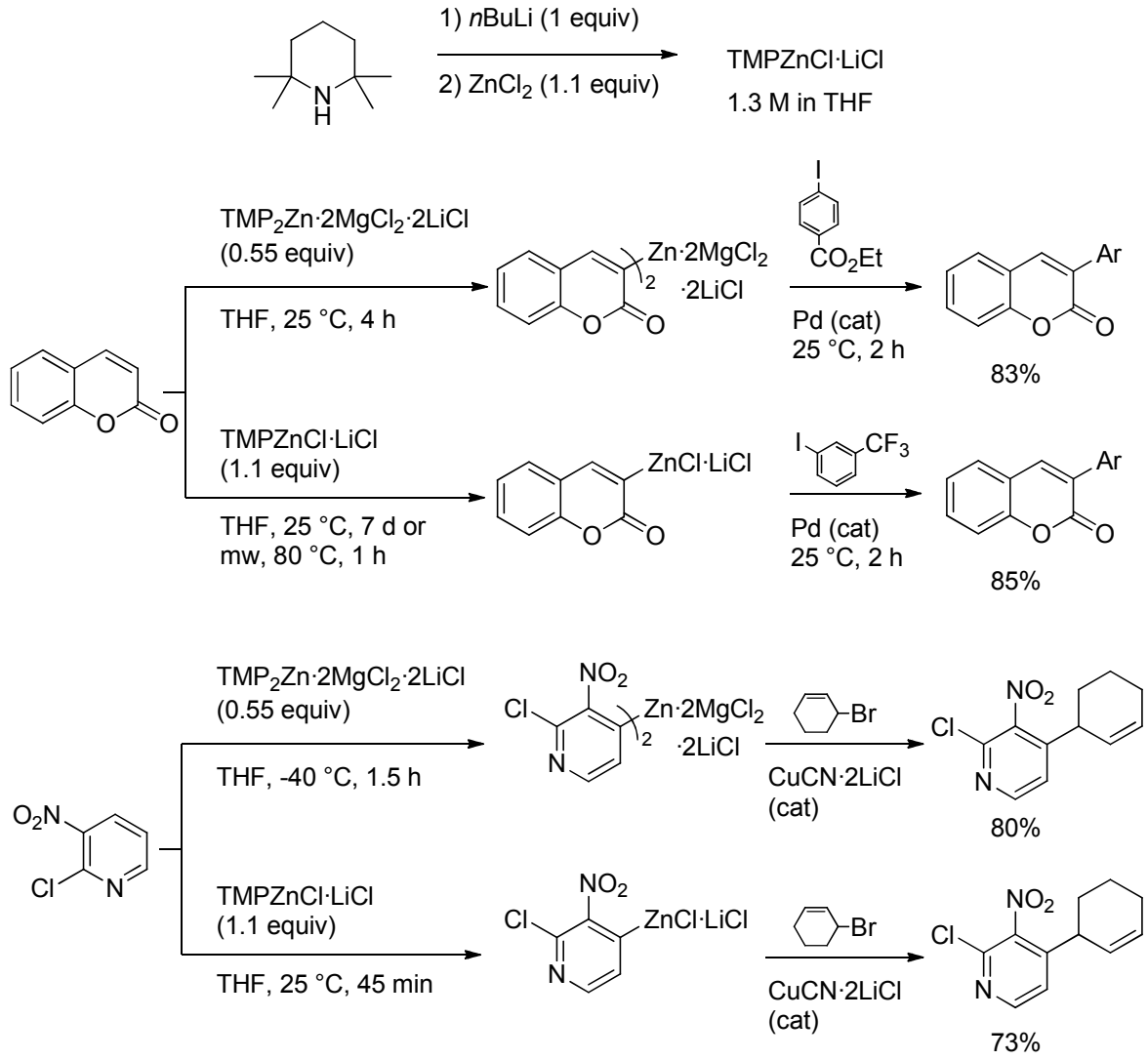


Scheme 17: Synthesis of new bisamide zinc bases for the generation of bisheteroarylzinc reagents and subsequent reaction with electrophiles.

The LiCl is an essential component for the solubility of these bases as already mentioned for the metal insertion, the halogen/ magnesium exchange and the directed metalation with magnesium amides. Moreover, the $MgCl_2$ increases the kinetic basicity.[29a] However, in the case of some electron-poor functionalized aromatics and heteroaromatics the already mentioned zinc bases reach their limits or have to be used at low temperatures. Recently, a milder and more selective zinc base (TMPZnCl·LiCl) was published which is normally used at ambient temperature[31] and can be used up to 160 °C under microwave conditions.[32] The preparation of this base and its reactivity compared to $TMP_2Zn·2MgCl_2·2LiCl$ is shown in Scheme 18.

[31] (a) Mosrin, M.; Knochel, P. *Org. Lett.* **2009**, *11*, 1837; (b) Mosrin, M.; Bresser, T.; Knochel, P. *Org. Lett.* **2009**, *11*, 3406; (c) Bresser, T.; Mosrin, M.; Monzon, G.; Knochel, P. *J. Org. Chem.* **2010**, *75*, 4686; (d) Bresser, T.; Monzon, G.; Mosrin, M.; Knochel, P. *Org. Process Res. Dev.* **2010**, *14*, 1299.

[32] Mosrin, M.; Monzon, G.; Bresser, T.; Knochel, P. *Chem. Commun.* **2009**, *37*, 5615.



Scheme 18: Synthesis of TMPZnCl·LiCl and its reactivity compared to $TMP_2Zn·2MgCl_2·2LiCl$.

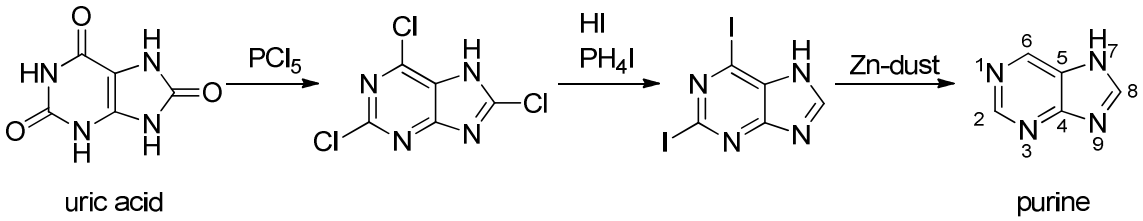
3. Functionalization of heterocycles

Condensed heterocycles gain importance due to their applications in biological and material science. Therefore, their functionalization is an active research field what is still affecting the demand on new synthetic methods.[33]

[33] (a) Kienle, M.; Wagner, A. J.; Dunst, C.; Knochel, P. *Chem. Asian. J.* **2011**, *6*, 517; (b) Zhu, J.; Xie, H.; Chen, Z.; Li, S.; Wu, Y. *Chem. Commun.* **2011**, *47*, 1512; (c) Kim, S. H.; Chang, S. *Org. Lett.* **2010**, *12*, 1868.

3.1. Functionalization of the purine scaffold

Purine itself is a synthetic compound which was named in 1884[34] and synthesized the first time 14 years later from uric acid[35] by E. Fischer (Scheme 19). Its naturally occuring derivatives are omnipresent as it's part of the DNA and of lots of co-factors.



Scheme 19: Purine synthesis by E. Fischer.

As a result of the vast quantity of biologically active compounds bearing this heterocyclic unit the purine scaffold became an important class of pharmacophores that has been extensively explored in the last decades.[36] For example, the 2-morpholino purine **I** and the 2-benzimidazolo purine **II** are potential kinase inhibitors[37] or display immunosuppressant[38] activity, the purine derivative **III** is a potential pharmaceutical for psychiatric disorders and neurological diseases (Scheme 20).

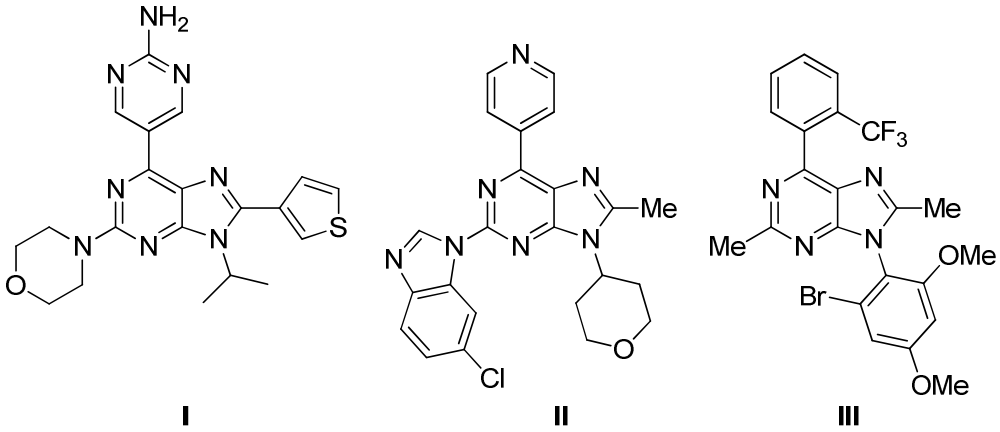
[34] E. Fischer *Berichte der Deutschen Chemischen Gesellschaft* **1884**, *17*, 328.

[35] E. Fischer *Berichte der Deutschen Chemischen Gesellschaft* **1898**, *31*, 2550.

[36] Reviews: (a) Legraverend, M. *Tetrahedron* **2008**, *64*, 8585; (b) Brændvang, M.; Gundersen, L. *Bioorg. Med. Chem.* **2007**, *15*, 7144; (c) Legraverend, M.; Grierson, D. S. *Bioorg. Med. Chem.* **2006**, *14*, 3987; (d) Rosemeyer, H. *Chem. Biodiv.* **2004**, *1*, 361.

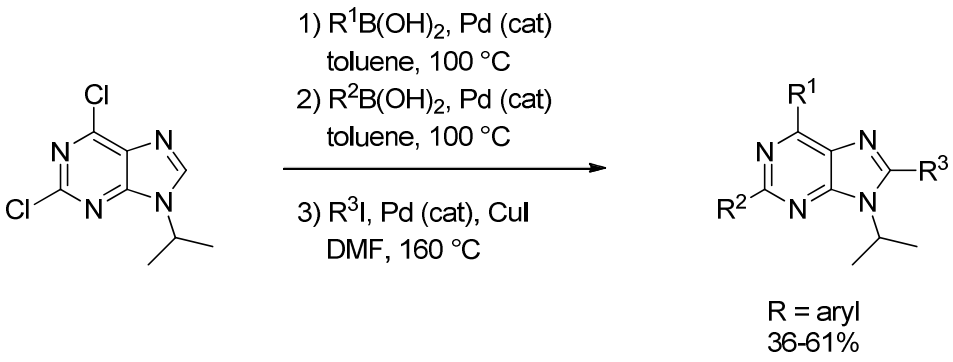
[37] Chen, D.; Nagaraj, H. K. M.; Williams, M. WO 2010/114494, 2010.

[38] Neagu, I.; Diller, D.; Kingsbury, C.; Bohnstedt, A. C.; Ohlmeyer, M. J.; Paradkar, V.; Ansari, N. US 20080214580, 2008.



Scheme 20: Biologically active purine derivatives.

Large combinatorial libraries of several types of substituted purines have been prepared by heterocyclizations,[39] direct C-H arylations,[40] or by regioselective nucleophilic substitutions of dihalopurines with amines in combination with cross-coupling reactions.[41] For the introduction of C-substituents to the 2-, 6-, and 8-positions of the purine moiety transition metal-catalyzed cross-coupling reactions of purine halides are usually used as shown in Scheme 21.[40b] Hereby, the functional group tolerance is restricted to methoxy- and fluorine-substituents.

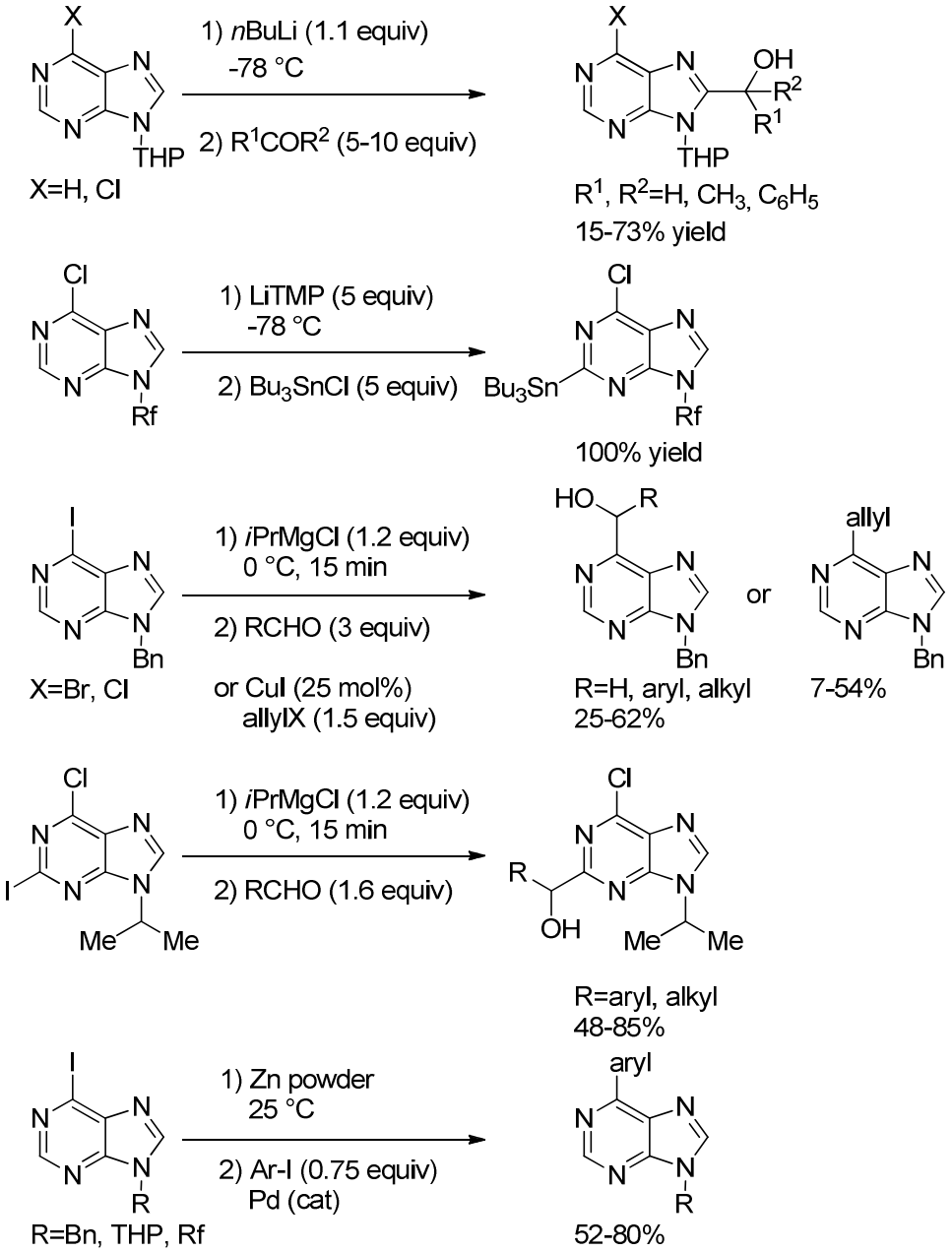


Scheme 21: General reaction scheme for the triple cross-coupling sequence published by Hocek.

[39] (a) Kalla, R. V.; Elzei, E.; Perry, T.; Li, X.; Gimbel, A.; Yang, M.; Zeng, D; Zablocki, J. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1397; (b) He, R.; Ching, S. M.; Lam, Y. *J. Comb. Chem.* **2006**, *8*, 923; (c) Lin, X.; Robins, M. J. *Collect. Czech. Chem. Commun.* **2006**, *71*, 1029.

[40] (a) Čerňa, I.; Pohl, R.; Klepetářová, B.; Hocek, M. *J. Org. Chem.* **2010**, *75*, 2302; (b) Čerňa, I.; Pohl, R.; Klepetářová, B.; Hocek, M. *J. Org. Chem.* **2008**, *73*, 9048.

[41] (a) Piguel, S.; Legraverend, M. *J. Org. Chem.* **2007**, *72*, 7026; (b) Hocek, M.; Pohl, R. *Synthesis* **2004**, 2869; (c) Hocek, M.; Hocková, D.; Dvořáková, H. *Synthesis* **2004**, 889.



Scheme 22: Reported metalations of single positions of the purine scaffold.

The opposite approach, coupling of metalated purine derivatives with appropriate C-electrophiles, has been less developed and is only known for single positions of the purine scaffold (Scheme 22). The preparation and the reactivity of lithiated purines *via* halogen/ lithium exchange or deprotonation,[42] magnesiated purines *via* iodine/ magnesium exchange,[43] and 6-zincated purines *via* zinc insertion[44] have been reported.

[42] a) Leonard, N. J.; Bryant, D. J. *J. Org. Chem.* **1979**, *44*, 4612; b) Tanaka, H.; Uchida, Y.; Shinozaki, M.; Hayakawa, H.; Matsuda, A.; Miyasaka, T. *Chem. Pharm. Bull.* **1983**, *31*, 787; c) Kato, K.; Hayakawa, H.;

While the organolithium compounds are only stable at very low temperatures and have low functional group tolerance, the exchange reactions with *i*PrMgCl and the Zn-insertion require iodinated purines which can be exclusively synthesized under harsh reaction conditions. Thus, there's still a lack of methodology for new and easy accessible multi or even full functionalized purine derivatives with a high functional group tolerance.

3.2. Functionalization of the benzo[*c*][1,2,5]thiadiazole scaffold

The benzothiadiazole scaffold is part of many important compounds such as the muscle relaxant tizanidine (Scheme 23) which is used for the treatment of chronical migraine and as antispastic agent.[45] Moreover, it is a suitable building block for semi-conducting polymers and copolymers[46] as well as for printable organic semiconductors (Scheme 23)[47] which find application as organic thin film transistors (OTFT), organic photovoltaic cells (OPV), light-emitting diodes (LED) or as fluorescent probes for bio-imaging.[48]

Tanaka, H.; Kumamoto, H.; Shindoh, S.; Shuto, S.; Miyasaka, T. *J. Org. Chem.* **1997**, *62*, 6833; d) Ghosh, A. K.; Lagisetty, P.; Zajc, B. *J. Org. Chem.* **2007**, *72*, 8222.

[43] a) Tobrman, T.; Dvořák, D. *Org. Lett.* **2003**, *5*, 4289; b) Tobrman, T.; Dvořák, D. *Org. Lett.* **2006**, *8*, 1291; c) Klečka, M.; Tobrman, T.; Dvořák, D. *Collect. Czech. Chem. Commun.* **2006**, *71*, 1221.

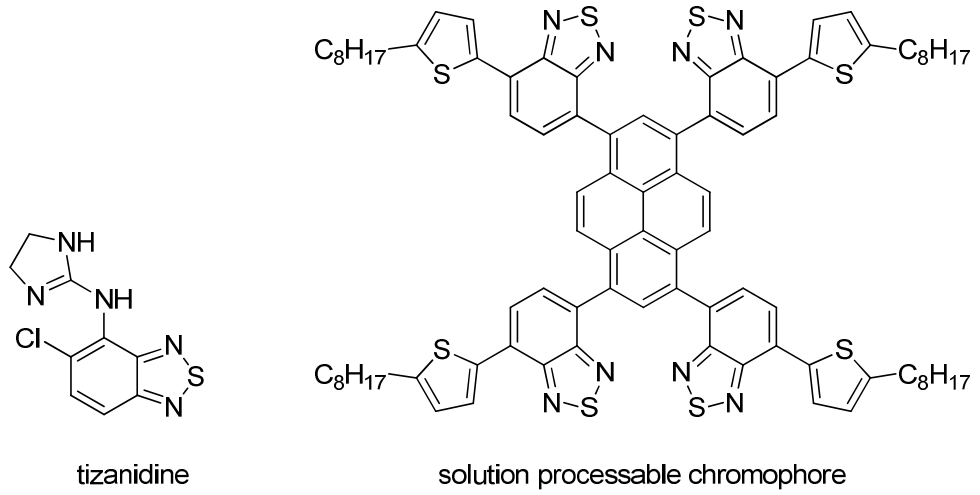
[44] a) Stevenson, T. M.; Prasad, A. S. B.; Citineni, J. R.; Knochel P. *Tetrahedron Lett.* **1996**, *37*, 8375; b) Prasad, A. S. B.; Stevenson, T. M.; Citineni, J. R.; Nyzam, V.; Knochel, P. *Tetrahedron* **1997**, *53*, 7237.

[45] (a) Lovell, B. V.; Marmura, M. J. *Current Opinion in Neurology* **2010**, *23*, 254; (b) Kamen, L.; Henney III, H. R.; Runyan, J. D. *Current Medical Research and Opinion* **2008**, *24*, 425.

[46] (a) Zheng, Q.; Chen, S.; Zhang, B.; Wang, L.; Tang, C.; Katz, H. E. *Org. Lett.* **2011**, *13*, 324; (b) Xu, E.; Zhong, H.; Lai, H.; Zeng, D.; Zhang, J.; Zhu, W.; Fang, Q. *Macromol. Chem. Phys.* **2010**, *211*, 651; (c) Clarke, T.; Ballantyne, A.; Jamieson, F.; Brabec, C.; Nelson, J.; Durrante, J. *Chem. Commun.* **2009**, 89.

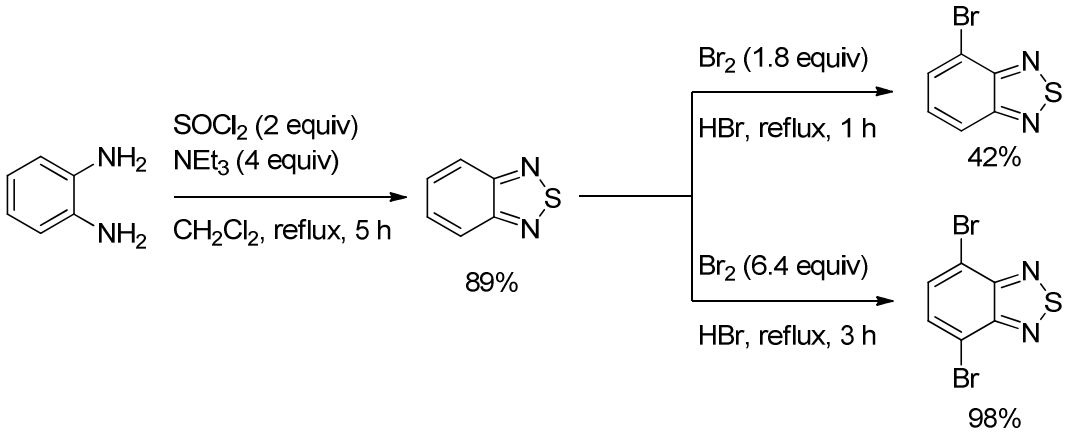
[47] Sonar, P.; Soh, M. S.; Cheng, Y. H.; Henssler, J. T.; Sellinger, A. *Org. Lett.* **2010**, *12*, 3292.

[48] Pu, K.-Y.; Li, K.; Liu, B. *Adv. Funct. Mater.* **2010**, *20*, 2770.



Scheme 23: Examples for a biologically active benzo[*c*][1,2,5]thiadiazole derivative and printable organic semiconductor.

Despite their versatile use, only few methods for the direct functionalization of this heterocycle have been reported.[49] The most common methods are the bromination[50] (Scheme 24) and the nitration[51] (Scheme 25) with further functionalization by transformation



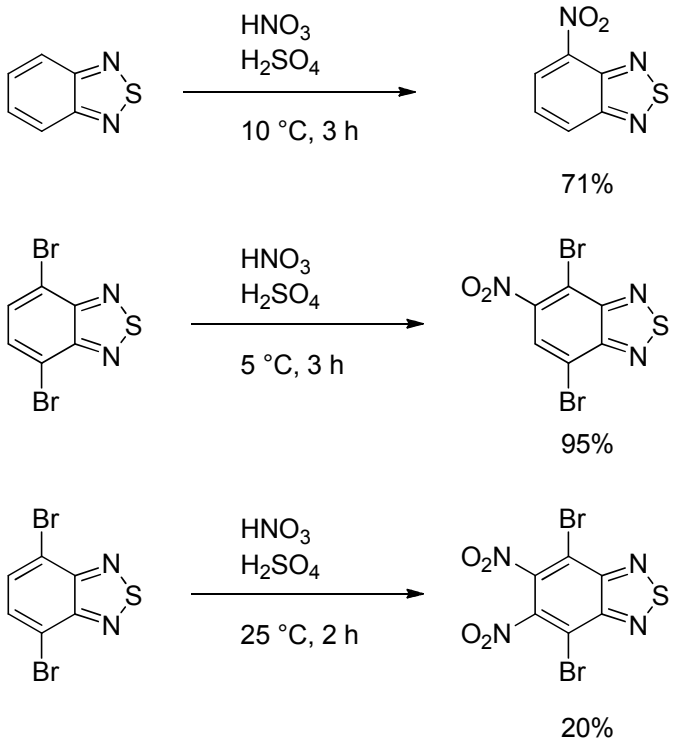
Scheme 24: Synthesis of benzo[*c*][1,2,5]thiadiazole and its bromination reaction.

[49] (a) Du, J.; Xu, E.; Zhong, H.; Yu, F.; Liu, C.; Wu, H.; Zeng, D.; Ren, S.; Sun, J.; Liu, Y.; Cao, A.; Fang, Q. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 1376; (b) Ju, J. U.; Jung, S. O.; Zhao, Q. H.; Kim, Y. H.; Je, J. T.; Kwon, S. K. *Bull. Korean Chem. Soc.* **2008**, *29*, 335; (c) Lash, T. D.; Wijesinghe, C.; Osuma, A. T.; Patel, J. R. *Tetrahedron Lett.* **1997**, *38*, 2031; (d) Takagi, K.; Tomoeda, M. *Chem. Pharm. Bull.* **1980**, *28*, 1909; (e) Komin, A. P.; Carmack, M. *J. Heterocycl. Chem.* **1975**, *12*, 829.

[50] Pilgram, K.; Skiles, R. D. *J. Heterocycl. Chem.* **1970**, *7*, 629.

[51] (a) Uno, T.; Takagi, K.; Tomoeda, M. *Chem. Pharm. Bull.* **1980**, *28*, 1909; (b) Uno, T.; Takagi, K.; Tomoeda, M. *Chem. Pharm. Bull.* **1978**, *26*, 3896; (c) Komin, A. P.; Carmack, M. *J. Heterocycl. Chem.* **1075**, *12*, 829.

of these substituents. The synthesis of some unsymmetrically functionalized benzo[*c*][1,2,5]thiadiazoles has also been reported.[52]

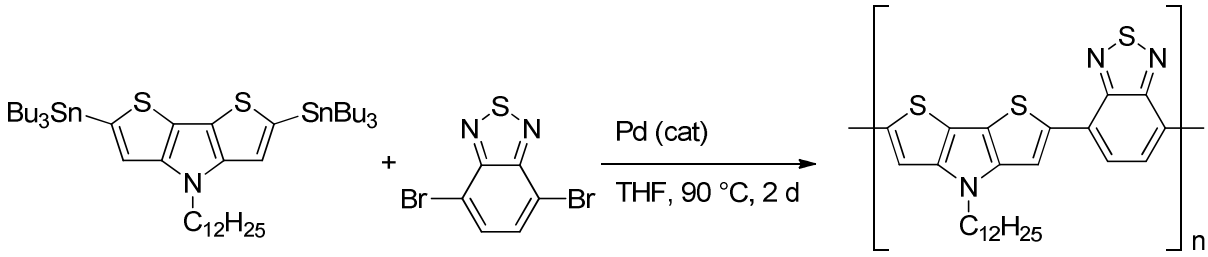


Scheme 25: Nitration of the benzo[*c*][1,2,5]thiadiazole scaffold.

Usually, 4,7-dibromobenzo[*c*][1,2,5]thiadiazole is used in cross-coupling reactions to provide the corresponding polymers or copolymers as shown for one example in Scheme 26.[53]

[52] (a) Bijleveld, J. C.; Shahid, M.; Gilot, J.; Wienk, M. M.; Janssen, R. A. J. *Adv. Funct. Mater.* **2009**, *19*, 3262; (b) Sonar, P.; Singh, S. P.; Leclère, P.; Surin, M.; Lazzaroni, R.; Lin, T. T.; Dodabalapur, A.; Sellinger, A. *J. Mater. Chem.* **2009**, *19*, 3228; (c) Wunderlich, S. H.; Kienle, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2009**, *48*, 7256; (d) Jørgensen, M.; Krebs, F. C. *J. Org. Chem.* **2005**, *70*, 6004; (e) Pilgram, K.; Zupan, M. *J. Org. Chem.* **1971**, *36*, 207.

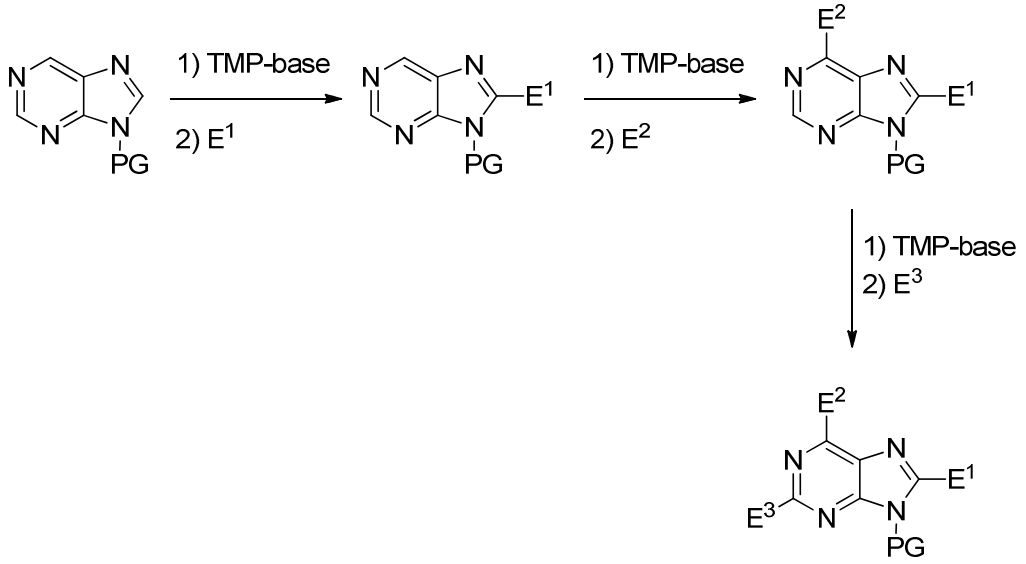
[53] (a) Lu, Y.; Chen, H.; Hou, X.; Hu, X.; Ng, S.-C. *Synth. Met.* **2010**, *160*, 1438; (b) Zoombelt, A. P.; Fonrodona, M.; Wienk, M. M.; Sieval, A. B.; Hummelen, J. C.; Janssen, R. A. J. *Org. Lett.* **2009**, *11*, 903; (c) Melucci, M.; Favaretto, L.; Bettini, C.; Gazzano, M.; Camaioni, N.; Maccagnani, P.; Ostoja, P.; Monari, M.; Barbarella, G. *Chem. Eur. J.* **2007**, *13*, 10046; (d) Zhang, M.; Tsao, H. N.; Pisula, W.; Yang, C.; Mishra, A. K.; Müllen, K. *J. Am. Chem. Soc.* **2007**, *129*, 3472; (e) Yao, Y.-H.; Kung, L.-R.; Hsu, C.-S. *J. Polym. Res.* **2006**, *13*, 277; (f) van Mullekom, H. A. M.; Vekemans, J. A. J. M.; Meijer, E. W. *Chem. Eur. J.* **1998**, *4*, 1235.



Scheme 26: Example for the copolymerization of 4,7-dibromobenzo[*c*][1,2,5]thiadiazole.

4. Objectives

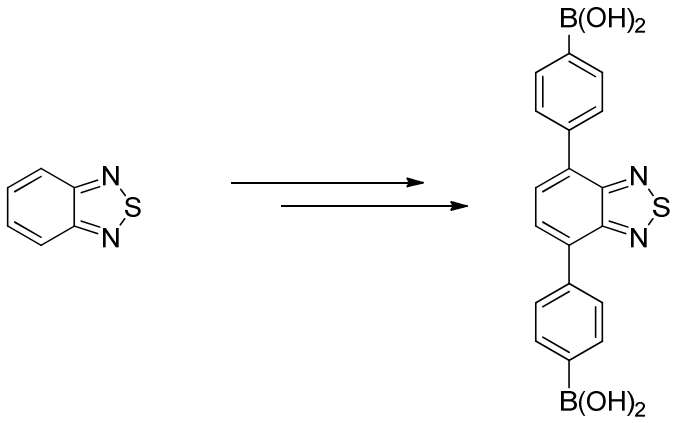
As the purine scaffold is known for providing many biologically active compounds the development of a general process to build up full functionalized purines *via* organometallic intermediates had to be accomplished. Thus, a versatile tool with a high functional group tolerance should be created.



Scheme 27: General reaction scheme for the functionalization of the purine scaffold *via* organometallic intermediates using TMP-bases.

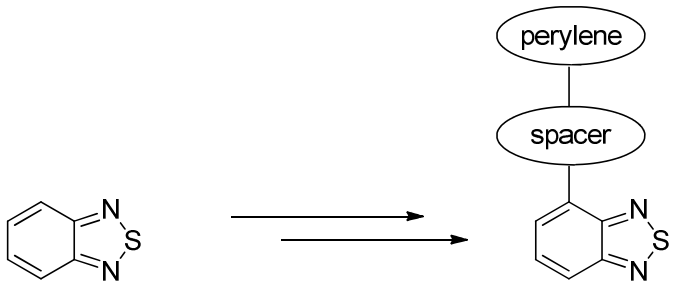
The second project was to explore the functionalization of benzo[*c*][1,2,5]thiadiazole derivatives for the development of new materials for electronic and optic applications. The

synthesis of a bisboronic acid used as a linear linker for the fornation of a new covalent organic framework (COF) based on benzothiadiazole should be explored.



Scheme 28: Synthesis of a benzo[*c*][1,2,5]thiadiazole derived linker for the generation of a new covalent organic framework with potential electronic properties.

Different substitution patterns should be investigated for the application in the field of new fluorescent benzothiadiazoloperylene dyes.

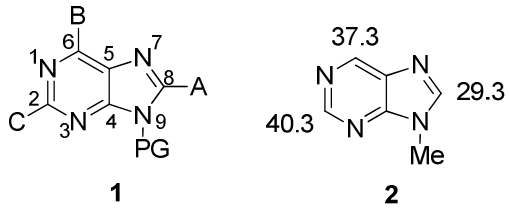


Scheme 29: Synthesis of new benzo[*c*][1,2,5]thiadiazoloperylene dyes.

B. RESULTS AND DISCUSSION

1. Functionalization of the Purine scaffold

As mentioned in a publication of Fu and Guo[54] who calculated amongst others the pK_a values of 9-methyl-9*H*-purine **2** (Scheme 30) in DMSO, the acidity of the three protons is disparate and therefore the regioselective deprotonation may represent a facile access to polyfunctionalized purines. Though, the successive functionalization of positions 8, 6 and 2 of one certain purine building block using organometallic intermediates is complicated and depends highly on the choice of the masked functional groups A, B and C at these positions as well as the protecting group (PG) of the purine **1** (Scheme 30).



Scheme 30: General figure of a purine precursor (**1**) and calculated pK_a values of 9-methyl-9*H*-purine **(2**) in DMSO.

1.1. Selection of the protection group

As most of the biologically active purine derivatives bear a ribofuranosyl (Rf) or ribofuranosyl-like backbone at position 7 or 9 it would be important to use a protecting group (PG) that is easily removed in the end of the functionalization pathway without touching the functional groups. Still, it has to be stable against organometallic reagents and further reaction conditions with various electrophiles. Thus, it would be possible to attach a functionalized and therefore expensive group to the finally functionalized purine building block, while this group has not to be stable against organometallic reagents.

4-Methoxybenzenesulfonyl (Mbs) is an interesting option as PG due to its high stability in acidic media. Unfortunatly, the deprotonation of position 8 of the purine scaffold was not achieved using either TMPZn- or TMPMg-bases (Table 1, entry 1). The benzylic PG (Bn) has a similar stability (entry 2) and purine derivatives bearing this PG could be metalated and

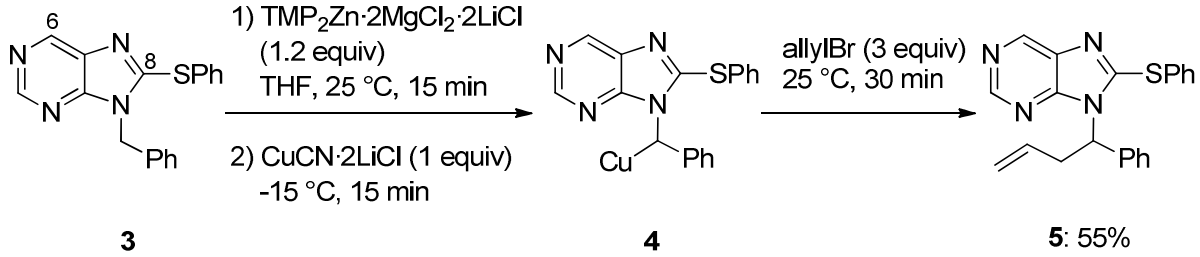
[54] Shen, K.; Fu, Y.; Li, J.; Liu, L.; Guo, Q. *Tetrahedron* **2007**, *63*, 1568.

functionalized at position 8. Nevertheless, deprotonation at position 6 was not achieved due to the higher acidity of the benzylic protons. Therefore, the copper intermediate **4** reacts with allylbromide providing **5** in 55% yield (Scheme 31).

Table 1: Stability and reactivity of different protection groups (PGs).

Entry	PG	acidic cleavage	reactivity towards TMP-bases
1	Mbs	HBr reflux	no deprotonation at position 8
2	Bn	HBr reflux	benzylic protons too acidic
3	MOM	1N HCl	deprotonation
4	THP	HOAc/ NaOAc	deprotonation

Mbs=4-methoxybenzenesulfonyl, Bn=benzyl, MOM=methoxymethyl, THP=2,2,3,3-tetrahydropyranyl.



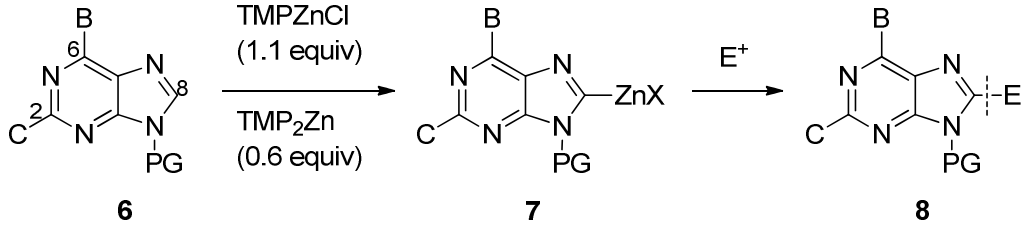
Scheme 31: Deprotonation of the benzylic protons of the purine derivative **3**.

Methoxymethyl (MOM) as PG is still quite stable, can be removed more easily than before mentioned PGs by using 1N HCl or Lewis acids and the deprotonation and functionalization was readily achieved at positions 8 and 6 (entry 3).[55] The 2,2,3,3-tetrahydropyranyl group (THP) is even more labile and therefore easy to cleave (entry 4). The deprotonation is equally achieved but the yield concerning a reaction with iodine was much lower and a cross-coupling product could not be isolated due to the cleavage of the PG.[56] In summary, the MOM-PG was chosen because of its concerted stability and reactivity.

[55] For deprotonation and functionalization compare: Chapters B.1.2. and B.1.4.

[56] Compare therefor: Chapter B.1.2. Table 2, entries 1-3 and Table 3, entry 3

1.2. Successive deprotonation of purine derivatives at positions 8 and 6



6 **7** **8**

Scheme 32: General reaction scheme for the zincation of purine derivatives of type **6** at position 8 and subsequent reaction with an electrophile.

The most acidic proton of the purine scaffold at position 8 can be abstracted with TMPMgCl·LiCl at -60 °C or with each TMP derived zinc base at 25 °C within 15 to 30 min (Scheme 32). The mildest possible method by using TMPZnCl·LiCl for the deprotonation and subsequent reaction with iodine provides the iodinated compounds **8a-c** in 60 to 98% yield (Table 2, entries 1-3). If TMPMgCl·LiCl is used at low temperature the yield is only slightly affected (entry 2). This displays an alternative for reactions that require magnesiated intermediates but is restricted to substrates which have a good solubility at low temperature and bear stable functional groups. The bromination with 1,2-dibromo-1,1,2,2-tetrachloroethane proceeds under Barbier-conditions[57] at 25 °C using $TMP_2Zn·2LiCl$ (entries 4-5) or after deprotonation with the more reactive bisamide zinc base $TMP_2Zn·2MgCl_2·2LiCl$ and subsequent reaction with the brominating agent mentioned above (entry 6). The 8-brominated compounds **8d-f** are obtained in 75% to 87% yield. Similarly, **6b** reacts with *S*-phenyl benzenesulfonothioate under Barbier-conditions at 0 °C providing **3** in 60% yield (entry 7). In contrast, the zincated intermediate of **6e** does not react with *S*-phenyl benzenesulfonothioate. To attach the thioether to the MOM-protected derivative the 8-lithiated intermediate was reacted with the electrophile giving product **8g** in 40% yield (entry 8). A copper(I)-catalyzed allylation[8] (10 mol% CuCN·2LiCl) with allyl bromide (-50 to 25 °C, 10 h) leads to the 8-allylated purine (**8h**) in 84% yield (entry 9).

[57] Blomberg, C.; Hartog, F. *Synthesis* **1977**, 18.

Table 2: Reaction of the zincated purine **7** with some electrophiles.

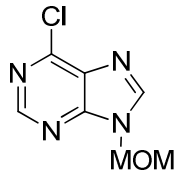
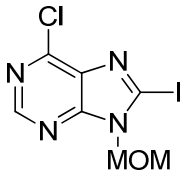
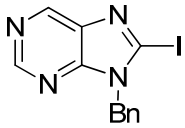
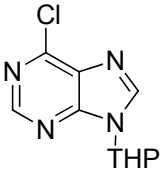
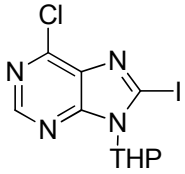
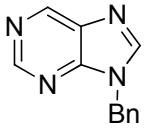
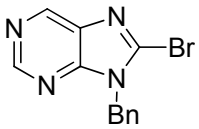
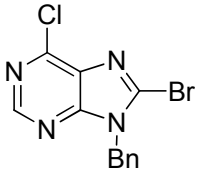
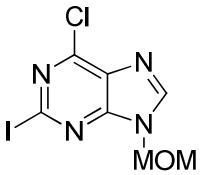
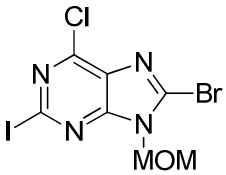
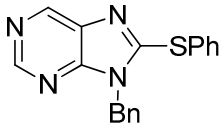
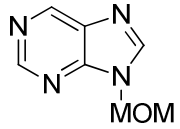
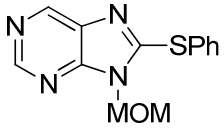
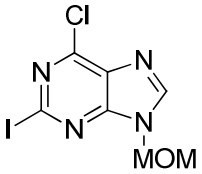
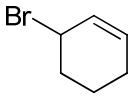
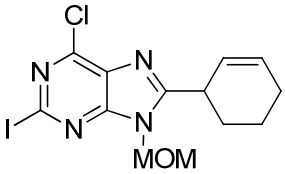
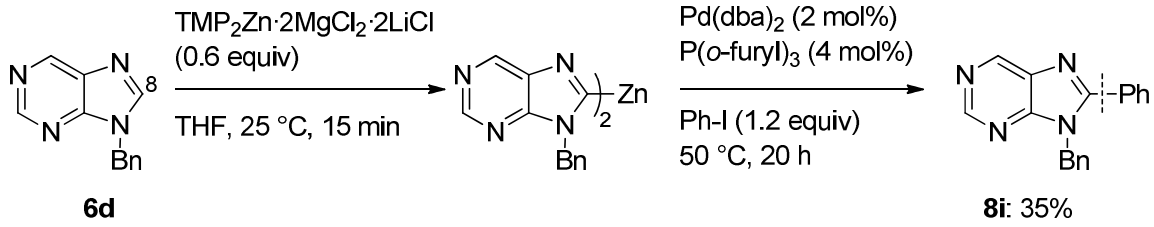
Entry	starting material	electrophile	product	yield, %[a]
1	 **6a**	I_2	 **8a**	98[b]
2	 **6b**	I_2	 **8b**	80 (84)[b]
3	 **6c**	I_2	 **8c**	60[b]
4	 **6b**	$(CCl_2Br)_2$	 **8d**	82[c]
5	 **6d**	$(CCl_2Br)_2$	 **8e**	75[c]
6	 **6e**	$(CCl_2Br)_2$	 **8f**	87[d]
7	 **6b**	$PhSO_2SPh$	 **3**	60[e]

Table 2 continued

8	 **6f**	$PhSO_2SPh$	 **8g**	40[f]
9	 **6e**		 **8h**	84[g]

[a] Isolated, analytically pure product; the yields in parentheses were obtained after deprotonation with TMPMgCl·LiCl (1.1 equiv) at -60 °C. [b] 1) TMPZnCl·LiCl (1.1 equiv), 25 °C, 1 h; 2) I_2 (1.2 equiv), 25 °C, 1 h. [c] 1) electrophile (1.0 equiv); 2) $TMP_2Zn·2LiCl$ (0.6 equiv), 25 °C, 10 min. [d] 1) $TMP_2Zn·2MgCl_2·2LiCl$ (1.1 equiv), 0 °C to 25 °C, 15 min; 2) electrophile (1.4 equiv). [e] 1) electrophile (1.0 equiv); 2) $TMP_2Zn·2LiCl$ (1.2 equiv), 0 °C, 10 min. [f] 1) *n*BuLi (1.05 equiv), -78 °C, 30 min; 2) $PhSO_2SPh$ (1.3 equiv), to 25°C in 14 h; [g] 1) $TMPZnCl·MgCl_2·LiCl$ (1.05 equiv), -50 °C, 30 min; 2) CuCN·2LiCl (10 mol%), 10 min; 3) electrophile (1.4 equiv).

Bisarylzinc reagents, which are obtained *via* deprotonation with TMP_2Zn bases[58] or with TMPMgCl·LiCl and transmetalation with 0.5 equivalents of $ZnCl_2$, react very slow in Pd-catalyzed Negishi cross-couplings,[7,59] even at 50 °C (Scheme 33). Due to the long reaction times a lot of starting material decomposes and the yield drops to 35% for the example of **8i**. Under microwave irradiation the product is obtained in traces only.



6d **8i**: 35%

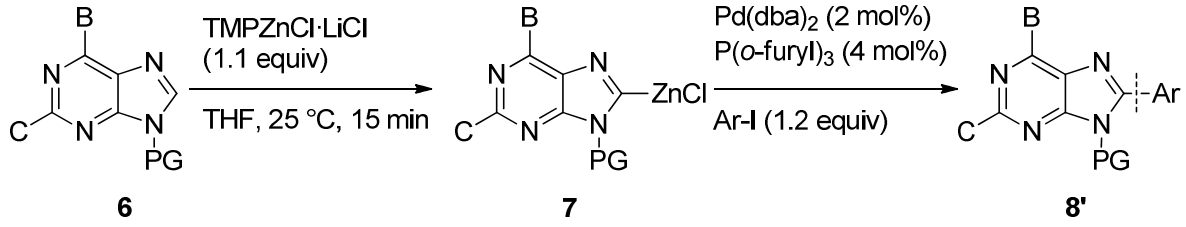
Scheme 33: Preparation of a bispurinylzinc reagent and subsequent cross-coupling reaction with iodobenzene.

The 8-zincated intermediates of type **7** undergo Pd-catalyzed Negishi cross-coupling reactions with $Pd(dba)_2$, P(*o*-furyl)$_3$[60] and aryl iodides within a few hours at 25 °C to give the 8-arylated compounds of type **8'** (Scheme 34).

[58] Prepared in the presence or absence of $MgCl_2$.

[59] (a) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340; (b) Negishi, E.; Valente, L. F.; Kobayashi, M. *J. Am. Chem. Soc.* **1980**, *102*, 3298.

[60] Farina, V.; Baker, S. R.; Benigni, D. A.; Sapino, C. *Tetrahedron Lett.* **1988**, *29*, 5739.



Scheme 34: General reaction scheme for a Negishi cross-coupling at position 8 with an aryl iodide.

If ethyl 4-iodobenzoate is used in this cross-coupling reaction, the yield crucially depends on the substituents B and C. If both positions bear a proton, the cross-coupling product **8j** is isolated in 97% yield (Table 3, entry 1). Similarly, the reaction of the 6-chloropurine derivative **6a** provides **8k** in 91% yield (entry 2). If a THP protection group is attached to the 6-chloropurine, the corresponding product **8l** is detected in traces, because of the deprotection of this more labile protective group (entry 3). The 2-chloropurine derivative **6g** reacts within 40 h to produce the 8-arylated compound **8m** in 58% yield (entry 4), as the chloro-substituent is partially substituted by TMP. At higher temperatures this substitution reaction proceeds faster than the cross-coupling reaction. Therefore, only electrophiles which react at low temperatures, as for example allylating agents, provide high yielding reaction pathways. The cross-coupling reaction of the 2,6-dichloropurine derivative **6h** furnishes the corresponding product **8n** in 62% yield within 20 h (entry 5). The cross-coupling reaction of the 2-TMS-purine derivative **6i** provides the purine **8o** in 52% yield, even though the starting material is consumed within 3 h (entry 6). If, additionally, a chloro-substituent is attached at position 6 the corresponding product **8p** is isolated in 91% yield (entry 7). In summary, as long as the substituent at position 6 (B) is a chloro atom, the substituent at position 2 (C) can be either a proton or a TMS-group without affecting the yield of the cross-coupling reaction.

Table 3: Negishi cross-coupling with ethyl 4-iodobenzoate.

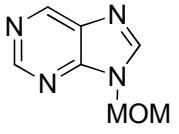
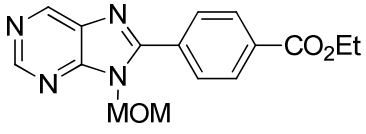
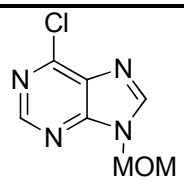
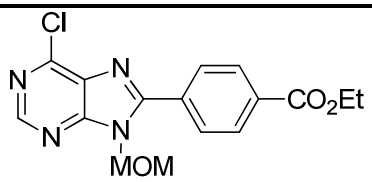
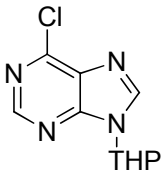
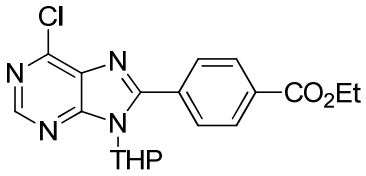
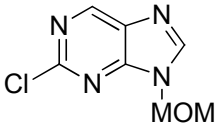
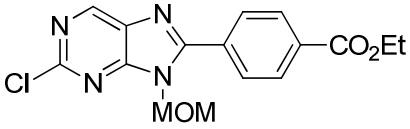
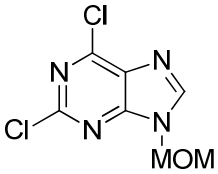
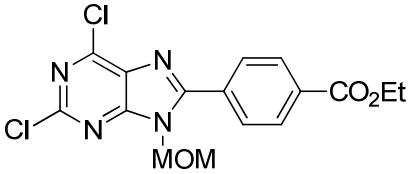
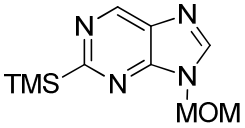
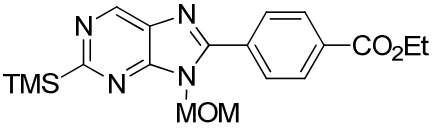
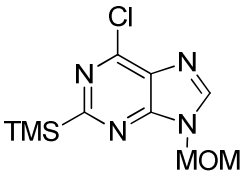
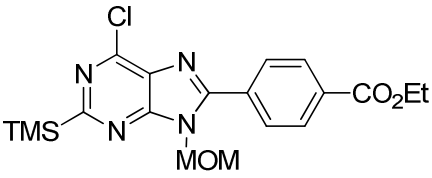
Entry	starting material	product	yield, %[a]
1	 **6e**	 **8j**	97[b]

Table 3 continued

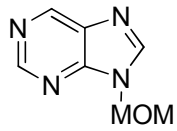
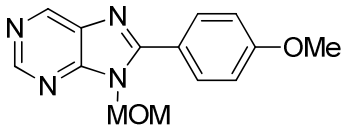
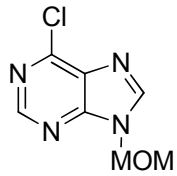
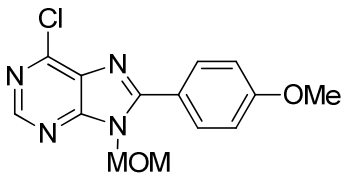
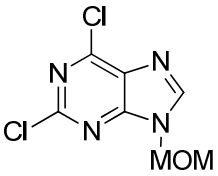
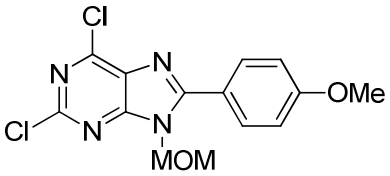
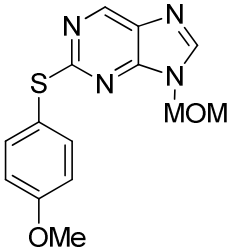
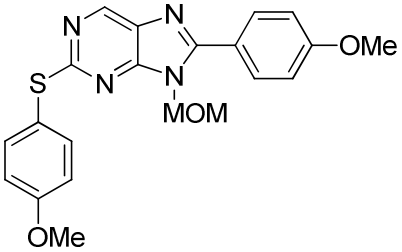
2	 **6a**	 **8k**	91[b]
3	 **6c**	 **8l**	traces[c]
4	 **6g**	 **8m**	58[b]
5	 **6h**	 **8n**	62[b]
6	 **6i**	 **8o**	52[b]
7	 **6j**	 **8p**	91[b]

[a] Isolated, analytically pure product. [b] Obtained by Pd-catalyzed cross-coupling reaction using $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%) as catalyst. [c] Deprotected product is isolated in 75% yield.

Similar results are obtained when 4-iodoanisole is used for the Negishi cross-coupling (Table 4). The main difference is observed when the purine **6e** without any substituents at positions 2 and 6 is used as a substrate. Thereby, the corresponding cross-coupling product **8q** is isolated in 61% yield (Table 4, entry 1). Compared to the cross-coupling with ethyl 4-iodobenzoate, almost the same results are achieved, when the 6-chloropurine (**6a**) and the 2,6-

dichloropurine derivative (**6h**) are deprotonated and cross-coupled with 4-iodoanisole. The 8-arylated compounds **8r** and **8s** are produced in 95% and 71% yield, respectively (entries 2-3). Functional groups like thioethers are tolerated in both positions, 2 and 6, during deprotonation and cross-coupling reactions. Thereby, the reaction of **6k** provides the corresponding product **8t** in 85% yield (entry 4).

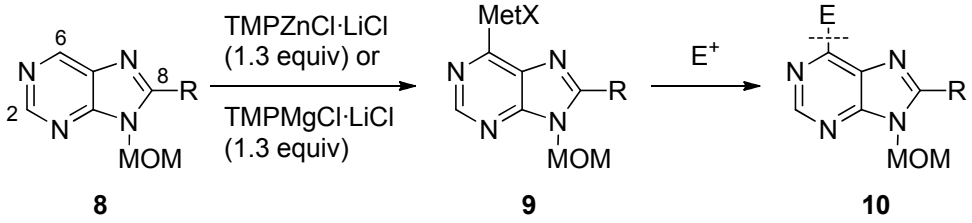
Table 4: Negishi cross-coupling with iodo-4-methoxybenzene.

Entry	starting material	product	yield, %[a]
1	 **6e**	 **8q**	61[b]
2	 **6a**	 **8r**	95[b]
3	 **6h**	 **8s**	71[b]
4	 **6k**	 **8t**	85[b]

[a] Isolated, analytically pure product. [b] Obtained by Pd-catalyzed cross-coupling reaction using $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%) as catalyst.

Further attempts with arylbromides or heteroarylhalides as electrophiles for this cross-coupling reaction failed.

The deprotonation at position 6 of the purine scaffold is achieved with TMPZnCl·LiCl at 25 °C or with TMPMgCl·LiCl at -20 °C, depending on the substrate (Scheme 35). Subsequent reaction with iodine provides the 6-iodinated compounds **10a-c** in 50% to 70% yield (Table 5, entries 1-3). Negishi cross-coupling reactions with iodobenzene or ethyl 4-iodobenzoate give the 6,8-bisarylated products **10d-f** in 53% to 63% yield (entries 4-6).



8 **9** **10**

Scheme 35: Deprotonation of purine derivatives of type **8** at position 6 and subsequent reaction with electrophiles.

Table 5: Deprotonation and functionalization at position 6 of type **8** purines.

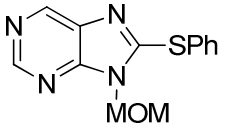
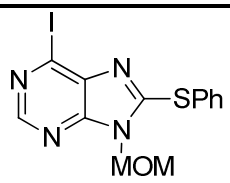
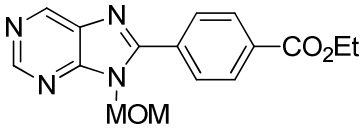
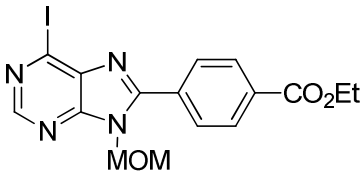
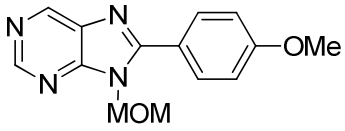
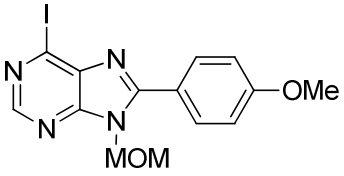
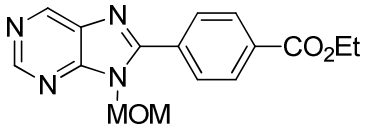
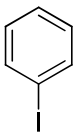
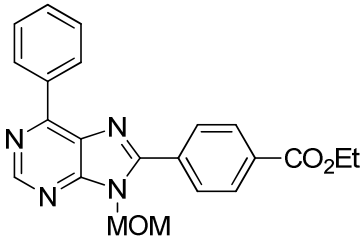
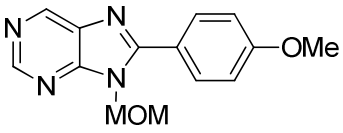
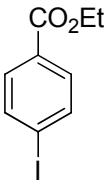
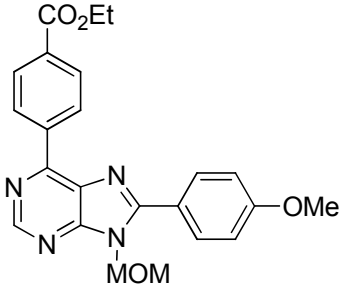
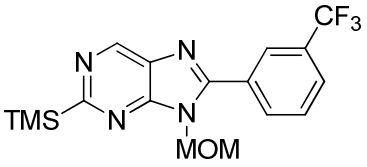
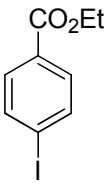
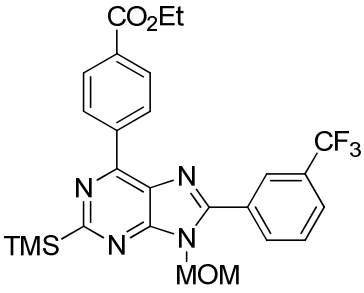
Entry	starting material	electrophile	product	yield, %[a]
1	 **8g**	I_2	 **10a**	50[b]
2	 **8j**	I_2	 **10b**	70[c]
3	 **8q**	I_2	 **10c**	60[c]

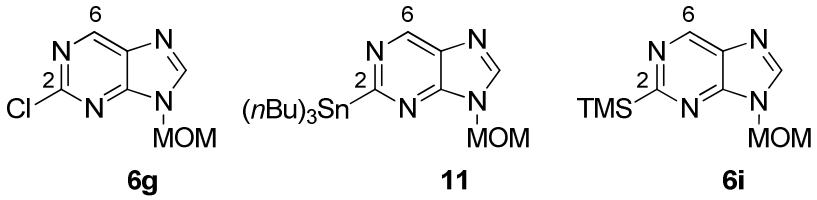
Table 5 continued

4	 **8j**		 **10d**	63[c, d]
5	 **8q**		 **10e**	55[c, d]
6	 **8u**		 **10f**	53[c, d]

[a] Isolated, analytically pure product. [b] TMPZnCl·LiCl (1.3 equiv), 25 °C, 2 h. [c] TMPMgCl·LiCl (1.3 equiv) -20 °C, 20 min. [d] 1) $ZnCl_2$ (1.5 equiv), -20 °C to 25 °C, 15 min; 2) $Pd(dba)_2$ (2 mol%), P(*o*-furyl)$_3$ (4 mol%), aryl iodide (1.2 equiv).

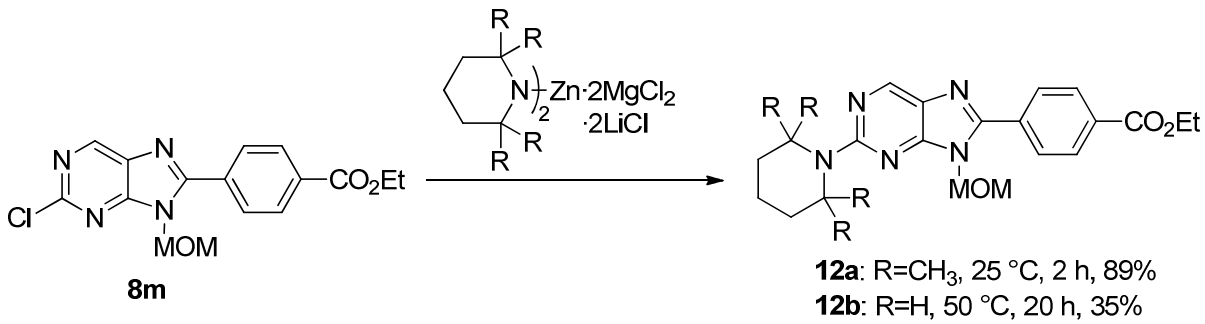
The deprotonation at postition 2 of different 6,8-disubstituted purine derivatives failed using TMPZnCl bases, TMP_2Zn bases, TMPMgCl·LiCl, $TMP_2Mg{\cdot}2LiCl$ and $TMP_2Mn{\cdot}2MgCl_2{\cdot}4LiCl$ as base at -20 to 25 °C. If no decomposition was observed the reaction mixture was heated to 50 °C or was exposed to microwave irradiation.

1.3. Selection of the masked function at position 2



Scheme 36: Different 2-substituted purine derivatives under consideration for the full functionalization pathway.

The 2-chloropurine derivatives have been reported in the literatur and can be synthesized *via* 2,6-dichloropurine which is commercially available.[61] The limitation has been already shown in the chapter above (B.1.2. Successive deprotonation of purine derivatives at positions 8 and 6) as the cross-coupling reaction with 2-chloro-9-MOM-9*H*-purine (**6g**) is not as high yielding as with other substrates. Moreover, the deprotonation of the 8-arylated compound **8m** with $TMP_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ is not possible, because of the almost quantitative substitution of the chlorine substituent which provides compound **12a** in 2 h at 25 °C in 89% yield (Scheme 37). If a less sterically hindered base like a bispiperidide is used, the reaction is less efficient and proceeds at higher temperature under formation of the corresponding amine **12b** in 35% yield.



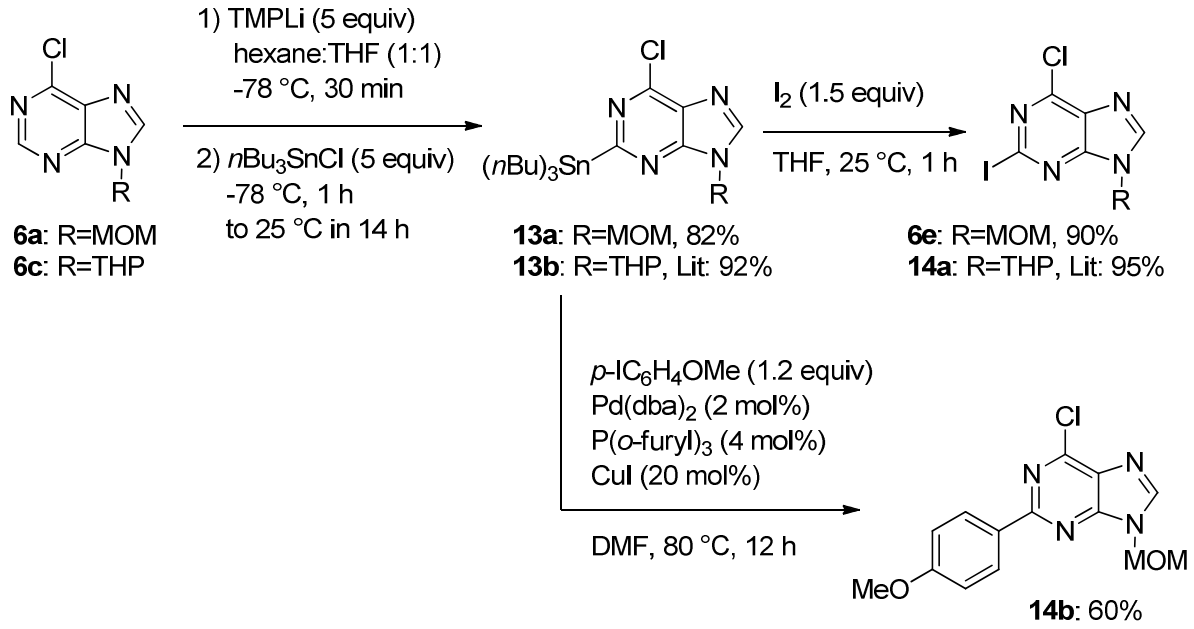
Scheme 37: Substitution of the 2-chloro substituent with bisamides.

A high yielding procedure for the synthesis of 6-chloro-9-THP-2-(tributylstannyl)-9*H*-purine is known in the literature.[62] The conversion of the tributylstannyl group to an iodo-substituent is easily achieved with iodine and known as well (Scheme 38). On the one hand, this method is easily adopted to synthesize 6-chloro-9-MOM-2-(tributylstannyl)-9*H*-purine (**13a**) in 82%

[61] Unciti-Broceta, A.; Pineda de las Infantas, M.; Gallo, M.; Espinosa, A. *Chem. Eur. J.* **2007**, *13*, 1754.

[62] (a) Brun, V.; Legraverend, M.; Grierson, D. *Tetrahedron Lett.* **2001**, *42*, 8161; (b) Taddei, D.; Kilian, P.; Slawin, A.; Woollins, J. D. *Org. Biomol. Chem.* **2004**, *2*, 665.

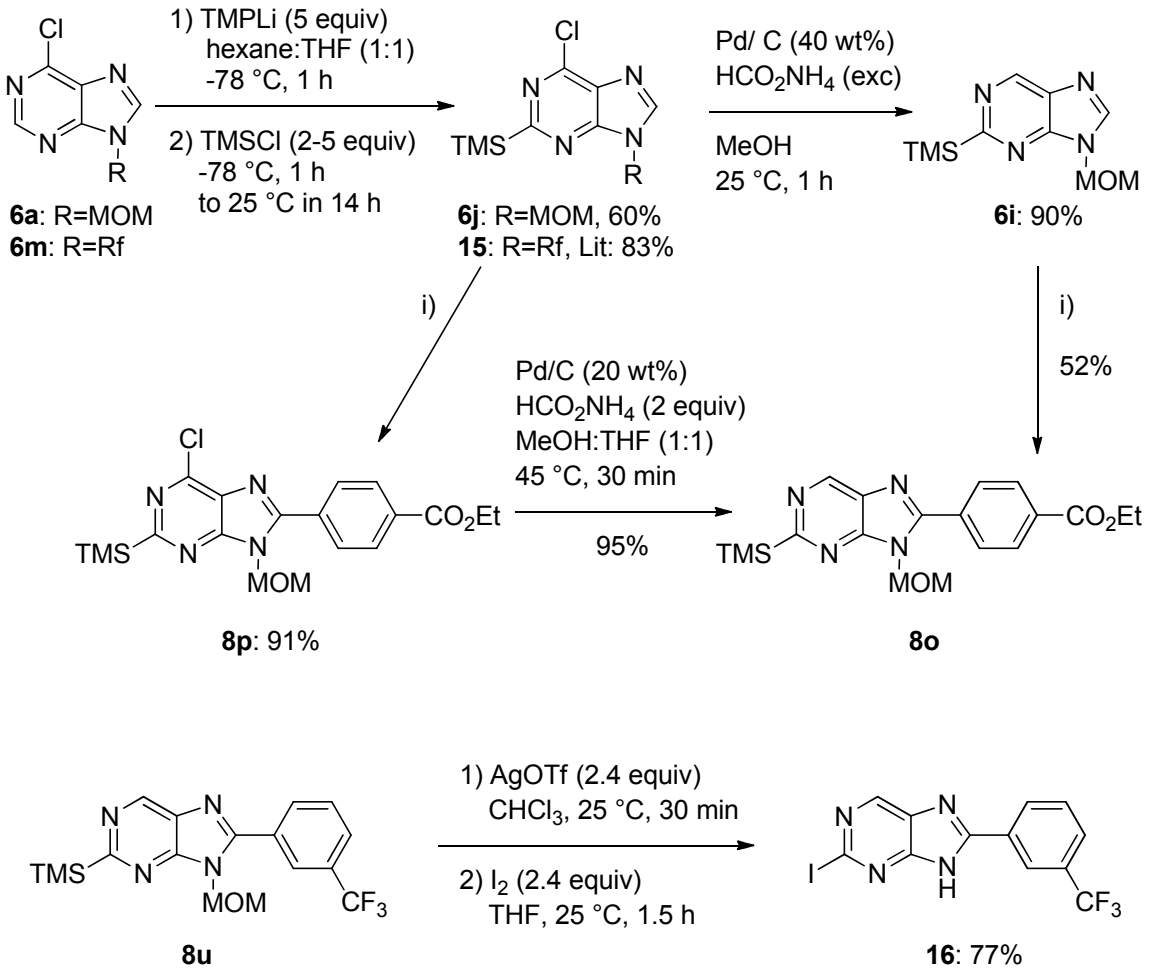
yield and the corresponding iodinated compound (**6e**) in 90% yield. On the other hand, the chloro-substituent cannot be reduced without cleaving the carbon-tin bond. Therefore, the only possible functionalization pathway is the Stille cross-coupling at position 2, first. Thus, cross-coupling reactions would be the only possibility for functionalization at this position, which is no improvement in comparison to the already known methods.



Scheme 38: Synthesis of 6-chloro-9-MOM-2-(tributylstannyl)-9*H*-purine and further functionalizations at position 2.

The synthesis of 6-chloro-9-Rf-2-(trimethylsilyl)-9*H*-purine is known[63] and can be adapted to synthesize 6-chloro-9-MOM-2-(trimethylsilyl)-9*H*-purine (**6j**) in 60% yield (Scheme 39). The selective reduction of the 6-chloro-substituent is possible before or after the cross-coupling reaction at position 8. If the first step is the Negishi cross-coupling and the second step is the reduction, the overall yield amounts to 86% for the final product **8o**, whereas the other pathway provides the same product in an overall yield of 47%. Due to these results, we have chosen the first described pathway for the following full functionalization of the purine scaffold. Preliminary results for the iodination at position 2 of the purine derivative **8u** with silver salts were successful. The iodinated compound **16** was obtained in 77% yield.

[63] Kato, K.; Hayakawa, H.; Tanaka, H.; Kumamoto, H.; Miyasaka, T. *Tetrahedron Lett.* **1995**, *36*, 6507.



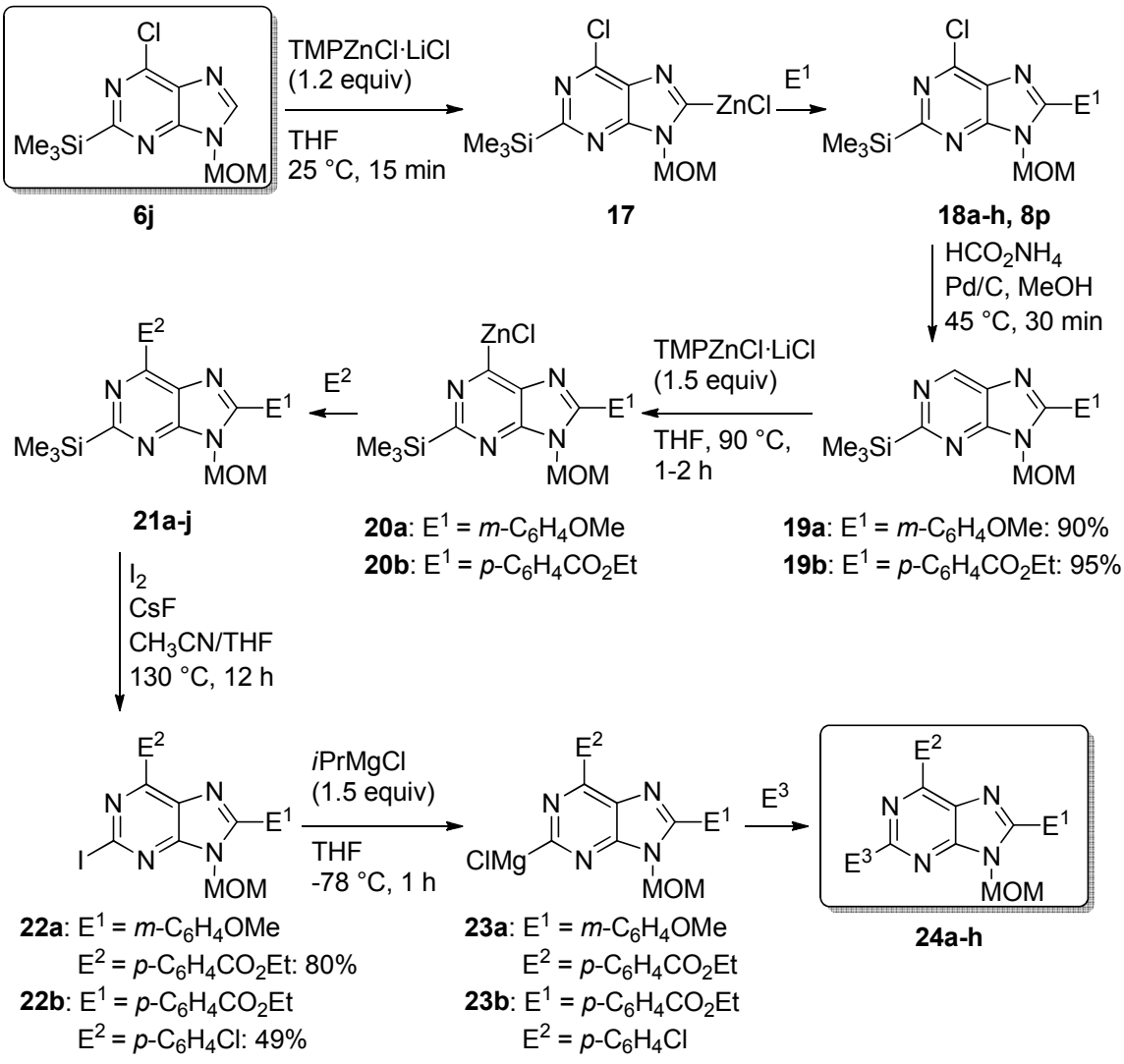
Scheme 39: Synthesis of 6-chloro-9-MOM-2-(trimethylsilyl)-9*H*-purine (**6j**) and further functionalizations. i) TMPZnCl·LiCl (1.1 equiv), 25 °C, 15 min; $Pd(dba)_2$ (2 mol%), P(*o*-furyl)$_3$ (4 mol%), ethyl 4-iodobenzoate (1.2 equiv), 25 °C, 3-14 h.

1.4. Full functionalization of the purine scaffold

Starting from an appropriate 6-chloro-9-MOM-2-TMS-purine derivative (**6j**), a regioselective functionalization of the purine scaffold was achieved successively at position 8, 6 and 2 *via* zinc and magnesium intermediates which were generated either by a direct zincation with TMPZnCl·LiCl[31,32] or by an I/ Mg exchange using *i*PrMgCl.

Starting from 6-chloropurine, 6-chloro-9-methoxymethyl-2-trimethylsilyl-9*H*-purine (**6j**) is prepared as described above (B.1.3. Selection of the masked function at position 2). Thus, this purine is readily metalated at position 8 using TMPZnCl·LiCl within 15 min at 25 °C leading to the zincated purine **17** (Scheme 40). Iodolysis of **17** produces the expected 8-iodopurine (**18a**) in 77% yield (Table 6, entry 1). Copper(I)-catalyzed allylation[8] (5 mol% CuCN·2LiCl)

with 3-bromocyclohexene (-30 °C to 25 °C, 10 h) leads to the 8-allylated purine (**18b**) in 91% yield (entry 2). Pd-catalyzed acylations ($Pd(PPh_3)_4$ (2 mol%))[64] with 2-furoyl chloride or 3-chlorobenzoyl chloride (0 to 25 °C, 6 h) provide the ketones **18c-d** in 46% and 55% yield, respectively (entries 3-4). Negishi cross-coupling reactions[7,59] with various aryl iodides using $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%) afford the 8-arylated purines **18e-g** and **8p** in 72-91% yield (entries 4-9). An alkynyl group can also be introduced *via* Sonogashira[65] coupling by preparing the iodide **18a** *in situ*. Its reaction with *p*-anisylacetylene (NEt_3 (1.2 equiv), CuI (4 mol%), $Pd(dba)_2$ (2 mol%), P(*o*-furyl)$_3$ (4 mol%), 25 °C, 3 h) leads to the 8-alkynylated purine **18h** in 75% yield.



Scheme 40: General reaction scheme for the full functionalization of the purine scaffold.

[64] Negishi, E.; Bagheri, V.; Chatterjee, S.; Luo, F.; Miller, J. A.; Stoll, A. T. *Tetrahedron Lett.* **1983**, *24*, 5181.

[65] Sonogashira, K.; Thoda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.

Table 6: Functionalization of position 8 *via* zincated purine **17**.

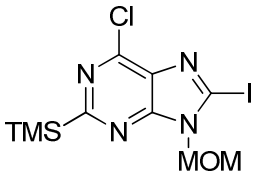
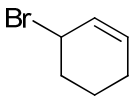
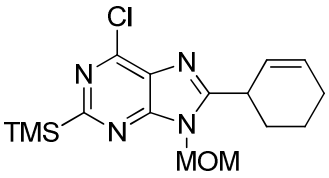
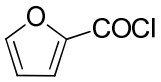
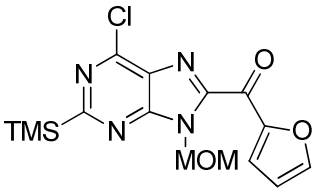
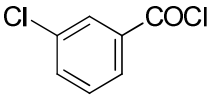
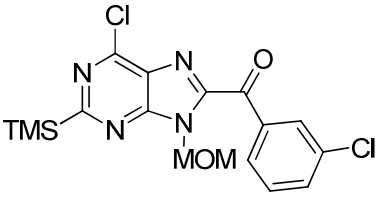
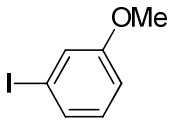
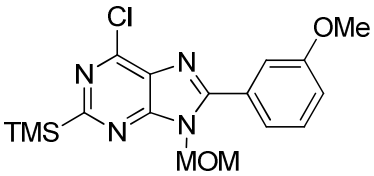
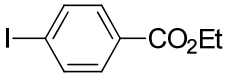
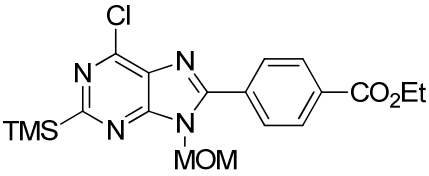
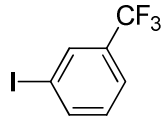
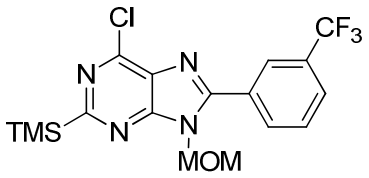
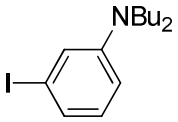
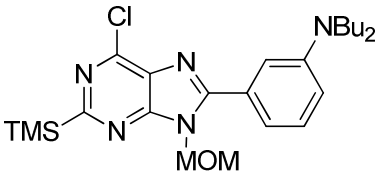
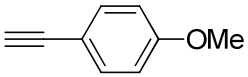
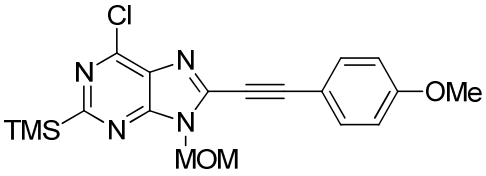
Entry	electrophile	product	yield, %[a]
1	I_2	 **18a**	77
2		 **18b**	91[b]
3		 **18c**	55[c]
4		 **18d**	46[c]
5		 **18e**	72[d]
6		 **8p**	91[d]

Table 6 continued

7		 **18f**	89[d]
8		 **18g**	74[d]
9		 **18h**	75[e]

[a] Isolated, analytically pure product. [b] Obtained after addition of CuCN·2LiCl (5 mol%). [c] Obtained by Pd-catalyzed acylation reaction using $Pd(PPh_3)_4$ (2 mol%). [d] Obtained by Pd-catalyzed cross-coupling reaction using $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%) as catalyst. [e] Obtained from **18a** by Pd-catalyzed coupling reaction using NEt_3 (1.2 equiv), CuI (4 mol%), $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%).

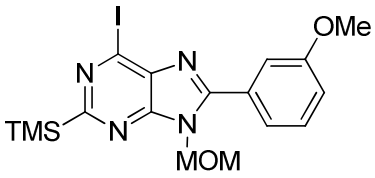
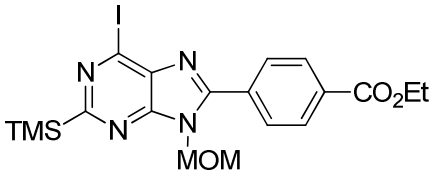
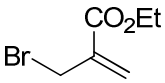
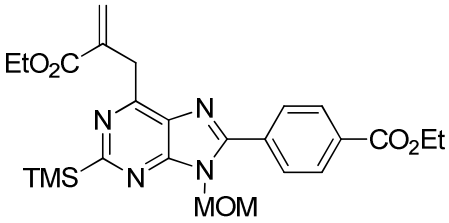
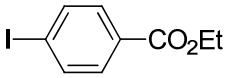
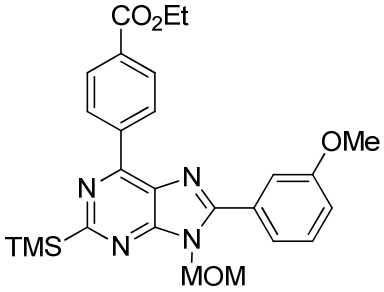
The chloro-substituent at position 6 is then removed using a Pd-catalyzed reduction with HCO_2NH_4 (20 wt% Pd/ C, MeOH/ EtOH or MeOH/ THF, 45 °C, 15-30 min). Under these conditions, the 6-chloropurines **18e** and **8p** led to the dechlorinated products **19a-b** in 90-95% yield (Scheme 40). Purines of type **19** are readily metalated at position 6. Thus, treatment of **19a** with TMPZnCl·$MgCl_2$·LiCl (1.5 equiv) leads to a complete zincation under microwave irradiation[30] (sealed vessel, 90 °C, 1 h) providing the 6-zincated purine **20a** (E^1=3-methoxyphenyl). The purine **19b**, which proved to be more acidic at position 6 than **19a** reacts with TMPZnCl·LiCl (prepared in the absence of $MgCl_2$)[66] leading to **20b** (E^1=4-carbethoxyphenyl, 90 °C, 2 h). The resulting zinc reagents (**20a-b**) react with a range of electrophiles (Table 7). Thus, iodolysis produces the 6-iodopurines **21a-b** in 64-76% yield (Table 7, entries 1-2). The copper-catalyzed allylation of **20b** with ethyl (2-bromomethyl)acrylate[67] leads to purine **21c** in 68% yield (entry 3). A range of aryl iodides

[66] The kinetic basicity of TMPZnCl·LiCl can be increased by adding $MgCl_2$ (1 equiv), see: Wunderlich, S. H.; Knochel, P. *Angew. Chem. Int. Ed.* **2007**, *46*, 7685.

[67] (a) Rambaud, M.; Villiéras, J. *Synthesis* **1984**, 406; (b) Villiéras, J.; Rambaud, M. *Org. Synth.* **1988**, *66*, 220.

bearing either electron-withdrawing substituents (CO_2Et, CF_3, Cl), electron-donating substituents (NBu_2) or a heterocyclic backbone (2-thienyl) undergo Negishi cross-coupling reactions[7,59] with **20a-b** (25 °C, 8-40 h) affording the 2,6-*bis*-arylated purines **21d-i** in 43-64% yield (entries 4-9). *In situ* generation of iodide **21b** followed by a Pd-catalyzed cross-coupling with *N*-allyl-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide[68] affords the 6-alkynylated purine **21j** in 75% yield (entry 10).

Table 7: Functionalization of position 6 *via* zincated purines **20a-b**.

entry	electrophile	product	yield, %[a]
1	I_2	 **21a**	64
2	I_2	 **21b**	76
3		 **21c**	68[b]
4		 **21d**	64[c]

[68] Patel, M. C.; Livinghouse, T.; Pagenkopf, B. L. *Org. Synth.* **2003**, *80*, 93.

Table 7 continued

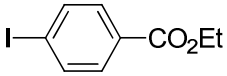
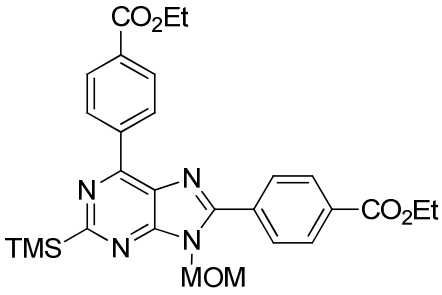
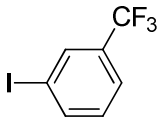
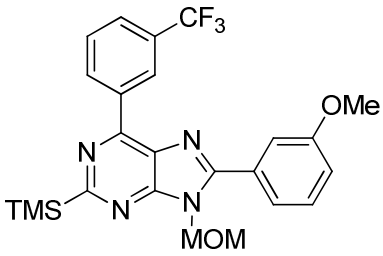
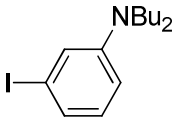
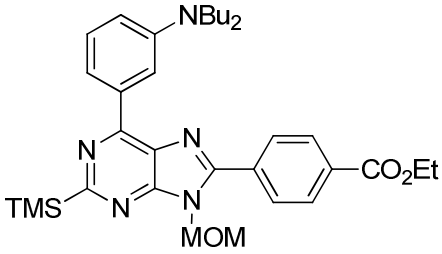
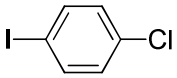
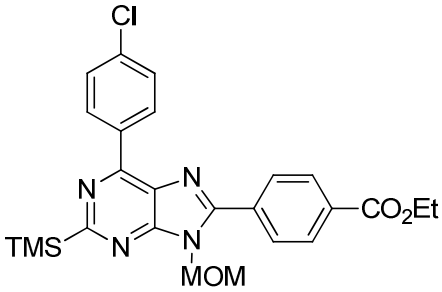
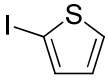
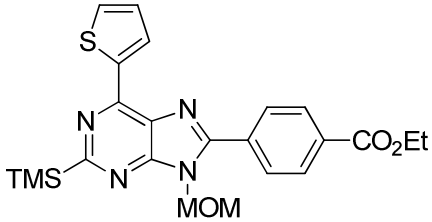
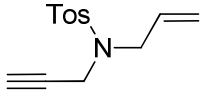
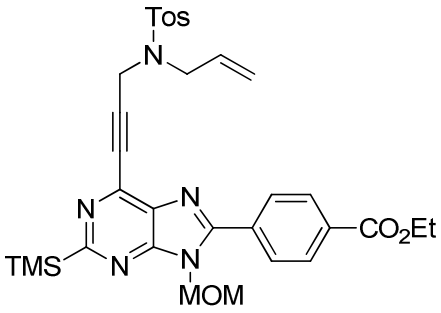
5		 **21e**	53[c]
6		 **21f**	55[c]
7		 **21g**	62[c]
8		 **21h**	55[c]
9		 **21i**	43[c]

Table 7 continued

10		 **21j**	75[d]

[a] Isolated, analytically pure product. [b] Obtained after addition of CuCN·2LiCl (25 mol%). [c] Obtained by Pd-catalyzed cross-coupling reaction using $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%) as catalyst. [d] Obtained from **22b** by Pd-catalyzed coupling reaction using NEt_3 (1.5 equiv), CuI (4 mol%), $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%).

After having functionalized positions 8 and 6, we have converted the 2-TMS-substituent of **21d** and **21g** by treatment with I_2 (1.4 equiv, 1:1 CH_3CN:THF, microwave irradiation, sealed vessel, 110 - 130 °C, 12 h) in the presence of CsF (2 equiv) to achieve the corresponding 2-iodopurines (**22a-b**) in 49-80% yield.[69] Under these reaction conditions, the PG is not cleaved, as observed for the reaction with silver trifluoromethanesulfonate (Scheme 39). I/ Mg exchange of **22a-b** with *i*PrMgCl (1.5 equiv, THF, -78 °C, 1 h) furnishes the Mg-reagents **23a-b**. Their reaction with various electrophiles such as allyl bromides (Table 8, entry 1), aldehydes (entry 2), immonium reagents[70] (entry 3) or a range of functionalized aryl and heteroaryl iodides (entries 4-7) and the Sonogashira cross-coupling of **22a** (entry 8) provides the fully 2,6,8-substituted purines in 55-94% yield.

[69] (a) Latouche, R.; Texier-Boullet, F.; Hamelin, J. *Tetrahedron Lett.* **1991**, *32*, 1179; (b) Furin, G. G.; Vyazankina, O. A.; Gostevsky, B. A.; Vyazankin, N. S. *Tetrahedron* **1988**, *44*, 2675; (c) Clark, J. H. *Chem. Rev.* **1980**, *80*, 429.

[70] Kinast, G.; Tietze, L. F. *Angew. Chem. Int. Ed.* **1976**, *15*, 239; *Angew. Chem.* **1976**, *88*, 261.

Table 8: Functionalization of position 2 *via* magnesiated purines 23a-b.

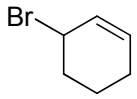
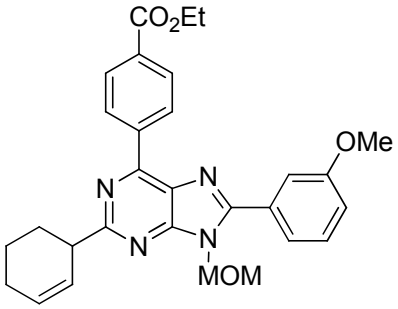
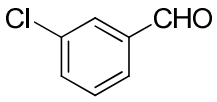
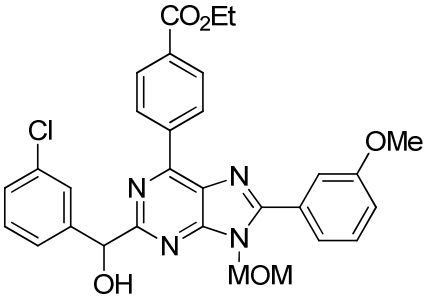
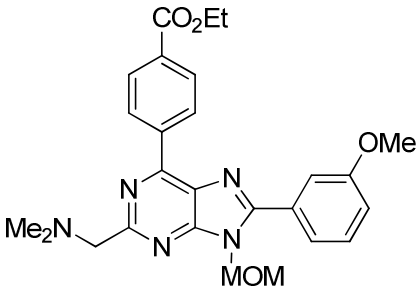
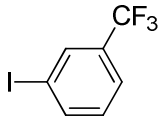
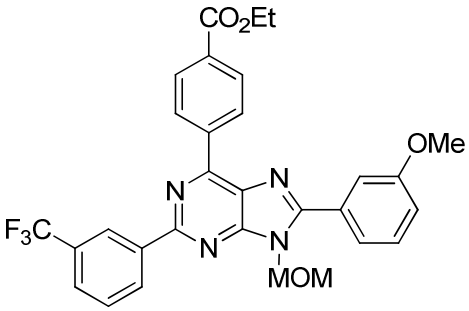
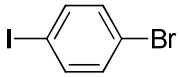
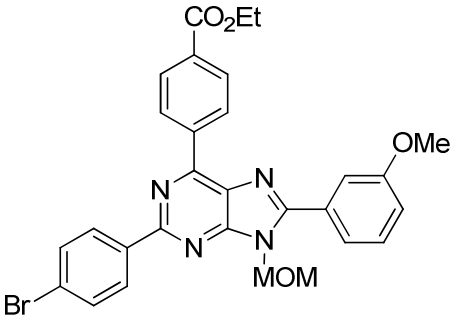
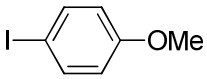
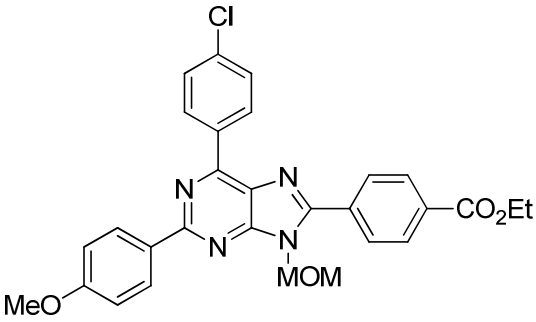
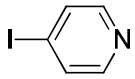
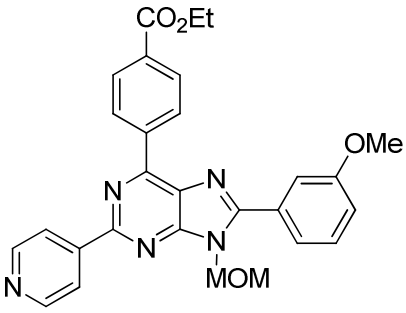
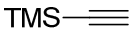
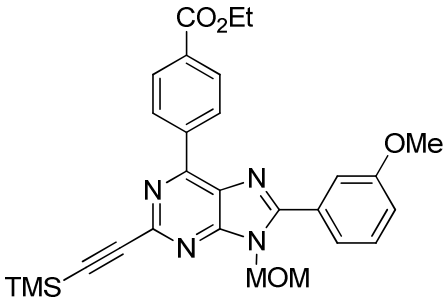
entry	electrophile	product	yield, %[a]
1		 **24a**	68[b]
2		 **24b**	94
3	$CF_3CO_2^-$ $CH_2NMe_2^+$	 **24c**	86
4		 **24d**	65[c]

Table 8 contiunued

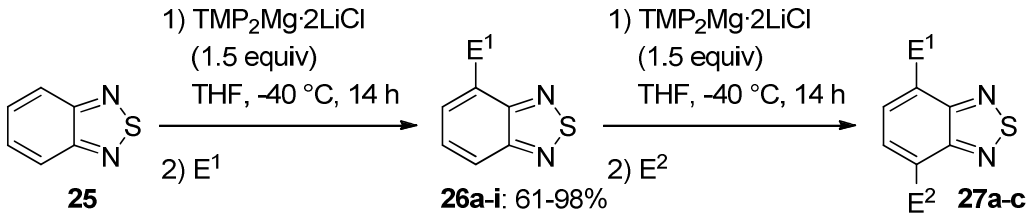
5		 **24e**	63[c]
6		 **24f**	58[c]
7		 **24g**	55[c]
8		 **24h**	76[d]

[a] Isolated, analytically pure product. [b] Obtained after addition of CuCN·2LiCl (25 mol%). [c] Obtained after transmetallation with $ZnCl_2$ (1.6 equiv) by Pd-catalyzed cross-coupling reaction using $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%) as catalyst [d] Obtained from **22a** by Pd-catalyzed coupling reaction using NEt_3 (1.5 equiv), CuI (4 mol%), $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%).

2. Functionalization of the benzo[*c*][1,2,5]thiadiazole and the benzo[*c*][1,2,5]oxadiazole scaffold

2.1. Functionalization of the benzo[*c*][1,2,5]thiadiazole scaffold via Zn-, Mg- and Mn-Intermediates

The direct access to unsymmetrically substituted benzo[*c*][1,2,5]thiadiazole derivatives is demanding and can be achieved *via* organometallic intermediates. Benzo[*c*][1,2,5]thiadiazole (**25**)[71] was readily magnesiated at position 4 with $TMP_2Mg\cdot 2LiCl$[25] at -40 °C to give the magnesiated intermediate within 14 h (Scheme 41).[72] Transmetalation with $ZnCl_2$ and Pd-mediated Negishi cross-coupling reactions[7,59] with various aryl halides and iodothiophenes provide the fluorescent compounds **26a-h** in 61 to 98% yield (Table 9, entries 1-8). Iodination gives the corresponding 4-halogenated compound **26i** in 85% yield (entry 9).



27a: E^1=C_6H_5
E^2=Br, 55%
27b: E^1=*p*-$C_6H_5CO_2Et$
E^2=C_6H_5, 74%
27c: E^1=*p*-$C_6H_5CO_2Et$
E^2=*p*-C_6H_5OMe, 84%

Scheme 41: Successive deprotonation and functionalization at positions 4 and 7.

Also, a second metalation at position 7 is achieved with $TMP_2Mg\cdot 2LiCl$ (Scheme 41). The organometallic reagent derived from **26c** reacts with 1,2-dibromo-1,1,2,2-tetrachloroethane to give the 7-brominated compound (**27a**) in 55% yield. Deprotonation of precursor **26d** and

[71] (a) Michaelis, A.; Storbeck, O. *Liebigs Ann. Chem.* **1893**, *274*, 263. (b) Michaelis, A.; Erdmann, G. *Chem. Ber.* **1895**, *28*, 2192.

[72] Those results are mentioned for the sake of completeness and have already been reported: Zimdars, S.; Diploma Thesis, Ludwig-Maximilians-Universität München, München, 2007.

subsequent transmetalation with $ZnCl_2$ followed by Negishi cross-coupling reactions[7,59] with aryl iodides provides the 4,7-bis-aryl compounds **27b**,**c** in 74 and 84% yield, respectively. Interestingly, all compounds which bear a phenol subunit (**26e**,**f**, **27c**) display a large Stokes shift of 122 to 123 nm.

Table 9: Functionalization of benzo[*c*][1,2,5]thiadiazole at position 4.

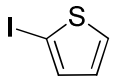
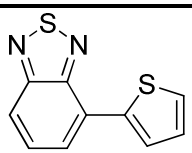
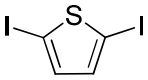
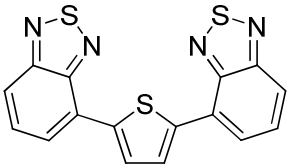
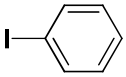
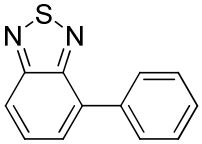
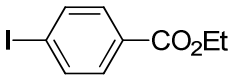
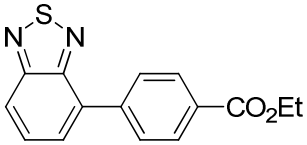
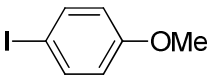
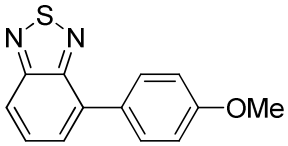
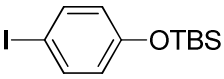
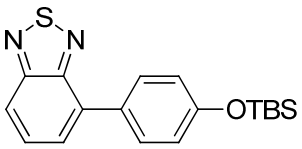
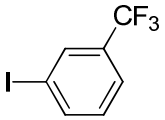
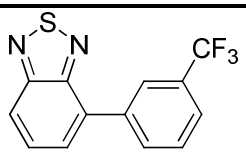
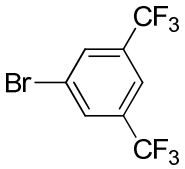
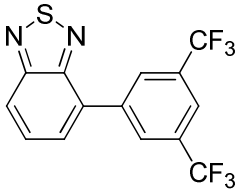
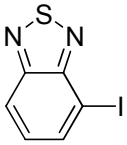
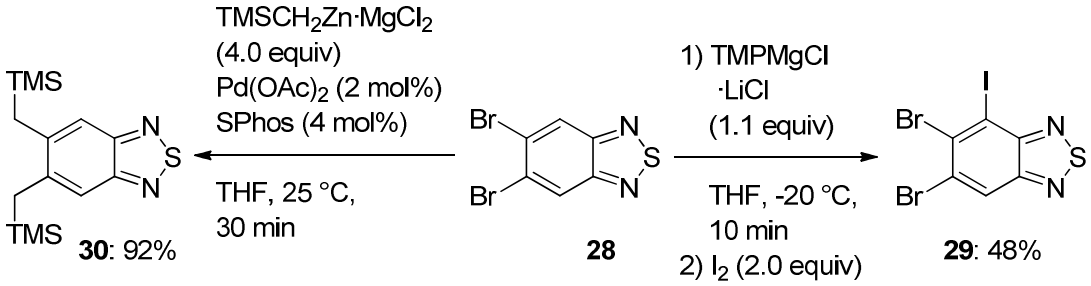
entry	electrophile	product	yield, %[a]
1		 **26a**	61[b]
2		 **26b**	98[b,c]
3		 **26c**	83[b]
4		 **26d**	72[b]
5		 **26e**	74[b]
6		 **26f**	82[b]

Table 9 continued

7		 **26g**	63[b]
8		 **26h**	61[b]
9	I_2	 **26i**	85[d]

[a] Isolated, analytically pure product. [b] Obtained by Pd-catalyzed cross-coupling reaction with $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%) as catalyst. [c] Obtained by cross-coupling reaction with 0.4 equiv of the electrophile. [d] Obtained by the reaction with I_2 (3.0 equiv).

5,6-Dibromobenzo[*c*][1,2,5]thiadiazole (**28**)[50] is magnesiated with TMPMgCl·LiCl[24] at -20 °C within 10 min followed by an iodolysis to provide compound **29** in 48% yield (Scheme 42). Alternatively, a Pd-catalyzed cross-coupling of **28** with trimethylsilylmethylzinc chloride[73] proceeds almost quantitative to give the benzothiadiazole derivative **30** in 92% yield.

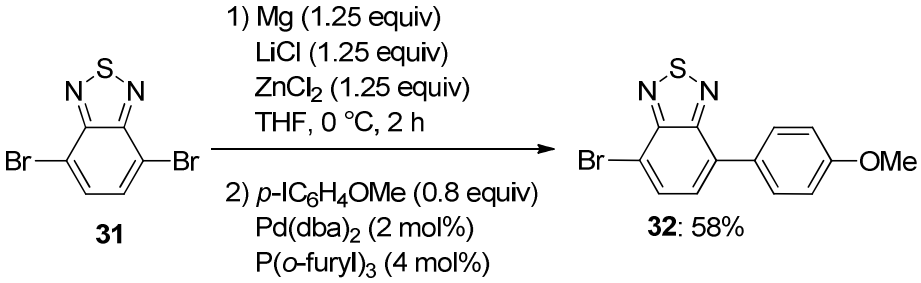


Scheme 42: Functionalization of 5,6-dibromobenzo[*c*][1,2,5]thiadiazole (**28**).

Metalation at position 4 of the benzothiadiazole scaffold can also be achieved by an oxidative Mg-insertion[11] when 4,7-dibromobenzo[*c*][1,2,5]thiadiazole (**31**)[50] is used as substrate

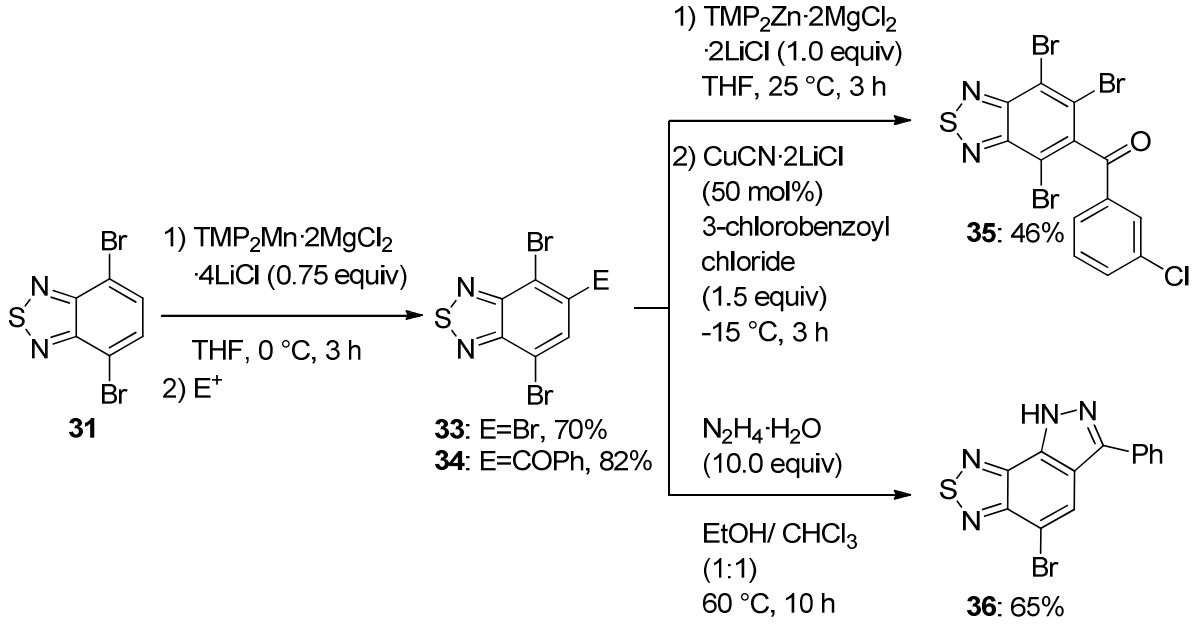
[73] Hosomi, A.; Shirahata, A.; Araki, Y.; Sakurai, H. *J. Org. Chem.* **1981**, *46*, 4631.

(Scheme 43). After *in situ* transmetalation with $ZnCl_2$ and a cross-coupling reaction with 4-iodoanisole the 4,7-di-substituted compound **32** is obtained in 58% yield.



Scheme 43: Functionalization of 4,7-dibromobenzo[*c*][1,2,5]thiadiazole (**31**) *via* Mg-insertion.

Deprotonation of **31** at position 5 is achieved with $TMP_2Mn \cdot 2MgCl_2 \cdot 4LiCl$.[52c] The resulting organomanganese reagent reacts with 1,2-dibromo-1,1,2,2-tetrachloroethane to give the 4,5,7-tribromo compound (**33**) in 70% yield. This 4,5,7-tribromobenzo[*c*][1,2,5]thiadiazole (**33**) is readily metalated with $TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (1.0 equiv, 25 °C, 3 h) and a Cu-catalyzed acylation reaction[8] with 3-chlorobenzoyl chloride furnishes the tetrasubstituted benzothiadiazole derivative **35** in 46% yield. The ketone **34** was synthesized according to a reported method,[52c] and further reaction with hydrazine gives the fused thiadiazoloindazole (**36**) in 65% yield.

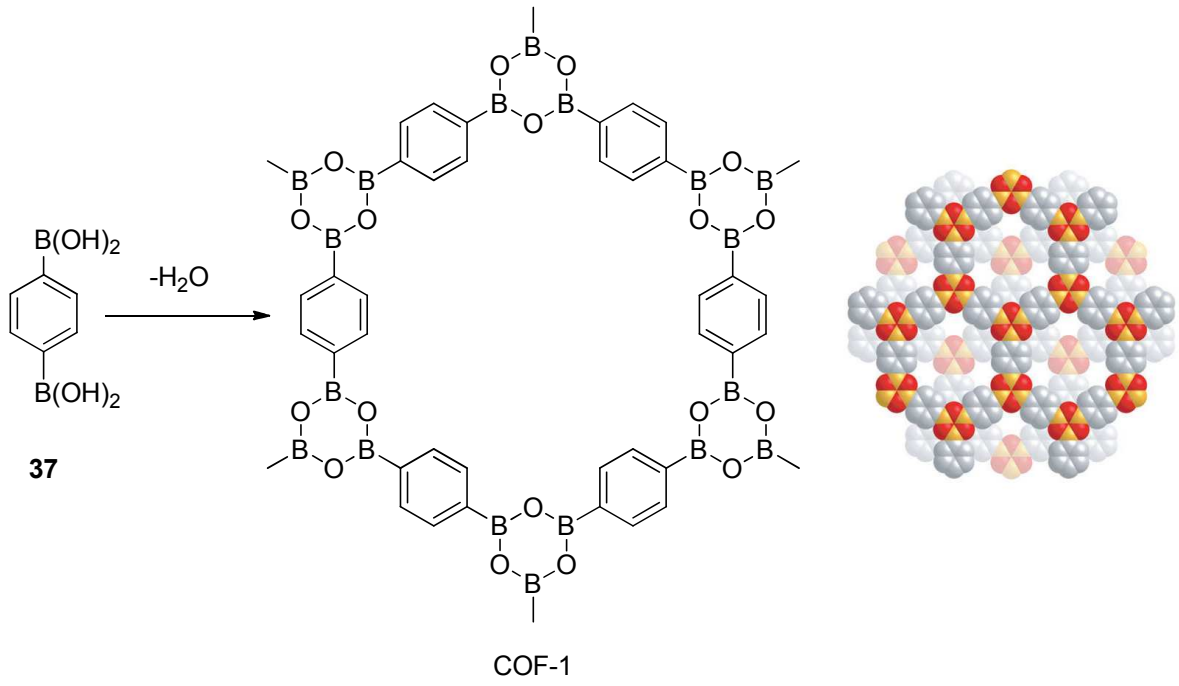


Scheme 44: Deprotonation of 4,7-dibromobenzo[*c*][1,2,5]thiadiazole (**31**).

2.2. Synthesis of a new covalent organic framework

2.2.1. Introduction

The first porous, crystalline, covalent organic framework (COF) derived from 1,4-benzenediboronic acid (**37**) by selfcondensation was published in 2005 by Yaghi.[74] The layered, hexagonal framework (COF-1) has a pore diameter of about 1.5 nm and forms a graphite like structure (Scheme 45). These porous materials are under consideration for applications like gas storage[75]and optics[76] as they have an exceptional thermal stability, a low density and a high, permanent porosity.



Scheme 45: Self condensation of BDBA and the resulting structure published by Yaghi.

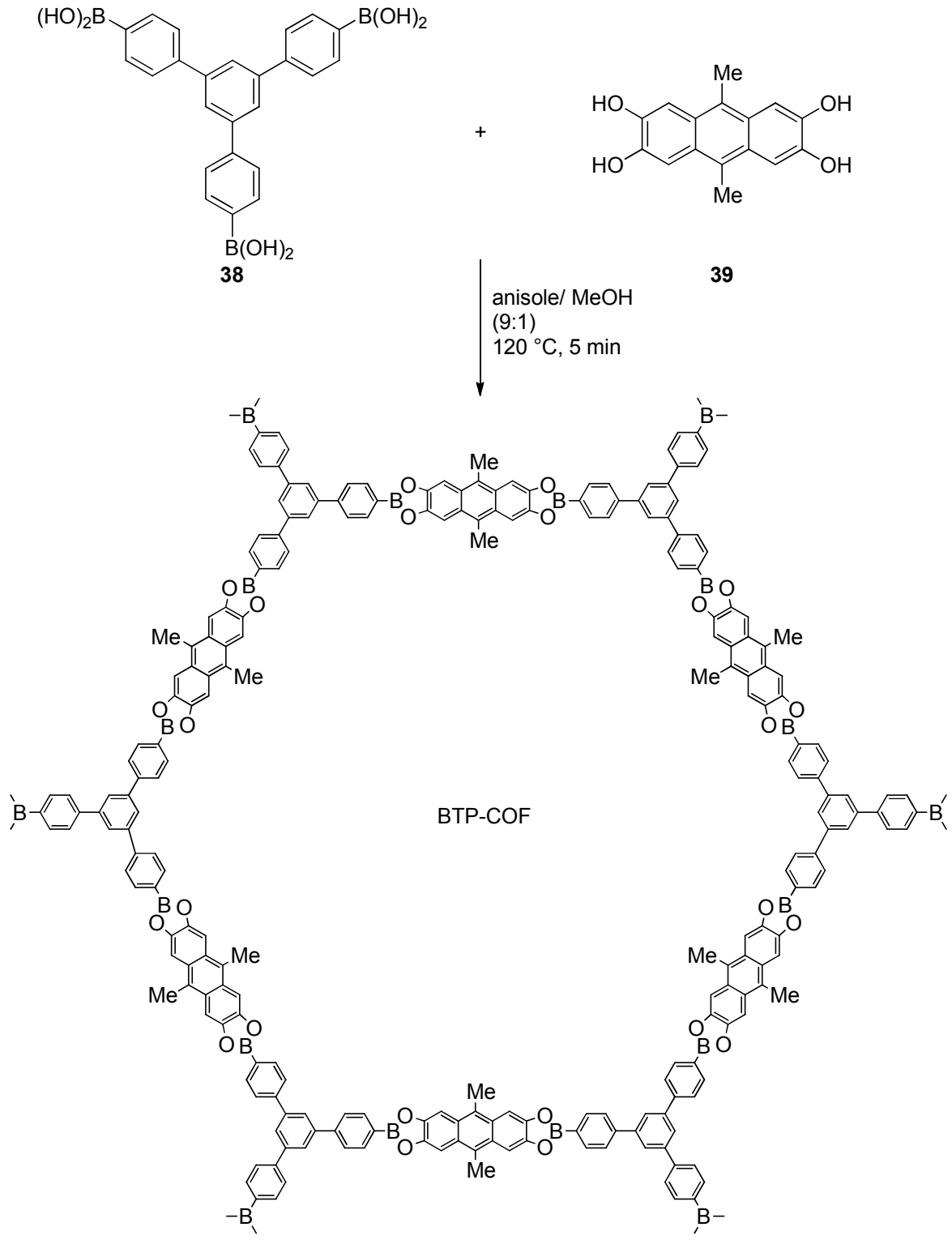
Recently, Bein characterized a COF structure with 4 nm open pores which was obtained by the co-condensation of a trigonal boronic acid (**38**) and a linear polyol (**39**) as described in

[74] Côté, A. P.; Benin, A. I.; Ockwig, N. W.; O'Keeffe, M.; Matzger, A. J.; Yaghi, O. M. *Science* **2005**, *310*, 1166.

[75] Li, J.-R.; Kuppler, R. J.; Zhou, H.-C. *Chem. Soc. Rev* **2009**, *38*, 1477.

[76] Kobler, J.; Lotsch, B. V.; Ozin, G. A.; Bein, T. *ACS Nano* **2009**, *3*, 1669.

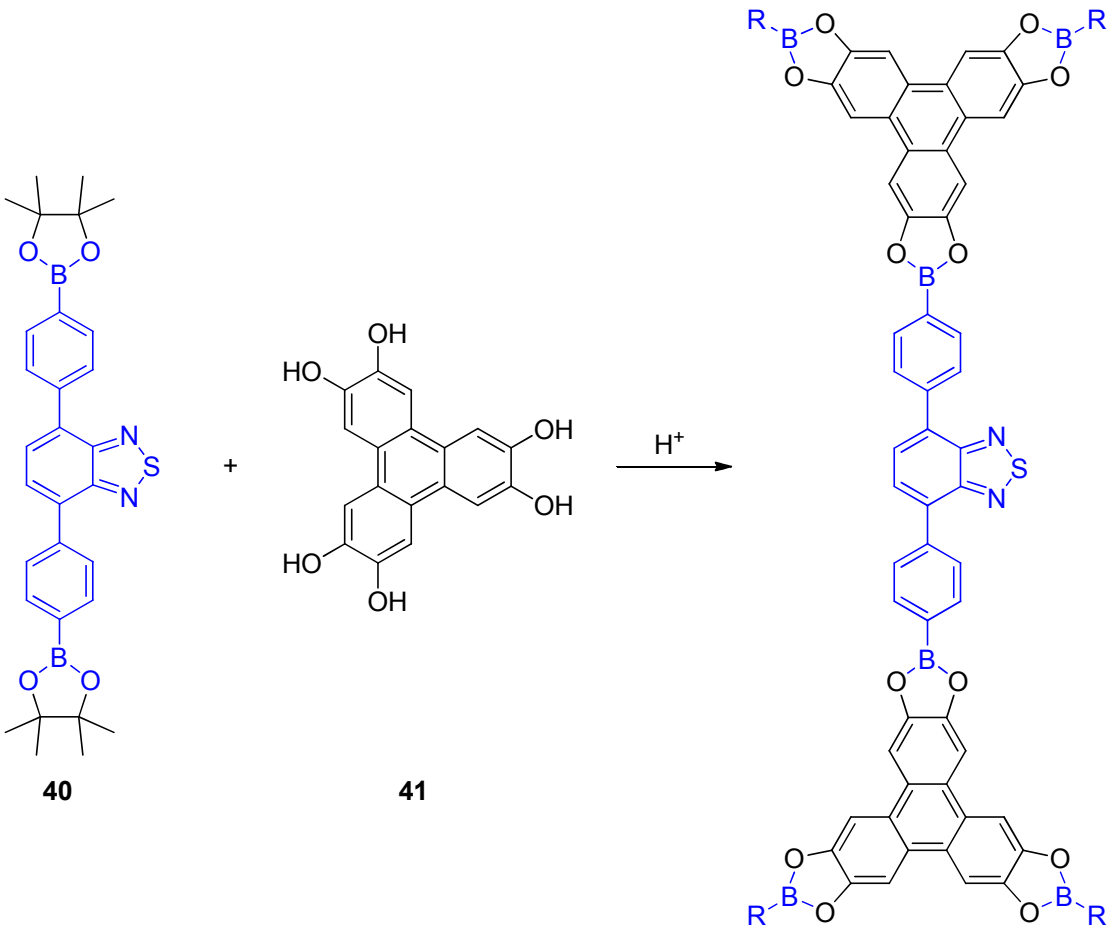
Scheme 46.[77]



Scheme 46: Condensation reaction for the BTP-COF described by Bein.

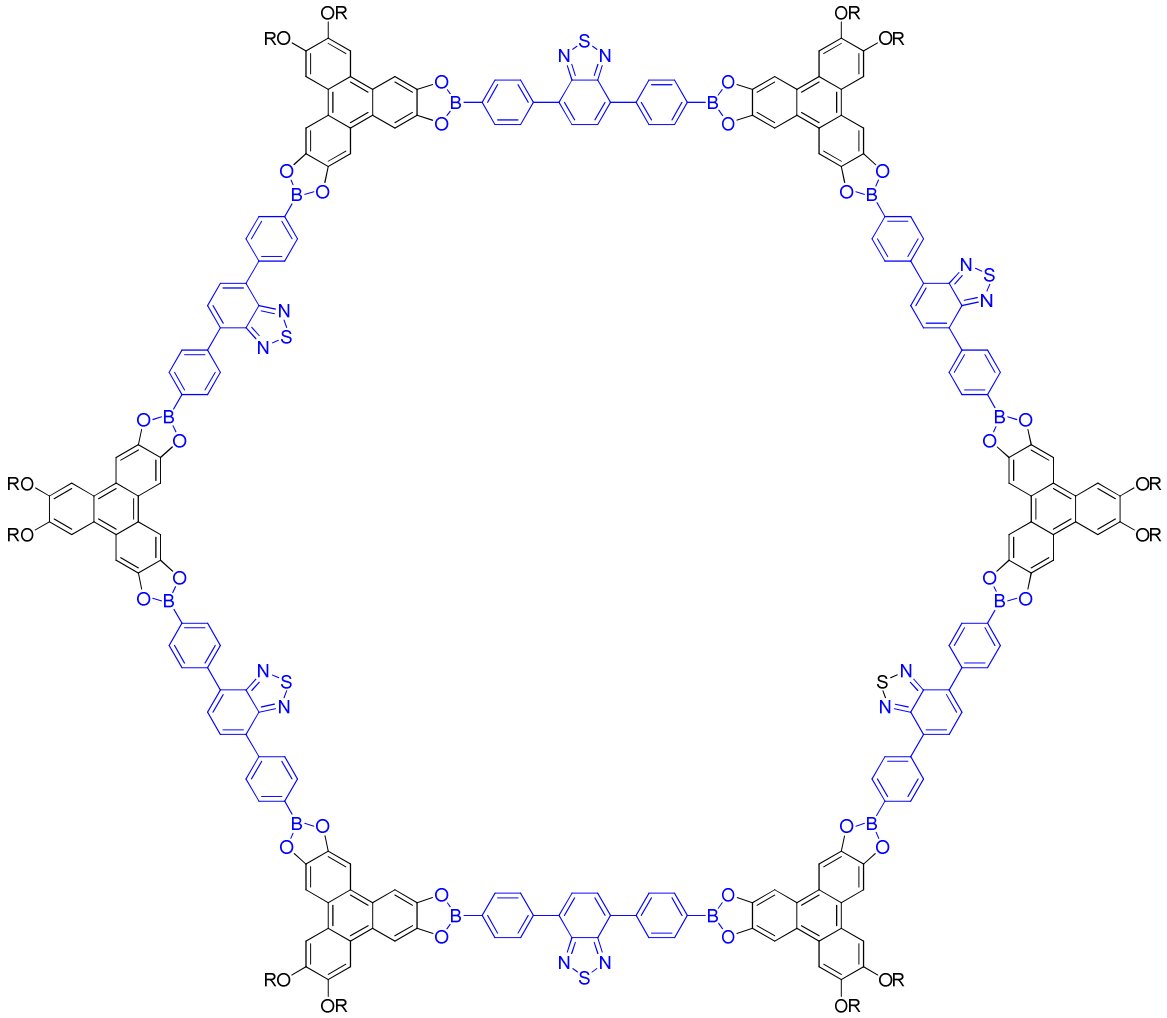
[77] Dogru, M.; Sonnauer, A.; Gavryushin, A.; Knochel, P.; Bein, T. *Chem. Commun.* **2011**, *47*, 1707.

In order to build up a COF with potential new electronical or optical properties, the synthesis of a linear linker (**40**) based on the benzo[*c*][1,2,5]thiadiazole scaffold was made up. The connection *via* co-condensation with the trigonal polyol (**41**) should form a COF as described in Scheme 47.



Scheme 47: General reaction scheme for the condensation reaction to form a COF with the benzo[*c*][1,2,5]thiadiazole derived linker (**40**).

The formed honeycomb shaped (Scheme 48) layers of this COF could either stack in an AB-fashion like graphite or an AA-fashion like boron nitride. Thus, either cavities or channels with a pore diameter of about 3.5 nm would be build up.



Scheme 48: Honeycomb-like structure of the BTD-COF.

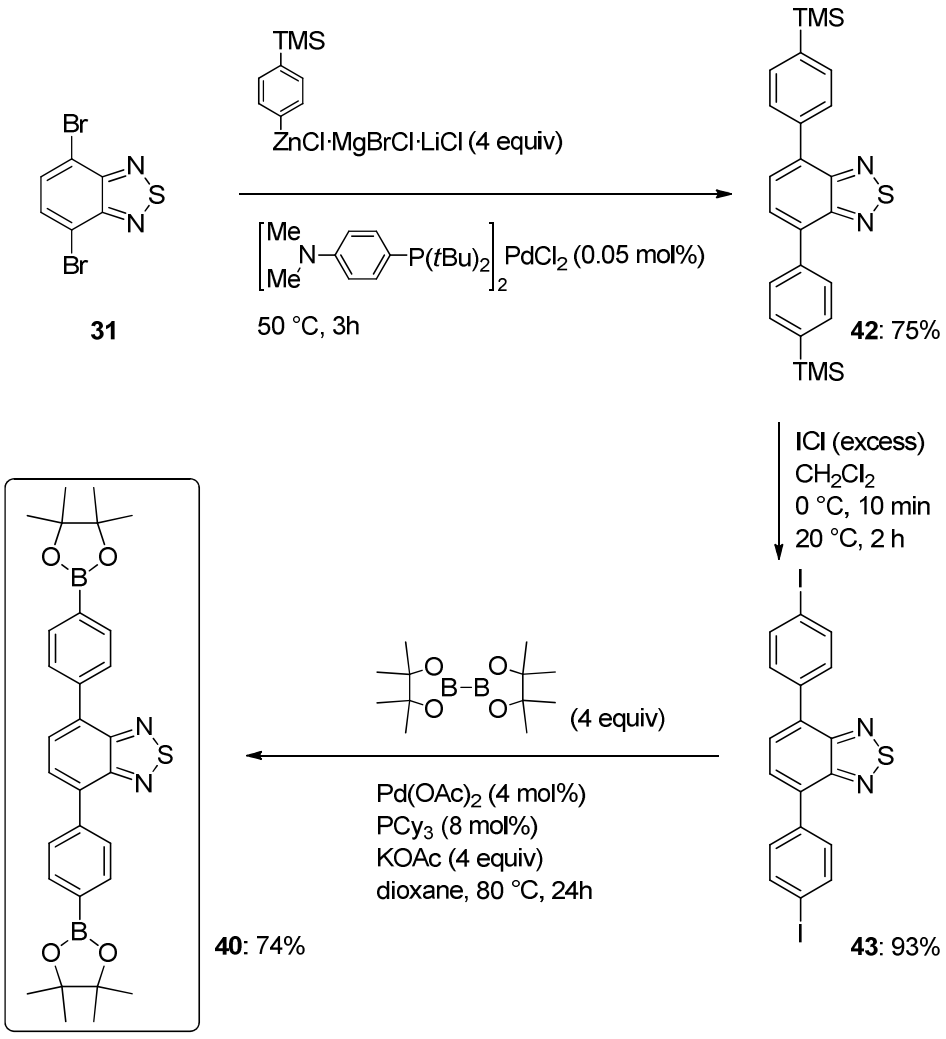
2.2.2. Synthesis of 4,7-bis(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[*c*][1,2,5]thiadiazole as precursor for a COF

The Negishi cross-coupling of 4,7-dibromobenzo[*c*][1,2,5]thiadiazole (**31**) with (4-(trimethylsilyl)phenyl)zinc(II) chloride·MgBrCl using $PdCl_2$(dppf) as catalyst has been reported to afford the product (**42**) in 55% yield.[78] We found a combination of a similar zinc reagent which was prepared in the presence of LiCl with a more efficient Pd-catalyst furnishing the desired compound within 3 h at 50 °C in 75% yield (Scheme 49).

4,7-Bis(4-(trimethylsilyl)phenyl)benzo[*c*][1,2,5]thiadiazole (**42**) reacts almost quantitative with ICl to give the corresponding bis-iodinated compound **43** in 93% yield. This step was

[78] Ito, Y.; Kjima, Y; Suginome, M.; Murakami, M. *Heterocycles* **1996**, *42*, 597.

neccessary because the direct conversion to a boronic acid was not successful as the benzo[*c*][1,2,5]thiadiazole subunit was not stable when it was exposed to BBr_3 or BCl_3. A Suzuki cross-coupling with bis(pinacolato)diboron furnishes the final product (**40**) in 74% yield.



Scheme 49: Synthesis of the benzo[*c*][1,2,5]thiadiazole derived linker (**40**).

2.3. New benzo[*c*][1,2,5]thiadiazole and benzo[*c*][1,2,5]oxadiazole based perylene dyes

2.3.1. Introduction

Organic functional materials with electronic and optical properties are of increasing interest in science and technology,[79] especially in cases where the variability and the saving of resources are important features. Organic light emitting diodes (OLEDs) or organic photovoltaic devices based on extended π-systems of polycyclic aromatic or heteroaromatic compounds are of great interest, especially perylene monoimides and bisimides[80] because of their high chemical and photochemical stability.[81] However, such systems exhibit strong tendencies for crystallization which is problematic for functional materials since the molecular packing, which invariably determines the crystal lattice, can be hardly predicted. Moreover, there are interfering border effects between the crystallites. The availability of amorphous organic materials[82] would solve these problems.

2.3.2. Preparation of precursors for new benzo[*c*][1,2,5]thiadiazole and benzo[*c*][1,2,5]oxadiazole based perylene dyes

To attach a benzo[*c*][1,2,5]thiadiazole or benzo[*c*][1,2,5]oxadiazole unit to a perylene core with or without a spacer in between there are two pathways which can be followed (Scheme 50). The first possibility is the metalation of the heterocycle and subsequent cross-coupling reaction with a halogenated perylene. The second one is the condensation of a

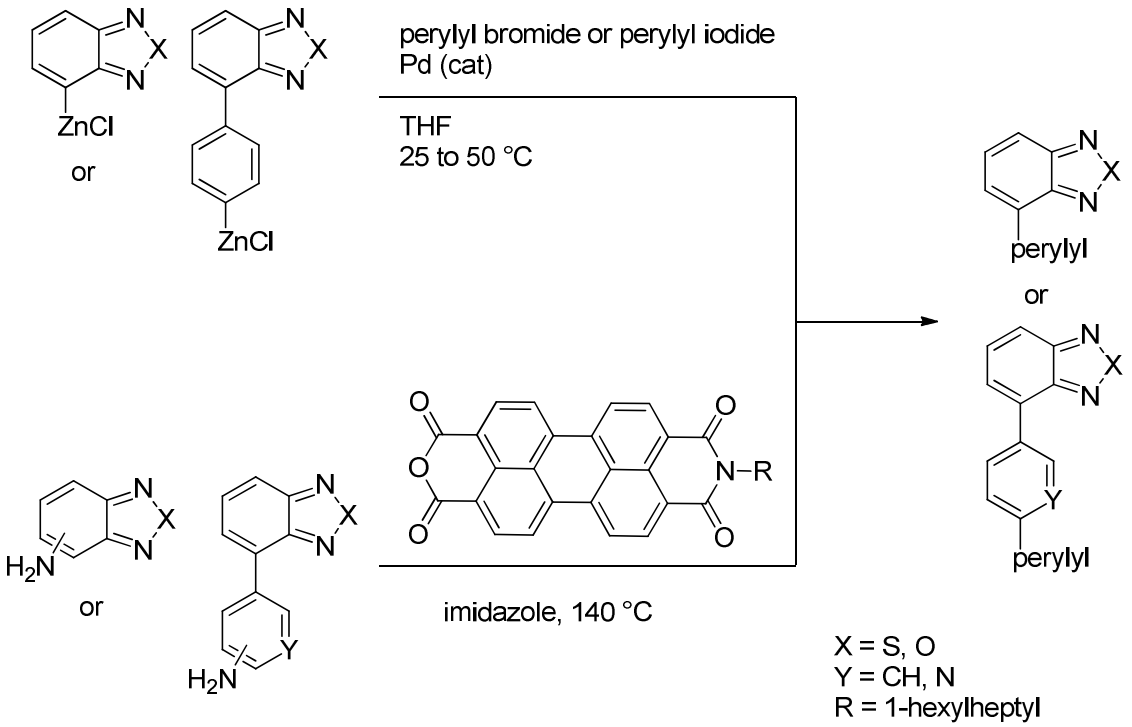
[79] (a) Brabec, C. J.; Sariciftci, N. S.; Hummelen, J. C. *Adv. Funct. Mater*. **2001**, *11*, 15; (b) Günes, S.; Neugebauer, H.; Sariciftci, N. S. *Chem. Rev.* **2007**, *107*, 1324; (c) Grätzel, M. *Nature* **2001**, *414*, 338; (d) Choi, H.; Kim, S.; Kang, S. O.; Ko, J.; Kang, M.-S.; Clifford, J. N.; Forneli, A.; Palomares, E.; Nazeeruddin, M. K.; Grätzel, M. *Angew. Chem. Int. Ed.* **2008**, *47*, 8259.

[80] (a) Langhals, H. *Heterocycles*, **1995**, *40*, 477; (b) Langhals, H. *Helv. Chim. Acta.* **2005**, *88*, 1309; (c) Li, C.; Schöneboom, J.; Liu, Z.; Pschirer, N. G.; Erk, P.; Herrmann, A.; Müllen, K. *Chem. Eur. J.* **2009**, *15*, 878.

[81] (a) Langhals, H.; Demmig, S.; Huber, H. *Spectrochim. Acta* **1988**, *44A*, 1189; (b) Langhals, H; Kollefrath, R.; Lindner, J. *Macromol. Rep.* **1995**, *A32*, 415; (c) Langhals, H.; Gold, J. *J. Prakt. Chem.* **1996**, *338*, 654; (d) Langhals, H.; Jona, W. *Angew. Chem. Int. Ed.* **1998**, *37*, 952.

[82] (a) Saragi, T. P. I.; Spehr, T.; Siebert, A.; Fuhrmann-Lieker, T.; Salbeck, J. *Chem. Rev.* **2007**, *107*, 1011; (b) Silaghi, S. D.; Spehr, T.; Cobet, C.; Saragi, T. P. I.; Werner, C.; Salbeck, J.; Esser, N. *J. Appl. Phys.* **2008**, *103*, 043503/1.

aminated heterocycle and an perylene anhydride.[83] A spacer unit can be attached to the heterocycle and/ or to the perylene.

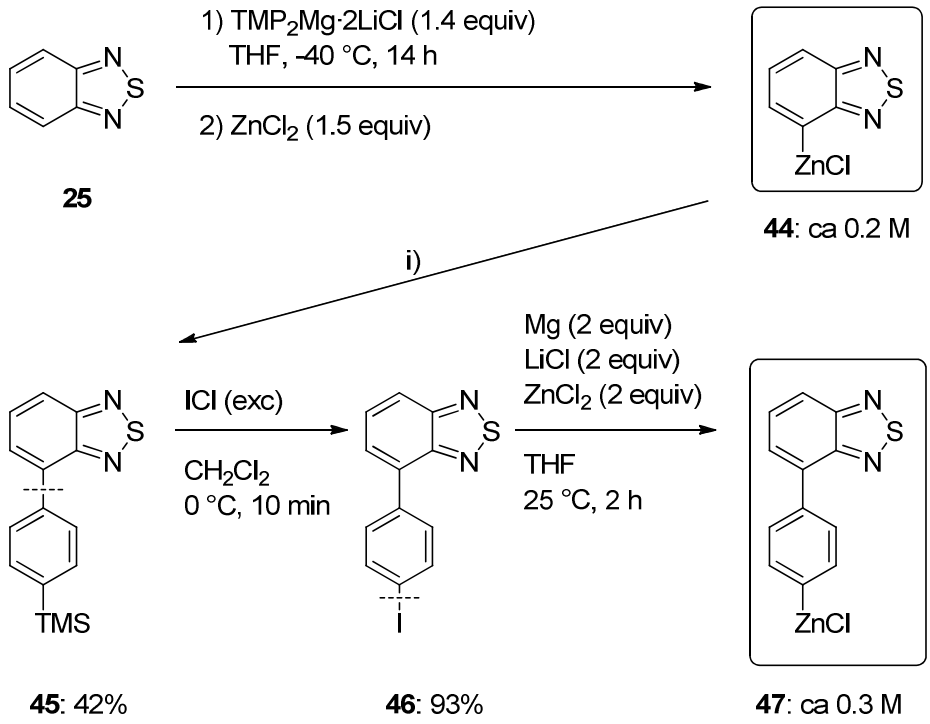


Scheme 50: Possible pathways for the attachment of the benzo[*c*][1,2,5]thiadiazole or the benzo[*c*][1,2,5]oxadiazole scaffold to perylenes via cross-coupling reaction or condensation.

For the direct cross-coupling with a halogenated perylene or benzoperylene the benzo[*c*][1,2,5]thiadiazole derived zinc reagents **44** and **47** are prepared as shown in Scheme 51. Therefore, benzo[*c*][1,2,5]thiadiazole (**25**) is metalated according to a procedure described in a previous chapter (2.1. Functionalization of the benzo[*c*][1,2,5]thiadiazole scaffold via Zn-, Mg- and Mn-Intermediates) and furnishes the zinc reagent **44** with a concentration of 0.2 M in THF. The cross-coupling of **44** with (4-iodophenyl)trimethylsilane provides compound **45** in 38% yield. The reaction of this compound with ICl occurs almost quantitative and gives the iodinated product **46** in 93% yield. The complete metalation *via* Mg insertion in the presence of $ZnCl_2$ is achieved in 2 h at 25 °C and leads to the zinc reagent **47** with a concentration of 0.25 M in THF. The cross-coupling reactions were performed at 25 °C

[83] (a) Kaiser, H.; Lindner, J.; Langhals, H. *Chem. Ber.* **1991**, *124*, 529; (b) Langhals, H.; Demmig, S.; Fotrawa, T. *J. Prakt. Chem.* **1991**, *333*, 733.

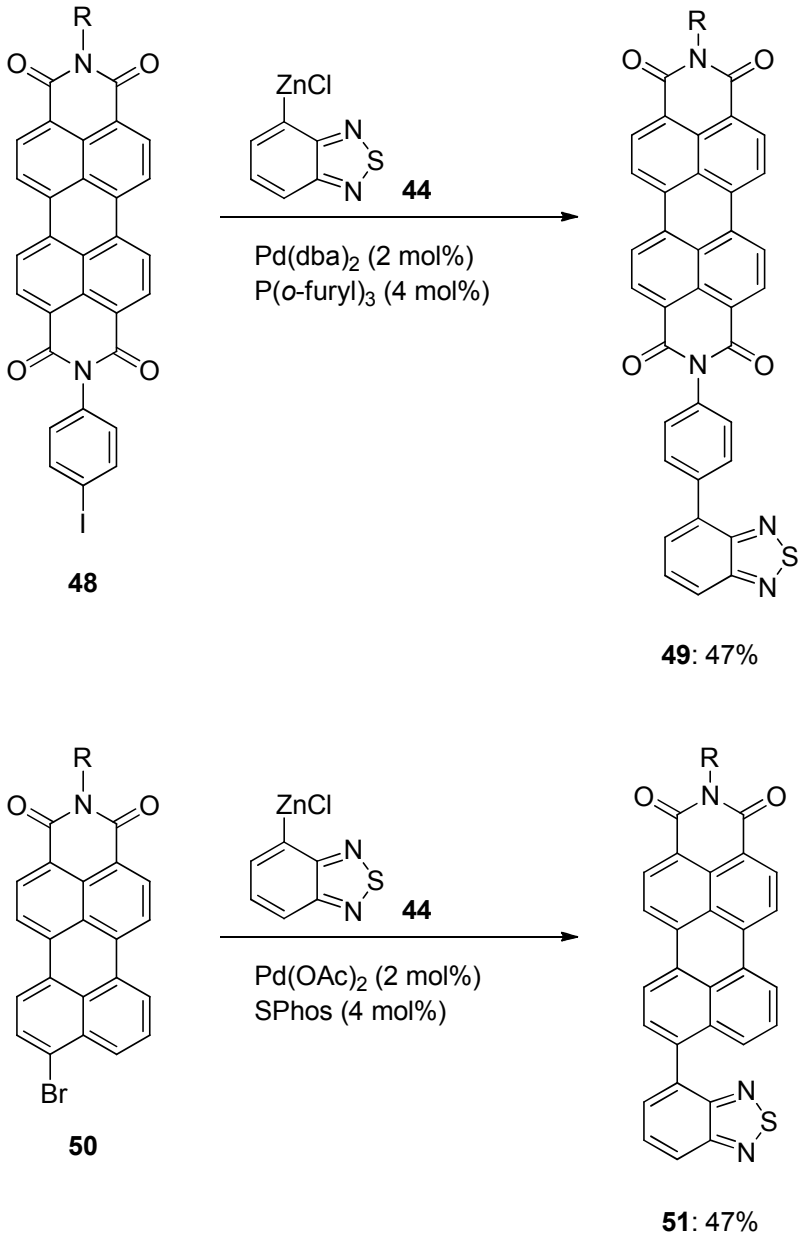
under Pd catalysis with either $Pd(dba)_2$ (2 mol%) and P(*o*-furyl)$_3$ (4 mol%) for iodinated perylenes or $Pd(OAc)_2$ (2 mol%) and SPhos (4 mol%) for brominated perylenes.[84]



Scheme 51: Preparation of benzo[*c*][1,2,5]thiadiazol derived zinc reagents. i) $TMP_2Mg\cdot 2LiCl$ (1.3 equiv), -40 °C, 14 h; $ZnCl_2$ (1.4 equiv), -40 to 25 °C, 30 min, $Pd(OAc)_2$ (2 mol%), SPhos (4 mol%), (4-iodophenyl)trimethylsilane (1.2 equiv), 25 °C, 10 h.

The direct Negishi cross-coupling reaction of the zinc reagent **44** with halogenated perylenes (R=1-hexylheptyl) is shown in Scheme 52.

[84] Purification and characterization of these cross-coupling products were performed by Andreas Walter and Andreas Esterbauer.

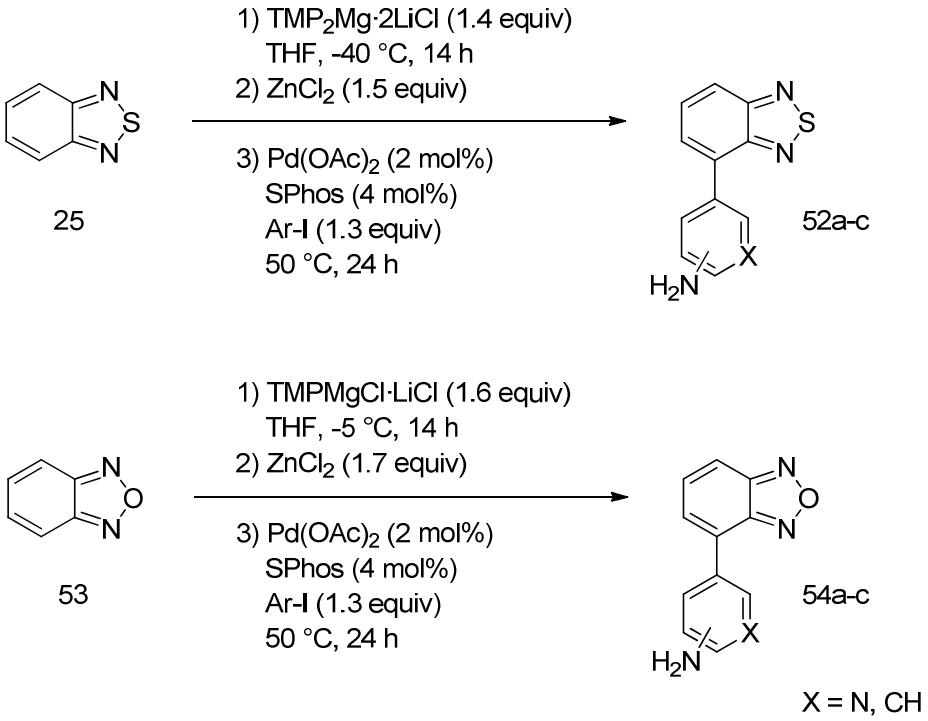


Scheme 52: Direct cross-coupling of the zinc reagent **44** with perylene dyes.

When we found, that the obtained materials had an amorphous morphology, a quantum yield close to 100% and a quantitative Förster type energy transfer[85] from the benzothiadiazole unit to the perylene chromophore, we synthesized a small library of heterocyclic compounds bearing an amine as functional group (Scheme 53, Table 10). Those compounds can be condensed with different perylene anhydrides to find out if and how the properties are tuneable.

[85] (a) Foerster, T. *Naturwiss.* **1946**, *33*, 166; (b) Foerster, T. *Ann. Phys.* **1948**, *2*, 55.

The zinc reagent **44** which is derived from **25** reacts with 4-iodoaniline, 3-iodoaniline and 5-iodopyridin-2-amine to give the compounds **52a-c** in 45 to 52% yield (Table 10, entries 1-3). Similarly, benzo[*c*][1,2,5]oxadiazole (**53**) is metalated with TMPMgCl·LiCl (-5 °C, 14 h), and funishes after transmetalation with $ZnCl_2$ and cross-coupling reaction the compounds **54a-c** in 43 to 47% yield (entries 4-6).



Scheme 53: Preparation of heterocyclic compounds bearing an amine as functional group for further transformation.

Table 10: Heterocyclic compounds bearing an amine as functional group derived from 25 and 53.

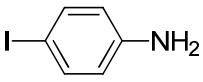
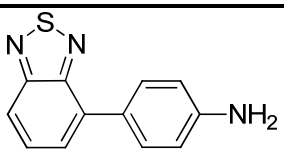
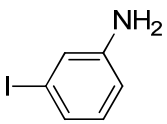
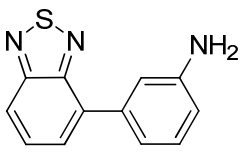
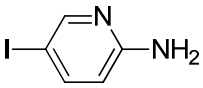
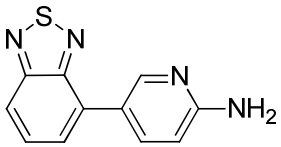
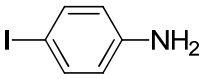
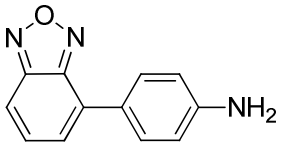
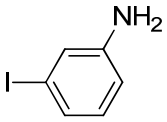
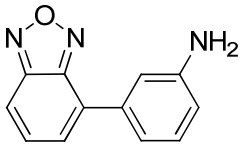
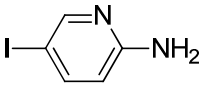
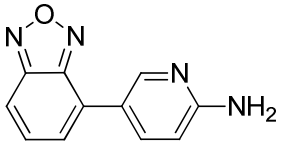
entry	electrophile	product	yield, %[a]
1		 **52a**	61[b]
2		 **52b**	61[b]

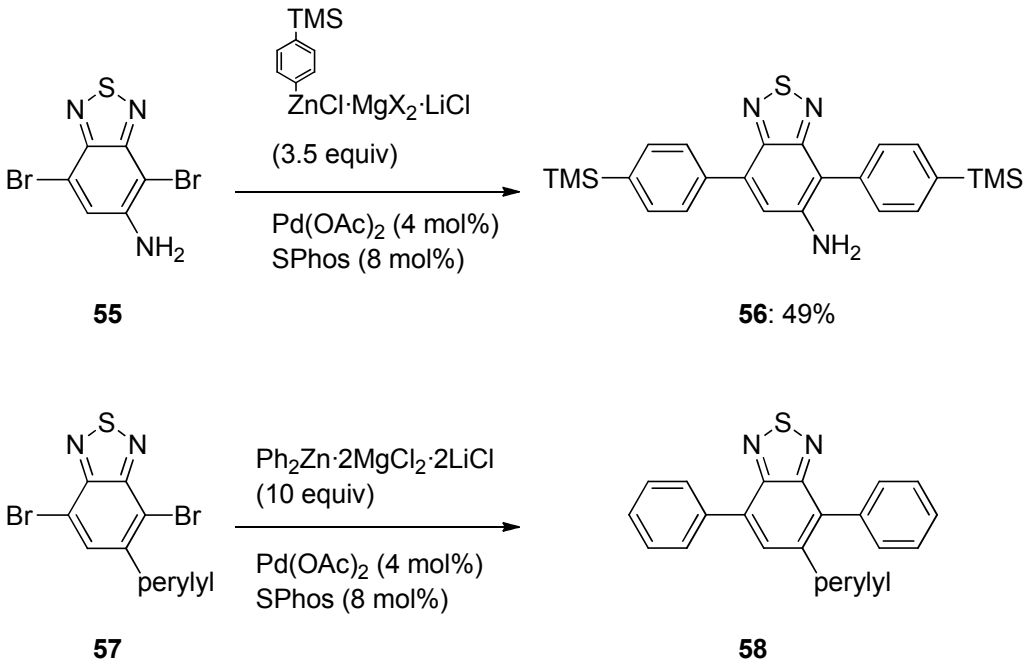
Table 10 continued

3		 **52c**	53[b]
4		 **54a**	59[b]
5		 **54b**	55[b]
6		 **54c**	54[b]

[a] Isolated, analytically pure product. [b] Obtained by Pd-catalyzed cross-coupling reaction with $Pd(OAc)_2$ (2 mol%) and SPhos (4 mol%) as catalyst.

In addition, we synthesized 5-aminated benzo[*c*][1,2,5]thiadiazoles to see if and how the connection of perylenes in this position affects the properties of these new materials (Scheme 54). Therefore, the readily available 4,7-dibromobenzo[*c*][1,2,5]thiadiazol-5-amine (**55**) was reacted with (4-trimethylsilyl)phenylzinc(II) chloride in the presence of a Pd catalyst and provided the compound **56** in 49% yield. Afterwards, compound **56** can be used for the already described condensation reaction. Moreover, we found that the Negishi cross-coupling is even possible, when the perylene is already connected to the 4,7-dibromobenzo[*c*][1,2,5]thiadiazol derivative (**57**).[86]

[86] Purification and characterization were performed by Andreas Walter.

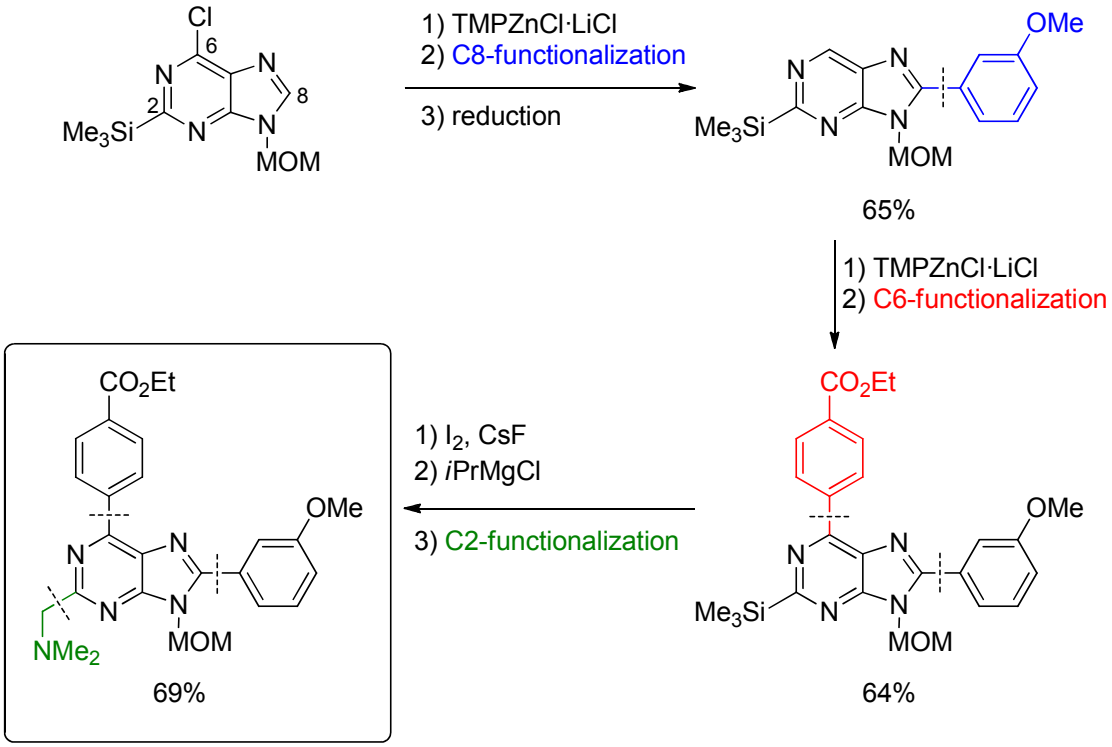


Scheme 54: Connection of the perylene core to position 5 of benzo[*c*][1,2,5]thiadiazole.

3. Summary and Outlook

3.1. Functionalization of the purine scaffold

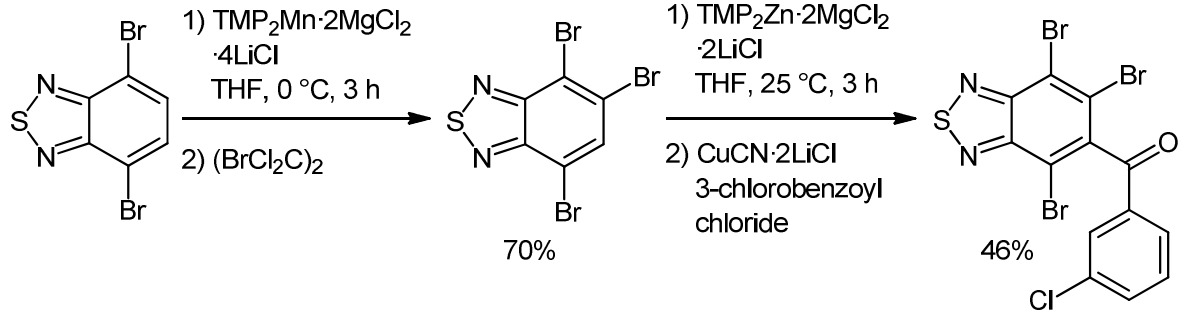
In summary, we have described a novel triple functionalization sequence of the purine scaffold starting from the readily available 6-chloropurine **6j** *via* 8-zincated, 6-zincated and 2-magnesiated intermediates using either a selective zincation with TMPZnCl·LiCl or an I/ Mg-exchange triggered by *i*PrMgCl. Our new functionalization approach of the purine skeleton allows besides cross-coupling reactions, the performance of novel functionalizations such as allylations, acylations and aminomethylations. In conclusion, this new method offers a general access to a large variety of highly functionalized purine derivatives (Scheme 55).



Scheme 55: Full functionalization of the purine scaffold.

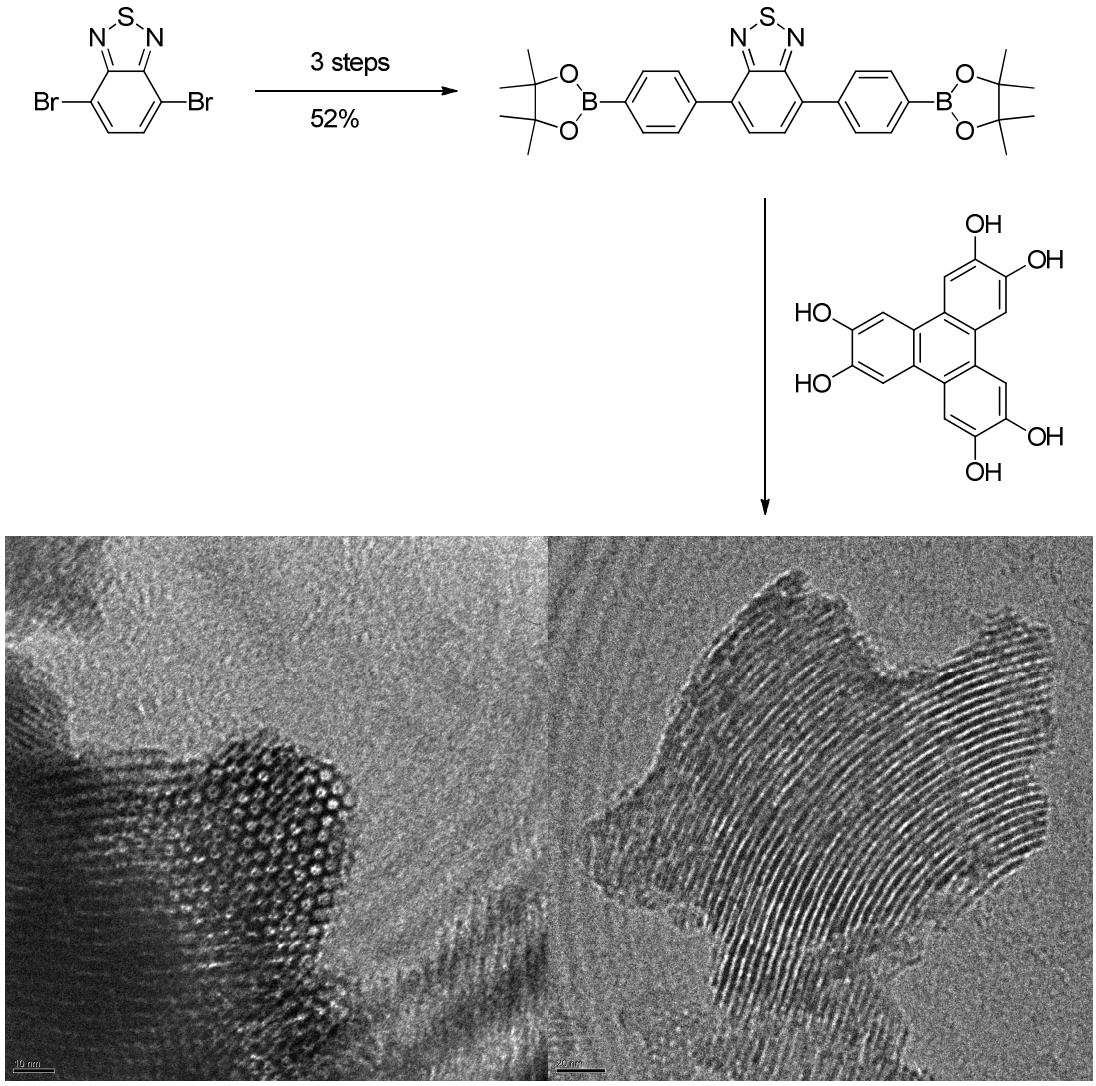
3.2. Functionalization of the benzothiadiazole and benzofurazan scaffold

The metalation of all positions of the benzo[*c*][1,2,5]thiadiazole scaffold using LiCl-solubilized TMP-bases is demonstrated on various substrates. Thus, unsymmetrically substituted benzothiadiazole derivatives and a new fused thiadiazoloindazole have been prepared.



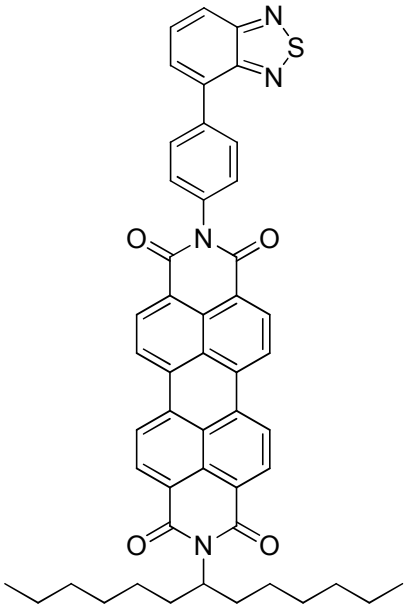
Scheme 56: Examples for the synthesis of unsymmetrically functionalized benzo[*c*][1,2,5]thiadiazole derivatives.

Furthermore, the synthesis of a benzothiadiazole derived linker for the formation of a new COF was accomplished in a 3 step synthesis with an overall yield of 52%.



Scheme 57: Synthesis of the benzothiadiazole derived linker and resulting TEM pictures of the formed COF.

Benzo[*c*][1,2,5]thiadiazole and benzo[*c*][1,2,5]oxadiazole were magnesiated with $TMP_2Mg \cdot 2LiCl$ and TMPMgCl·LiCl and efficiently attached to perylene and benzoperylene building blocks by using a Pd-catalyzed cross-coupling reactions. The resulting bichromophores exhibit efficient FRET as indicated by high fluorescence quantum yields. These new materials were obtained as amorphous solids and are therefore of interest for material science.



Scheme 58: One example of an amorphous, fluorescent benzothiadiazoloperylene dye.

C. EXPERIMENTAL SECTION

1. General Considerations

All reactions were carried out with magnetic stirring under argon atmosphere in flame-dried glassware if not indicated otherwise. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use.

Solvents were dried according to standard procedures by distillation from drying agents and stored under argon.
CH_2Cl_2 was continuously refluxed and freshly distilled from P_2O_5.
DME was heated to reflux over and freshly distilled from sodium benzophenone ketyl.
DMF was heated to reflux for 14 h over CaH_2 and distilled from CaH_2.
Et_2O was predried over CaH_2 and dried with the solvent purification system SPS-400-2 from INNOVATIVE TECHNOLOGIES INC.
EtOH was treated with phthalic anhydride (25 g/L) and sodium, heated to reflux for 6 h and distilled.
THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen.

Solvents for column chromatography were distilled prior to use.

Reagents

Acid chlorides, liquid aldehydes, TMPH and NEt_3 were distilled prior to use. All compounds which were purchased from commercial sources were used without further purification. Pd/ C (10% Pd, 50% wet with water) was purchased from Acros Organics.
Following compounds were prepared according to literature procedures:
6-Chloro-9-(methoxymethyl)-9*H*-purine (**6a**),[87] 9-benzyl-9*H*-purine (**6b**),[88] 6-chloro-9-(tetrahydro-2-pyranyl)-9*H*-purine (**6c**),[89] 6-chloro-9-benzyl-9*H*-purine (**6d**),[90] 9-

[87] Maurer, H. K. Ph.D. Dissertation, Universität Heidelberg, Heidelberg, Germany, 1963.

[88] Montgomery, J.; Temple, C. *J. Am. Chem. Soc.* **1961**, *83*, 630.

[89] Robins, R.; Godefroi, E.; Taylor, E.; Lewis, L.; Jackson, A. *J. Am. Chem. Soc.* **1961**, *83*, 2574.

[90] Tromp, R.; Spanjersberg, R.; von Frijtag Drabbe Künzel, J.; IJzermann, A. *J. Med. Chem.* **2005**, *48*, 321.

(methoxymethyl)-9*H*-purin-6-amine, [91] 2-chloropurine,[61] MOMCl solution in toluene,[92] benzo[*c*][1,2,5]thiadiazole (**25**),[93] 5,6-dibromobenzo[*c*][1,2,5]thiadiazole (**28**),[50] 4,7-dibromobenzo[*c*][1,2,5]thiadiazole (**31**),[50] (4-bromophenyl)trimethylsilane,[94] 4,7-dibromobenzo[*c*][1,2,5]thiadiazol-5-amine (**51**).[95]

Reactions were monitored by gas chromatography (GC, GC-MS) or thin layer chromatography (TLC). The completion of deprotonations was determined *via* quenching of reaction aliquots with iodine. Microwave reactions were performed in sealed reaction vessels under argon atmosphere with a high powered, focused microwave (Biotage initiator™ 2.5).

***i*PrMgCl·LiCl** and ***i*PrMgCl** solutions in THF were purchased from Chemetall (Frankfurt/ Main, Germany).

***n*BuLi** solution in hexane was purchased from Chemetall.

$TMP_2Mg·2LiCl$[25] 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 (8.3 mL, 1.2 M in THF, 10 mmol) was added dropwise. The resulting mixture was stirred for 30 min, warmed up to 25 °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.

TMPMgCl·LiCl[24] solution (1.2 M in THF) was prepared by the slow addition of TMPH (17.8 g, 126 mmol) to a *i*PrMgCl·LiCl solution (100 mL, 1.2 M in THF, 120 mmol) and stirring of the resulting mixture at 25 °C for 3 days.

$TMP_2Zn·2LiCl$ solution (1.3 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 $ZnCl_2$ (5.0 mL, 1.0 M in THF, 5.0 mmol) was added dropwise. The solution was warmed up to 25 °C, the solvent was evaporated under vacuum (10^{-3} mbar) and THF was added slowly under vigorous stirring until the salts were completely dissolved.

[91] Fuji, T.; Saito, T.; Fujisawa, T. *Heterocycles* **1988**, *27*, 1163.

[92] Berliner, M.; Belecki, K. *Org. Synth.* **2007**, *84*, 102.

[93] Tsubata, Y.; Suzuki, T.; Miyashi, T. *J. Org. Chem.* **1992**, *57*, 6749.

[94] Itami, K.; Terakawa, K.; Yoshida, J.; Kajimoto, O. *J. Am. Chem. Soc.* **2003**, *125*, 6058.

[95] Pilgram, K.; Skiles, R. D. *J. Heterocycl. Chem.* **1974**, *11*, 777.

$TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$[29] solution (0.9 M in THF) was prepared by the slow addition of $ZnCl_2$ (5 mL, 1.0 M in THF, 5 mmol) to a solution of TMPMgCl·LiCl (8.3 mL, 1.2 M in THF, 10 mmol) and stirring for 30 min at 25 °C.

$PIP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ solution (0.4 M in THF) was prepared similar to the $TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ solution by the slow addition of *i*PrMgCl·LiCl (7.3 mL, 1.31 M in THF, 9.5 mmol) to a solution of piperidine (0.85 g, 10 mmol) in THF (10 mL). After stirring for 7 h at 25 °C, $ZnCl_2$ (5.0 mL, 1.0 M in THF, 5.0 mmol) was added and the resulting solution was stirred for 30 min.

$TMPZnCl \cdot MgCl_2 \cdot LiCl$ solution (0.5 M in THF) was prepared by the slow addition of $ZnCl_2$ (10 mL, 1.0 M in THF, 10 mmol) to a solution of TMPMgCl·LiCl (8.3 mL, 1.2 M in THF, 10 mmol) and stirring for 30 min at 25 °C.

TMPZnCl·LiCl[31] solution (1.2 M in THF) was prepared by the slow addition of *n*BuLi (25 mL of a 2.4 M in hexane, 60 mmol) to a solution of TMPH (8.48 g, 60 mmol) in THF (60 mL) at -40 °C. The reaction mixture was allowed to warm up slowly to -10 °C within 1 h. $ZnCl_2$ (66 mL, 1.0 M in THF, 66 mmol) was added dropwise and the resulting solution was stirred for 30 min at -10 °C and then for 30 min at 25 °C. The solvent was removed under vacuum affording a yellowish solid. THF was then added slowly under vigorous stirring until the salts were completely dissolved (ca 1 h).

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 (10^{-3} mbar) at 140 °C for 6 h. After cooling, dry THF (80 mL) was added and stirring was continued until all the salts were dissolved (approx. 24 h). The slightly yellow solution was stored under argon.

$ZnCl_2$ solution (1.0 M in THF) was prepared by drying $ZnCl_2$ (137 g, 100 mmol) in a Schlenk-flask under vacuum (10^{-3} mbar) at 140 °C for 6 h. After cooling, dry THF (100 mL) was added and stirring was continued until all salts were dissolved (approx. 5 h). The colorless solution was stored under argon over molecular sieves (4 Å).

(4-Trimethylsilylphenyl)zinc(II) chloride·MgBrCl·LiCl[96] solution (0.35 M in THF) was prepared by drying LiCl (212 mg, 5 mmol) under vacuum (10^{-3} mbar) at 140 °C. After cooling Mg (146 mg, 6.0 mmol), THF (5 mL) and (4-bromophenyl)trimethylsilane (917 mg, 4.0 mmol) were successively added. The mixture was stirred for 2 h at 25 °C, was canulate to a solution of $ZnCl_2$ (5 mL, 1.0 M in THF, 5.0 mmol) and was stirred for 15 min at 25 °C.

[96] Rahman, M. J.; Yamakawa, J.; Matsumoto, A.; Enozawa, H.; Nishinaga, T.; Kamada, K.; Iyoda, M. *J. Org. Chem.* **2008**, *73*, 5542.

Diphenylzinc(II)·MgClI·LiCl solution (0.5 M in THF) was prepared by drying LiCl (318 mg, 7.5 mmol) under vacuum (10^{-3} mbar) at 140 °C. After cooling Mg (182 mg, 7.5 mmol), THF (5 mL) and iodobenzene (1.02 g, 5.0 mmol) were successively added. The mixture was stirred for 2 h at 25 °C, was canulate to a solution of $ZnCl_2$ (2.25 mL, 1.0 M in THF, 2.25 mmol) and was stirred for 30 min at 25 °C.

Content Determination of Organometallic Reagents

Organzinc and organomagnesium reagents were titrated against I_2 in a 0.5 M LiCl solution in THF.[97]

Organolithium reagents were titrated against menthol using 1,10-phenanthroline as indicator in THF.[98]

TMP derived Mg and Zn bases were titrated against benzoic acid using 4-(phenylazo)diphenylamine as indicator in THF.[99]

Chromatography

Flash column chromatography (FCC) was performed using silica gel 60 (0.040-0.063 mm) from Merck.

Thin layer chromatography (TLC) was performed using SiO_2 pre-coated aluminium plates (Merck 60, F-254). The chromatograms were examined under UV light at 254 nm.

Analytical Data

NMR spectra were recorded on VARIAN Mercury 200, BRUKER AXR 300, VARIAN VXR 400 S and BRUKER AMX 600 instruments. Chemical shifts are reported as δ-values in ppm relative to the residual solvent peak of $CHCl_3$ (δ_H : 7.25, δ_C : 77.0). For the characterization of the observed signal multiplicities the following appreviations were used: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) as well as br (broad).

[97] Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 890.

[98] Lin, H.-S.; Paquette, A. *Synth. Commun.* **1994**, *24*, 2503.

[99] Hammett, L. P.; Walden, G. H.; Edmonds, S. M. *J. Am. Chem. Soc.* **1934**, *56*, 1092.

Mass spectroscopy: High resolution (HR-MS) and low resolution (MS) spectra were recorded on a FINNIGAN MAT 95Q instrument. Electron impact ionization (EI) was conducted with an electron energy of 70 eV.

For the combination of gas chromatography with mass spectroscopic detection, a GC/MS from HEWLETT-PACKARD HP 6890 / MSD 5973 was used.

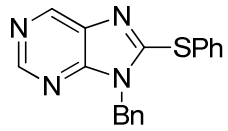
Infrared spectra (IR) were recorded from 4500 cm^{-1} to 650 cm^{-1} on a PERKIN ELMER Spectrum BX-59343 instrument. For detection a SMITHS DETECTION DuraSampl*IR* II Diamond ATR sensor was used. The absorption bands are reported in wavenumbers (cm^{-1}).

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

2. Functionalization of the purine scaffold

2.1. Synthesis of compounds 3-16

Synthesis of 9-benzyl-8-(phenylthio)-9*H*-purine (3)



In a Schlenk-tube $TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (2.6 mL, 0.95 M in THF, 2.4 mmol) was added within 1.5 h to a solution of 9-benzyl-9*H*-purine (**6d**, 410 mg, 2.0 mmol) and $PhSO_2SPh$ (500 mg, 2.0 mmol) in THF (4 mL) at 0 °C and the resulting reaction mixture was stirred for 10 min. After addition of $NH_{3(conc)}$/ $NH_4Cl_{(sat)}$ (1:3, 10 mL) the reaction mixture was warmed up to 25 °C, the aqueous layer was extracted with CH_2Cl_2 (4 x 50 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, CH_2Cl_2/ MeOH gradient = 400:1, 400:2, 400:3, 400:4) yielded 9-benzyl-8-(phenylthio)-9*H*-purine (**3**, 380 mg, 60%) as a colorless solid.

mp (°C): 134-135.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3056 (w), 3030 (w), 3010 (w), 2970 (vw), 2474 (vw), 2360 (m), 2342 (w), 1948 (vw), 1892 (w), 1806 (vw), 1738 (w), 1578 (s), 1496 (w), 1468 (s), 1458 (m), 1444

(m), 1424 (s), 1374 (s), 1354 (m), 1344 (s), 1312 (w), 1298 (vs), 1230 (s), 1222 (s), 1180 (m), 1130 (w), 1094 (m), 1074 (m), 1020 (w), 1000 (w), 988 (w), 924 (m), 914 (w), 892 (w), 826 (w), 792 (w), 776 (w), 748 (m), 726 (s), 708 (m), 696 (s), 688 (s), 676 (m), 624 (w).

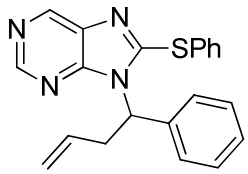
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.94 (s, 1H), 8.93 (s, 1H), 7.61-7.57 (m, 2H), 7.46-7.41 (m, 3H), 7.40-7.31 (m, 5H), 5.50 ppm (s, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 155.6, 153.5, 151.7, 145.7, 134.9, 134.3, 134.2, 129.9, 129.8, 129.0, 128.4, 128.0, 127.2, 46.5 ppm.

MS (70 eV, EI): m/z (%) = 319 (17), 318 (83), 317 (54), 227 (7), 209 (30), 167 (39), 92 (7), 91 (100), 65 (12).

HRMS (EI): m/z calc. for [$C_{18}H_{14}N_4S$] 318.0939; found: 318.0935.

Synthesis of 9-(1-phenylbut-3-en-1-yl)-8-(phenylthio)-9*H*-purine (5)

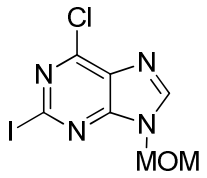


In a Schlenk-tube $TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (1.3 mL, 0.95 M in THF, 1.2 mmol) was added dropwise to a solution of 9-benzyl-8-(phenylthio)-9*H*-purine (**3**, 318 mg, 1.0 mmol) in THF (3.5 mL) and the resulting reaction mixture was stirred for 15 min. At -20 °C $CuCN \cdot 2LiCl$ (1.0 mL, 1.0 M in THF, 1.0 mmol) was added dropwise and after 10 min allyl bromide (0.26 mL, 3 mmol) was added. After warming up to 25 °C and further stirring for 30 min, a mixture of $NH_{3(conc)}$/ $NH_4Cl_{(sat)}$ (1:3, 10 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, CH_2Cl_2/ MeOH gradient = 400:0.5, 400:1, 400:2, 400:4) yielded 9-(1-phenylbut-3-en-1-yl)-8-(phenylthio)-9*H*-purine (**5**, 196 mg, 55%) as a slightly yellow oil.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3058 (w), 3030 (w), 3008 (w), 2980 (w), 2920 (w), 1952 (vw), 1874 (vw), 1642 (w), 1582 (s), 1496 (w), 1454 (s), 1428 (s), 1372 (m), 1330 (s), 1302 (s), 1278 (s), 1234 (s), 1190 (m), 1180 (m), 1158 (w), 1116 (w), 1092 (m), 1024 (m), 1000 (m), 992 (m), 960 (m), 912 (s), 846 (w), 832 (w), 790 (m), 770 (w), 746 (s), 714 (m), 696 (vs), 686 (vs), 652 (m), 616 (m).

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.90 (s, 1H), 8.89 (s, 1H), 7.59-7.55 (m, 4H), 7.45-7.41 (m, 3H), 7.37-7.34 (m, 2H), 7.33-7.30 (m, 1H), 5.88 (dd, *J* = 10.5, 5.7 Hz, 1H), 5.69-5.62 (m, 1H), 5.06-5.03 (m, 1H), 4.96-4.94 (m, 1H), 3.84-3.79 (m, 1H), 3.27-3.22 ppm (m 1H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 155.6, 153.6, 151.1, 145.7, 138.1, 134.2, 134.0, 133.4, 129.7, 129.7, 128.8, 128.4, 127.8, 127.7, 118.9, 60.5, 36.3 ppm.
MS (70 eV, EI): m/z (%) = 358 (62), 357 (44), 317 (39), 249 (21), 239 (21), 228 (40), 227 (100), 131 (35), 130 (37), 129 (29), 91 (37).
HRMS (EI): m/z calc. for [$C_{21}H_{18}N_4S$] 358.1252; found: 358.1252.

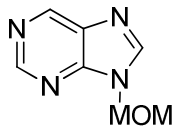
Synthesis of 6-chloro-2-iodo-9-(methoxymethyl)-9*H*-purine (6e)



In a Schlenk-flask I_2 (950 mg, 3.75 mmol) dissolved in THF (4 mL) was added dropwise to a solution of 6-chloro-9-MOM-2-(tributylstannyl)-9*H*-purine (**13a**, 1.22 g, 2.5 mmol) in THF (12 mL). After stirring the resulting reaction mixture for 1 h, $Na_2S_2O_3$ solution (10 mL) and EtOAc (50 mL) were added. The organic layer was washed with H_2O (30 mL) and $NaCl_{(sat)}$ solution, was dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. Purification *via* trituration with pentane yielded 6-chloro-2-iodo-9-(methoxymethyl)-9*H*-purine (**6e**, 730 mg, 90%) as a pale yellow solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.17 (s, 1H), 5.60 (s, 2H), 3.42 ppm (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 152.9, 150.8, 145.0, 131.5, 117.2, 74.8, 57.7 ppm.
MS (70 eV, EI): m/z (%) = 325 (9), 324 (28), 296 (33), 294 (100), 197 (7), 45 (16).
HRMS (EI): m/z calc. for [$C_7H_6ClIN_4O$] 323.9275; found: 323.9252.

Synthesis of 9-(methoxymethyl)-9*H*-purine (6f)



In a round bottom flask with reflux condenser *t*BuONO (0.5 mL, 4 mmol) was added to a solution of 9-(methoxymethyl)-9*H*-purin-6-amine (558 mg, 2 mmol) in THF (10 mL). The reaction mixture was refluxed for 3 h, *tert*-butyl nitrite (0.5 mL, 4 mmol) was added and the mixture was refluxed for further 3 h. The solvents were evaporated *in vacuo*. Purification *via* column chromatography (silicagel, CH_2Cl_2/ MeOH gradient = 100:0, 100:1 to 30:1) yielded 9-(methoxymethyl)-9*H*-purine (**6f**, 230 mg, 70%) as a pale yellow solid.

mp (°C): 87-88.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3102 (vw), 3044 (w), 2992 (w), 2948 (w), 2834 (vw), 1860 (vw), 1692 (w), 1596 (m), 1580 (s), 1504 (m), 1470 (w), 1456 (w), 1418 (w), 1394 (m), 1356 (m), 1342 (m), 1304 (m), 1292 (m), 1256 (w), 1230 (m), 1218 (m), 1200 (m), 1178 (m), 1126 (m), 1088 (vs), 1018 (m), 936 (w), 922 (w), 908 (m), 892 (m), 794 (m), 754 (s), 658 (m), 636 (s), 606 (vw).

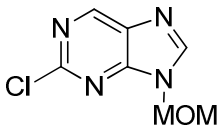
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.17 (s, 1H), 9.01 (s, 1H), 8.24 (s, 1H), 5.64 (s, 2H), 3.38 ppm (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.1, 148.8, 145.2, 133.8, 73.9, 57.3 ppm.

MS (70 eV, EI): m/z (%) = 164 (8), 135 (11), 134 (100), 133 (38), 79 (5), 52 (7), 45 (86).

HRMS (EI): m/z calc. for [$C_7H_8N_4O$] 164.0698; found: 164.0697.

Synthesis of 2-chloro-9-(methoxymethyl)-9*H*-purine (6g)

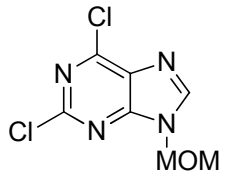


In a round bottom flask NEt_3 (7.2 mL, 52 mmol) was added to a solution of 2-chloropurine (4 g, 26 mmol) in DME (300 mL). MOMCl (30 mL, 2.0 M in toluene, 60 mmol) was added dropwise. The reaction mixture was stirred until the starting material was completely consumed. K_2CO_3 (10 g) and H_2O (200 mL) were added. The solvents were evaporated *in vacuo*, the crude solid triturated with EtOAc and the solvent evaporated. Purification *via*

column chromatography (silicagel, CH_2Cl_2/ EtOH 20:1) yielded 2-chloro-9-(methoxymethyl)-9*H*-purine (**6g**, 3.0 g, 58%) as a colorless solid.

mp (°C): 113-115.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3078 (w), 3058 (w), 2950 (w), 2838 (w), 2362 (w), 2340 (vw), 2280 (vw), 1736 (w), 1696 (w), 1664 (w), 1594 (m), 1570 (s), 1502 (m), 1444 (w), 1430 (m), 1402 (m), 1358 (s), 1342 (s), 1298 (m), 1234 (m), 1218 (m), 1204 (s), 1180 (s), 1150 (s), 1110 (s), 1086 (vs), 1020 (s), 946 (w), 910 (s), 790 (m), 770 (s), 702 (m), 682 (m), 636 (m), 610 (vw).
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.24 (s, 1H), 5.61 (s, 2H), 3.41 ppm (s, 3H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 155.0, 153.5, 150.4, 145.9, 132.9, 74.1, 57.5 ppm.
MS (70 eV, EI): m/z (%) = 200 (7), 198 (20), 170 (24), 169 (15), 168 (84), 167 (36), 52 (5), 45 (100).
HRMS (EI): m/z calc. for [$C_7H_7ClN_4O$] 198.0308; found: 198.0309.

Synthesis of 2,6-dichloro-9-(methoxymethyl)-9*H*-purine (6h)



In a round bottom flask K_2CO_3 (6.2 g, 45 mmol) was added to a solution of 2,6-dichloropurine (1.89 g, 10 mmol) in DMF (20 mL). MOMCl (7.5 mL, 2.0 M in toluene, 15 mmol) was added dropwise. The reaction mixture was stirred until the starting material was completely consumed. H_2O (20 mL) was added. The solvents were evaporated *in vacuo*, the crude solid triturated with EtOAc and the solvent evaporated. Purification *via* column chromatography (silicagel, CH_2Cl_2/ EtOH gradient = 100:0, 500:1 to 100:1) yielded 2,6-dichloro-9-(methoxymethyl)-9*H*-purine (**6h**, 860 mg, 37%) as a colorless solid.

mp (°C): 126-127.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3106 (w), 3084 (vw), 3014 (vw), 2970 (vw), 2946 (w), 2846 (vw), 2836 (vw), 1834 (vw), 1696 (vw), 1596 (m), 1556 (s), 1496 (m), 1456 (w), 1442 (w), 1418 (w), 1396 (w), 1386 (w), 1360 (m), 1342 (m), 1310 (m), 1272 (m), 1254 (w), 1222 (s), 1182 (m), 1170 (s), 1138 (s), 1100 (vs), 1046 (w), 1024 (m), 956 (m), 936 (w), 912 (s), 880 (s), 786 (s), 720 (m), 682 (w), 658 (w), 626 (m).

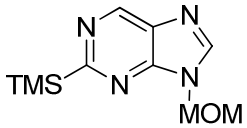
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.27 (s, 1H), 5.61 (s, 2H), 3.41 ppm (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.6, 152.1, 145.7, 130.6, 74.7, 57.6 ppm.

MS (70 eV, EI): m/z (%) = 232 (9), 212 (9), 211 (12), 204 (40), 203 (20), 202 (62), 201 (21), 196 (12), 45 (100).

HRMS (EI): m/z calc. for [$C_7H_6Cl_2N_4O$] 231.9919; found: 231.9919.

Synthesis of 9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (6i)



In a round bottom flask Pd/ C (40 wt%) and HCO_2NH_4 (1.25 g, 35 mmol) were added to a solution of the 6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 2.5 mmol) in MeOH (5 mL) at 45 °C. When the reaction started proceeding (intensive bubbling) the mixture was stirred for further 30 min until the starting material was completely consumed as monitored by TLC. The solution was filtered through celite®. After washing the cake with EtOH (400 mL) and concentration *via* rotary evaporation, the crude material was redissolved in CH_2Cl_2 (100 mL) and the undissolved HCO_2NH_4 was filtered off. The solvents were evaporated *in vacuo*. Purification *via* column chromatography (silicagel, EtOAc) yielded 9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6i**, 550 mg, 90%) as a pale yellow oil.

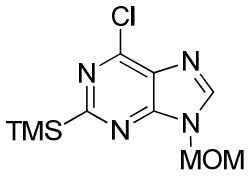
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3418 (brw), 2956 (w), 2900 (vw), 2830 (vw), 1740 (vw), 1588 (m), 1562 (m), 1498 (w), 1442 (w), 1426 (w), 1396 (w), 1364 (m), 1350 (m), 1330 (w), 1290 (w), 1246 (m), 1180 (m), 1092 (s), 1024 (w), 918 (m), 898 (w), 838 (vs), 756 (s), 696 (w), 670 (w), 658 (vw), 636 (m), 622 (w).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.12 (s, 1H), 8.14 (s, 1H), 5.58 (s, 2H), 3.32 (s, 3H), 0.30 ppm (s. 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 174.6, 150.9, 147.1, 144.7, 132.3, 73.6, 57.5, -1.9 ppm.

HRMS (ESI): m/z calc. for [$C_{10}H_{16}N_4OSi+H^+$] 237.1166; found: 237.1166.

Synthesis of 6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (6j)



In a 1L Schlenk-flask equipped with a large stirring bar and septum *n*BuLi (76.6 mL, 2.61 M in hexane, 200 mmol) was added to a solution of TMPH (28.25 g, 200 mmol) in THF (100 mL) at -78 °C and the reaction mixture was stirred for 1 h. Subsequently, a solution of 6-chloro-9-(methoxymethyl)-9*H*-purine (7.94 g, 40 mmol) in THF (80 mL) was added dropwise within 1 h and the reaction mixture was stirred for 2 h. Then, TMSCl (21.7 g, 200 mmol) was added dropwise within 20 min and stirred for 1 h. After addition of $NaHCO_{3(sat)}$ (20 mL) and $NaCl_{(sat)}$ (20 mL) the mixture was slowly warmed up to 25 °C. After addition of $NH_4Cl_{(sat)}$ (500 mL) the aqueous layer was extracted with CH_2Cl_2 (3 x 200 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc gradient = 5:1, 4:1, 3:1) yielded 6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 6.50 g, 60%) as a bright yellow oil.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957 (w), 1708 (w), 1586 (m), 1540 (m), 1492 (w), 1462 (w), 1360 (m), 1350 (m), 1307 (w), 1247 (m), 1183 (m), 1133 (m), 1101 (s), 1027 (w), 950 (w), 917 (w), 874 (m), 838 (vs), 776 (m), 759 (m), 650 (w).

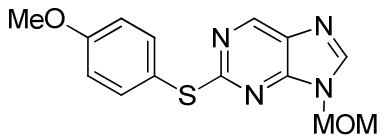
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.19 (s, 1H), 5.63 (s, 2H), 3.39 (s, 3H), 0.37 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 175.6, 151.5, 150.1, 144.4, 130.1, 74.4, 57.7, -1.9 ppm.

MS (70 eV, EI): m/z (%) = 270 (20), 257 (24), 255 (71), 240 (22), 235 (41), 225 (28), 95 (32), 93 (100), 73 (88), 45 (99).

HRMS (EI): m/z calc. for [$C_{10}H_{15}ClN_4OSi$] 270.0704; found: 270.0691.

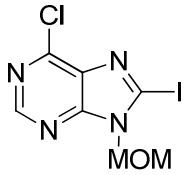
Synthesis of 9-(methoxymethyl)-2-((4-methoxyphenyl)thio)-9*H*-purine (6k)



4-Methoxy thiophenol (168 mg, 1.2 mmol) was added to a solution of *t*BuOK (224 mg, 2.0 mmol) in NMP (2 mL). After the mixture was stirred for 5 min at 110 °C, 2-chloro-9-(methoxymethyl)-9*H*-purine (**6g**, 193 mg, 1.0 mmol) was added and the resulting mixture was heated for 1 h. After cooling to 25 °C, EtOAc (30 mL) was added, the organic layer was washed with H_2O (3 x 15 mL) and $NaCl_{(sat)}$ (15 mL). The organic layer was dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, EtOAc) yielded 9-(methoxymethyl)-2-((4-methoxyphenyl)thio)-9*H*-purine (**6k**, 160 mg, 53%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.87 (s, 1H), 8.03 (s, 1H), 7.55-7.50 (m, 2H), 6.95-6.90 (m, 2H), 5.37 (s, 2H), 3.82 (s, 3H), 3.23 ppm (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.2, 160.6, 152.8, 149.1, 144.2, 137.2, 131.1, 120.7, 114.6, 73.7, 57.7, 55.4 ppm.
MS (70 eV, EI): m/z (%) = 304 (5), 303 (17), 302 (100), 301 (88), 272 (6), 271 (19), 259 (7), 257 (23), 139 (7), 45 (27).
HRMS (EI): m/z calc. for [$C_{14}H_{14}N_4O_2S$] 302.0837; found: 302.0829.

Synthesis of 6-chloro-8-iodo-9-(methoxymethyl)-9*H*-purine (8a)

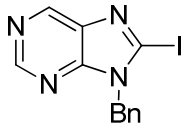


TMPZnCl·LiCl (0.92 mL, 1.2 M in THF, 1.1 mmol) was added dropwise to a solution of 6-chloro-9-(methoxymethyl)-9*H*-purine (**6a**, 199 mg, 1.0 mmol) in THF (1.5 mL). After stirring for 30 min, a solution of I_2 (305 mg, 1.2 mmol) in THF (4 mL) was added dropwise and the reaction mixture stirred for 1 h. Then, a mixture of $Na_2S_2O_{3(sat)}$/ $NH_4Cl_{(sat)}$ (1:2, 10 mL) was added, the aqueous layer was extracted with Et_2O (3 x 30 mL), the combined organic layers were washed with $NaCl_{(sat)}$ solution (10 mL) and dried (Na_2SO_4). The solvent was evaporated

in vacuo. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 1:2) yielded 6-chloro-8-iodo-9-(methoxymethyl)-9*H*-purine (**8a**, 317 mg, 98%) as a beige solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.71 (s, 1H), 5.61 (s, 2H), 3.42 ppm (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.5, 152.3, 149.6, 133.7, 107.4, 76.0, 57.6 ppm.
MS (70 eV, EI): m/z (%) = 323 (20), 296 (28), 295 (9), 294 (94), 292 (8), 197 (7), 169 (29), 168 (9), 167 (100), 77 (7), 45 (66).
HRMS (EI): m/z calc. for [$C_7H_6ClIN_4O$] 323.9275; found: 323.9266.

Synthesis of 9-benzyl-8-iodo-9*H*-purine (8b)



Method A: TMPZnCl·LiCl (0.92 mL, 1.2 M in THF, 1.1 mmol) was added dropwise to a solution of 9-benzyl-9*H*-purine (**6b**, 210 mg, 1.0 mmol) in THF (1.5 mL). After stirring for 30 min, a solution of I_2 (305 mg, 1.2 mmol) in THF (2 mL) was added dropwise and the reaction mixture stirred for 1 h. Then, a mixture of $Na_2S_2O_{3(sat)}$/ $NH_4Cl_{(sat)}$ (1:2, 10 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ Et_2O = 1:9) yielded 8-iodo-9-benzyl-9*H*-purine (**8b**, 270 mg, 80%) as a colorless solid.
Method B: TMPMgCl·LiCl (0.95 mL, 1.16 M in THF, 1.1 mmol) was added very slow to a solution of 9-benzyl-9*H*-purine (**6b**, 210 mg, 1.0 mmol) in THF (4 mL) at -60 °C. After 15 min of stirring, a solution of I_2 (380 mg, 1.5 mmol) in THF (3 mL) was added dropwise and the reaction mixture stirred for 2.5 h. After work-up and purification as described above 8-iodo-9-benzyl-9*H*-purine is obtained (**8b**, 284 mg, 84%) as a colorless solid.

mp (°C): 211-213.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3066 (w), 3026 (w), 2360 (m), 2340 (m), 1894 (w), 1738 (m), 1578 (s), 1494 (m), 1468 (m), 1448 (m), 1436 (m), 1420 (s), 1398 (s), 1364 (m), 1342 (s), 1328 (s), 1302 (s), 1294 (s), 1244 (s), 1218 (m), 1196 (m), 1164 (s), 1132 (m), 1094 (m), 1072 (m), 1028 (m), 1002 (w), 984 (m), 922 (m), 908 (m), 888 (m), 858 (w), 812 (m), 790 (m), 772 (m), 724 (vs), 692 (s), 672 (m), 648 (m), 622 (w).

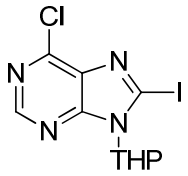
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.08 (s, 1H), 8.95 (s, 1H), 7.35-7.31 (m, 5H), 5.48 ppm (s, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 152.8, 147.1, 136.4, 134.7, 128.9, 128.5, 127.9, 108.3, 49.0 ppm.

MS (70 eV, EI): m/z (%) = 337 (5), 336 (41), 335 (18), 210 (16), 209 (100), 208 (9), 104 (6), 92 (7), 91 (84), 65 (16).

HRMS (EI): m/z calc. for [$C_{12}H_8IN_4$] 335.9872; found: 335.9859.

Synthesis of 6-chloro-8-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (8c)



TMPZnCl·LiCl (1.0 mL, 1.1 M in THF, 1.1 mmol) was added dropwise to a solution of 6-chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (**6c**, 239 mg, 1.0 mmol) in THF (1.5 mL). After stirring for 30 min, a solution of I_2 (305 mg, 1.2 mmol) in THF (2 mL) was added dropwise and the reaction mixture stirred for 1 h. Then, a mixture of $Na_2S_2O_3/NH_4Cl_{(sat)}$ (1:2, 10 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, CH_2Cl_2) yielded 6-chloro-8-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (**8c**, 220 mg, 60%) as a colorless solid.

mp (°C): 143-145.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3068 (w), 2970 (w), 2954 (w), 2938 (w), 2918 (w), 2840 (w), 2728 (w), 2594 (w), 2362 (vw), 2340 (vw), 1736 (vw), 1592 (vs), 1568 (s), 1554 (s), 1444 (s), 1432 (s), 1406 (m), 1384 (s), 1352 (m), 1334 (m), 1314 (s), 1280 (m), 1250 (s), 1224 (s), 1194 (m), 1174 (m), 1152 (s), 1124 (m), 1082 (s), 1062 (m), 1040 (vs), 1008 (s), 998 (s), 960 (m), 930 (s), 912 (s), 864 (s), 822 (m), 788 (m), 702 (w), 694 (vw), 660 (w), 626 (m), 618 (m).

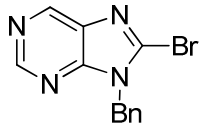
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.68 (s, 1H), 5.67 (dd, *J* = 11.4, 2.4 Hz, 1H), 4.25-4.19 (m, 1H), 3.79-3.71 (m, 1H), 3.20-3.07 (m, 1H), 2.20-2.13 (m, 1H), 1.94-1.63 ppm (m, 4H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 152.5, 151.6, 149.5, 134.3, 106.6, 87.4, 69.3, 28.8, 24.6, 23.3 ppm.

MS (70 eV, EI): m/z (%) = 282 (27), 281 (6), 280 (100), 245 (27), 127 (6), 118 (7), 99 (7), 91 (6), 85 (6).

HRMS (EI): m/z calc. for [$C_{10}H_{10}ClIN_4O$] 363.9588; found: 363.9580.

Synthesis of 9-benzyl-8-bromo-9*H*-purine (8d)



$TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (1.7 mL, 0.76 M in THF, 1.3 mmol) was added dropwise to a solution of 9-benzyl-9*H*-purine (**6b**, 210 mg, 1.0 mmol) and 1,2-dibromo-1,1,2,2-tetrachloroethane (326 mg, 1.0 mmol) in THF (2 mL). After 15 min of stirring, a mixture of $NH_{3(conc)}$/ $NH_4Cl_{(sat)}$ (1:3, 10 mL) was added, the aqueous layer was extracted with Et_2O (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, CH_2Cl_2/ MeOH gradient = 200:0, 200:1 to 100:1) yielded 9-benzyl-8-bromo-9*H*-purine (**8d**, 238 mg, 82%) as a colorless solid.

mp (°C): 130-131.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3028 (w), 2964 (vw), 2358 (vw), 2342 (vw), 1948 (vw), 1892 (vw), 1738 (w), 1582 (s), 1494 (w), 1472 (s), 1448 (m), 1432 (s), 1410 (m), 1372 (m), 1348 (s), 1330 (m), 1304 (s), 1242 (s), 1178 (s), 1134 (w), 1098 (m), 1074 (w), 1026 (w), 992 (w), 978 (w), 920 (w), 910 (m), 888 (w), 820 (w), 790 (w), 774 (w), 724 (vs), 692 (m), 676 (m), 624 (w), 604 (w).

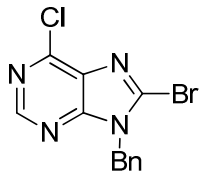
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.05 (s, 1H), 8.99 (s, 1H), 7.37-7.31 (m, 5H), 5.49 ppm (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 152.9, 152.5, 147.2, 134.5, 134.3, 134.2, 129.0, 128.5, 127.9, 47.6 ppm.

MS (70 eV, EI): m/z (%) = 290 (36), 289 (20), 288 (37), 287 (16), 209 (100),92 (13), 91 (87), 65 (28).

HRMS (EI): m/z calc. for [$C_{12}H_9BrN_4$] 288.0011; found: 287.9994.

Synthesis of 9-benzyl-8-bromo-6-chloro-9*H*-purine (8e)



$TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (1.3 mL, 0.95 M in THF, 1.2 mmol) was added dropwise to a solution of 9-benzyl-6-chloro-9*H*-purine (**6d**, 245 mg, 1.0 mmol) and 1,2-dibromo-1,1,2,2-tetrachloroethane (326 mg, 1.0 mmol) in THF (2 mL). After 15 min of stirring, a mixture of $NH_{3(conc)}$/ $NH_4Cl_{(sat)}$ (1:3, 10 mL) was added, the aqueous layer was extracted with Et_2O (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ CH_2Cl_2 gradient = 1:5 to 1:7) yielded 9-benzyl-8-bromo-6-chloro-9*H*-purine (**8e**, 240 mg, 75%) as a colorless solid.

mp (°C): 87-88.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3028 (w), 2960 (w), 2942 (w), 2360 (m), 2342 (w), 2216 (w), 1890 (vw), 1736 (m), 1696 (m), 1586 (s), 1556 (s), 1494 (m), 1464 (m), 1452 (s), 1434 (s), 1408 (m), 1374 (m), 1350 (m), 1326 (vs), 1242 (s), 1200 (s), 1192 (s), 1158 (m), 1144 (s), 1076 (m), 1024 (w), 1000 (m), 966 (vw), 940 (m), 892 (m), 868 (m), 814 (w), 788 (w), 772 (w), 724 (s), 704 (s), 692 (s), 674 (m), 638 (w).

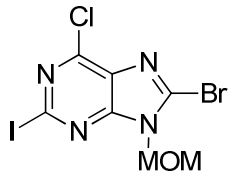
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.75 (s, 1H), 7.36-7.31 (m, 5H), 5.49 ppm (s, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 152.2, 152.1, 149.5, 134.3, 134.1, 134.0, 129.0, 128.7, 128.0, 48.3 ppm.

MS (70 eV, EI): m/z (%) = 324 (15), 323 (7), 322 (11), 245 (14), 244 (6), 243 (45), 92 (6), 91 (100), 65 (9).

HRMS (EI): m/z calc. for [$C_{12}H_8BrClN_4$] 321.9621; found: 321.9617.

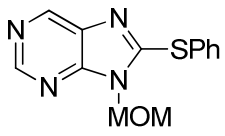
Synthesis of 8-bromo-6-chloro-2-iodo-9-(methoxymethyl)-9*H*-purine (8f)



$TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (1.3 mL, 0.95 M in THF, 1.2 mmol) was added dropwise to a solution of 6-chloro-2-iodo-9-(methoxymethyl)-9*H*-purine (**6e**, 325 mg, 1.0 mmol) and 1,2-dibromo-1,1,2,2-tetrachloroethane (456 mg, 1.4 mmol) in THF (2 mL). After stirring for 1 h, a mixture of $NH_{3(conc)}$/ $NH_4Cl_{(sat)}$ (1:3, 10 mL) was added, the aqueous layer was extracted with Et_2O (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc gradient = 3:1 to 2:1) yielded 8-bromo-6-chloro-2-iodo-9-(methoxymethyl)-9*H*-purine (**8f**, 348 mg, 87%) as a colorless solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.60 (s, 2H), 3.44 ppm (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.8, 149.0, 134.3, 131.6, 11.1, 74.9, 57.8 ppm.
MS (70 eV, EI): m/z (%) = 404 (16), 402 (13), 376 (12), 374 (48), 372 (35), 323 (15), 295 (13), 293 (40), 45 (100).
HRMS (EI): m/z calc. for [$C_7H_5BrClIN_4O$] 401.8380; found: 401.8376.

Synthesis of 9-methoxymethyl-8-(phenylthio)-9*H*-purine (8g)



*n*BuLi (0.86 mL, 2.44 M in hexane, 2.1 mmol) was added dropwise to a solution of 9-(methoxymethyl)-9*H*-purine (**6f**, 328 mg, 2.0 mmol) in THF (10 mL) at -78 °C. After 15 min of stirring, a solution of $PhSO_2SPh$ (651 mg, 2.6 mmol) in THF (2.6 mL) was added and the reaction mixture was slowly warmed up to 25 °C overnight. After addition of $NH_4Cl_{(sat)}$ (20 mL), the aqueous layer was extracted with CH_2Cl_2 (3 x 40 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, Et_2O) yielded 9-methoxymethyl-8-(phenylthio)-9*H*-purine (**8g**, 216 mg, 40%) as a colorless solid.

mp (°C): 79-80.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2936 (w), 2832 (w), 1704 (w), 1582 (m), 1562 (s), 1462 (m), 1450 (s), 1440 (s), 1410 (m), 1392 (m), 1348 (m), 1322 (s), 1286 (m), 1246 (s), 1232 (m), 1188 (m), 1140 (s), 1114 (vs), 1088 (m), 1060 (vs), 1024 (m), 1000 (w), 954 (w), 942 (w), 918 (s), 864 (w), 850 (w), 788 (w), 772 (m), 756 (vs), 720 (m), 704 (m), 690 (m), 682 (m), 638 (w), 622 (w), 606 (vw).

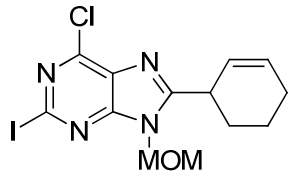
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.67 (s, 1H), 7.70-7.64 (m, 2H), 7.47-7.42 (m, 3H), 5.64 (s, 2H), 3.40 ppm (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 155.6, 154.0, 151.4, 148.5, 133.7, 131.6, 129.7, 129.6, 127.1, 73.7, 57.4 ppm.

MS (70 eV, EI): m/z (%) = 308 (18), 307 (16), 306 (47), 277 (15), 276 (20), 275 (38), 265 (30), 263 (100), 45 (96).

HRMS (EI): m/z calc. for [$C_{13}H_{11}ClN_4OS$] 306.0342; found: 306.0336.

Synthesis of 6-chloro-8-(cyclohex-2-en-1-yl)-2-iodo-9-(methoxymethyl)-9*H*-purine (8h)



TMPMgCl·LiCl (1 mL, 1.13 M in THF, 1.13 mmol) was added dropwise to a premixed solution of 6-chloro-2-iodo-9-(methoxymethyl)-9*H*-purine (**6e**, 325 mg, 1.0 mmol) in THF (1 mL) and $ZnCl_2$ (1.0 mL, 1.0 M in THF, 1.0 mmol) at -65 °C. After stirring for 30 min, CuCN·2LiCl (0.1 mL, 1.0 M in THF, 0.1 mmol) and 3-bromocyclohexene were added successive and the reaction mixture warmed up to 25 °C in 2 h. Then, a mixture of $NH_{3(conc)}$/ $NH_4Cl_{(sat)}$ (1:3, 10 mL) was added, the aqueous layer was extracted with Et_2O (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ Et_2O = 3:1) yielded 6-chloro-8-(cyclohex-2-en-1-yl)-2-iodo-9-(methoxymethyl)-9*H*-purine (**8h**, 340 mg, 84%) as a colorless solid.

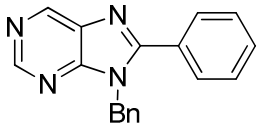
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 6.06-5.99 (m, 1H), 5.79-5.73 (m, 1H), 5.60 (s, 2H), 3.97-3.88 (m, 1H), 3.40 (s, 3H), 2.24-2.10 (m, 3H), 2.08-1.94 (m, 2H), 1.79-1.64 ppm (m, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 161.8, 154.5, 149.0, 130.8, 130.8, 124.3, 115.7, 73.2, 57.4, 35.5, 28.1, 24.5, 21.2 ppm.

MS (70 eV, EI): m/z (%) = 406 (13), 404 (39), 375 (13), 374 (28), 373 (19), 361 (28), 359 (23), 345 (14), 308 (15), 81 (14), 79 (14), 45 (100).

HRMS (EI): m/z calc. for [$C_{13}H_{14}ClIN_4O$] 403.9901; found: 403.9892.

Synthesis of 9-benzyl-8-phenyl-9*H*-purine (8i)



$TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (2.2 mL, 0.9 M in THF, 2 mmol) was added dropwise to a solution of 9-benzyl-9*H*-purine (**6d**, 210 mg, 1.0 mmol) in THF (2 mL). After stirring for 1 h, the resulting solution was treated with $Pd(dba)_2$ (38 mg, 5 mol%, 0.05 mmol), P(*o*-furyl)$_3$ (23 mg, 10 mol%, 0.1 mmol) and iodobenzene (225 mg, 1.1 mmol). The reaction mixture was stirred at 45 °C for 14 h, $NH_4Cl_{(sat)}$ (10 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, CH_2Cl_2) yielded 9-benzyl-8-phenyl-9*H*-purine (**8i**, 100 mg, 35%) as a colorless solid.

mp (°C): 119-120.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3034 (w), 2970 (vw), 2956 (vw), 2360 (w), 2342 (w), 1738 (w), 1608 (m), 1586 (s), 1520 (vw), 1496 (w), 1480 (m), 1454 (m), 1442 (m), 1422 (m), 1376 (m), 1364 (m), 1352 (s), 1298 (s), 1262 (m), 1250 (m), 1234 (m), 1152 (w), 1100 (w), 1076 (w), 1026 (w), 1004 (w), 990 (w), 930 (w), 918 (m), 910 (m), 888 (w), 856 (w), 830 (w), 798 (m), 780 (s), 718 (vs), 694 (vs), 650 (w), 622 (w), 606 (vw).

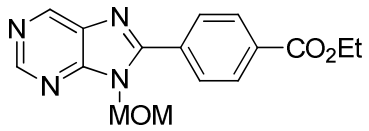
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.19 (s, 1H), 9.03 (s, 1H), 7.69-7.68 (m, 2H), 7.57-7.55 (m, 1H), 7.51-7.49 (m, 2H), 7.31-7.26 (m, 3H), 7.09-7.07 (m, 2H), 5.59 ppm (s, 2H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 156.5, 153.6, 152.3, 147.5, 135.8, 131.0, 129.3, 129.0, 128.9, 128.1, 126.7, 126.7, 47.0 ppm.

MS (70 eV, EI): m/z (%) = 287 (14), 286 (82), 285 (70), 272 (13), 209 (24), 182 (18), 91 (100), 65 (10).

HRMS (EI): m/z calc. for [$C_{18}H_{14}N_4$] 286.1218; found: 286.1217.

Synthesis of ethyl 4-(9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (8j)



TMPZnCl·LiCl (4.6 mL, 1.2 M in THF, 5.5 mmol) was added dropwise to a solution of 9-(methoxymethyl)-9*H*-purine (**6e**, 820 mg, 5.0 mmol) in THF (7 mL). After stirring for 1 h, the resulting solution was treated with $Pd(dba)_2$ (58 mg, 2 mol%, 0.1 mmol), P(*o*-furyl)$_3$ (46 mg, 4 mol%, 0.2 mmol) and ethyl 4-iodobenzoate (1.66 g, 6.0 mmol). The reaction mixture was stirred for 14 h, $NH_4Cl_{(sat)}$ (50 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, EtOAc) yielded ethyl 4-(9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**8j**, 1.51 g, 97%) as a colorless solid.

mp (°C): 117-119.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2978 (vw), 2932 (vw), 2830 (vw), 2362 (vw), 2340 (vw), 1712 (s), 1654 (vw), 1608 (w), 1594 (w), 1586 (w), 1570 (w), 1522 (vw), 1484 (w), 1466 (w), 1436 (w), 1410 (w), 1392 (w), 1370 (m), 1350 (m), 1314 (m), 1282 (vs), 1256 (s), 1218 (w), 1172 (w), 1156 (m), 1126 (m), 1112 (s), 1088 (s), 1034 (w), 1016 (m), 964 (w), 936 (w), 926 (w), 914 (w), 906 (w), 886 (w), 868 (m), 854 (w), 828 (vw), 792 (w), 778 (m), 764 (m), 718 (s), 696 (w), 656 (vw), 618 (vw), 608 (vw).

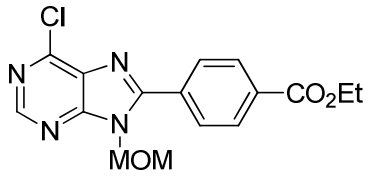
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.34 (s, 1H), 9.18 (s, 1H), 8.24-8.19 (m, 4H), 5.66 (s, 2H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.60 (s, 3H), 1.43 ppm (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 165.7, 156.8, 154.4, 152.8, 147.7, 133.3, 133.1, 132.0, 130.1, 129.8, 73.5, 61.5, 57.9, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 312 (18), 283 (13), 282 (64), 281 (77), 267 (17), 253 (13), 209 (17), 133 (11), 45 (100).

HRMS (EI): m/z calc. for [$C_{16}H_{16}N_4O_3$] 312.1222; found: 312.1216.

Synthesis of ethyl 4-(6-chloro-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (8k)



TMPZnCl·LiCl (1.1 mL, 1.0 M in THF, 1.1 mmol) was added dropwise to a solution of 6-chloro-9-(methoxymethyl)-9*H*-purine (**6a**, 199 mg, 1.0 mmol) in THF (2 mL). After 15 min of stirring, the resulting solution was treated with $Pd(dba)_2$ (8 mg, 1 mol%, 0.01 mmol), P(*o*-furyl)$_3$ (5 mg, 2 mol%, 0.02 mmol) and ethyl 4-iodobenzoate (348 mg, 1.2 mmol). The reaction mixture was stirred for 5 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 5:1) yielded ethyl 4-(6-chloro-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**8k**, 317 mg, 91%) as a colorless solid.

mp (°C): 142-144.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2940 (vw), 2830 (vw), 1714 (s), 1612 (vw), 1592 (m), 1566 (m), 1524 (vw), 1468 (w), 1448 (w), 1410 (w), 1388 (w), 1366 (w), 1342 (m), 1294 (m), 1266 (s), 1254 (s), 1238 (m), 1186 (w), 1176 (w), 1142 (s), 1090 (vs), 1032 (m), 1014 (m), 948 (m), 916 (m), 868 (m), 852 (w), 794 (w), 770 (m), 738 (m), 718 (m), 694 (w), 636 (vw), 620 (vw), 608 (w).

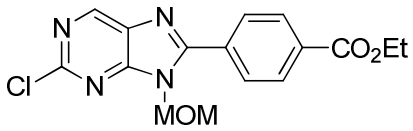
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.77 (s, 1H), 8.21-8.18 (m, 4H), 5.63 (s, 2H), 4.42 (q, *J* = 7.3 Hz, 2H), 3.58 (s, 3H), 1.42 ppm (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 165.7, 155.7, 154.2, 152.2, 150.6, 132.9, 132.0, 131.1, 130.0, 129.8, 73.9, 61.5, 57.8, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 348 (15), 346 (39), 317 (34), 316 (50), 315 (92), 314 (97), 300 (20), 286 (10), 271 (12), 243 (14), 45 (100).

HRMS (EI): m/z calc. for [$C_{16}H_{15}ClN_4O_3$] 346.0833; found: 346.0823.

Synthesis of ethyl 4-(2-chloro-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (8m)



TMPZnCl·LiCl (1.1 mL, 1.0 M in THF, 1.1 mmol) was added dropwise to a solution of 2-chloro-9-(methoxymethyl)-9*H*-purine (**6g**, 199 mg, 1.0 mmol) in THF (1 mL). After 15 min of stirring, the resulting solution was treated with $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and ethyl 4-iodobenzoate (348 mg, 1.2 mmol). The reaction mixture was stirred for 24 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 4:1) yielded ethyl 4-(2-chloro-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**8m**, 200 mg, 91%) as a colorless solid.

mp (°C): 142-143.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2986 (vw), 2946 (vw), 2362 (vw), 1716 (s), 1594 (m), 1578 (m), 1522 (vw), 1482 (w), 1464 (w), 1452 (w), 1412 (m), 1396 (w), 1364 (m), 1346 (s), 1312 (m), 1274 (s), 1252 (s), 1182 (w), 1168 (w), 1142 (s), 1124 (m), 1104 (s), 1082 (vs), 1034 (w), 1016 (s), 970 (vw), 932 (w), 910 (m), 874 (m), 856 (w), 794 (w), 776 (s), 732 (m), 720 (m), 704 (m), 690 (w), 676 (w), 636 (w), 612 (m).

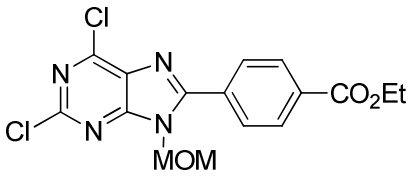
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.02 (s, 1H), 8.25-8.23 (m, 2H), 8.20-8.18 (m, 2H, 5.62 (s, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 3.61 (s, 3H), 1.44 ppm (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 165.7, 156.4, 155.6, 154.7, 149.8, 133.1, 132.4, 132.0, 130.2, 129.7, 73.4, 61.5, 57.8, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 348 (17), 346 (48), 318 (24), 317 (41), 316 (59), 315 (79), 301 (16), 287 (13), 271 (14), 243 (21), 45 (100).

HRMS (EI): m/z calc. for [$C_{16}H_{15}ClN_4O_3$] 346.0833; found: 346.0824.

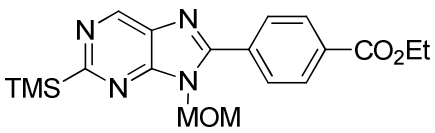
Synthesis of ethyl 4-(2,6-dichloro-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (8n)



TMPZnCl·LiCl (6.6 mL, 1.0 M in THF, 6.6 mmol) was added dropwise to a solution of 2,6-dichloro-9-(methoxymethyl)-9*H*-purine (**6h**, 1.4 g, 6.0 mmol) in THF (9 mL). After 15 min of stirring, the resulting solution was treated with $Pd(dba)_2$ (69 mg, 2 mol%, 0.12 mmol), P(*o*-furyl)$_3$ (56 mg, 4 mol%, 0.24 mmol) and ethyl 4-iodobenzoate (2.0 g, 7.2 mmol). The reaction mixture was stirred for 14 h, $NH_4Cl_{(sat)}$ (50 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 2:1) yielded ethyl 4-(2,6-dichloro-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**8n**, 1.4 g, 62%) as a beige solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.25-818 (m, 4H), 5.61 (s, 2H), 4.44 (q, *J* = 7.0 Hz, 2H), 3.61 (s, 3H), 1.44 ppm (t, *J* = 7.2 Hz, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.7, 156.4, 155.5, 153.1, 151.4, 133.3, 131.6, 130.3, 130.1, 129.9, 74.0, 61.5, 58.0, 14.3 ppm.
MS (70 eV, EI): m/z (%) = 382 (13), 380 (19), 352 (13), 351 (20), 350 (21), 349 (26), 335 (6), 274 (5), 45 (100).
HRMS (EI): m/z calc. for [$C_{16}H_{14}Cl_2N_4O_3$] 380.0443; found: 380.0437.

Synthesis of ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (8o)

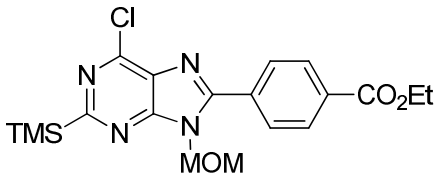


TMPZnCl·LiCl (1.0 mL, 1.18 M in THF, 1.2 mmol) was added dropwise to a solution of 9-(methoxymethyl)-2-(trimethylsily)-9*H*-purine (**6i**, 236 mg, 1.0 mmol) in THF (2 mL). After 15 min of stirring, the resulting solution was treated with $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and ethyl 4-iodobenzoate (348 mg, 1.2 mmol). The reaction mixture was stirred for 3 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the

aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 9:1) yielded ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**8o**, 200 mg, 52%) as a beige solid.

The analytical data match those of compound **20b**.

Synthesis of ethyl 4-(6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (8p)



TMPZnCl·LiCl (1.0 mL, 1.18 M in THF, 1.2 mmol) was added dropwise to a solution of 6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 271 mg, 1.0 mmol) in THF (2 mL). After 15 min of stirring, the resulting solution was treated with $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and ethyl 4-iodobenzoate (348 mg, 1.2 mmol). The reaction mixture was stirred at 45 °C for 14 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 10:1) yielded ethyl 4-(6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**8p**, 380 mg, 91%) as a colorless solid. The reaction was done also on 20 and 30 mmol scale furnishing the desired compound in 70% and 85% yield, respectively.

mp (°C): 121-122.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2902 (w), 1721 (m), 1552 (w), 1462 (w), 1365 (w), 1346 (w), 1274 (m), 1242 (m), 1111 (m), 1090 (s), 1022 (w), 1016 (w), 961 (w), 912 (w), 869 (w), 840 (vs), 775 (m), 759 (m), 718 (m), 620 (w).

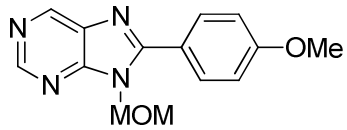
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.20 (s, 4H), 5.65 (s, 2H), 4.41 (q, *J*=7.1 Hz, 2H), 3.60 (s, 3H), 1.41 (t, *J*=7.1 Hz, 3H) 0.40 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 175.3, 165.8, 154.9, 153.5, 149.5, 132.8, 132.3, 130.0, 129.9, 129.8, 73.8, 61.4, 58.0, 14.3, -1.9 ppm.

MS (70 eV, EI): m/z (%) = 418 (55), 404 (100), 389 (64), 388 (51), 384 (100), 374 (72), 93 (57), 57 (46), 45 (83), 43 (56).

HRMS (EI): m/z calc. for [$C_{19}H_{23}ClN_4O_3Si$] 418.1228; found: 418.1225.

Synthesis of 9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purine (8q)



TMPZnCl·LiCl (1.0 mL, 1.18 M in THF, 1.2 mmol) was added dropwise to a solution of 9-(methoxymethyl)-9*H*-purine (**6e**, 164 mg, 1.0 mmol) in THF (2 mL). After 45 min of stirring, the resulting solution was treated with $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and 4-iodoanisole (281 mg, 1.2 mmol). The reaction mixture was stirred for 14 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, Et_2O) yielded 9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purine (**8q**, 165 mg, 61%) as a colorless solid.

mp (°C): 164-166.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3002 (vw), 2942 (w), 2842 (vw), 1610 (m), 1594 (m), 1572 (m), 1526 (w), 1474 (s), 1444 (m), 1420 (m), 1350 (s), 1318 (m), 1302 (m), 1290 (m), 1252 (s), 1228 (m), 1212 (m), 1184 (s), 1156 (m), 1128 (m), 1092 (vs), 1036 (s), 1016 (m), 978 (w), 920 (m), 906 (m), 854 (s), 826 (m), 796 (m), 766 (s), 742 (m), 704 (m), 664 (w), 644 (w), 636 (w).

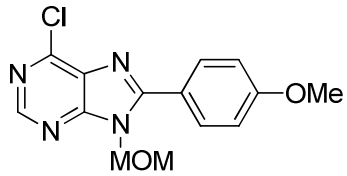
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.10 (s, 1H), 8.97 (s, 1H), 8.09-8.04 (m, 2H), 7.09-7.04 (m, 2H), 5.62 (s, 2H), 3.89 (s, 3H), 3.59 ppm (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 162.1, 156.8, 154.1, 152.3, 147.2, 133.6, 131.4, 120.9, 114.5, 73.2, 57.6, 55.5 ppm.

MS (70 eV, EI): m/z (%) = 270 (100), 240 (61), 239 (94), 227 (18), 226 (11), 225 (25), 209 (10), 134 (11), 133 (12), 45 (81).

HRMS (EI): m/z calc. for [$C_{14}H_{14}N_4O_2$] 270.1117; found: 270.1109.

Synthesis of 6-chloro-9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purine (8r)



TMPZnCl·LiCl (5.6 mL, 1.18 M in THF, 6.6 mmol) was added dropwise to a solution of 6-chloro-9-(methoxymethyl)-9*H*-purine (**6a**, 1.19 g, 6.0 mmol) in THF (9 mL). After 45 min of stirring, the resulting solution was treated with $Pd(dba)_2$ (69 mg, 2 mol%, 0.12 mmol), P(*o*-furyl)$_3$ (56 mg, 4 mol%, 0.24 mmol) and 4-iodoanisole (1.69 g, 7.2 mmol). The reaction mixture was stirred for 2 h, $NH_4Cl_{(sat)}$ (50 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, CH_2Cl_2, then pentane/ EtOAc gradient = 1:1 to 1:2) yielded 6-chloro-9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purine (**8r**, 1.74 g, 95%) as a colorless solid.

mp (°C): 157-159.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2816 (w), 1614 (s), 1568 (s), 1530 (m), 1480 (s), 1440 (m), 1420 (m), 1400 (m), 1364 (m), 1348 (s), 1306 (m), 1252 (s), 1240 (s), 1206 (m), 1180 (s), 1160 (s), 1140 (s), 1086 (vs), 1046 (s), 1024 (s), 962 (s), 946 (s), 870 (m), 844 (s), 814 (m), 784 (m), 744 (m), 718 (m), 704 (s), 646 (m), 618 (m).

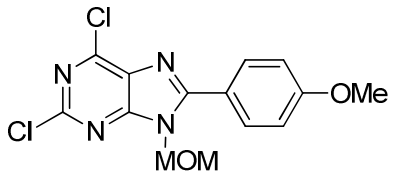
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.74 (s, 1H), 8.10 (d, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 9.1 Hz, 2H), 5.63 (s, 2H), 3.91 (s, 3H), 3.59 ppm (s, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 162.3, 157.0, 154.4, 151.5, 149.6, 131.6, 131.1, 120.3, 114.5, 73.9, 57.7, 55.5 ppm.

MS (70 eV, EI): m/z (%) = 306 (29), 305 (16), 304 (100), 276 (11), 275 (16), 274 (35), 273 (39), 261 (13), 259 (12), 45 (65).

HRMS (EI): m/z calc. for [$C_{14}H_{13}ClN_4O_2$] 304.0727; found: 304.0721.

Synthesis of 2,6-dichloro-9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purine (8s)



TMPZnCl·LiCl (8.8 mL, 1.25 M in THF, 11 mmol) was added dropwise to a solution of 2,6-dichloro-9-(methoxymethyl)-9*H*-purine (**6h**, 2.33 g, 10 mmol) in THF (10 mL). After 15 min of stirring, the resulting solution was treated with $Pd(dba)_2$ (58 mg, 1 mol%, 0.1 mmol), P(*o*-furyl)$_3$ (46 mg, 2 mol%, 0.2 mmol) and 4-iodoanisole (2.81 g, 12 mmol). The reaction mixture was stirred for 6 h, $NH_4Cl_{(sat)}$ (100 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 200 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, CH_2Cl_2) yielded 2,6-dichloro-9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purine (**8s**, 2.4 g, 71%) as a colorless solid.

mp (°C): 179-181.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2362 (m), 2340 (m), 1740 (vs), 1610 (w), 1560 (m), 1478 (w), 1458 (w), 1436 (w), 1424 (w), 1398 (w), 1366 (s), 1354 (s), 1314 (w), 1296 (w), 1262 (m), 1228 (m), 1218 (s), 1180 (m), 1158 (m), 1118 (w), 1082 (m), 1042 (w), 1020 (w), 964 (m), 882 (w), 840 (m), 802 (w), 742 (w), 666 (w).

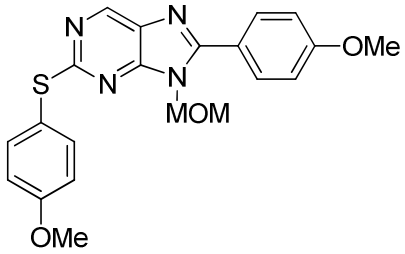
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.08-8.03 (m, 2H), 7.06-7.02 (m, 2H), 5.57 (s, 2H), 3.89 (s, 3H), 3.59 ppm (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 162.4, 157.6, 155.7, 152.2, 150.1, 131.6, 130.3, 120.0, 114.6, 74.0, 57.8, 55.5 ppm.

MS (70 eV, EI): m/z (%) = 340 (22), 338 (34), 310 (11), 309 (10), 308 (17), 307 (12), 295 (6), 293 (6), 133 (11), 45 (100).

HRMS (EI): m/z calc. for [$C_{14}H_{12}Cl_2N_4O_2$] 338.0337; found: 338.0327.

Synthesis of 9-(methoxymethyl)-8-(4-methoxyphenyl)-2-((4-methoxyphenyl)thio)-9*H*-purine (8t)



TMPZnCl·LiCl (1.5 mL, 0.72 M in THF, 1.1 mmol) was added dropwise to a solution of 9-(methoxymethyl)-2-((4-methoxyphenyl)thio)-9*H*-purine (**6k**, 302 mg, 1.0 mmol) in THF (2 mL). After 45 min of stirring the resulting solution was treated with $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and 4-iodoanisole (281 mg, 1.2 mmol). The reaction mixture was stirred for 14 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc gradient = 1:1 to 0:1) yielded 9-(methoxymethyl)-8-(4-methoxyphenyl)-2-((4-methoxyphenyl)thio)-9*H*-purine (**8t**, 345 mg, 85%) as an orange solid.

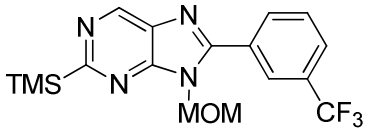
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.86 (s, 1H), 7.99 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 8.6 Hz, 2H), 7.02 (d, *J* = 9.1 Hz, 2H), 6.96 (d, *J* = 8.6 Hz, 2H), 5.35 (s, 2H), 3.86-3.85 (m, 6H), 3.35 ppm (s, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 166.0, 161.8, 160.4, 155.5, 154.9, 147.5, 137.2, 131.1, 130.7, 121.0, 120.8, 114.5, 114.4, 73.2, 57.7, 55.3, 55.3 ppm.

MS (70 eV, EI): m/z (%) = 409 (40), 408 (100), 407 (79), 363 (39), 69 (36), 57 (52), 55 (47), 44 (48), 43 (35), 41 (44).

HRMS (EI): m/z calc. for [$C_{21}H_{20}N_4O_3S$] 408.1256; found: 408.1252.

Synthesis of 9-(methoxymethyl)-8-(3-(trifluoromethyl)phenyl)-2-(trimethylsilyl)-9*H*-purine (8u)



TMPZnCl·LiCl (9.14 mL, 1.05 M in THF, 9.6 mmol) was added dropwise to a solution of 9-(methoxymethyl)-2-(trimethylsily)-9*H*-purine (**6i**, 1.9 g, 8.0 mmol) in THF (8 mL). After 15 min of stirring the resulting solution was treated with $Pd(dba)_2$ (92 mg, 2 mol%, 0.16 mmol), P(*o*-furyl)$_3$ (74 mg, 4 mol%, 0.32 mmol) and 1-iodo-3-(trifluoromethyl)benzene (3.05 g, 11.2 mmol). The reaction mixture was stirred for 24 h, $NH_4Cl_{(sat)}$ solution (50 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL), the combined organic layers were dried (MgSO4) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 3:1) yielded 9-(methoxymethyl)-8-(3-(trifluoromethyl)phenyl)-2-(trimethylsilyl)-9*H*-purine (**16**, 1.45 g, 48%) as a colorless solid.

mp (°C): 135-136.

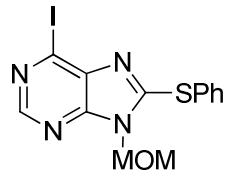
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3076 (vw), 2958 (w), 2902 (vw), 2840 (vw), 1620 (vw), 1574 (w), 1490 (vw), 1464 (w), 1434 (w), 1416 (m), 1368 (m), 1356 (m), 1322 (m), 1296 (w), 1280 (m), 1262 (w), 1250 (m), 1216 (w), 1180 (m), 1166 (m), 1154 (m), 1124 (s), 1110 (s), 1088 (s), 1034 (m), 928 (w), 912 (w), 840 (vs), 804 (s), 766 (m), 726 (m), 714 (w), 698 (m), 686 (w), 666 (vw), 652 (w), 624 (vw).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.27 (s, 1H), 8.46 (br, 1H), 8.36-8.34 (m, 1H), 7.85-7.83 (m, 1H), 7.73-7.69 (m, 1H), 5.69 (s, 2H), 3.64 (s, 3H), 0.44 ppm (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 174.7, 154.4, 153.0, 146.7, 132.8 (q, $^4J_{C\text{-}F}$=1 Hz), 132.1, 131.7 (q, $^2J_{C\text{-}F}$=33 Hz), 129.7, 129.6, 127.7 (q, $^3J_{C\text{-}F}$=4 Hz), 126.7 (q, $^3J_{C\text{-}F}$=4 Hz), 123.7 (q, $^1J_{C\text{-}F}$=272 Hz), 73.1, 57.9, -1.8 ppm.

HRMS (ESI): m/z calc. for [$C_{17}H_{19}F_3N_4OSi+H^+$] 381.1353; found: 381.1350.

Synthesis of 6-iodo-9-(methoxymethyl)-8-(phenylthio)-9*H*-purine (10a)



TMPZnCl·LiCl (1.2 mL, 1.0 M in THF, 1.2 mmol) was added dropwise to a solution of 9-(methoxymethyl)-8-(phenylthio)-9*H*-purine (**8g**, 272 mg, 1.0 mmol) in THF (10 mL). After stirring for 1 h, a solution of I_2 (305 mg, 1.2 mmol) in THF (3 mL) was added dropwise and the reaction mixture stirred for 1 h. Then, a mixture of $Na_2S_2O_{3(sat)}/NH_4Cl_{(sat)}$ (1:2, 10 mL) was added, the aqueous layer was extracted with Et_2O (3 x 30 mL), the combined organic layers were washed with $NaCl_{(sat)}$ solution (10 mL) and dried ($MgSO_4$). The solvents were evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc gradient = 3:1 to 2:1) yielded 6-iodo-9-(methoxymethyl)-8-(phenylthio)-9*H*-purine (**10a**, 200 mg, 50%) as a beige solid.

mp (°C): 106-108.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3042 (vw), 2994 (vw), 2932 (w), 2826 (vw), 1558 (s), 1444 (m), 1434 (s), 1416 (m), 1332 (m), 1314 (s), 1276 (m), 1238 (s), 1220 (m), 1180 (m), 1160 (w), 1126 (s), 1106 (vs), 1060 (s), 1026 (m), 974 (w), 932 (w), 908 (s), 854 (m), 786 (w), 764 (m), 752 (vs), 702 (m), 688 (m), 638 (w), 620 (w).

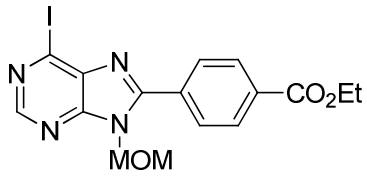
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.55 (s, 1H), 7.70-7.67 (m, 2H), 7.46-7.43 (m, 3H), 5.60 (s, 2H), 3.39 ppm (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 154.6, 151.6, 138.7, 134.7, 133.4, 129.6, 129.5, 127.6, 119.3, 73.8, 57.4 ppm.

MS (70 eV, EI): m/z (%) = 408 (24), 407 (16), 399 (13), 398 (96), 392 (11), 391 (100), 109 (12), 91 (14), 77 (11), 45 (51).

HRMS (EI): m/z calc. for [$C_{13}H_{11}IN_4OS$] 397.9698; found: 397.9669.

Synthesis of ethyl 4-(6-iodo-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (10b)



A solution of ethyl 4-(9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**8j**, 312 mg, 1.0 mmol) in THF (10 mL) was added dropwise to TMPMgCl·LiCl (1.3 mL, 0.94 M in THF, 1.2 mmol) at -20 °C. After stirring for 1 h, the resulting reaction mixture was added to a solution of I_2 (1.0 g, 3.9 mmol) in THF (2 mL) at 0 °C and the solution was stirred for 1 h. Then, a mixture of $Na_2S_2O_{3(sat)}$/ $NH_4Cl_{(sat)}$ (1:2, 20 mL) was added, the aqueous layer was extracted with EtOAc (3 x 50 mL), the combined organic layers were washed with $NaCl_{(sat)}$ solution (20 mL) and dried ($MgSO_4$). The solvents were evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 1:1) yielded ethyl 4-(6-iodo-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**10b**, 306 mg, 70%) as a beige solid.

mp (°C): 152-154.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2936 (vw), 2832 (vw), 2362 (vw), 1716 (s), 1580 (w), 1556 (s), 1522 (w), 1470 (m), 1434 (m), 1408 (w), 1386 (w), 1368 (w), 1338 (m), 1266 (s), 1254 (s), 1228 (m), 1186 (w), 1168 (m), 1132 (m), 1088 (vs), 1034 (m), 1014 (m), 912 (m), 870 (m), 848 (m), 792 (w), 776 (m), 768 (m), 732 (m), 716 (s), 696 (m), 634 (vw), 616 (vw).

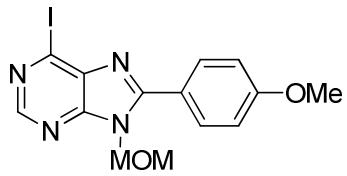
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.68 (s, 1H), 8.24-8.20 (m, 4H), 5.61 (s, 2H), 4.44 (q, *J* = 7.3 Hz, 2H), 3.59 (s, 3H), 1.44 ppm (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 165.7, 155.1, 152.2, 150.5, 138.1, 133.0, 132.1, 130.1, 129.9, 121.6, 73.8, 61.5, 57.8, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 439 (14), 438 (62), 409 (17), 408 (100), 407 (88), 393 (17), 239 (11), 238 (14), 221 (11), 207 (16), 45 (70).

HRMS (EI): m/z calc. for [$C_{16}H_{15}IN_4O_3$] 438.0189; found: 438.0182.

Synthesis of 6-iodo-9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purine (10c)



A solution of 9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purine (**8q**, 270 mg, 1.0 mmol) in THF (10 mL) was added dropwise to TMPMgCl·LiCl (1.3 mL, 0.94 M in THF, 1.2 mmol) at -20 °C. After stirring for 1 h, the resulting reaction mixture was added to a solution of I_2 (1.0 g, 3.9 mmol) in THF (2 mL) at -20 °C and the solution was stirred for 3 h. Then, a mixture of $Na_2S_2O_3$/ $NH_4Cl_{(sat)}$ (1:2, 20 mL) was added, the aqueous layer was extracted with EtOAc (3 x 50 mL), the combined organic layers were washed with $NaCl_{(sat)}$ (20 mL) and dried ($MgSO_4$). The solvents were evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ Et_2O = 1:1) yielded 6-iodo-9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purine (**10c**, 238 mg, 60%) as a beige solid.

mp (°C): 156-158.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2932 (w), 2832 (w), 1612 (m), 1562 (s), 1526 (m), 1466 (s), 1418 (m), 1358 (m), 1338 (m), 1296 (m), 1256 (s), 1246 (s), 1230 (m), 1184 (s), 1166 (m), 1138 (s), 1128 (s), 1090 (vs), 1038 (s), 1020 (m), 964 (w), 914 (s), 856 (m), 842 (s), 790 (m), 768 (s), 742 (m), 694 (m), 644 (m), 610 (m).

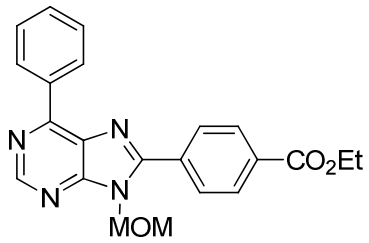
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.63 (s, 1H), 8.10-8.08 (m, 2H), 7.08-7.06 (m, 2H), 5.59 (s, 2H), 3.90 (s, 3H), 3.58 ppm (s, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 162.3, 156.3, 151.6, 150.6, 138.1, 131.7, 120.3, 120.2, 114.5, 73.9, 57.7, 55.5 ppm.

MS (70 eV, EI): m/z (%) = 397 (15), 396 (100), 366 (21), 365 (23), 269 (12), 239 (11), 238 (9), 197 (7), 133 (12), 45 (30).

HRMS (EI): m/z calc. for [$C_{14}H_{13}IN_4O_2$] 396.0083; found: 396.0074.

Synthesis of ethyl 4-(9-(methoxymethyl)-6-phenyl-9*H*-purin-8-yl)benzoate (10d)



A solution of ethyl 4-(9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**8j**, 312 mg, 1.0 mmol) in THF (10 mL) was added dropwise to TMPMgCl·LiCl (1.3 mL, 0.94 M in THF, 1.2 mmol) at -20 °C. After stirring for 1 h, $ZnCl_2$ (1.3 mL, 1.0 M in THF, 1.3 mmol) was added, the resulting reaction mixture was stirred for 30 min and warmed up to 25 °C. Then, $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and iodobenzene (265 mg, 1.3 mmol) were added. The reaction mixture was stirred for 14 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 5:1) yielded ethyl 4-(9-(methoxymethyl)-6-phenyl-9*H*-purin-8-yl)benzoate (**10d**, 245 mg, 63%) as a beige solid.

mp (°C): 156-157.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2938 (w), 2908 (w), 2838 (vw), 1708 (s), 1588 (m), 1560 (m), 1498 (w), 1466 (w), 1442 (w), 1428 (w), 1410 (w), 1368 (m), 1330 (m), 1282 (vs), 1254 (m), 1210 (m), 1184 (m), 1142 (m), 1126 (m), 1102 (s), 1082 (s), 1036 (m), 1018 (s), 980 (w), 954 (w), 934 (w), 914 (m), 874 (m), 864 (m), 854 (m), 770 (s), 752 (m), 718 (m), 694 (s), 686 (m), 670 (m), 646 (w), 626 (w).

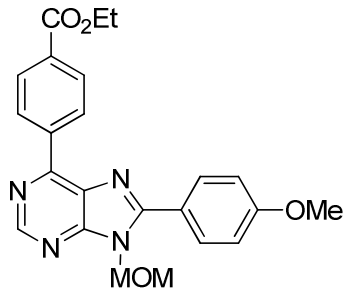
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.07 (s, 1H), 8.94-8.92 (m, 2H), 8.28-8.23 (m, 4H), 7.61-7.53 (m, 3H), 5.68 (s, 2H), 4.45 (q, *J* = 7.0 Hz, 2H), 3.62 (s, 3H), 1.45 ppm (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.8, 155.1, 154.7, 154.2, 152.4, 135.2, 132.8, 132.6, 131.2, 130.5, 130.0, 129.9, 129.8, 128.7, 73.4, 61.4, 57.6, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 388 (26), 359 (9), 358 (46), 357 (100), 343 (10), 329 (13), 285 (6), 209 (9), 45 (23).

HRMS (EI): m/z calc. for [$C_{22}H_{20}N_4O_3$] 388.1535; found: 388.1529.

Synthesis of ethyl 4-(9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purin-6-yl)benzoate (10e)



A solution of 9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purine (**8q**, 270 mg, 1.0 mmol) in THF (10 mL) was added dropwise to TMPMgCl·LiCl (1.3 mL, 0.94 M in THF, 1.2 mmol) at -20 °C. After stirring for 1 h, $ZnCl_2$ (1.3 mL, 1.0 M in THF, 1.3 mmol) was added, the resulting reaction mixture stirred for 30 min and warmed up to 25 °C. Then, $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and ethyl 4-iodobenzoate (359 mg, 1.3 mmol) were added. The reaction mixture was stirred for 14 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 3:1) yielded ethyl 4-(9-(methoxymethyl)-8-(4-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**10e**, 230 mg, 55%) as a beige solid.

mp (°C): 158-159.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2996 (vw), 2940 (w), 2930 (w), 2846 (vw), 1712 (m), 1614 (m), 1580 (m), 1558 (w), 1532 (w), 1476 (m), 1460 (m), 1448 (m), 1380 (w), 1364 (w), 1326 (m), 1294 (m), 1274 (s), 1254 (vs), 1182 (m), 1170 (m), 1144 (m), 1098 (s), 1082 (m), 1038 (m), 1020 (m), 914 (w), 878 (w), 838 (w), 770 (m), 744 (w), 706 (w), 642 (vw), 618 (vw).

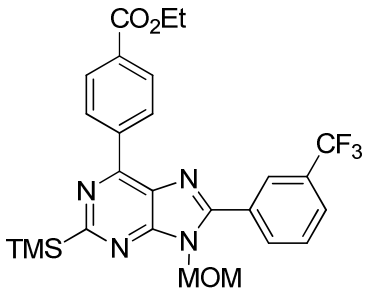
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.05-9.01 (m, 3H), 8.24-8.22 (m, 2H), 8.18-8.14 (m, 2H), 7.12-7.08 (m, 2H), 5.68 (s, 2H), 4.43 (q. *J* = 7.0 Hz, 2H), 3.92 (s, 3H), 3.62 (s, 3H), 1.44 ppm (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 166.3, 162.1, 156.4, 155.6, 151.7, 151.7, 139.5, 132.1, 131.5, 131.1, 129.8, 129.7, 121.0, 114.5, 73.4, 61.1, 57.5, 55.5, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 419 (21), 418 (86), 389 (9), 388 (43), 387 (100), 373 (17), 359 (15), 315 (9), 300 (9), 159 (8), 45 (28).

HRMS (EI): m/z calc. for [$C_{23}H_{22}N_4O_4$] 418.1641; found: 418.1640.

Synthesis of ethyl 4-(9-(methoxymethyl)-8-(3-(trifluoromethyl)phenyl)-2-(trimethylsilyl)-9*H*-purin-6-yl)benzoate (10f)



A solution of 9-(methoxymethyl)-8-(3-(trifluoromethyl)phenyl)-2-(trimethylsilyl)-9*H*-purine (**8u**, 380 mg, 1.0 mmol) in THF (1 mL) was added dropwise to TMPMgCl·LiCl (1.3 mL, 0.94 M in THF, 1.2 mmol) at -20 °C. After stirring for 1 h, $ZnCl_2$ (1.3 mL, 1.0 M in THF, 1.3 mmol) was added, the resulting reaction mixture stirred for 30 min and warmed up to 25 °C. Then, $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and ethyl 4-iodobenzoate (359 mg, 1.3 mmol) were added. The reaction mixture was stirred for 3h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ CH_2Cl_2 = 5:4) yielded ethyl 4-(9-(methoxymethyl)-8-(3-(trifluoromethyl)phenyl)-2-(trimethylsilyl)-9*H*-purin-6-yl)-benzoate (**10f**, 280 mg, 53%) as a beige solid.

mp (°C): 148-149.

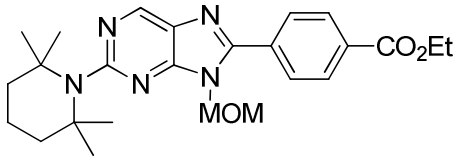
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2930 (vw), 2902 (vw), 2830 (vw), 1718 (s), 1598 (w), 1568 (m), 1506 (vw), 1464 (m), 1424 (w), 1388 (w), 1368 (w), 1326 (s), 1296 (m), 1270 (vs), 1246 (s), 1214 (w), 1190 (w), 1172 (m), 1156 (m), 1130 (s), 1102 (vs), 1088 (s), 1074 (s), 1042 (w), 1020 (m), 918 (w), 910 (w), 882 (w), 844 (vs), 822 (s), 808 (m), 774 (m), 758 (m), 728 (w), 694 (s), 670 (w), 652 (w).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.10-9.06 (m, 2H), 8.52 (br s, 1H), 8.45-8.42 (m, 1H), 8.27-8.23 (m, 2H), 7.87-7.84 (m, 1H), 7.76-7.71 (m, 1H), 5.72 (s, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 3.66 (s, 3H), 1.45 (t, *J* = 7.2 Hz, 3H), 0.49 (s, 9H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 174.0, 166.5, 154.6, 153.9, 150.8, 140.4, 133.0 (q, $^4J_{C\text{-}F}$=1 Hz), 131.9, 131.7 (q, $^2J_{C\text{-}F}$=33 Hz), 130.0, 129.8, 129.7, 129.7, 129.6, 127.5 (q, $^3J_{C\text{-}F}$=4 Hz), 126.8 (q, $^3J_{C\text{-}F}$=4 Hz), 123.8 (q, $^1J_{C\text{-}F}$=272 Hz), 73.2, 61.1, 57.8, 14.3, -1.7 ppm.

HRMS (ESI): m/z calc. for [$C_{26}H_{27}F_3N_4O_3Si+H^+$] 529.1877; found: 529.1872.

Synthesis of ethyl 4-(9-(methoxymethyl)-2-(2,2,6,6-tetramethylpiperidin-1-yl)-9*H*-purin-8-yl)benzoate (12a)



$TMP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (0.8 mL, 0.8 M in THF, 0.6 mmol) was added dropwise to a solution of ethyl 4-(2-chloro-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**8m**, 173 mg, 0.5 mmol) in THF (1 mL). After stirring for 2 h, $NH_4Cl_{(sat)}$ (10 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 4:1) yielded ethyl 4-(9-(methoxymethyl)-2-(2,2,6,6-tetramethylpiperidin-1-yl)-9*H*-purin-8-yl)benzoate (**12a**, 200 mg, 89%) as a yellow solid.

mp (°C): 193-195.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2968 (w), 2946 (w), 2872 (vw), 2362 (vw), 2340 (vw), 2148 (m), 1712 (m), 1618 (w), 1600 (s), 1578 (w), 1546 (s), 1534 (s), 1508 (w), 1472 (w), 1456 (w), 1418 (s), 1366 (m), 1336 (m), 1320 (w), 1278 (vs), 1254 (m), 1182 (w), 1158 (m), 1128 (m), 1106 (s), 1094 (s), 1068 (w), 1042 (w), 1014 (m), 992 (w), 970 (w), 940 (w), 914 (m), 880 (w), 870 (w), 856 (w), 788 (w), 776 (w), 738 (w), 710 (m), 684 (w).

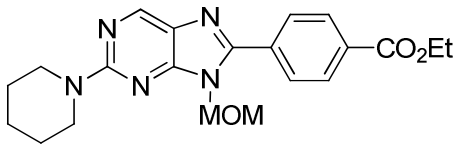
^{1}H-NMR (300 MHz, $CDCl_3$): δ =8.94 (s, 1H), 8.14-8.10 (m, 2H), 8.03-8.00 (m, 2H), 5.17 (s, 2H), 4.40 (q, *J*=7.1 Hz, 2H), 3.56 (s, 3H), 1.90-1.70 (m, 18H), 1.41 ppm (t, *J*=7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.0, 164.7, 148.3, 144.7, 133.5, 131.4, 129.8, 128.3, 120.0, 118.5, 72.9, 61.2, 57.4, 57.0, 53.4, 27.7, 14.8, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 451 (40), 328 (27), 327 (100), 297 (27), 296 (45), 268 (38), 232 (19), 171 (21), 69 (24), 45 (32).

HRMS (EI): m/z calc. for [$C_{25}H_{33}N_5O_3$] 451.2583; found: 451.2582.

Synthesis of ethyl 4-(9-(methoxymethyl)-2-(piperidin-1-yl)-9*H*-purin-8-yl)benzoate (12b)



$PIP_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (1.3 mL, 0.42 M in THF, 0.6 mmol) was added dropwise to a solution of ethyl 4-(2-chloro-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**8m**, 173 mg, 0.5 mmol) in THF (1 mL). After stirring for 2 h, the reaction mixture was heated to 50 °C for 20 h. $NH_4Cl_{(sat)}$ (10 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 4:1) yielded ethyl 4-(9-(methoxymethyl)-2-(piperidin-1-yl)-9*H*-purin-8-yl)benzoate (**12b**, 70 mg, 35%) as a pale yellow solid.

mp (°C): 206-207.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2931 (m), 2863 (m), 2830 (w), 2149 (m), 1704 (s), 1636 (s), 1610 (m), 1545 (vs), 1532 (s), 1474 (m), 1456 (m), 1443 (m), 1418 (m), 1398 (m), 1361 (m), 1320 (m), 1280 (s), 1272 (s), 1238 (s), 1200 (m), 1177 (m), 1096 (vs), 1071 (m), 1059 (m), 1016 (m), 1023 (m), 998 (m), 960 (w), 937 (w), 883 (w), 868 (m), 858 (m), 813 (w), 800 (w), 774 (s), 729 (w), 706 (m), 684 (m), 658(w).

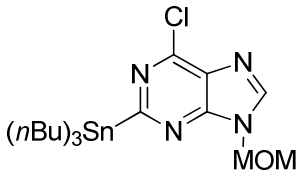
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.63 (s, 1H), 8.13-8.09 (m, 2H), 7.98-7.94 (m, 2H), 5.12 (s, 2H), 4.62-4.59 (m, 2H), 4.40 (q, *J*=7.1 Hz, 2H), 3.68-3.65 (m, 2H), 3.52 (s, 3H), 1.85-1.73 (br m, 6H), 1.40 ppm (t, *J*=7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.9, 165.4, 162.7, 147.5, 145.0, 133.2, 131.5, 129.8, 128.4, 117.8, 72.6, 61.2, 57.3, 49.6, 27.2, 25.9, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 396 (13), 395 (49), 380 (27), 364 (10), 352 (19), 351 (22), 350 (100), 323 (12), 322 (21), 294 (11), 45 (27), 41 (14).

HRMS (EI): m/z calc. for [$C_{21}H_{25}N_5O_3$] 395.1957; found: 395.1957.

Synthesis of 6-chloro-9-(methoxymethyl)-2-(tributylstannyl)-9*H*-purine (13a)



*n*BuLi (4.2 mL, 2.5 M in hexane, 10.5 mmol) was added to a solution of TMPH (1.41 g, 10 mmol) in THF (2.6 mL) and hexane (1.3 mL) at -78 °C and the reaction mixture was stirred for 1 h. Subsequently, a solution of 6-chloro-9-(methoxymethyl)-9*H*-purine (**8a**, 397 mg, 2.0 mmol) in THF (3.5 mL) was added dropwise and the reaction mixture was stirred for 1 h. Then, nBu$_3$SnCl (2.71 mL, 10 mmol) was added dropwise and stirred for 1 h. After addition of $NH_4Cl_{(sat)}$ (4 mL) the mixture was slowly warmed up to 25 °C within 14 h. After addition of $NaHCO_{3(sat)}$ (4 mL) the aqueous layer was extracted with Et_2O (3 x 20 mL). The combined organic layers were dried ($MgSO_4$), filtered over celite® and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc gradient = 6:1 to 4:1) yielded 6-chloro-9-(methoxymethyl)-2-(tributylstannyl)-9*H*-purine (**13a**, 822 mg, 84%) as a bright yellow oil.

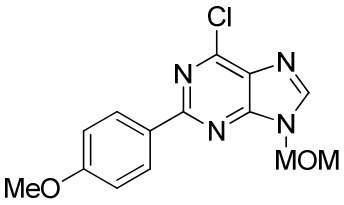
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (m), 2922 (m), 2872 (w), 2852 (m), 1582 (m), 1536 (s), 1492 (w), 1464 (m), 1410 (w), 1394 (w), 1376 (w), 1338 (s), 1304 (w), 1246 (m), 1178 (s), 1134 (s), 1102 (vs), 1076 (m), 1046 (w), 1024 (m), 960 (w), 942 (m), 918 (m), 876 (w), 858 (m), 794 (w), 764 (s), 694 (m), 668 (m), 650 (m).

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.15 (s, 1H), 5.64 (s, 2H), 3.40 (s, 3H), 1.64-1.59 (m, 6H), 1.37-1.20 (m, 12H), 0.89 ppm (t, *J*=7.4 Hz, 9H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 182.6, 151.3, 149.5, 143.6, 129.9, 74.2, 57.6, 28.9 (t, $^3J_{C\text{-}Sn}$=11 Hz), 27.2 (t, $^2J_{C\text{-}Sn}$=28 Hz), 13.7, 10.7 ppm (t, $^1J_{C\text{-}Sn}$=173 Hz).

HRMS (ESI): m/z calc. for [$C_{19}H_{33}ClN_4OSn+H^+$] 489.1438; found: 489.1443.

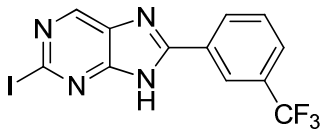
Synthesis of 6-chloro-9-(methoxymethyl)-2-(4-methoxyphenyl)-9*H*-purine (14b)



$Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol), 4-iodoanisole (280 mg, 1.2 mmol) and CuI (38 mg, 20 mol%, 0.20 mmol) were successively added to a solution of 6-chloro-9-(methoxymethyl)-2-(tributylstannyl)-9*H*-purine (**13a**, 488 mg, 1.0 mmol) in DMF (4 mL) and the resulting reaction mixture was stirred at 80 °C for 12 h. After cooling to 25 °C, the solution was diluted with Et_2O (50 mL). The organic layer was washed with H_2O (3 x 20 mL), was dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 1:2) and trituration with pentane yielded 6-chloro-9-(methoxymethyl)-2-(4-methoxyphenyl)-9*H*-purine (**14b**, 185 mg, 60%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.47-8.42 (m, 2H), 8.19 (s, 1H), 7.00-6.95 (m, 2H), 5.65 (s, 2H), 3.88 (s, 3H), 3.44 ppm (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 162.0, 159.7, 152.9, 151.0, 145.3, 144.6, 130.1, 129.0, 113.9, 74.4, 57.6, 55.4 ppm.
MS (70 eV, EI): m/z (%) = 306 (27), 305 (14), 304 (85), 276 (17), 275 (36), 274 (49), 273 (100), 239 (10), 225 (9), 45 (55).
HRMS (EI): m/z calc. for [$C_{14}H_{13}ClN_4O_2$] 304.0727; found: 304.0722.

Synthesis of 2-iodo-8-(3-(trifluoromethyl)phenyl)-purine (16)



I_2 (609 mg, 2.4 mmol) was added to a solution of 9-(methoxymethyl)-8-(3-(trifluoromethyl)phenyl)-2-trimethylsilyl-9*H*-purine (**8u**, 380 mg, 1.0 mmol) and AgOTf (617 mg, 2.4 mmol) in $CHCl_3$ (13 mL) and the resulting reaction mixture was stirred at 1.5 h. $NaHCO_{3(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (4 x 30 mL), the combined organic layers were dried ($MgSO_4$) and were filtered over celite®. The solvent

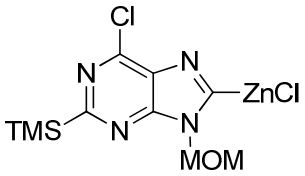
was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 3:1) yielded 2-iodo-8-(3-(trifluoromethyl)phenyl)-purine (**16**, 300 mg, 77%) as a white solid.

mp (°C): 249-254.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3064 (vw), 2938 (w), 2830 (br) 2782 (w), 2700 (w), 2662 (w), 1616 (w), 1586 (w), 1572 (m), 1520 (vw), 1464 (w), 1436 (vw), 1406 (w), 1338 (s), 1318 (s), 1274 (m), 1244 (w), 1226 (m), 1168 (m), 1112 (vs), 1094 (s), 1070 (m), 998 (vw), 938 (m), 924 (m), 862 (w), 846 (w), 808 (w), 788 (w), 728 (m), 704 (m), 690 (m), 666 (w), 652 (vw).
^{1}H-NMR (400 MHz, CD_3OD/ $CDCl_3$): δ = 8.74 (br s, 1H), 8.43 (br s, 1H), 8.36-8.34 (br m, 1H), 7.80-7.78 (br m, 1H), 7.70-7.66 (br m, 1H).
^{13}C-NMR (100 MHz, CD_3OD/ $CDCl_3$): δ = 181.7, 132.2 (q, $^{2}J_{C\text{-}F}$=33 Hz), 131.2 (br), 130.4, 129.6, 128.7 (q, $^{3}J_{C\text{-}F}$=4 Hz), 124.8 (q, $^{3}J_{C\text{-}F}$=4 Hz), 124.7 (q, $^{1}J_{C\text{-}F}$=272 Hz), 119.1 ppm.
HRMS (ESI): m/z calc. for [$C_{12}H_6F_3IN_4$+H^+] 390.9662; found: 390.9658.

2.2. Full functionalization of the purine scaffold

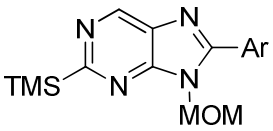
2.2.1. Typical procedures 1-5

TP1: Typical procedure for the preparation of (6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)zinc(II) chloride (17)



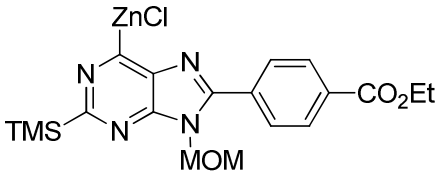
In a Schlenk-flask equipped with a stirring bar and septum TMPZnCl·LiCl (1.2 equiv, 1.0 M in THF) was added dropwise to a 1 M solution of 6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 1-30 mmol) in THF at 25 °C and stirred for 15 min resulting in a reddish-brown solution.

TP2: Typical procedure for the reduction of the 6-chloropurine derivatives 18e and 8p



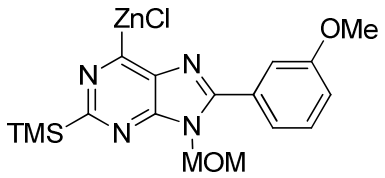
To a solution of the 6-chloropurine derivative **18e** or **8p** (5-20 mmol) in EtOH/ MeOH (1:1) or EtOH/ THF (1:1) at 45 °C were added Pd/ C (20 wt%) and HCO_2NH_4 (2 equiv). The solution was slowly stirred at 45 °C. When the reaction started proceeding (intensive bubbling) the mixture was stirred for further 30-60 min until the starting material was completely consumed as monitored by TLC. The solution was filtered through celite®. After washing the cake with plenty of EtOAc (400-750 mL) and concentration *via* rotary evaporation, the crude material was redissolved in CH_2Cl_2 (100 mL) and the undissolved HCO_2NH_4 was filtered off. After concentration *via* rotary evaporation, the crude material was purified by flash column chromatography.

TP3: Typical procedure for the preparation of (8-(4-(ethoxycarbonyl)phenyl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-6-yl)zinc(II) chloride (20b)



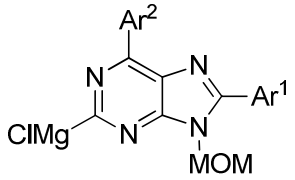
In a microwave-vessel equipped with a stirring bar and septum, ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**19b**, 1-10 mmol) was added to TMPZnCl·LiCl (1.5 equiv, 1.0 M in THF). After sealing the vessel, the reaction mixture was stirred at 90 °C for 2 h under microwave irradiation furnishing a very dark blue solution.

TP4: Typical procedure for the preparation of 9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purin-6-yl)zinc(II) chloride (20a)



In a microwave-vessel equipped with a stirring bar and septum, $ZnCl_2$ (1.6 equiv, 1.0 M in THF) was added to TMPMgCl·LiCl (1.5 equiv, 1.0 M in THF) and stirred at 25 °C for 1.5 h. 9-(Methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (**19a**, 1-5 mmol) was added. After sealing the vessel, the reaction mixture was stirred at 90 °C for 1 h under microwave irradiation furnishing a very dark green solution.

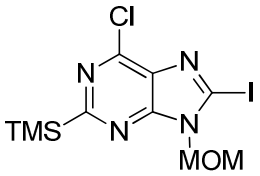
TP5: Typical procedure for the I/ Mg-exchange at C2 of the purine derivatives 23a-b



To a solution of the 2-iodopurine derivative **23a** or **23b** (1.0 mmol) in dry THF (10 mL), was added dropwise a solution of *i*PrMgCl (0.67 mL, 1.78 M in THF, 1.2 mmol) at -78 °C. The solution was stirred for 30 min at -78 °C prior to a second addition of *i*PrMgCl (0.3 mmol) and further stirring for 30 min.

2.2.2. Synthesis of compounds 18a-24h

Synthesis of 6-chloro-8-iodo-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (18a)

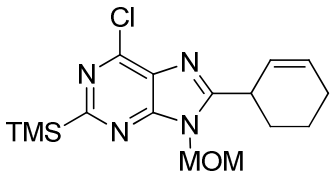


6-Chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 271 mg, 1.0 mmol) was metalated according to **TP1** and the resulting solution was added dropwise to a solution of I_2

(330 mg, 1.3 mmol) in THF (1.5 mL) at 0 °C. After stirring the reaction mixture at 25 °C for 1 h, $Na_2S_2O_{3(sat)}$ (10 mL) and $NH_4Cl_{(sat)}$ (10 mL) were added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 7:1) yielded 6-chloro-8-iodo-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**18a**, 300 mg, 77%) as a slightly yellow solid.

mp (°C): 98-99.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2955 (w), 2364 (w), 1741 (w), 1577 (w), 1547 (m), 1425 (w), 1398 (w), 1361 (w), 1331 (w), 1290 (w), 1244 (m), 1201 (m), 1177 (w), 1136 (w), 1106 (m), 1045 (w), 959 (w), 917 (w), 874 (m), 843 (vs), 777 (m), 758 (m).
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.60 (s, 2H), 3.39 (s, 3H), 0.37 ppm (s, 9H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 175.6, 152.9, 148.3, 132.4, 106.7, 75.7, 57.7, -2.0 ppm.
MS (70 eV, EI): m/z (%) = 396 (8), 383 (16), 381 (47), 366 (17), 361 (35), 351 (17), 269 (19), 95 (18), 93 (54), 73 (41), 45 (100).
HRMS (EI): m/z calc. for [$C_{10}H_{14}ClIN_4OSi$] 395.9670; found: 395.9664.

Synthesis of 6-chloro-8-(cyclohex-2-en-1-yl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (18b)



6-Chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 271 mg, 1.0 mmol) was metalated according to **TP1** and the resulting solution was cooled to -30 °C, treated with CuCN·2LiCl (0.05 mL, 1.0 M in THF, 5 mol%, 0.05 mmol) and 3-bromocyclohexene (193 mg, 1.2 mmol) and slowly warmed up to 25 °C. After stirring at this temperature for 12 h, $NH_4Cl_{(sat)}$ (10 mL) and $NH_{3(conc)}$ (1 mL) were added, the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 15:1) yielded 6-chloro-8-(cyclohex-2-en-1-yl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**18b**, 320 mg, 91%) as a colorless oil.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3029 (w), 2937 (w), 2837 (w), 2867 (w), 1740 (w), 1534 (m), 1495 (w), 1461 (w), 1449 (w), 1431 (w), 1358 (m), 1246 (m), 1204 (w), 1182 (w), 1138 (m), 1128 (m), 1084 (m), 968 (w), 917 (w), 896 (w), 874 (w), 837 (vs), 805 (w), 776 (m), 75 (m), 722 (w), 702 (w), 624 (m), 637 (m).

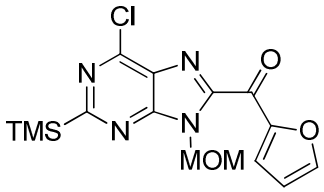
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.98-5.91 (m, 1H), 5.76-5.71 (m, 1H), 5.65 (s, 2H), 3.94-3.86 (m, 1H), 3.35 (s, 3H), 2.18-1.88 (m, 5H), 1.74-1.62 (m, 1H), 0.34 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 174.0, 160.7, 153.0, 148.4, 130.2, 129.4, 124.7, 72.8, 57.3, 35.5, 28.1, 24.4, 21.3, -1.9 ppm.

MS (70 eV, EI): m/z (%) = 352 (35), 351 (23), 350 (100), 335 (25), 320 (23), 307 (52), 305 (27), 93 (67), 73 (45), 45 (71).

HRMS (EI): m/z calc. for [$C_{16}H_{23}ClN_4OSi$] 350.1330; found: 350.1328.

Synthesis of (6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)(furan-2-yl)methanone (18c)



6-Chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 271 mg, 1.0 mmol) was metalated according to **TP1** and the resulting solution was cooled to 0 °C, treated with $Pd(PPh_3)_4$ (25 mg, 2 mol%, 0.02 mmol), and furan-2-carbonyl chloride (170 mg, 1.3 mmol) and slowly warmed up to 25 °C. After stirring at this temperature for 6 h, $NH_4Cl_{(sat)}$ (10 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 9:1) yielded (6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)(furan-2-yl)methanone (**18c**, 200 mg, 55%) as a yellowish solid.

mp (°C): 119-120.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3151 (w), 3121 (w), 2956 (w), 2899 (w), 1654 (m), 1577 (w), 1546 (m), 1467 (m), 1447 (m), 1393 (m), 1375 (w), 1345 (w), 1257 (m), 1245 (m), 1189 (w), 1156 (w), 1138 (m), 1119 (m), 1085 (m), 1033 (w), 1021 (w), 976 (w), 948 (w), 920 (w), 881 (m), 839 (vs), 771 (s), 644 (w), 622 (w).

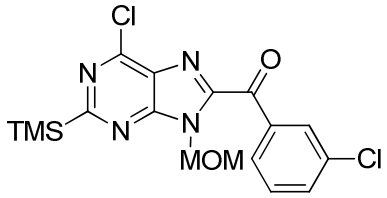
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.23 (dd, *J* = 3.7, 0.8 Hz, 1H), 7.81 (dd, *J* = 1.7, 0.7 Hz, 1H), 6.68 (dd, *J* = 3.7, 1.7 Hz, 1H), 6.12 (s, 2H), 3.40 (s, 3H), 0.41 ppm (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 178.2, 171.0, 152.3, 152.2, 150.7, 149.3, 146.3, 129.1, 126.0, 113.2, 74.6, 57.8, -2.0 ppm.

MS (70 eV, EI): m/z (%) = 364 (33), 349 (42), 329 (30), 321 (32), 319 (28), 269 (69), 95 (77), 93 (100), 81 (23), 73 (59), 45 (100).

HRMS (EI): m/z calc. for [$C_{15}H_{17}ClN_4O_3Si$] 364.0758; found: 364.0758.

Synthesis of (6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)(3-chlorophenyl)methanone (18d)



6-Chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 271 mg, 1.0 mmol) was metalated according to **TP1** and the resulting solution cooled to 0 °C, treated with $Pd(PPh_3)_4$ (25 mg, 2 mol%, 0.02 mmol), and 3-chlorobenzoyl chloride (228 mg, 1.3 mmol) and slowly warmed up to 25 °C. After stirring at this temperature for 6 h, $NH_4Cl_{(sat)}$ (10 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 20:1) yielded (6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)(3-chlorophenyl)methanone (**18d**, 187 mg, 46%) as a pale yellow oil.

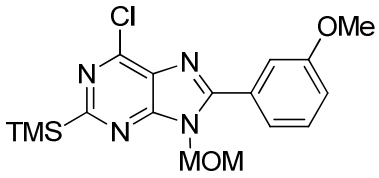
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2957 (w), 1727 (w), 1665 (m), 1574 (m), 1544 (m), 1456 (m), 1430 (w), 1371 (m), 1354 (w), 1235 (s), 1185 (m), 1140 (m), 1121 (m), 1081 (s), 982 (w), 848 (w), 934 (w), 877 (m), 841 (vs), 760 (s), 725 (m), 694 (w), 684 (w).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.34-8.33 (m, 1H), 8.32-8.29 (m, H), 7.65-7.62 (m, 1H), 7.51-7.47 (m, 1H), 6.07 (s, 2H), 3.38 (s, 3H), 0.42 ppm (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 183.7, 178.4, 152.6, 52.1, 146.7, 136.9, 134.9, 134.3, 131.1, 129.9, 129.6, 129.0, 74.7, 57.8, -2.0 ppm.

MS (70 eV, EI): m/z (%) = 408 (25), 393 (45), 365 (35), 269 (48), 139 (62), 93 (67), 85 (38), 73 (36), 71 (64), 57 (100), 56 (36), 45 (51), 43 (81), 41 (37).
HRMS (EI): m/z calc. for [$C_{17}H_{18}Cl_2N_4O_2Si$] 408.0576; found: 408.0569.

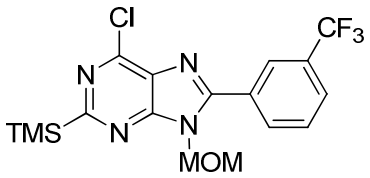
Synthesis of 6-chloro-9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (18e)



6-Chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 2.30 g, 8.5 mmol) was metalated according to **TP1** and the resulting solution was treated with $Pd(dba)_2$ (129 mg, 2 mol%, 0.17 mmol), P(*o*-furyl)$_3$ (79 mg, 4 mol%, 0.34 mmol) and iodo-3-methoxybenzene (2.59 g, 11.1 mmol). After stirring the reaction mixture at 45 °C for 14 h, $NH_4Cl_{(sat)}$ (50 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc gradient = 20:1, 10:1, 5:1) yielded 6-chloro-9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (**18e**, 2.3 g, 72%) as a colorless solid. The reaction was also done on 20 and 25 mmol scale furnishing the desired compound in 67% and 65% yield, respectively.

mp (°C): 169-170.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 1739 (w), 1606 (w), 1581 (w), 1550 (w), 1486 (w), 1352 (w), 1252 (m), 1138 (w), 1094 (m), 1079 (w), 1047 (m), 964 (w), 914 (w), 884 (w), 869 (m), 841 (vs), 791 (m), 778 (m), 758 (w), 728 (w).
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.70-7.65 (m, 2H), 7.46-7.41 (m, 1H), 7.11-7.08 (m, 1H), 5.65 (s, 2H), 3.88 (s, 3H), 3.60 (s, 3H), 0.40 ppm (s, 9H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 174.8, 159.9, 156.1, 153.6, 149.1, 130.1, 129.9, 129.5, 122.2, 117.7, 114.7, 73.8, 58.0, 55.5, -1.9 ppm.
MS (70 eV, EI): m/z (%) = 378 (32), 376 (88), 361 (67), 346 (34), 345 (45), 341 (74), 331 (58), 296 (36), 73 (50), 45 (100).
HRMS (EI): m/z calc. for [$C_{17}H_{21}ClN_4O_2Si$] 376.1122; found: 376.1119.

Synthesis of 6-chloro-9-(methoxymethyl)-8-(3-(trifluoromethyl)phenyl)-2-(trimethylsilyl)-9*H*-purine (18f)



6-Chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 271 mg, 1.0 mmol) was metalated according to **TP1** and the resulting solution was treated with $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and iodo-3-(trifluoromethyl)benzene (354 mg, 1.3 mmol). After stirring the reaction mixture at 45 °C for 14 h, $NH_4Cl_{(sat)}$ (10 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 10:1) yielded 6-chloro-9-(methoxymethyl)-8-(3-(trifluoromethyl)phenyl)-2-(trimethylsilyl)-9*H*-purine (**18f**, 370 mg, 89%) as a colorless solid.

mp (°C): 123.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2961 (w), 1602 (w), 1579 (w), 1544 (m), 1463 (w), 1368 (w), 1328 (m), 1306 (m), 1263 (m), 1249 (m), 1128 (vs), 1106 (s), 1093 (s), 1079 (m), 914 (m), 877 (m), 845 (s), 815 (s), 773 (m), 729 (w), 702 (m), 689 (m), 654 (w).

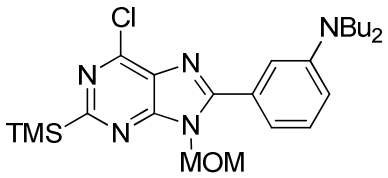
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.43 (s, 1H), 8.33 (d, *J*=7.87 Hz, 1H), 7.82 (d, *J*=7.87 Hz, 1H), 7.69 (t, *J*=7.87 Hz, 1H), 5.65 (s, 2H), 3.61 (s, 3H), 0.41 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 175.4, 154.4, 153.4, 148.6, 133.0 (q, $^4J_{C\text{-}F}$=1 Hz), 131.6 (q, $^2J_{C\text{-}F}$=33 Hz), 129.9, 129.6, 129.3, 127.8 (q, $^3J_{C\text{-}F}$=4 Hz), 126.8 (q, $^3J_{C\text{-}F}$=4 Hz), 123.6 (q, $^1J_{C\text{-}F}$=272 Hz), 73.7, 57.9, -1.9 ppm.

MS (70 eV, EI): m/z (%) = 414 (13), 399 (40), 384 (22), 383 (18), 379 (38), 369 (25), 334 (20), 93 (44), 73 (31), 45 (100).

HRMS (EI): m/z calc. for [$C_{17}H_{18}ClF_3N_4OSi$] 414.0891; found: 414.0882.

Synthesis of *N*,*N*-dibutyl-3-(6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)aniline (18g)



6-Chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 271 mg, 1.0 mmol) was metalated according to **TP1** and the resulting solution was treated with $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and *N*,*N*-dibutyl-3-iodoaniline (431 mg, 1.3 mmol). After stirring the reaction mixture at 45 °C for 3 h, $NH_4Cl_{(sat)}$ (10 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 19:1) yielded *N*,*N*-dibutyl-3-(6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)aniline (**18g**, 475 mg, 74%) as a yellow solid.

mp (°C): 98-99.

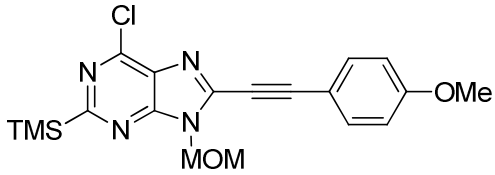
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2934 (w), 2872 (w), 2360 (w), 2342 (vw), 1736 (w), 1606 (w), 1572 (m), 1548 (m), 1494 (m), 1464 (m), 1456 (m), 1398 (w), 1366 (m), 1348 (m), 1310 (w), 1286 (w), 1258 (m), 1244 (m), 1214 (m), 1200 (w), 1158 (w), 1138 (m), 1098 (s), 1046 (m), 1012 (vw), 992 (vw), 962 (w), 912 (w), 878 (w), 840 (vs), 830 (s), 776 (s), 756 (m), 728 (m), 696 (m), 670 (w), 616 (w).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.36-7.28 (m, 3H), 6.82-6.79 (m, 1H), 5.68 (s, 2H), 3.62 (s, 3H), 3.36-3.31 (m, 4H), 1.65-1.55 (m, 4H), 1.43-1.31 (m, 4H), 0.99-0.94 (m, 6H), 0.42 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 174.1, 157.4, 153.6, 148.8, 148.3, 130.0, 129.7, 129.1, 116.5, 114.0, 112.6, 73.8, 57.9, 50.8, 29.3, 20.3, 13.9, -1.9 ppm.

HRMS (ESI): m/z calc. for [$C_{24}H_{36}ClN_5OSi+H^+$] 474.2450; found: 474.2448.

Synthesis of 6-chloro-9-(methoxymethyl)-8-((4-methoxyphenyl)ethynyl)-2-(trimethylsilyl)-9*H*-purine (18h)



6-Chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine (**6j**, 271 mg, 1.0 mmol) was metalated according to **TP1** and the resulting solution was added dropwise to a solution of I_2 (300 mg, 1.2 mmol) in THF (1.0 mL) at 0 °C. After stirring the reaction mixture at 25 °C for 1 h, NEt_3 (121 mg, 1.2 mmol), CuI (8 mg, 4 mol%, 0.04 mmol), $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.02 mmol) and ethynyl-4-methoxybenzene (172 mg, 1.3 mmol) were successively added. After stirring the resulting mixture at 25 °C for 3 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 7:1) yielded 6-chloro-9-(methoxymethyl)-8-((4-methoxyphenyl)ethynyl)-2-(trimethylsilyl)-9*H*-purine (**18h**, 300 g, 75%) as a colorless solid.

mp (°C): 167-168.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2968 (w), 2935 (w), 2896 (w), 2836 (w), 2218 (w), 1605 (w), 1579 (w), 1544 (m), 1516 (m), 1456 (w), 1341 (w), 1296 (w), 1254 (m), 1244 (s), 1202 (w), 1170 (m), 1133 (m), 1113 (s), 1079 (m), 1030 (m), 965 (w), 917 (w), 841 (s), 828 (vs), 769 (m), 700 (m), 622 (m), 615 (m).

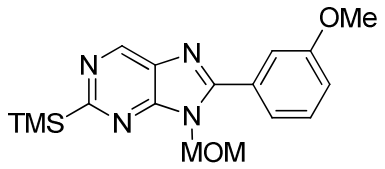
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 9.0 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 5.74 (s, 2H), 3.84 (s, 3H), 3.46 (s, 3H), 0.39 ppm (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 175.9, 161.4, 151.4, 149.3, 139.6, 134.2, 130.1, 114.4, 112.0, 98.6, 77.0, 73.9, 57.9, 55.4, -1.9 ppm.

MS (70 eV, EI): m/z (%) = 402 (38), 401 (32), 400 (96), 385 (45), 365 (65), 55 (35), 95 (34), 93 (100), 73 (44), 45 (84).

HRMS (EI): m/z calc. for [$C_{19}H_{21}ClN_4O_2Si$] 400.1122; found: 400.1114.

Synthesis of 9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (19a)



6-Chloro-9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (**18e**, 5.87 g, 15.6 mmol) dissolved in MeOH/ THF (70 mL/ 70 mL) was reduced according to **TP2**. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 3:1) afforded 9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (**19a**, 4.83 g, 90%) as a white solid.

mp (°C): 116-117.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2998 (vw), 2956 (vw), 2898 (vw), 2836 (vw), 1574 (m), 1506 (vw), 1486 (w), 1464 (w), 1440 (w), 1426 (w), 1418 (vw), 1400 (vw), 1368 (w), 1354 (w), 1320 (w), 1288 (w), 1256 (w), 1246 (m), 1240 (m), 1234 (m), 1212 (w), 1202 (w), 1182 (w), 1144 (w), 1110 (w), 1086 (m), 1054 (m), 1030 (m), 932 (vw), 910 (vw), 902 (w), 880 (w), 840 (vs), 794 (w), 782 (m), 768 (m), 754 (m), 726 (m), 690 (w), 672 (w), 662 (w), 620 (w).

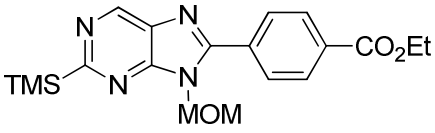
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.21 (s, 1H), 7.69-7.65 (m, 2H), 7.44 (t, *J* = 7.9 Hz, 1H), 7.11-7.07 (m, 1H), 5.66 (s, 2H), 3.87 (s, 3H), 3.61 (s, 3H), 0.41 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 174.0, 160.0, 156.1, 153.3, 146.1, 132.2, 130.1, 130.0, 122.0, 117.6, 114.5, 73.2, 57.9, 55.5, -1.8 ppm.

MS (70 eV, EI): m/z (%) = 343 (27), 342 (74), 341 (27), 327 (58), 312 (26), 311 (41), 297 (100), 212 (41), 89 (46), 73 (30), 45 (52).

HRMS (EI): m/z calc. for [$C_{17}H_{22}N_4O_2Si$] 342.1512; found: 342.1504.

Synthesis of ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (19b)



Ethyl 4-(6-chloro-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**8p**, 8.0 g, 19 mmol) dissolved in MeOH/ EtOH (50 mL/ 50 mL) was reduced according to **TP2**. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 3:1) yielded ethyl 4-

(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**19b**, 7.1 g, 95%) as a colorless solid.

mp (°C): 179-180.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (w), 2937 (w), 2900 (w), 2832 (w), 1714 (m), 1586 (w), 1575 (w), 1473 (w), 1461 (w), 1411 (w), 1361 (m), 13141 (w), 1298 (w), 1271 (m), 1245 (m), 1184 (m), 1152 (m), 1105 (m), 1105 (m), 1084 (s), 1014 (w), 928 (w), 910 (w), 839 (vs), 776 (m), 756 (m), 718 (m), 700 (w).

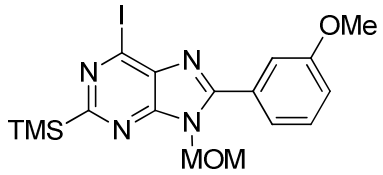
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.24 (s, 1H), 8.20 (s, 4H), 5.67 (s, 2H), 4.40 (q, *J* = 7.2 Hz, 2H), 3.60 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H), 0.41 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 174.7, 165.8, 154.8, 153.0, 146.8, 132.9, 132.6, 132.2, 130.0, 129.6, 73.1, 61.4, 57.9, 14.3, -1.8 ppm.

MS (70 eV, EI): m/z (%) = 384 (79), 383 (25), 369 (61), 351 (30), 350 (30), 338 (25), 337 (100), 89 (36), 73 (24), 45 (31).

HRMS (EI): m/z calc. for [$C_{19}H_{24}N_4O_3Si$] 384.1618; found: 384.1620.

Synthesis of 6-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (21a)



9-(Methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (**19a**, 685 mg, 2.0 mmol) was metalated according to **TP4** and the resulting solution was added dropwise to a solution of I_2 (609 mg, 2.4 mmol) in THF (2 mL) at 0 °C. After stirring the reaction mixture at 25 °C for 1 h, $Na_2S_2O_{3(sat)}$ (10 mL) and $NH_4Cl_{(sat)}$ (10 mL) were added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 15:1) yielded 6-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (**21a**, 600 mg, 64%) as a colorless solid.

mp (°C): 164-166.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3000 (vw), 2952 (vw), 2938 (vw), 2894 (vw), 2836 (vw), 2364 (vw), 2340 (vw), 1736 (vw), 1606 (vw), 1590 (vw), 1570 (w), 1538 (m), 1504 (w), 1484 (w), 1462 (w), 1444 (w), 1428 (w), 1414 (w), 1388 (w), 1372 (w), 1352 (w), 1324 (w), 1314 (w), 1288 (vw), 1246 (s), 1210 (m), 1188 (w), 1154 (w), 1148 (w), 1120 (w), 1092 (s), 1078 (m), 1048 (m), 994 (vw), 952 (vw), 912 (w), 886 (m), 844 (vs), 830 (s), 794 (m), 768 (s), 758 (m), 730 (m), 692 (w), 668 (w), 658 (w), 624 (vw).

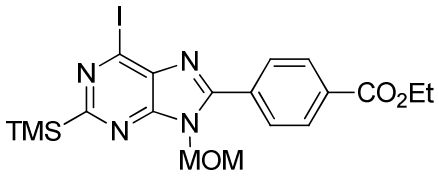
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.69-7.64 (m, 2H), 7.44 (t, *J* = 8.1 Hz, 1H), 7.11-7.07 (m, 1H), 5.61 (s, 2H), 3.88 (s, 3H), 3.59 (s, 3H), 0.39 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 175.3, 159.9, 155.2, 149.8, 136.8, 130.1, 129.7, 122.3, 121.2, 117.5, 114.9, 73.8, 58.0, 55.5, -1.8 ppm.

MS (70 eV, EI): m/z (%) = 468 (67), 453 (27), 438 (21), 423 (18), 342 (19), 341 (74), 185 (30), 73 (91), 69 (21), 45 (100).

HRMS (EI): m/z calc. for [$C_{17}H_{21}IN_4O_2Si$] 468.0478; found: 468.0480.

Synthesis of ethyl 4-(6-iodo-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (21b)



Ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**19b**, 385 mg, 1.0 mmol) was metalated according to **TP3** and the resulting solution was added dropwise to a solution of I_2 (440 mg, 1.7 mmol) in THF (1.5 mL) at 0 °C. After stirring the reaction mixture at 25 °C for 30 min, $Na_2S_2O_{3(sat)}$ (10 mL) and $NH_4Cl_{(sat)}$ (10 mL) were added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 15:1) yielded ethyl 4-(6-iodo-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**21b**, 390 mg, 76%) as a colorless solid.

mp (°C): 137-139.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2984 (vw), 2954 (w), 2900 (w), 2840 (vw), 1718 (m), 1614 (vw), 1578 (w), 1560 (w), 1540 (m), 1516 (w), 1460 (w), 1426 (w), 1408 (vw), 1386 (w), 1364 (w), 1354

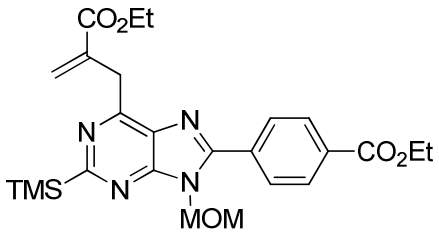
(w), 1344 (m), 1296 (w), 1274 (s), 1252 (s), 1244 (s), 1210 (m), 1180 (w), 1154 (m), 1124 (m), 1110 (m), 1090 (vs), 1034 (m), 1016 (m), 942 (w), 914 (w), 840 (vs), 798 (m), 774 (s), 760 (m), 746 (m), 718 (m), 698 (m), 690 (m), 662 (vw), 642 (vw), 628 (w), 616 (m).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.22 (s, 4H), 5.63 (s, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 3.61 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H), 0.41 ppm (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 175.8, 165.8, 154.1, 149.7, 136.7, 132.7, 132.4, 130.0, 129.9, 121.7, 73.7, 61.4, 58.0, 14.3, -1.9 ppm.

HRMS (ESI): m/z calc. for [$C_{19}H_{23}IN_4O_3Si+H^+$] 511.0657; found: 511.0652.

Synthesis of ethyl 4-(6-(2-(ethoxycarbonyl)allyl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (21c)



Ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**19b**, 385 mg, 1.0 mmol) was metalated according to **TP3** and the resulting solution cooled to -20 °C. After dropwise addition of CuCN·2LiCl (0.25 mL, 1.0 M in THF, 25 mol%, 0.25 mmol) the mixture was stirred for 15 min and ethyl 2-(bromomethyl)acrylate[67] was added. The reaction mixture was slowly warmed to 25 °C (within 8 h) and quenched by the addition of $NH_4Cl_{(sat)}$ (20 mL) and $NH_{3(conc)}$ (2 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 5:1) yielded ethyl 4-(6-(2-(ethoxycarbonyl)allyl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**21c**, 220 mg, 68%) as a pale yellow oil.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2980 (w), 2958 (w), 2904 (w), 1716 (s), 1636 (w), 1615 (w), 1587 (m), 1566 (m), 1464 (w), 1369 (w), 1344 (w), 1272 (s), 1246 (m), 1152 (m), 1094 (s), 1016 (m), 925 (m), 841 (vs), 778 (m), 722 (m), 700 (m), 693 (m), 622 (m).

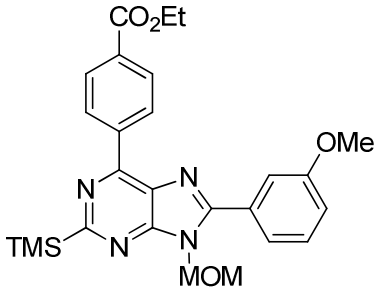
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.16 (s, 4H), 6.29 (s, 1H), 5.61-5.60 (m, 3H), 4.41-4.34 (m, 2H), 4.29 (s, 2H), 4.19-4.12 (m, 2H), 3.57 (s, 3H), 1.41-1.36 (m, 3H), 1.22-1.17 (m, 3H), 0.32 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 174.0, 167.0, 165.9, 157.0, 153.5, 152.6, 137.5, 133.2, 132.3, 130.8, 129.9, 129.7, 126.4, 73.2, 61.3, 60.6, 57.8, 35.4, 14.3, 14.1, -1.9 ppm.

MS (70 eV, EI): m/z (%) = 496 (72), 467 (28), 452 (40), 451 (100), 424 (62), 423 (85), 379 (34), 75 (31), 73 (94), 45 (70).

HRMS (EI): m/z calc. for [$C_{25}H_{32}N_4O_5Si$] 496.2142; found: 496.2140.

Synthesis of ethyl 4-(9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purin-6-yl)benzoate (21d)



9-(Methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (**19a**, 1.71 g, 5.0 mmol) was metalated according to **TP4** and the resulting solution was added dropwise to a solution of $Pd(dba)_2$ (57 mg, 2 mol%, 0.10 mmol), $P(o\text{-furyl})_3$ (46 mg, 4 mol%, 0.20 mmol) and ethyl 4-iodobenzoate (2.42 g, 8.5 mmol) in dry THF (8 mL) at 25 °C. The reaction mixture was stirred for 12 h, $NH_4Cl_{(sat)}$ (10 mL) was added, the aqueous layer was extracted with EtOAc (2 x 20 mL), the combined organic layers were dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. The crude material was purified by flash column chromatography (silicagel, isohexane/ CH_2Cl_2 gradient = 1:2, 1:3) to afford ethyl 4-(9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purin-6-yl)benzoate (**21d**, 1.56 g, 63%) as an off-white powder.

mp (°C): 134-136.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2992 (vw), 2948 (vw), 2934 (vw), 2898 (vw), 2832 (vw), 1714 (m), 1572 (m), 1558 (m), 1484 (w), 1462 (w), 1412 (w), 1390 (w), 1362 (w), 1346 (w), 1282 (s), 1252 (m), 1214 (m), 1202 (w), 1188 (w), 1150 (w), 1130 (m), 1104 (m), 1086 (m), 1052 (m), 1026 (m), 964 (vw), 916 (w), 888 (w), 854 (s), 840 (vs), 790 (m), 780 (m), 762 (m), 728 (w), 702 (w), 676 (w), 664 (w), 624 (vw).

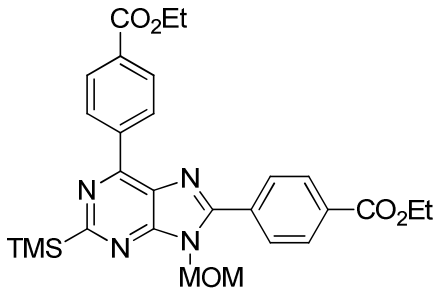
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.09-9.05 (m, 2H), 8.24-8.20 (m, 2H), 7.78-7.74 (m, 2H), 7.47 (t, *J* = 8.1 Hz, 1H), 7.13-7.09 (m, 1H), 5.72 (s, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 3.90 (s 3H), 3.63 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H), 0.47 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 173.4, 166.5, 160.0, 155.5, 154.8, 150.3, 140.5, 131.8, 130.3, 130.1, 130.0, 129.8, 129.6, 122.2, 117.1, 115.0, 73.4, 61.1, 57.9, 55.5, 14.4, -1.7 ppm.

MS (70 eV, EI): m/z (%) = 491 (26), 490 (86), 489 (100), 476 (18), 475 (52), 460 (22), 459 (31), 446 (20), 445 (63), 45 (20).

HRMS (EI): m/z calc. for [$C_{26}H_{30}N_4O_4Si$] 490.2036; found: 490.2021.

Synthesis of diethyl 4,4'-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine-6,8-diyl)dibenzoate (21e)



Ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**19b**, 385 mg, 1.0 mmol) was metalated according to **TP3** and the resulting solution added dropwise to a mixture of $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and ethyl 4-iodobenzoate (470 mg, 1.7 mmol) in THF (1 mL). After stirring the reaction mixture for 20 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 15:1) yielded diethyl 4,4'-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purine-6,8-diyl)dibenzoate (**21e**, 280 mg, 53%) as a colorless solid.

mp (°C): 184-186.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2982 (w), 2958 (w), 2903 (w), 1717 (s), 1584 (w), 1572 (m), 1464 (w), 1366 (w), 1342 (w), 1256 (s), 1247 (s), 1195 (m), 1183 (m), 1159 (m), 1099 (s), 1087 (s), 1019 (m), 914 (w), 873 (m), 842 (vs), 817 (m), 787 (m), 777 (m), 757 (m), 727 (m), 705 (m), 618 (w).

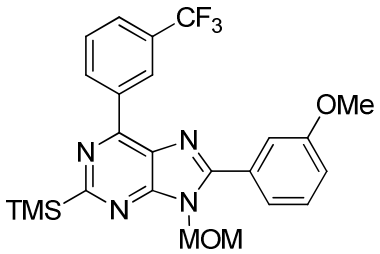
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.08-9.04 (m, 2H), 8.30-8.20 (m, 6H), 5.71 (s, 2H), 4.47-4.38 (m, 4H), 3.62 (s, 3H), 1.45-1.40 (m, 6H), 0.46 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 173.9, 166.5, 165.9, 154.7, 154.3, 150.8, 140.5, 133.1, 132.5, 131.9, 130.0, 129.9, 129.8, 129.7, 129.6, 73.3, 61.4, 61.1, 57.9, 14.3, 14.3, -1.7 ppm.

MS (70 eV, EI): m/z (%) = 532 (72), 531 (100), 517 (72), 502 (34), 501 (33), 487 (82), 89 (32), 73 (38), 45 (68).

HRMS (EI): m/z calc. for [$C_{28}H_{32}N_4O_5Si$] 532.2142; found: 532.2206.

Synthesis of 9-(methoxymethyl)-8-(3-methoxyphenyl)-6-(3-(trifluoromethyl)phenyl)-2-(trimethylsilyl)-9*H*-purine (21f)



9-(Methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purine (**19a**, 342 mg, 1.0 mmol) was metalated according to **TP4** and the resulting solution was added dropwise to a solution of $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(o-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and 1-iodo-3-(trifluoromethyl)benzene (462 mg, 1.7 mmol) in THF (1 mL) at 25 °C. The reaction mixture was stirred for 24 h, $NH_4Cl_{(sat)}$ (10 mL) was added. The aqueous layer was extracted with EtOAc (2 x 20 mL), the combined organic layers were washed with $NaCl_{(sat)}$ (20 mL) and dried (Na_2SO_4). The solvents were evaporated *in vacuo*. The crude material was purified by flash column chromatography (silicagel, pentane/ CH_2Cl_2 gradient = 4:1, 2:1) to afford 9-(methoxymethyl)-8-(3-methoxyphenyl)-6-(3-(trifluoromethyl)phenyl)-2-(trimethylsilyl)-9*H*-purine (**21f**, 268 mg, 55%) as an off-white powder.

mp (°C): 167-169.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3078 (vw), 3002 (vw), 2962 (vw), 2902 (vw), 2838 (vw), 1576 (m), 1494 (m), 1464 (w), 1442 (w), 1412 (w), 1340 (m), 1314 (m), 1302 (m), 1288 (m), 1262 (m), 1242 (m), 1216 (w), 1200 (w), 1188 (w), 1158 (m), 1124 (s), 1112 (s), 1094 (m), 1072 (m), 1048 (w), 920 (w), 904 (w), 878 (m), 842 (vs), 802 (m), 790 (m), 780 (m), 762 (w), 726 (w), 698 (m), 682 (w), 626 (vw), 610 (vw).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.30 (s, 1H), 9.24 (d, *J* = 7.8 Hz, 1H), 7.79-7.68 (m, 4H), 7.48 (t, *J* = 8.3 Hz, 1H), 7.12 (m, 1H), 5.74 (s, 2H), 3.91 (s, 3H), 3.64 (s, 3H), 0.48 ppm (s, 9H).

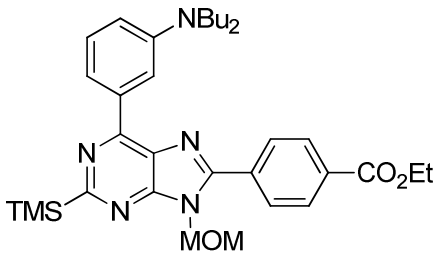
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 173.4, 160.0, 155.6, 154.8, 149.8, 137.0, 133.3, 131.0 ($^{2}J_{C-F}$=33 Hz), 130.2, 130.1, 129.6, 129.0, 126.9 ($^{3}J_{C-F}$=4 Hz), 126.6 ($^{3}J_{C-F}$=4 Hz), 124.3 ($^{1}J_{C-F}$=272 Hz), 122.1, 117.4, 114.8, 73.4, 57.9, 55.4, -1.7 ppm.

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.66 ppm.

MS (70 eV, EI): m/z (%) = 487 (29), 486 (85), 485 (100), 472 (24), 471 (70), 456 (26), 455 (39), 450 (22), 448 (69), 89 (21), 45 (34).

HRMS (EI): m/z calc. for [$C_{24}H_{25}F_3N_4O_2Si$] 486.1699; found: 486.1676.

Synthesis of ethyl 4-(6-(3-(dibutylamino)phenyl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (21g)



Ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**19b**, 385 mg, 1.0 mmol) was metalated according to **TP3** and the resulting solution added dropwise to a mixture of $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and *N*,*N*-dibutyl-3-iodoaniline (563 mg, 1.7 mmol) in THF (1 mL). After stirring the reaction mixture 20 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 19:1) afforded ethyl 4-(6-(3-(dibutylamino)phenyl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)-benzoate (**21g**, 365 mg, 62%) as a thick yellow oil. The reaction was also done on a 10 mmol scale furnishing the desired compound in 62% yield.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2956 (m), 2933 (w), 2873 (w), 1719 (m), 1600 (m), 1568 (m), 1556 (m), 1494 (m), 1460 (m), 1398 (w), 1367 (m), 1339 (m), 1272 (s), 1245 (m), 1220 (m), 1186 (m),

1155 (m), 1105 (s), 1091 (s), 1017 (m), 914 (w), 840 (vs), 777 (s), 758 (m), 722 (m), 699 (m), 622 (w), 614 (w).

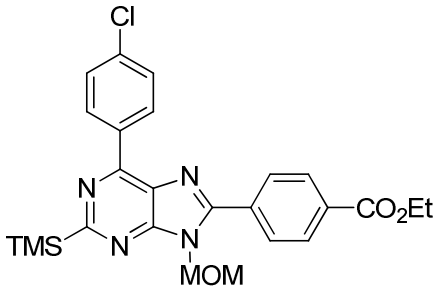
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.43-8.40 (m, 1H), 8.33-8.19 (m, 5H), 7.39 (t, *J* = 7.9 Hz, 1H), 6.80 (dd, *J* = 8.4, 2.6 Hz, 1H), 5.72 (s, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 3.64 (s, 3H), 3.42-3.37 (m, 4H), 1.74-1.64 (m, 4H), 1.49-1.36 (m, 7H), 1.03-0.94 (m, 6H), 0.49 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 173.4, 166.0, 154.4, 153.4, 153.0, 148.3, 137.0, 133.6, 132.1, 129.9, 129.7, 129.6, 129.3, 117.3, 114.1, 113.2, 73.2, 61.3, 57.8, 51.2, 29.6, 20.5, 14.4, 14.1, -1.7 ppm.

MS (70 eV, EI): m/z (%) = 587 (25), 546 (13), 545 (37), 544 (100), 503 (13), 503 (10), 502 (32), 73 (13), 45 (15), 43 (14), 43 (12).

HRMS (EI): m/z calc. for [$C_{33}H_{45}N_5O_3Si$] 587.3292; found: 587.3290.

Synthesis of ethyl 4-(6-(4-chlorophenyl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (21h)

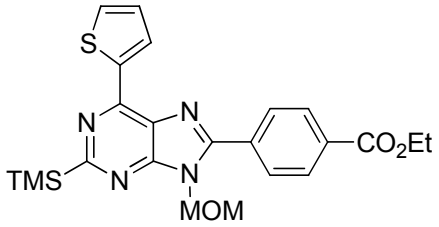


Ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**19b**, 385 mg, 1.0 mmol) was metalated according to **TP3** and the resulting solution added dropwise to a mixture of $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and chloro-4-iodobenzene (405 mg, 1.7 mmol) in THF (1 mL). After stirring the reaction mixture for 8 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 10:1) yielded ethyl 4-(6-(4-chlorophenyl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)-benzoate (**21h**, 288 mg, 58%) as a colorless solid. The reaction was also done on a 5 mmol scale furnishing the desired compound in 52% yield.

mp (°C): 145-146.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3068 (vw), 2988 (vw), 2960 (vw), 2934 (vw), 2902 (vw), 2830 (vw), 2360 (vw), 2342 (vw), 1718 (m), 1614 (vw), 1576 (m), 1554 (w), 1520 (vw), 1490 (m), 1466 (w), 1444 (w), 1430 (w), 1416 (vw), 1404 (w), 1390 (w), 1368 (w), 1340 (w), 1318 (w), 1306 (w), 1290 (w), 1264 (s), 1248 (m), 1216 (w), 1200 (w), 1186 (w), 1174 (w), 1158 (w), 1102 (m), 1090 (s), 1034 (w), 1016 (m), 958 (vw), 914 (w), 880 (w), 842 (vs), 808 (m), 788 (m), 776 (m), 762 (m), 728 (w), 718 (m), 704 (w), 690 (w), 670 (w), 658 (vw), 630 (w), 622 (w).
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.06-8.90 (m, 2H), 8.34-8.18 (m, 4H), 7.61-7.49 (m, 2H), 5.72 (s, 2H), 4.45 (q, *J* = 7.1 Hz, 2H), 3.64 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H), 0.47 ppm (s, 9H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 173.8, 165.9, 154.4, 154.0, 150.7, 136.7, 134.8, 133.1, 132.4, 131.2, 130.0, 129.7, 129.4, 128.7, 73.2, 61.4, 57.8, 14.3, -1.7 ppm.
HRMS (ESI): m/z calc. for [$C_{25}H_{27}ClN_4O_3Si+H^+$] 495.1614; found: 495.1612.

Synthesis of ethyl 4-(9-(methoxymethyl)-6-(thiophen-2-yl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (21i)



Ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**19b**, 385 mg, 1.0 mmol) was metalated according to **TP3** and the resulting solution added dropwise to a mixture of $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and 2-iodothiophene (357 mg, 1.7 mmol) in THF (1 mL). After stirring the reaction mixture for 40 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc = 19:1) yielded ethyl 4-(9-(methoxymethyl)-6-(thiophen-2-yl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**21i**, 200 mg, 43%) as a yellow solid.

mp (°C): 171-172.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2983 (w), 2956 (w), 2938 (w), 2903 (w), 1723 (m), 1575 (m), 1472 (w), 1421 (w), 1397 (w), 1363 (w), 1338 (w), 1273 8m), 1237 (m), 1185 (w), 1101 8m), 1086 (m),

1037 (w), 1018 (w), 868 (m), 844 (vs), 838 (s), 809 (m), 776 (m), 758 (m), 714 (s), 694 (m), 675 (w), 618 (w).

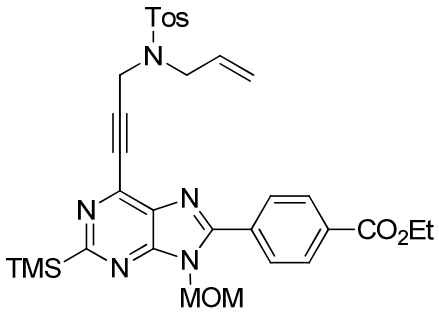
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.74 (dd, *J* = 3.8, 1.1 Hz, 1H), 8.29-8.20 (m, 4H), 7.56 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.24-7.22 (m, 1H), 5.68 (s, 2H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.60 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H), 0.44 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 174.1, 166.0, 153.9, 153.9, 147.9, 141.3, 133.3, 132.3, 132.2, 130.3, 130.0, 129.7, 128.6, 127.4, 73.2, 61.4, 57.8, 14.3, -1.8 ppm.

MS (70 eV, EI): m/z (%) = 466 (87), 465 (58), 451 (63), 436 (48), 435 (65), 433 (36), 421 (88), 393 (40), 89 (37), 73 (49), 45 (100).

HRMS (EI): m/z calc. for [$C_{23}H_{26}N_4O_3SSi$] 466.1495; found: 466.1483.

Synthesis of ethyl 4-(6-(3-(*N*-allyl-4-methylphenylsulfonamido)prop-1-yn-1-yl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (21j)



Ethyl 4-(9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**19b**, 385 mg, 1.0 mmol) was metalated according to **TP3** and the resulting solution was added dropwise to a solution of I_2 (380 mg, 1.5 mmol) in THF (1.0 mL) at 0 °C. After stirring the reaction mixture at 25 °C for 1 h, NEt_3 (152 mg, 1.5 mmol), CuI (8 mg, 4 mol%, 0.04 mmol), $Pd(dba)_2$ (12 mg, 2 mol%, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 4 mol%, 0.04 mmol) and *N*-allyl-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (172 mg, 1.3 mmol) were successively added. After stirring the resulting mixture for 1 h $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ EtOAc gradient = 10:1, 9:1, 8:1) yielded ethyl 4-(6-(3-(*N*-allyl-4-methylphenylsulfonamido)prop-1-yn-1-yl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**21j**, 472 mg, 75%) as a thick colorless oil.

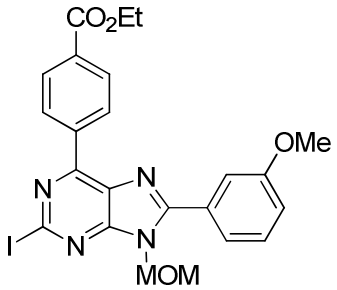
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2958 (w), 2874 (vw), 2366 (vw), 2238 (vw), 1718 (m), 1644 (vw), 1614 (vw), 1580 (m), 1522 (vw), 1464 (w), 1428 (w), 1410 (w), 1392 (w), 1346 (s), 1328 (m), 1272 (s), 1248 (m), 1214 (w), 1180 (m), 1160 (s), 1094 (s), 1068 (w), 1050 (w), 1032 (w), 1016 (m), 994 (w), 930 (w), 912 (w), 896 (w), 842 (vs), 812 (m), 778 (m), 756 (m), 724 (m), 704 (m), 692 (m), 664 (s), 624 (m).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.23 (s, 4H), 7.91-7.78 (m, 2H), 7.16-7.11 (m, 2H), 5.93-5.76 (m, 1H), 5.66 (s, 2H), 5.55-5.44 (m, 1H), 5.33-5.25 (m, 1H), 4.51 (s, 2H), 4.44 (q, *J* = 7.1 Hz, 2H), 4.04-4.02 (m, 2H), 3.61 (s, 3H), 2.11 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H), 0.42 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 174.5, 165.8, 154.8, 153.0, 143.2, 139.2, 135.8, 132.9, 132.6, 131.8, 130.0, 129.7, 129.5, 127.7, 120.4, 91.1, 81.6, 73.3, 61.4, 57.8, 49.4, 37.1, 23.8, 21.2, 14.3, -1.8 ppm.

HRMS (ESI): m/z calc. for [$C_{32}H_{37}N_5O_5SSi+H^+$] 632.2357; found: 632.2368.

Synthesis of ethyl 4-(2-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (22a)



A microwave vial was charged with CsF (335 mg, 2.2 mmol) which was dried under high vacuum (10^{-3} mbar) at 120 °C for 3 h. Ethyl 4-(9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(trimethylsilyl)-9*H*-purin-6-yl)benzoate (**21d**, 543 mg, 1.1 mmol), I_2 (419 mg, 1.65 mmol), THF (5 mL) and CH_3CN (5 mL) were successively added. The microwave vial was sealed and the reaction mixture was stirred under microwave irradiation at 110 °C for 12 h. The excess iodine was quenched with $Na_2S_2O_{3(sat)}$ (5 mL) and the mixture was diluted with EtOAc (5 mL). The aqueous layer was extracted with EtOAc (2 x 5 mL), the combined organic layers were washed with $NaCl_{(sat)}$ (10 mL) and were dried (Na_2SO_4). After concentration *via* rotary evaporation, the crude mixture was purified by flash column chromatography (silicagel, isohexane/ CH_2Cl_2 = 1:6) to afford ethyl 4-(2-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**22a**, 484 mg, 80%) as a white powdery solid.

mp (°C): 164-165.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3006 (w), 2980 (w), 2970 (w), 2942 (w), 2908 (w), 2838 (vw), 1706 (m), 1568 (m), 1556 (m), 1486 (m), 1464 (w), 1382 (w), 1368 (w), 1352 (w), 1320 (s), 1304 (m), 1274 (s), 1246 (vs), 1210 (m), 1188 (m), 1164 (m), 1136 (s), 1126 (s), 1102 (s), 1080 (m), 1046 (s), 1020 (m), 948 (m), 910 (m), 892 (m), 880 (m), 872 (m), 848 (w), 796 (m), 772 (s), 728 (w), 702 (m), 696 (m), 670 (w), 654 (m), 608 (vw).

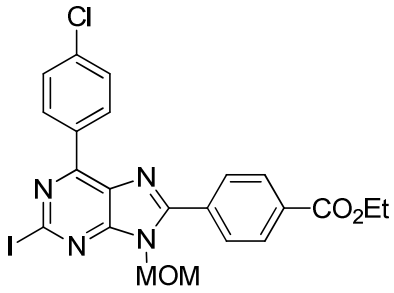
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.94 (d, *J* = 8.4 Hz, 2H), 8.18 (d, *J* = 9.0 Hz, 2H), 7.72 (ddd, *J* = 7.2, 1.2, 0.6 Hz, 1H), 7.69 (dd, *J* = 2.4, 1.2 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.13 (ddd, *J* = 8.4, 3.0, 1.2 Hz, 1H), 5.62 (s, 2H), 4.42 (q, *J* = 7.2 Hz, 2H), 3.90 (s, 3H), 3.60 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H) ppm.

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 166.2, 159.9, 156.2, 156.0, 153.8, 138.6, 132.6, 130.8, 130.2, 129.9, 129.7, 129.4, 122.2, 118.9, 117.5, 115.0, 73.5, 61.2, 57.8, 55.5, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 544 (13), 513 (18), 418 (11), 388 (21), 387 (35), 58 (33), 45 (24), 44 (13), 43 (100).

HRMS (EI): m/z calc. for [$C_{23}H_{21}IN_4O_4$] 544.0607; found: 544.0594.

Synthesis of ethyl 4-(6-(4-chlorophenyl)-2-iodo-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (22b)



A microwave vial was charged with CsF (304 mg, 2.0 mmol) which was dried under high vacuum (10^{-3} mbar) at 120 °C for 3 h. Ethyl 4-(6-(4-chlorophenyl)-9-(methoxymethyl)-2-(trimethylsilyl)-9*H*-purin-8-yl)benzoate (**21h**, 494 mg, 1.0 mmol), I_2 (355 mg, 1.4 mmol), THF (1 mL) and CH_3CN (1 mL) were successively added. The microwave vial was sealed and the reaction mixture was stirred under microwave irradiation at 110 °C for 12 h. The excess iodine was quenched with $Na_2S_2O_{3(sat)}$ (5 mL) and the solution was diluted with EtOAc (5 mL). The aqueous layer was extracted with EtOAc (2 x 5 mL), the combined organic layers were washed with $NaCl_{(sat)}$ (10 mL) and were dried (Na_2SO_4). After concentration *via* rotary evaporation, the crude mixture was purified by flash column chromatography (silicagel,

isohexane/ EtOAc = 10:1) to afford ethyl 4-(6-(4-chlorophenyl)-2-iodo-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**22b**, 266 mg, 49%) as a white powder.

mp (°C): 162-164.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3074 (vw), 2982 (w), 2938 (w), 2906 (w), 2874 (vw), 2818 (vw), 1726 (s), 1586 (m), 1566 (s), 1554 (m), 1492 (m), 1478 (m), 1462 (w), 1444 (w), 1434 (w), 1400 (m), 1376 (w), 1366 (w), 1342 (w), 1316 (m), 1292 (m), 1274 (s), 1250 (s), 1228 (m), 1196 (m), 1180 (m), 1156 (w), 1140 (m), 1126 (m), 1110 (s), 1098 (m), 1080 (vs), 1036 (m), 1014 (m), 966 (m), 940 (m), 876 (m), 866 (w), 838 (m), 804 (w), 794 (m), 774 (m), 716 (m), 694 (m), 666 (w), 656 (w), 628 (w).

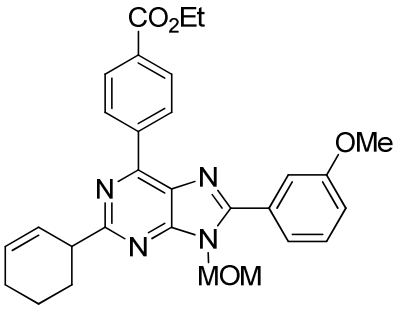
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.79 (d, *J* = 7.8 Hz, 2H), 8.21 (s, 4H), 7.76 (d, *J* = 8.4 Hz, 2H), 5.58 (s, 2H), 4.43 (q, *J* = 6.9 Hz, 2H), 3.59 (s, 3H), 1.44 ppm (t, *J* = 6.9 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.7, 155.8, 154.5, 154.0, 137.9, 132.9, 132.8, 132.2, 131.3, 130.2, 130.0, 129.7, 128.8, 119.3, 73.4, 61.4, 57.7, 14.3.

MS (70 eV, EI): m/z (%) = 548 (48), 520 (17), 518 (49), 517 (100), 391 (18), 130 (11), 128 (18), 127 (11), 45 (81).

HRMS (EI): m/z calc. for [$C_{22}H_{18}ClIN_4O_3$] 548.0112; found: 548.0105.

Synthesis of ethyl 4-(2-(cyclohex-2-en-1-yl)-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (24a)



Ethyl 4-(2-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**22a**, 544 mg, 1.0 mmol) was magnesiated according to **TP5** and a solution of CuCN·2LiCl (1.65 mL, 1.0 M in THF, 1.65 mmol) was added dropwise to the reaction mixture at -78 °C. The solution was warmed up to -40 °C and 3-bromocyclohexene (322 mg, 2.0 mmol) was added dropwise. The reaction mixture was warmed up to -10 °C within 3 h and quenched with $NH_4Cl_{(sat)}$/ $NH_{3(conc)}$ (9 mL/ 1 mL). The aqueous layer was extracted with EtOAc (2 x 10 mL),

the combined organic layers were washed with $NaCl_{(sat)}$ (10 mL) and were dried (Na_2SO_4). After concentration *via* rotary evaporation, the crude mixture was purified by flash column chromatography (silicagel, isohexane/ EtOAc gradient = 27:4, 21:4) to afford ethyl 4-(2-(cyclohex-2-en-1-yl)-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoat (**24a**, 342 mg, 69%) as a pale yellow powdery solid.

mp (°C): 145-147.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3022 (vw), 2986 (w), 2930 (w), 2910 (w), 2890 (w), 2836 (w), 1714 (s), 1610 (vw), 1578 (s), 1558 (m), 1510 (w), 1478 (m), 1466 (m), 1448 (w), 1424 (w), 1406 (w), 1366 (m), 1354 (m), 1314 (m), 1282 (vs), 1248 (s), 1236 (s), 1216 (m), 1206 (m), 1182 (m), 1154 (m), 1126 (m), 1100 (s), 1086 (s), 1048 (m), 1028 (s), 972 (w), 962 (w), 908 (m), 896 (m), 876 (m), 860 (w), 816 (w), 796 (m), 776 (m), 758 (m), 734 (w), 716 (w), 700 (s), 666 (m), 650 (w).

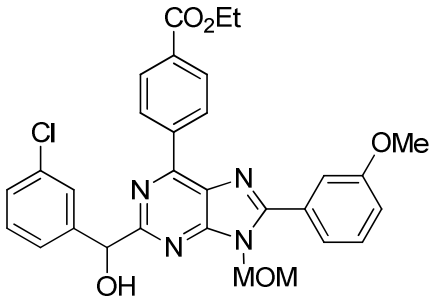
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.05-9.03 (m, 2H), 8.23-8.21 (m, 2H), 7.76-7.73 (m, 2H), 7.50-7.47 (m, 1H), 7.12 (ddd, *J* = 8.4, 2.7, 0.9 Hz, 1H), 6.16-6.13 (m, 1H), 5.93-5.90 (m, 1H), 5.69 (s, 2H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.95-3.91 (m, 4H), 3.63 (s, 3H), 2.31-2.27 (m, 1H), 2.22-2.10 (m, 3H), 2.03-1.97 (m, 1H), 1.83-1.76 (m, 1H), 1.44 ppm (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.2, 166.5, 159.9, 156.1, 155.6, 152.0, 140.2, 131.9, 130.3, 130.1, 129.8, 129.6, 129.1, 129.0, 127.8, 122.1, 117.1, 114.9, 73.3, 61.1, 57.8, 55.5, 44.7, 28.8, 25.0, 21.6, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 500 (6), 499 (31), 498 (100), 497 (15), 469 (8), 453 (13), 432 (6), 425 (7), 349 (7), 45 (12).

HRMS (EI): m/z calc. for [$C_{29}H_{30}N_4O_4$] 498.2267; found: 498.2258.

Synthesis of ethyl 4-(2-((3-chlorophenyl)(hydroxy)methyl)-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (24b)



Ethyl 4-(2-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**22a**, 544 mg, 1.0 mmol) was magnesiated according to **TP5** and 3-chlorobenzaldehyde (281 mg, 2.0 mmol) was added dropwise. The mixture was stirred for 2 h and the temperature was slowly risen to 0 °C. The reaction mixture was quenched with H_2O (10 mL) and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with $NaCl_{(sat)}$ (10 mL) and were dried (Na_2SO_4). After concentration *via* rotary evaporation the crude mixture was purified by flash column chromatography (silicagel, isohexane/ EtOAc = 1:2) to afford ethyl 4-(2-((3-chlorophenyl)(hydroxy)methyl)-9-(methoxymethyl)-8-(3-methoxy-phenyl)-9*H*-purin-6-yl)benzoate (**24b**, 524 mg, 94%) as a white powder.

mp (°C): 134-136.

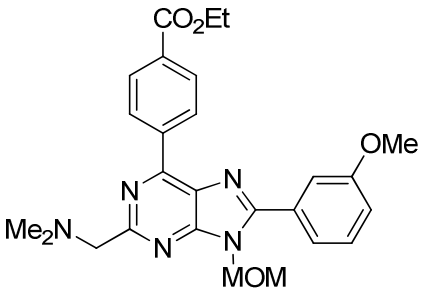
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3434 (br, w), 3068 (w), 2990 (m), 2938 (m), 2832 (w), 2360 (m), 2336 (m), 1738 (w), 1722 (m), 1712 (m), 1692 (m), 1588 (m), 1574 (m), 1462 (m), 1354 (m), 1328 (w), 1274 (vs), 1244 (s), 1212 (m), 1186 (m), 1154 (m), 1102 (s), 1056 (m), 1020 (m), 904 (m), 872 (w), 850 (w), 786 (w), 776 (m), 764 (m), 728 (m), 706 (m), 690 (m).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.01 (d, *J* = 8.4 Hz, 2H), (d, *J* = 8.4 Hz, 2H), 7.78-7.68 (m, 3H), 7.58 (dt, *J* = 7.2, 1.8 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.33-7.20 (m, 2H), 7.13 (brd, *J* = 8.4 Hz, 1H), 6.04 (s, 1H), 5.67 (m, 2H), 5.27 (bs, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 3.91 (s, 3H), 3.58 (s, 3H), 1.46 ppm (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.2, 162.7, 159.9, 156.7, 156.0, 151.7, 144.7, 139.0, 134.0, 132.4, 130.1, 130.0, 129.7, 129.7, 129.6, 129.4, 127.6, 126.8, 124.7, 122.1, 117.3, 114.9, 74.7, 73.6, 61.2, 57.9, 55.4, 14.3 ppm.

HRMS (ESI): m/z calc. for [$C_{30}H_{27}ClN_4O_5$+H^+] 559.1748; found: 559.1751.

Synthesis of ethyl 4-(2-((dimethylamino)methyl)-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (24c)



Ethyl 4-(2-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**22a**, 544 mg, 1.0 mmol) was magnesiated according to **TP5** and $ZnCl_2$ (1.65 mL, 1.0 M in THF, 1.65 mmol) was added dropwise to the reaction mixture at -78 °C. The solution was warmed up to 0 °C within 1 h. The reaction mixture was added dropwise to a solution of *N*-methyl-*N*-methylenemethanaminium 2,2,2-trifluoroacetate[100] (2.0 mL, 1.0 M solution in CH_2Cl_2, 2.0 mmol) at 0 °C, was stirred for 2 h and then quenched with H_2O (10 mL). After extraction of the aqueous layer with EtOAc (2 x 10 mL), the combined organic layers were washed with $NaCl_{(sat)}$ (10 mL) and were dried (Na_2SO_4). After concentration *via* rotary evaporation, the crude mixture was purified by flash column chromatography (silicagel, EtOAc/ MeOH = 9:1) to afford ethyl 4-(2-((dimethylamino)methyl)-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**24c**, 406 mg, 86%) as an orange powdery solid.

mp (°C): 120-121.

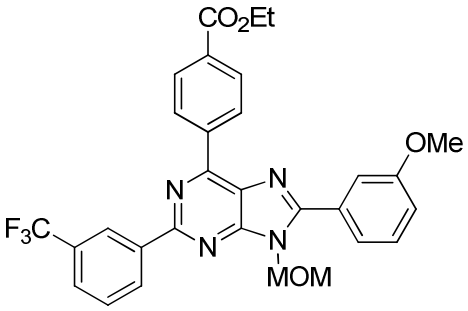
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3096 (vw), 3070 (vw), 2976 (w), 2936 (w), 2820 (w), 2770 (w), 1714 (s), 1578 (s), 1558 (m), 1508 (w), 1484 (m), 1472 (m), 1354 (m), 1336 (m), 1314 (m), 1280 (vs), 1256 (s), 1238 (s), 1208 (m), 1182 (m), 1156 (m), 1124 (m), 1100 (s), 1086 (s), 1046 (s), 1026 (s), 976 (w), 910 (w), 896 (w), 868 (m), 860 (m), 798 (w), 772 (m), 758 (m), 736 (m), 722 (w), 700 (s), 672 (m).

^{1}H-NMR (300 MHz, $CDCl_3$): 9.05-9.01 (m, 2H), 8.24-8.20 (m, 2H), 7.77-7.73 (m, 2H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.13 (ddd, *J* = 8.4, 2.6, 1.0 Hz, 1H), 5.72 (s, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 4.07 (s, 2H), 3.92 (s, 3H), 3.61 (s, 3H), 2.57 (s, 6H), 1.43 ppm (t, *J* = 7.1 Hz, 3H).

[100] (a) Ahond, A.; Cavé, A.; Kann-Fan, C.; Husson, H.; de Rostolan, J.; Potier, P. *J. Am. Chem. Soc.* **1968**, *90*, 5622; (b) Holy, N.; Fowler, R.; Burnett, E.; Lorenz, R. *Tetrahedron* **1979**, *35*, 613.

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.4, 159.9, 156.1, 155.9, 152.2, 139.8, 132.1, 130.1, 130.0, 129.8, 129.6, 129.5, 122.1, 117.2, 114.9, 73.3, 65.4, 61.1, 57.5, 55.5, 45.3, 14.3 ppm.
MS (70 eV, EI): m/z (%) = 474 (0.5), 433 (28), 432 (100), 402 (8), 401 (10), 388 (10), 45 (9).
HRMS (EI): m/z calc. for [$C_{26}H_{29}N_5O_4$] 475.2220; found: 475.2140.

Synthesis of ethyl 4-(9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(3-(trifluoromethyl)-phenyl)-9*H*-purin-6-yl)benzoate (24d)



Ethyl 4-(2-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**22a**, 544 mg, 1.0 mmol) was magnesiated according to **TP5** and $ZnCl_2$ (1.65 mL, 1.0 M in THF, 1.65 mmol) was added dropwise to the reaction mixture at -78 °C. The solution was warmed up to -20 °C within 1 h, $Pd(dba)_2$ (17 mg, 3 mol%, 0.03 mmol), P(*o*-furyl)$_3$ (14 mg, 6 mol%, 0.06 mmol) and 3-iodobenzotrifluoride (505 mg, 1.8 mmol) were added. The solution was stirred for 4 h at 25 °C. H_2O (10 mL) and EtOAc (10 mL) were added, the aqueous layer was extracted with EtOAc (2 x 10 mL), the combined organic layers were washed with $NaCl_{(sat)}$ (10 mL) and were dried (Na_2SO_4). After concentration *via* rotary evaporation the crude mixture was purified by flash column chromatography (silicagel, isohexane/ CH_2Cl_2 = 1:2) to afford ethyl 4-(9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(3-(trifluoromethyl)phenyl)-9*H*-purin-6-yl)benzoate (**24d**, 370 mg, 65%) as a white powdery solid.

mp (°C): 153-154.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2984 (vw), 2958 (vw), 2936 (vw), 2906 (vw), 1716 (m), 1600 (w), 1580 (m), 1560 (m), 1506 (vw), 1486 (w), 1472 (w), 1442 (w), 1404 (w), 1380 (w), 1368 (m), 1350 (w), 1324 (s), 1280 (vs), 1242 (s), 1216 (m), 1170 (m), 1160 (m), 1110 (s), 1098 (s), 1050 (m), 1022 (m), 958 (vw), 916 (w), 900 (w), 872 (w), 862 (w), 836 (vw), 802 (w), 790 (w), 774 (m), 754 (w), 730 (w), 694 (m), 674 (m).

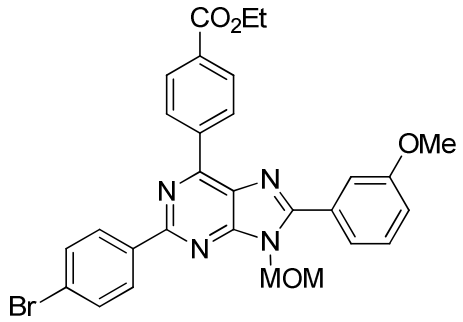
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.13 (d, *J* = 8.4 Hz, 2H), 8.93 (s, 1H), 8.88 (d, *J* = 7.8 Hz, 1H), 8.27 (d, *J* = 8.4 Hz, 2H), 7.79 (bd, *J* = 7.8 Hz, 1H), 7.77 (dd, *J* = 2.4, 1.8 Hz, 1H), 7.75 (bd, *J* = 7.8 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.15 (ddd, *J* = 8.4, 3.0, 1.2 Hz, 1H), 5.77 (s, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 3.69 (s, 3H), 1.45 ppm (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 166.4, 159.9, 156.9, 156.6, 156.3, 152.2, 139.9, 138.9, 132.2, 131.4, 131.0 (q, $^{2}J_{C-F}$ = 33 Hz), 130.2, 130.1, 129.9, 129.8, 129.7, 129.0, 126.6 (q, $^{3}J_{C-F}$ = 4 Hz), 124.9 (q, $^{3}J_{C-F}$ = 4 Hz), 124.2 (q, $^{1}J_{C-F}$ = 272 Hz), 122.1, 117.3, 114.9, 73.5, 61.1, 57.9, 55.5, 14.3 ppm.

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.6 ppm.

HRMS (EI): m/z calc. for [$C_{30}H_{25}F_3N_4O_4$+H^+] 563.1906; found: 563.1896.

Synthesis of ethyl 4-(2-(4-bromophenyl)-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (24e)



Ethyl 4-(2-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**22a**, 544 mg, 1.0 mmol) was magnesiated according to **TP5** and $ZnCl_2$ (1.65 mL, 1.0 M in THF, 1.65 mmol) was added dropwise to the reaction mixture at -78 °C. The solution was warmed up to -20 °C within 1 h, $Pd(dba)_2$ (17 mg, 3 mol%, 0.03 mmol), P(*o*-furyl)$_3$ (14 mg, 6 mol%, 0.06 mmol) and 1-bromo-4-iodobenzene (438 mg, 1.8 mmol) were added at -20 °C. The solution was stirred for 4 h at 25 °C. H_2O (10 mL) and EtOAc (10 mL) were added. The aqueous layer was extracted with EtOAc (2 x 10 mL), the combined organic layers were washed with $NaCl_{(sat)}$ (10 mL) and were dried (Na_2SO_4). After concentration *via* rotary evaporation the crude mixture was purified by flash column chromatography (silicagel, isohexane/ CH_2Cl_2 gradient = 1:2 to 1:3) to afford ethyl 4-(2-(4-bromophenyl)-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**24e**, 361 mg, 63%) as a white powdery solid.

mp (°C): 190-194.

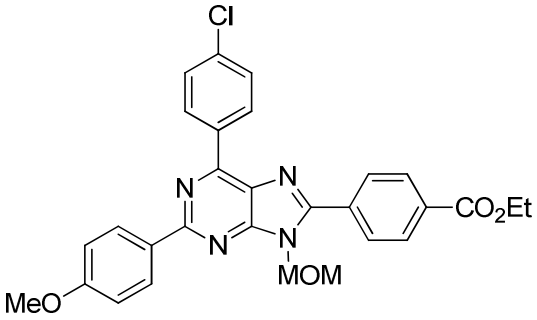
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3784 (vw), 3698 (vw), 2988 (w), 2942 (w), 2830 (vw), 2360 (vw), 1714 (m), 1582 (m), 1562 (m), 1486 (m), 1462 (m), 1398 (w), 1366 (m), 1314 (m), 1280 (vs), 1254 (m), 1242 (s), 1214 (m), 1194 (w), 1162 (w), 1128 (m), 1100 (s), 1070 (m), 1050 (m), 1022 (m), 1012 (m), 952 (w), 920 (w), 890 (w), 880 (w), 868 (w), 836 (w), 774 (m), 730 (w), 714 (w), 698 (m), 674 (w).

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.09 (d, *J* = 8.4 Hz, 2H), 8.52 (d, *J* = 9.0 Hz, 2H), 8.23 (d, *J* = 9.0 Hz, 2H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.75 (bs, 1H), 7.64 (d, *J* = 9.0 Hz, 2H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.13 (dd, *J* = 7.8, 2.4 Hz, 1H), 5.70 (s, 2H), 4.43 (d, *J* = 7.2 Hz, 2H), 3.92 (s, 3H), 3.66 (s, 3H), 1.44 (t, *J* = 7.2 Hz, 3H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 166.4, 159.9, 157.4, 156.3, 156.2, 152.0, 140.0, 137.0, 132.1, 131.6, 130.1, 130.0, 129.8, 129.7, 129.7, 129.6, 124.8, 122.1, 117.2, 114.9, 73.4, 61.1, 57.9, 55.5, 14.3 ppm.

HRMS (ESI): m/z calc. for [$C_{29}H_{26}{}^{79}BrN_4O_4$+$H^+$] 573.1137; found: 573.1132.

Synthesis of ethyl 4-(6-(4-chlorophenyl)-9-(methoxymethyl)-2-(4-methoxyphenyl)-9*H*-purin-8-yl)benzoate (24f)



Ethyl 4-(6-(4-chlorophenyl)-2-iodo-9-(methoxymethyl)-9*H*-purin-8-yl)benzoate (**22b**, 548 mg, 1.0 mmol) was magnesiated according to **TP5** and $ZnCl_2$ (1.65 mL, 1.0 M in THF, 1.65 mmol) was added dropwise to the reaction mixture at -78 °C. The solution was warmed up to -20 °C within 1 h, $Pd(dba)_2$ (17 mg, 3 mol%, 0.03 mmol), P(*o*-furyl)$_3$ (14 mg, 6 mol%, 0.06 mmol) and 1-iodo-4-methoxybenzene (416 mg, 1.8 mmol) were added at -20 °C. The solution was stirred for 12 h at 25 °C. H_2O (10 mL) and EtOAc (10 mL) were added. The aqueous layer was extracted with EtOAc (2 x 10 mL), the combined organic layers were washed with $NaCl_{(sat)}$ (10 mL) and were dried (Na_2SO_4). After concentration *via* rotary evaporation the crude mixture was purified by flash column chromatography (silicagel,

isohexane/ EtOAc = 21:4) to afford ethyl 4-(6-(4-chlorophenyl)-9-(methoxymethyl)-2-(4-methoxyphenyl)-9*H*-purin-8-yl)benzoate (**24f**, 307 mg, 58%) as an off-white solid.

mp (°C): 234-236.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2980 (w), 2958 (vw), 2936 (w), 2904 (vw), 2874 (vw), 2834 (vw), 1722 (s), 1610 (w), 1586 (s), 1556 (m), 1514 (w), 1490 (m), 1476 (w), 1452 (w), 1432 (w), 1398 (m), 1370 (s), 1346 (m), 1300 (m), 1264 (s), 1250 (vs), 1218 (m), 1210 (m), 1188 (w), 1178 (w), 1162 (s), 1098 (s), 1086 (s), 1076 (s), 1034 (m), 1014 (m), 960 (w), 950 (vw), 912 (m), 880 (w), 872 (w), 848 (m), 842 (m), 820 (w), 800 (s), 778 (m), 748 (w), 726 (m), 718 (m), 706 (m), 690 (m), 648 (w), 638 (vw).

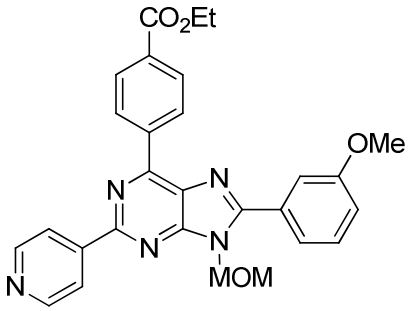
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.00 (d, *J* = 8.4 Hz, 2H), 8.60 (d, *J* = 9.0 Hz, 2H), 8.27 (d, *J* = 9.0 Hz, 2H), 8.24 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 9.0 Hz, 2H), 5.70 (s, 2H), 4.45 (q, *J* = 7.2 Hz, 2H), 3.91 (s, 3H), 3.67 (s, 3H), 1.45 ppm (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 165.9, 161.6, 158.6, 156.1, 154.2, 152.5, 137.0, 134.6, 133.0, 132.3, 131.2, 130.8, 130.0, 129.8, 129.6, 128.8, 128.7, 113.8, 73.3, 61.3, 57.8, 55.4, 14.3 ppm.

MS (70 eV, EI): m/z (%) = 630 (24), 529 (22), 528 (67), 500 (12), 499 (37), 498 (35), 497 (100), 484 (12), 483 (11), 349 (17), 175 (16), 45 (34).

HRMS (EI): m/z calc. for [$C_{29}H_{25}ClN_4O_4$] 528.1564; found: 528.1560.

Synthesis of ethyl 4-(9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(pyridin-4-yl)-9*H*-purin-6-yl)benzoate (24g)



Ethyl 4-(2-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**22a**, 544 mg, 1.0 mmol) was magnesiated according to **TP5** and $ZnCl_2$ (1.65 mL, 1.0 M in THF, 1.65 mmol) was added dropwise to the reaction mixture at -78 °C. The solution was warmed up to -20 °C within 1 h, $Pd(dba)_2$ (17 mg, 3 mol%, 0.03 mmol), P(*o*-furyl)$_3$ (14 mg, 6 mol%,

0.06 mmol) and 4-iodopyridine (380 mg, 1.8 mmol) were added at -20 °C. The solution was stirred for 4 h at 25 °C. H_2O (10 mL) and EtOAc (10 mL) were added. The aqueous layer was extracted with EtOAc (2 x 10 mL), the combined organic layers were washed with $NaCl_{(sat)}$ (10 mL) and were dried (Na_2SO_4). After concentration *via* rotary evaporation, the crude mixture was purified by flash column chromatography (silicagel, CH_2Cl_2/ EtOAc gradient = 5:1, 1:1) to afford ethyl 4-(9-(methoxymethyl)-8-(3-methoxyphenyl)-2-(pyridin-4-yl)-9*H*-purin-6-yl)benzoate (**24g**, 268 mg, 55%) as a white solid.

mp (°C): 147-148.

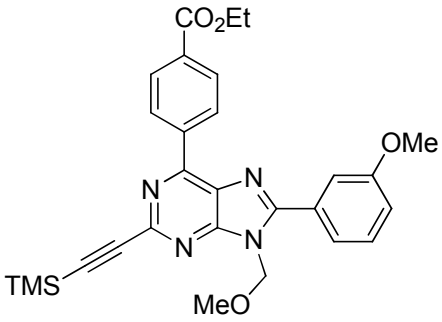
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3444 (vw), 3070 (vw), 2988 (vw), 2936 (w), 2906 (vw), 2832 (vw), 2360 (vw), 2342 (vw), 2332 (vw), 1712 (m), 1692 (m), 1588 (s), 1580 (m), 1562 (m), 1510 (w), 1488 (m), 1474 (m), 1466 (m), 1426 (w), 1416 (w), 1354 (m), 1322 (w), 1274 (vs), 1238 (s), 1212 (m), 1186 (m), 1154 (m), 1104 (s), 1056 (s), 1030 (m), 1020 (m), 902 (m), 872 (m), 850 (w), 812 (vw), 786 (m), 776 (m), 764 (m), 728 (m), 706 (m), 690 (m).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.11 (d, *J* = 8.7 Hz, 2H), 8.81 (d, *J* = 4.2 Hz, 2H), 8.50 (d, *J* = 6.0 Hz, 2H), 8.23 (d, *J* = 8.7 Hz, 2H), 7.78 (m, 2H), 7.50 (t, *J* = 8.1 Hz, 1H), 7.15 (ddd, *J* = 8.4, 2.7, 0.9 Hz, 1H), 5.75 (s, 2H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.92 (s, 3H), 3.68 (s, 3H), 1.44 ppm (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.3, 160.0, 157.0, 156.2, 155.9, 152.2, 150.2, 145.5, 139.7, 132.3, 130.6, 130.2, 129.8, 129.7, 129.7, 122.2, 122.1, 117.4, 115.0, 73.6, 61.2, 57.9, 55.5, 14.3 ppm.

HRMS (ESI): m/z calc. for [$C_{28}H_{25}N_5O_4$+H^+] 496.1985; found: 496.1975.

Synthesis of ethyl 4-(9-(methoxymethyl)-8-(3-methoxyphenyl)-2-((trimethylsilyl)-ethynyl)-9*H*-purin-6-yl)benzoate (24h)



$Pd(dba)_2$ (17 mg, 3 mol%, 0.03 mmol), P(*o*-furyl)$_3$ (14 mg, 6 mol%, 0.06 mmol), CuI (6 mg, 3 mol%, 0.03 mmol), NEt_3 (122 mg, 1.2 mmol) and trimethylsilylacetylene (98 mg, 1.0 mmol) were successively added to a solution of ethyl 4-(2-iodo-9-(methoxymethyl)-8-(3-methoxyphenyl)-9*H*-purin-6-yl)benzoate (**22a**, 544 mg, 1.0 mmol) in THF (10 mL). The solution was stirred for 24 h and H_2O (10 mL) was added. After extraction with EtOAc (2 x 10 mL), the combined organic layers were washed with $NaCl_{(sat)}$ (10 mL) and dried (Na_2SO_4). The solvents were evaporated *in vacuo*. Purification *via* column chromatography (silicagel, isohexane/ CH_2Cl_2 = 1:1) yielded ethyl 4-(9-(methoxymethyl)-8-(3-methoxyphenyl)-2-((trimethylsilyl)-ethynyl)-9*H*-purin-6-yl)benzoate (**24h**, 388 mg, 76%) as an off-white solid.

m.p (°C): 175-177.

IR (ATR): 3000 (vw), 2984 (vw), 2964 (vw), 2940 (vw), 2836 (vw), 2164 (vw), 1720 (m), 1612 (w), 1586 (w), 1572 (m), 1560 (m), 1468 (m), 1434 (w), 1400 (w), 1360 (s), 1308 (w), 1276 (s), 1252 (m), 1210 (w), 1180 (w), 1152 (m), 1124 (w), 1104 (m), 1086 (m), 1058 (w), 1032 (m), 996 (w), 916 (w), 900 (w), 866 (s), 844 (vs), 794 (m), 772 (s), 758 (m), 730 (m), 722 (w), 702 (m), 696 (m), 674 (w), 646 (w).

^{1}H-NMR ($CDCl_3$, 600 MHz): δ = 9.00 (d, *J* = 9.0 Hz, 2H), 8.21 (d, *J* = 9.0 Hz, 2H), 7.75 (ddd, *J* = 7.8 Hz, 1.2 Hz, 0.6 Hz, 1H), 7.72 (dd, *J* = 2.4 Hz, 1.2 Hz, 1H), 7.48 (t, *J* = 8.4 Hz, 1H), 7.13 (ddd, *J* = 8.4 Hz, 3.0Hz, 1.2 Hz, 1H), 5.69 (s, 2H), 4.42 (q, *J* = 7.2 Hz, 2H), 3.90 (s, 3H), 3.61 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H), 0.36 ppm (s, 9H).

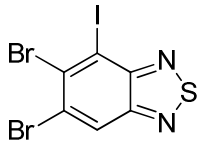
^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 166.3, 159.9, 157.0, 155.3, 152.8, 145.5, 139.2, 132.3, 130.2, 130.1, 130.0, 129.7, 129.6, 122.2, 117.4, 114.9, 103.5, 92.1, 73.3, 61.1, 57.6, 55.5, 14.3, -0.2 ppm.

HRMS (ESI): m/z calc. for $[C_{28}H_{31}N_4O_4Si+H^+]$ 515.2115, found: 515.2104.

3. Functionalization of the benzo[*c*][1,2,5]thiadiazole and benzo[*c*][1,2,5]oxadiazole scaffold

3.1. Functionalization of the benzo[*c*][1,2,5]thiadiazole scaffold via Zn-, Mg- and Mn-Intermediates

Synthesis of 5,6-dibromo-4-iodobenzo[*c*][1,2,5]thiadiazole (29)



In a Schlenk-tube TMPMgCl·LiCl (1.0 mL, 1.1 M in THF, 1.1 mmol) was added dropwise to a solution of 5,6-dibromobenzo[*c*][1,2,5]thiadiazole (**28**, 294 mg, 1.0 mmol) in THF (4 mL) at -20 °C. After stirring at this temperature for 10 min, I_2 (2.0 mL, 1.0 M in THF, 2.0 mmol) was added dropwise and the reaction mixture was slowly warmed up to 25 °C in 5 h. $NH_4Cl_{(sat)}$ (10 mL) and $Na_2S_2O_{3(sat)}$ (5 mL) were added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The crude residue was purified by flash chromatography (silicagel, pentane/ Et_2O = 200:1), providing the compound **29** (200 mg, 48%) as a yellow solid.

mp (°C): 171-172.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3066 (vw), 2922 (w), 2852 (vw), 1712 (w), 1560 (w), 1472 (m), 1418 (m), 1368 (w), 1330 (w), 1296 (w), 1244 (w), 1230 (s), 1176 (w), 1160 (w), 1118 (w), 1104 (m), 1096 (m), 964 (w), 952 (m), 908 (m), 876 (m), 856 (vs), 840 (s), 758 (w), 734 (w), 718 (m), 682 (w), 622 (w).

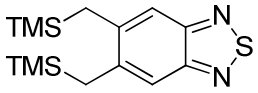
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.38 (s, 1H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 156.2, 150.7, 135.5, 126.2, 124.6, 95.8 ppm.

MS (70 eV, EI): m/z (%) = 422 (56), 420 (100), 418 (53), 214 (25), 212 (23), 133 (19), 128 (42), 127 (33), 80 (20), 43 (22).

HRMS (EI): m/z calc. for [$C_6HBr_2IN_2S$] 417.7272; found: 417.7274.

Synthesis of 5,6-bis((trimethylsilyl)methyl)benzo[*c*][1,2,5]thiadiazole (30)



In a Schlenk-tube $TMSCH_2MgCl$ (3.39 mL, 1.18 M in Et_2O, 4.0 mmol) was added dropwise to dry $ZnCl_2$ (550 mg, 4.0 mmol) in THF (4 mL) at 0 °C and the mixture was warmed up to 25 °C. 5,6-Dibromobenzo[*c*][1,2,5]thiadiazole (**28**, 294 mg, 1.0 mmol), $Pd(OAc)_2$ (5 mg, 2 mol%, 0.02 mmol) and SPhos (16 mg, 4 mol%, 0.04 mmol) were successively added. After stirring for 30 min, $NH_4Cl_{(sat)}$ (10 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The crude residue was purified by flash chromatography (silicagel, pentane/ Et_2O = 100:1), providing the compound **30** (283 mg, 92%) as a colorless solid.

mp (°C): 90-91.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2954 (w), 2898 (vw), 1492 (w), 1458 (w), 1420 (w), 1400 (w), 1268 (w), 1246 (m), 1160 (w), 1140 (m), 1084 (w), 886 (w), 868 (m), 834 (vs), 820 (s), 778 (m), 758 (w), 712 (w), 694 (m), 664 (w).

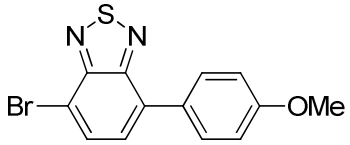
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.53 (s, 2H), 2.24 (s, 4H), 0.04 (s, 18H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.6, 142.7, 117.7, 25.5, -1.4 ppm.

MS (70 eV, EI): m/z (%) = 308 (11), 295 (6), 294 (11), 291 (43), 74 (9), 73 (100), 45 (17), 43 (12).

HRMS (EI): m/z calc. for [$C_{14}H_{24}N_2SSi_2$] 308.1199; found: 308.1192.

Synthesis of 4-bromo-7-(4-methoxyphenyl)benzo[*c*][1,2,5]thiadiazole (32)



In a Schlenk-tube dry LiCl (106 mg, 2.5 mmol), Mg (61 mg, 2.5 mmol), $ZnCl_2$ (2.5 mL, 1.0 M in THF, 2.5 mmol) and THF (5 mL) were successively added. At 0 °C 4,7-dibromobenzo[*c*][1,2,5]thiadiazole (**31**, 588 mg, 2.0 mmol) was added and the reaction mixture stirred for 2 h. The resulting brown solution was canulated to a mixture of $Pd(dba)_2$ (30 mg, 2 mol%, 0.04 mmol), P(*o*-furyl)$_3$ (16 mg, 4 mol%, 0.08 mmol) and 4-iodoanisole

(374 mg, 1.6 mmol) in THF (2 mL). After stirring at 25 °C for 5 h, $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 40 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The crude residue was purified by flash chromatography (silicagel, pentane/ Et_2O = 50:1), providing the compound **32** (300 mg, 58%) as a yellow solid.

mp (°C): 133-136.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3048 (vw), 2990 (vw), 2934 (vw), 2896 (vw), 2836 (vw), 1896 (vw), 1608 (m), 1530 (w), 1508 (m), 1482 (m), 1462 (w), 1454 (w), 1438 (w), 1342 (vw), 1308 (w), 1282 (m), 1272 (w), 1248 (s), 1180 (s), 1152 (w), 1116 (w), 1084 (w), 1030 (s), 972 (vw), 942 (w), 930 (w), 880 (s), 838 (m), 826 (vs), 796 (m), 732 (w), 654 (vw), 628 (vw).

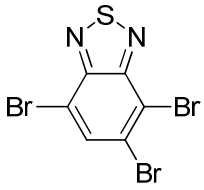
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.91-7.84 (m, 3H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.09-7.04 (m, 2H), 3.90 (s, 3H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.1, 153.9, 153.2, 133.6, 132.3, 130.3, 129.0, 127.4, 114.1, 112.2, 55.4 ppm.

MS (70 eV, EI): m/z (%) = 323 (16), 322 (100), 321 (15), 320 (98), 307 (35), 305 (35), 279 (20), 277 (21), 198 (26).

HRMS (EI): m/z calc. for [$C_{13}H_9BrN_2OS$] 319.9619; found: 319.9615.

Synthesis of 4,5,7-tribromobenzo[*c*][1,2,5]thiadiazole (33)



In a Schlenk-tube $TMP_2Mn{\cdot}2MgCl_2{\cdot}4LiCl$ (7.5 mL, 0.5 M in THF, 3.75 mmol) was added dropwise to a solution of 4,7-dibromobenzo[*c*][1,2,5]thiadiazole (**31**, 1.47 g, 5.0 mmol) in THF (5 mL) at 0 °C. After stirring at this temperature for 3 h, $(BrCl_2C)_2$ (7.5 mL, 1.0 M in THF, 7.5 mmol) was added dropwise and the reaction mixture was slowly warmed up to 25 °C in 5 h. $NH_4Cl_{(sat)}$ (20 mL) was added, the aqueous layer was extracted with CH_2Cl_2 (3 x 40 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The crude residue was purified by flash chromatography (silicagel, pentane/ Et_2O = 100:1), providing compound **33** (1.3 g, 70%) as a yellow solid.

mp (°C): 153-154.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 1736 (vw), 1570 (w), 1540 (vw), 1508 (vw), 1488 (w), 1478 (w), 1452 (w), 1368 (vw), 1302 (w), 1294 (w), 1260 (vw), 1222 (m), 1184 (w), 1138 (w), 1124 (w), 972 (m), 940 (w), 878 (vs), 864 (m), 844 (m), 750 (w), 690 (w).

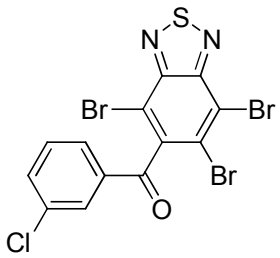
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.08 (s, 1H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.5, 153.0, 135.9, 127.1, 116.6, 113.7 ppm.

MS (70 eV, EI): m/z (%) = 376 (32), 374 (100), 372 (97), 370 (30), 295 (15), 293 (29), 291 (14), 216 (18), 214 (19), 58 (24), 43 (67).

HRMS (EI): m/z calc. for [$C_6HBr_3N_2S$] 369.7411; found: 369.7413.

Synthesis of (3-chlorophenyl)(4,6,7-tribromobenzo[*c*][1,2,5]thiadiazol-5-yl)methanone (35)



In a Schlenk-tube $TMP_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (2.0 mL, 0.5 M in THF, 1.0 mmol) was added dropwise to a solution of 4,6,7-tribromobenzo[*c*][1,2,5]thiadiazole (**33**, 373 mg, 1.0 mmol) in THF (1 mL). After stirring for 3 h, $CuCN{\cdot}2LiCl$ (0.5 mL, 1.0 M in THF, 50 mol%, 0.5 mmol), 3-chlorobenzoyl chloride (263 mg, 1.5 mmol) were successively added at -15 °C and the reaction mixture stirred for 3 h. $NH_4Cl_{(sat)}$ (20 mL) and $NH_{3(conc)}$ (5 mL) were added, the aqueous layer was extracted with CH_2Cl_2 (3 x 40 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The crude residue was purified by flash chromatography (silicagel, pentane/ Et_2O = 20:1), providing the compound **35** (233 mg, 46%) as a yellow solid.

mp (°C): 195-198.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3096 (w), 3072 (w), 2930 (w), 2872 (w), 1748 (w), 1722 (m), 1680 (s), 1644 (m), 1622 (m), 1588 (m), 1570 (m), 1466 (w), 1448 (m), 1422 (m), 1380 (m), 1370 (m), 1346 (w), 1278 (m), 1264 (vs), 1246 (vs), 1188 (s), 1172 (s), 1132 (s), 1074 (m), 1052 (m),

1000 (w), 968 (w), 942 (w), 908 (m), 884 (s), 846 (w), 810 (m), 788 (m), 758 (s), 738 (vs), 720 (s), 672 (s), 604 (w).

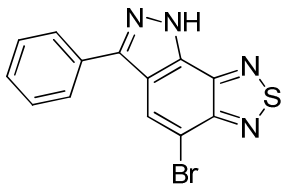
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.89-7.88 (m, 1H), 7.74-7.71 (m, 1H), 7.66-7.63 (m, 1H), 7.49-7.46 (m, 1H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 190.7, 153.1, 151.4, 141.8, 135.7, 135.6, 134.7, 130.6, 129.5, 129.4, 128.0, 123.8, 118.8, 111.3 ppm.

MS (70 eV, EI): m/z (%) = 510 (28), 433 (55), 431 (78), 429 (33), 401 (16), 399 (16), 141 (31), 139 (100), 111 (65), 75 (35).

HRMS (EI): m/z calc. for [$C_{13}H_4Br_3ClN_2OS$] 507.7283; found: 507.7275.

4-bromo-6-phenyl-8*H*-[1,2,5]thiadiazolo[3,4-*g*]indazole (36)



In a round bottom flask, $N_2H_4 \cdot H_2O$ (0.5 g, 10.0 mmol) was added dropwise to a solution of (4,7-dibromobenzo[*c*][1,2,5]thiadiazol-5-yl)(phenyl)methanone (**34**, 398 mg, 1.0 mmol) in EtOH/ $CHCl_3$ (6 mL each). The reaction mixture was stirred at 60 °C for 10 h, the solvent was evaporated *in vacuo* and the crude residue was purified by flash chromatography (silicagel, isohexane/ EtOAc gradient = 5:1 to 3:1), providing the compound **36** (214 mg, 65%) as a yellow solid.

mp (°C): 270-272.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3264 (m), 1746 (vw), 1610 (vw), 1516 (vw), 1496 (w), 1446 (w), 1396 (w), 1362 (m), 1338 (w), 1274 (vw), 1246 (w), 1230 (w), 1140 (vw), 1112 (w), 1104 (w), 1074 (w), 978 (w), 888 (m), 870 (vs), 838 (m), 764 (w), 718 (s), 694 (s), 674 (m), 634 (w).

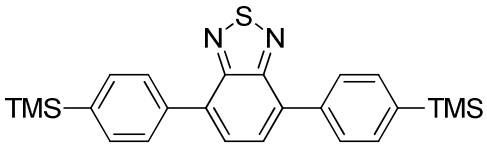
^{1}H-NMR (400 MHz, d6-DMSO): δ = 8.47 (m, 1H), 7.99-7.90 (m, 2H), 7.63-7.45 (m, 3H) ppm.

MS (70 eV, EI): m/z (%) = 333 (16), 332 (100), 331 (20), 330 (92), 329 (5), 218 (9), 164 (5), 77 (15).

HRMS (EI): m/z calc. for [$C_{13}H_7BrN_4S$] 329.9575; found: 329.9566.

3.2. Synthesis of the BTD-COF precursor 40

Synthesis of 4,7-bis(4-(trimethylsilyl)phenyl)benzo[*c*][1,2,5]thiadiazole (42)



In a 250 mL Schlenk-flask bis(di-*tert*-butyl(4-dimethylaminophenyl)phosphine) dichloropalladium(II) (28 mg, 0.04 mmol) and 4,7-dibromobenzo[*c*][1,2,5]thiadiazole (**31**, 1.47 g, 5.0 mmol) were successively added to a solution of (4-(trimethylsilyl)phenyl)zinc(II) chloride (36.4 mL, 0.55 M in THF, 20 mmol) and the resulting greenish reaction mixture was stirred at 50 °C for 3 h. After addition of $NH_4Cl_{(sat)}$ (100 mL), the aqueous layer was extracted with CH_2Cl_2 (3 x 200 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane) afforded 4,7-bis(4-(trimethylsilyl)phenyl)benzo[*c*][1,2,5]thiadiazole (**42**, 1.6 g, 75%) as a bright yellow solid.

mp (°C): 151-153.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3016 (w), 2952 (w), 2894 (w), 1554 (w), 1480 (w), 1400 (w), 1247 (m), 1095 (w), 837 (vs), 818 (s), 813 (s), 757 (m), 721 (m), 691 (w).

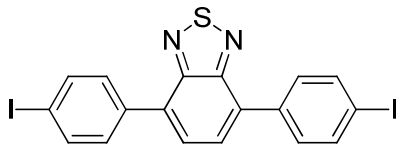
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.96-7.92 (m, 4H), 7.79 (s, 2H), 7.73-7.70 (m, 4H), 0.34 ppm (s, 18H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 154.2, 140.8, 137.8, 133.7, 133.5, 128.5, 128.1, -1.1 ppm.

MS (70 eV, EI): m/z (%) = 434 (10), 433 (32), 432 (79), 419 (17), 418 (40), 417 (100), 202 (14), 201 (35), 73 (18), 57 (10).

HRMS (EI): m/z calc. for [$C_{24}H_{28}N_2SSi_2$] 432.1512; found: 432.1509.

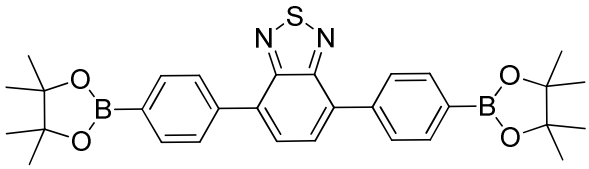
Synthesis of 4,7-bis(4-iodophenyl)benzo[*c*][1,2,5]thiadiazole (43)



In a 500 mL round bottom flask 4,7-bis(4-(trimethylsilyl)phenyl)benzo[*c*][1,2,5]thiadiazole (**42**, 10 g, 23 mmol) was dissolved in CH_2Cl_2 (200 mL) and cooled to 0 °C. ICl (2.0 mL, excess) was added dropwise and the reaction mixture was stirred at 0 °C for 10 min. After warming up to 25 °C the solution was stirred for further 2 h. Filtration afforded 4,7-bis(4-iodophenyl)benzo[*c*][1,2,5]thiadiazole (**43**, 11.6 g, 93%) as a yellow solid.

mp (°C): 214-218.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2920 (w), 2851 (w), 1586 (w), 1552 (w), 1472 (m), 1402 (w), 1116 (w), 1102 (w), 1060 (w), 1006 (m), 972 (w), 943 (w), 886 (w), 849 (w), 806 (vs), 710 (w).
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.90-7.85 (m, 4H), 7.76 (s, 2H), 7.73-7.68 ppm (m, 4H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.8, 137.8, 136.7, 132.6, 131.0, 127.9, 94.6 ppm.
MS (70 eV, EI): m/z (%) = 542 (6), 541 (21), 540 (100), 288 (11), 286 (9), 143 (6).
HRMS (EI): m/z calc. for [$C_{18}H_{10}I_2N_2S$] 539.8654; found: 539.8650.

Synthesis of 4,7-bis(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo [*c*][1,2,5]thiadiazole (40)



In a 250 mL Schlenk-flask equipped with a big stirring bar KOAc (4.9 g, 50 mmol) was dried under high vacuum (10^{-3} mbar) at 100 °C. After successive addition of 1,4-dioxane (100 mL), 4,7-bis(4-iodophenyl)benzo[*c*][1,2,5]thiadiazole (**43**, 5.4 g, 10 mmol), and 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (10.2 g, 40 mmol) the reaction mixture was degassed for 30 min. $Pd(OAc)_2$ (90 mg, 0.4 mmol) and $P(Cy)_3$ (220 mg, 0.8 mmol) were added and the resulting greenish reaction mixture was stirred at 80 °C for 24 h. After addition of $NaHCO_{3(sat)}$ (100 mL) the aqueous layer was extracted with Et_2O (4 x 200 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Recrystallization from

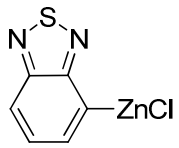
Et_2O afforded 4,7-bis(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[*c*][1,2,5] thiadiazole (**43**, 4.1 g ,74%) as a bright yellow solid.

mp (°C): 184-186.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2975 (w), 1609 (w), 1550 (w), 1519 (w), 1396 (m), 1356 (vs), 1320 (m), 1294 (m), 1214 (w), 1143 (s), 1122 (m), 1105 (m), 1084 (m), 1020 (w), 961 (w), 890 (w), 856 (m), 821 (s), 744 (w), 657 (m).
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.00-7.95 (m, 8H), 7.80 (s, 2H), 1.37 ppm (s, 24H).
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 154.0, 140.0, 135.0, 133.5, 128.5, 128.2, 83.9, 24.9 ppm.
MS (70 eV, EI): m/z (%) = 542 (10), 541 (34), 540 (100), 539 (44), 441 (14), 440 (11), 341 (24), 340 (22), 339 (9).
HRMS (EI): m/z calc. for [$C_{30}H_{34}B_2N_2O_4S$] 540.2425; found: 540.2419.

3.3. Synthesis of perylenedye precursors

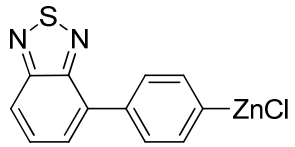
3.3.1. Typical procedures 6-8

TP6: Typical procedure for the synthesis of reagent 44



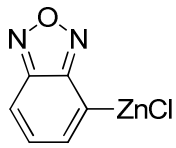
In a Schlenk-tube $TMP_2Mg{\cdot}2LiCl$ (23.0 mL, 0.6 M in THF, 13.8 mmol) was added dropwise to a solution of benzo[*c*][1,2,5]thiadiazole (**25**, 1.4 g, 10 mmol) in THF (10 mL) at -40 °C. After 14 h of stirring at -40 °C, $ZnCl_2$ (15 mL, 1.0 M in THF, 15 mmol) was added dropwise. Further stirring at -40 °C for 30 min and warming up to 25 °C provides the zinc reagent **44** in ca 85% yield as a dark brown solution (0.2 M in THF).

TP7: Typical procedure for the synthesis of reagent 47



In a Schlenk-tube LiCl (170 mg, 4.0 mmol) was dried under vacuum (10^{-3} mbar) at 140 °C. After cooling, Mg (97 mg, 4.0 mmol), $ZnCl_2$ (4.0 mL, 1.0 M in THF, 4.0 mmol) and 4-(4-iodophenyl)benzo[*c*][1,2,5]thiadiazole (**46**, 676 mg, 2 mmol) were successively added. The reaction mixture was stirred for 2 h at 25 °C. Canulation to a second Schlenk-tube furnishes the zinc reagent **47** in ca 80% yield as a dark brown solution (0.3 M in THF).

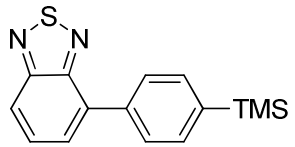
TP8: Typical procedure for the metalation of benzo[*c*][1,2,5]oxadiazole (51)



In a Schlenk-tube TMPMgCl·LiCl (1.7 mL, 1.2 M in THF, 2.0 mmol) was added dropwise to a solution of benzo[*c*][1,2,5]oxadiazole (**51**, 220 mg, 1.8 mmol) in 2 mL THF at -5 °C. After 14 h of stirring, $ZnCl_2$ (2.1 mL, 1.0 M in THF, 2.1 mmol) was added dropwise. Further stirring at -5 °C for 30 min and warming up to 25 °C provides the desired zinc reagent in ca 80% yield as a dark brown solution (0.25 M in THF).

3.3.2. Synthesis of compounds 45-58

Synthesis of 4-(4-(trimethylsilyl)phenyl)benzo[*c*][1,2,5]thiadiazole (45)



$Pd(dba)_2$ (35 mg, 2 mol%, 0.06 mmol), P(*o*-furyl)$_3$ (28 mg, 4 mol% 0.12 mmol) and (4-iodophenyl)trimethylsilane (1.24 g, 4.5 mmol) were successively added to the zinc reagent **44** prepared by **TP6** (15 mL, 0.2 M in THF, 3 mmol). After stirring at 25 °C for 24 h, the reaction mixture was quenched by the addition of $NH_4Cl_{(sat)}$ (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent

was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane) afforded 4-(4-(trimethylsilyl)phenyl)benzo[c][1,2,5]thiadiazole (**45**, 355 mg, 42%) as a bright yellow solid.

mp (°C): 120.6-122.4.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3058 (w), 1946 (w), 1912 (w), 1874 (w), 1798 (w), 1727 (w), 1656 (w), 1595 (w), 1580 (w), 1537 (w), 1491 (w), 1474 (w), 1412 (w), 1377 (w), 1351 (w), 1168 (w), 1064 (w), 1003 (w), 896 (m), 850 (m), 834 (m), 825 (m), 799 (vs), 751 (s), 713 (w).

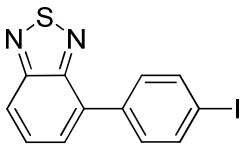
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.01-7.97 (m, 1H), 7.91-7.88 (m, 2H), 7.71-7.66 (m, 4H), 0.32 ppm (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 155.6, 153.6, 140.9, 137.7, 134.7, 133.6, 129.6, 128.5, 127.7, 120.6, -1.1 ppm.

MS (70 eV, EI): m/z (%) = 286 (3), 285 (5), 284 (22) [M^+], 272 (2), 271 (9), 270 (19), 269 (100), 253 (2), 239 (6), 135 (4).

HRMS (EI): m/z calc. for [$C_{15}H_{16}N_2SSi$] 284.0803; found: 284.0799.

Synthesis of 4-(4-iodophenyl)benzo[*c*][1,2,5]thiadiazole (46)



In a round bottom flask ICl (2 mL) was added dropwise to a solution of 4-(4-(trimethylsilyl)phenyl)benzo[*c*][1,2,5]thiadiazole (284 mg, 1 mmol) in CH_2Cl_2 (2 mL) at 0 °C and stirred for 3 h. The reaction mixture was quenched by the addition of $Na_2S_2O_{3(sat)}$ (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ Et_2O = 200:1) afforded 4-(4-iodophenyl)-benzo[*c*][1,2,5]thiadiazole (**46**, 316 mg, 93%) as a bright yellow solid.

mp (°C): 71-73.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3063 (w), 3014 (w), 2953 (w), 2894 (w), 1594 (w), 1544 (w), 1482 (w), 1408 (w), 1381 (w), 1249 (m), 1130 (w), 1107 (w), 1096 (w), 895 (w), 840 (s), 823 (s), 803 (s), 756 (vs), 723 (m), 696 (m), 678 (m).

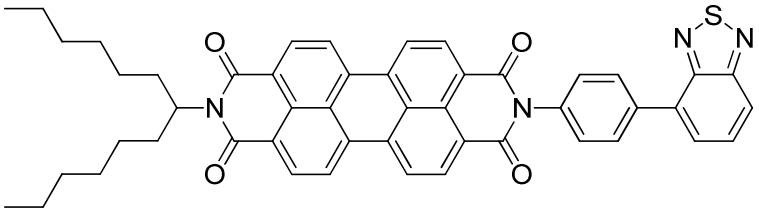
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.06-8.00 (m, 1H), 7.90-7.85 (m, 2H), 7.72-7.67 ppm (m, 4H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 155.6, 153.2, 137.8, 136.8, 133.4, 131.0, 129.6, 127.6, 121.0, 94.5 ppm.

MS (70 eV, EI): m/z (%) = 339 (15), 338 (100), 212 (10), 211 (57), 178 (15), 165 (7), 152 (9), 140 (12), 58 (11), 43 (39).

HRMS (EI): m/z calc. for [$C_{12}H_7IN_2S$] 337.9375; found: 337.9370.

Synthesis of 2-(4-benzo[*c*][1,2,5]thiadiazol-4-ylphenyl)-9-(1-hexylheptyl)anthra[2,1,9-*def*;6,5,10-*d'e'f'*]diisoquinoline-1,3,8,10-tetraon (49)



$Pd(dba)_2$ (12 mg, 0.02 mmol), P(*o*-furyl)$_3$ (9 mg, 0.04 mmol) and 2-(1-hexylheptyl)-9-(4-iodophenyl)anthra[2,1,9-def;6,5,10-d'e'f']diisoquinoline-1,3,8,10-tetraone (**48**, 100 mg, 129 μmol) were successively added to the zinc reagent **44** prepared by **TP6** (4.3 mL, 0.2 M in THF, 0.85 mmol). After stirring at 25 °C for 24 h, the reaction mixture was quenched by the addition of $NH_4Cl_{(sat)}$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. The crude solid was dissolved in CH_2Cl_2 and precipitated with MeOH. Filtration afforded 2-(4-benzo[*c*][1,2,5]thiadiazol-4-ylphenyl)-9-(1-hexylheptyl)anthra[2,1,9-*def*;6,5,10-*d'e'f'*]-diisoquinoline-1,3,8,10-tetraon (**49**, 47 mg, 47%) as a bright red solid.

mp (°C): > 300.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3476 (w), 2956 (m), 2926 (m), 2857 (m), 1696 (s), 1660 (s), 1594 (s), 1578 (m), 1543 (w), 1512 (w), 1483 (w), 1466 (w), 1434 (w), 1406 (m), 1352 (s), 1254 (s), 1178 (m), 1138 (w), 1126 (w), 1111 (w), 1067 (w), 1024 (w), 965 (w), 900 (w), 874 (w), 864 (m), 841 (w), 810 (s), 793 (m), 746 (m), 726 (w), 688 (w).

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.74-8.64 (m, 8 H), 8.18 (d, *J* = 8.3 Hz, 2 H, 8.05 (d, *J* = 8.8 Hz, 2 H), 7.81 (d, *J* = 7.1 Hz, 2 H), 7.73 (m, 2 H), 7.53 (d, *J* = 8.2 Hz, 1 H), 5.23 -5.16

(m, 1 H), 2.29-2.23 (m, 2 H), 1.92-1.83 (m, 2 H), 1.39-1.19 (m, 16 H), 0.83 ppm (t, *J* = 7.0 Hz, 6 H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.6, 135.3, 132.0, 130.3, 129.6, 128.8, 128.1, 123.4, 123.1, 54.8, 32.4, 31.8, 29.7, 29.2, 26.9, 22.6, 14.0 ppm.

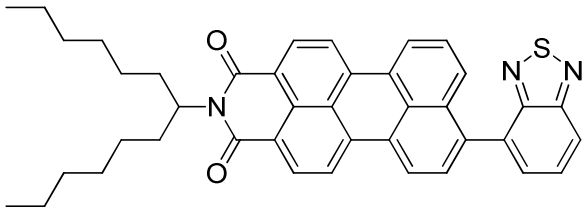
MS (70 eV, EI): m/z (%) = 783 (36), 600 (100).

HRMS (EI): m/z calc. for [$C_{49}H_{42}N_4O_4S$] 782.2927; found: 782.2845.

UV/VIS ($CHCl_3$): λ_{max} (ε) = 315.9 (17400), 352.0 (10500), 459.1 (19100), 491.0 (52700), 527.4 nm (87900).

Fluorescence ($CHCl_3$): λ_{max} (I_{rel}) = 534.2 (1.00), 576.8 (0.51), 625.1 nm (0.12).

Synthesis of 8-(benzo[*c*][1,2,5]thiadiazol-4-yl)-2-(1-hexylheptyl)-1*H*-perylo[3,4-*cd*]pyridine-1,3(2*H*)-dione (51)



$Pd(OAc)_2$ (5 mg, 0.02 mmol), SPhos (16 mg, 0.04 mmol) and 8-bromo-2-(1-hexylheptyl)-1*H*-perylo[3,4-*cd*]pyridine-1,3(2*H*)-dione (**50**, 63 mg, 0.13 mmol) were successively added to the zinc reagent **44** prepared by **TP6** (4.3 mL, 0.2 M in THF, 0.85 mmol). After stirring at 25 °C for 24 h, the reaction mixture was quenched by the addition of $NH_4Cl_{(sat)}$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, CH_2Cl_2) afforded a red solid which was dissolved in CH_2Cl_2 and precipitated with MeOH. Filtration provided 8-(benzo[*c*][1,2,5]thiadiazol-4-yl)-2-(1-hexylheptyl)-1*H*-perylo[3,4-*cd*]pyridine-1,3(2*H*)-dione (**51**, 39 mg, 47%) as a red solid.

mp (°C): 184-185.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3050 (w), 2953 (m), 2924 (s), 2855 (m), 1688 (s), 1650 (s), 1616 (w), 1592 (s), 1576 (s), 1542 (w), 1507 (w), 1487 (w), 1456 (m), 1434 (w), 1349 (w), 1374 (w), 1352 (s), 1295 (m), 1247 (m), 1214 (w), 1174 (w), 1139 (w), 1105 (w), 1028 (w), 980 (w), 902 (w), 854 (m), 841 (m), 808 (s), 752 (s), 726 (w), 688 (w), 668 (w).

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.59-8.47 (m, 3H), 8.39 (m, 3H), 8.17 (dd, *J* = 8.7, 1.2 Hz, 1H), 7.84-7.80 (m, 1H), 7.77-7.72 (m, 2H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.47 (m, 1H), 5.24-5.17 (m, 1H), 2.31-2.22 (m, 2H), 1.91-1.83 (m, 2H), 1.40-1.20 (m, 16H), 0.83 ppm (t, *J* = 7.0 Hz, 6 H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.1, 164.1, 155.1, 154.3, 138.1, 136.8, 136.5, 133.2, 132.8, 132.0, 131.1, 130.3, 129.8, 129.7, 129.5, 129.4, 129.1, 128.8, 128.3, 127.0, 126.5, 123.7, 123.0, 121.6, 120.4, 120.3, 54.4, 32.4, 31.8, 29.3, 27.0, 22.6, 14.1 ppm.

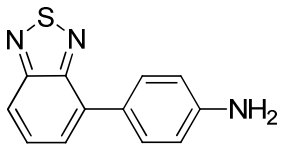
MS (70 eV, EI): m/z (%) = 637 (42), 455 (100).

HRMS (EI): m/z calc. for [$C_{41}H_{39}N_3O_2S$] 637.2763; found: 637.2751.

UV/VIS ($CHCl_3$): λ_{max} (ε) = 314.0 (15600), 489.5 (37500), 513.3 nm (38400).

Fluorescence ($CHCl_3$): λ_{max} = 557.3 nm.

Synthesis of 4-(benzo[*c*][1,2,5]thiadiazol-4-yl)aniline (52a)



$Pd(OAc)_2$ (14 mg, 2 mol%, 0.06 mmol), SPhos (49 mg, 4 mol%, 0.12 mmol) and 4-iodoaniline (855 mg, 3.9 mmol) were successively added to the zinc reagent **44** prepared by **TP6** (15 mL, 0.2 M in THF, 3.0 mmol). After stirring at 50 °C for 24 h, the reaction mixture was quenched by the addition of $NH_4Cl_{(sat)}$ (15 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, CH_2Cl_2) afforded 4-(benzo[*c*][1,2,5]thiadiazol-4-yl)aniline (**52a**, 415 mg, 61%) as an orange solid.

mp (°C): 132-133.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3441 (w), 3349 (w), 3216 (w), 2924 (w), 2853 (w), 1738 (w), 1627 (m), 1608 (m), 1541 (w), 1512 (s), 1479 (m), 1327 (w), 1297 (m), 1276 (m), 1181 (m), 1167 (w), 1124 (m), 1078 (w), 894 (w), 827 (m), 802 (s), 753 (vs).

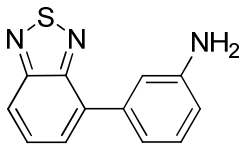
^{1}H-NMR (400 MHz, d6-DMSO): δ = 7.94-7.88 (m, 1H), 7.76-7.67 (m, 4H), 6.72-6.68 (m, 2H), 5.40 ppm (br s, 2H).

^{13}C-NMR (100 MHz, d6-DMSO): δ = 155.3, 152.8, 149.2, 134.0, 130.3, 129.9, 125.4, 123.9, 118.3, 113.6 ppm.

MS (70 eV, EI): m/z (%) = 229 (5), 228 (15), 227 (100), 226 (15), 211 (5), 194 (5), 181 (4), 168 (3), 140 (4), 114 (5).

HRMS (EI): m/z calc. for [$C_{12}H_9N_3S$] 227.0517; found: 227.0517.

Synthesis of 3-(benzo[*c*][1,2,5]thiadiazol-4-yl)aniline (52b)



$Pd(OAc)_2$ (14 mg, 2 mol%, 0.06 mmol), SPhos (49 mg, 4 mol%, 0.12 mmol) and 3-iodoaniline (855 mg, 3.9 mmol) were successively added to the zinc reagent **44** prepared by **TP6** (15 mL, 0.2 M in THF, 3 mmol). After stirring at 50 °C for 24 h, the reaction mixture was quenched by the addition of $NH_4Cl_{(sat)}$ (15 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 3:1) afforded 3-(benzo[*c*][1,2,5]thiadiazol-4-yl)aniline (**52b**, 414 mg, 61%) as an orange solid.

mp (°C): 93-95.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3435 (m), 3346 (m), 3214 (w), 3041 (w), 1738 (w), 1623 (m), 1607 (m), 1582 (m), 1541 (w), 1494 (w), 1478 (m), 1454 (m), 1331 (w), 1288 (w), 1247 (w), 1165 (m), 994 (w), 908 (w), 881 (w), 850 (m), 827 (m), 813 (m), 778 (s), 760 (vs), 698 (s).

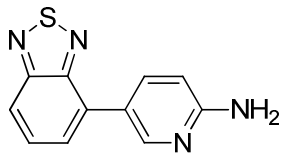
^{1}H-NMR (400 MHz, d6-DMSO): δ = 8.03 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.78-7.71 (m, 2H), 7.18-7.14 (m, 2H), 7.05-7.03 (m, 1H), 6.67-6.64 (m, 1H), 5.20 ppm (br s, 2H).

^{13}C-NMR (100 MHz, d6-DMSO): δ = 155.1, 152.8, 148.7, 137.5, 134.4, 130.1, 128.9, 127.5, 119.9, 116.8, 114.6, 114.0 ppm.

MS (70 eV, EI): m/z (%) = 229 (4), 228 (11), 227 (100), 226 (14), 211 (5), 200 (3), 199 (3), 194 (2), 181 (3), 140 (3), 114 (3).

HRMS (EI): m/z calc. for [$C_{12}H_9N_3S$] 227.0517; found: 227.0503.

Synthesis of 5-(benzo[*c*][1,2,5]thiadiazol-4-yl)pyridin-2-amine (52c)



$Pd(OAc)_2$ (14 mg, 2 mol%, 0.06 mmol), SPhos (49 mg, 4 mol%, 0.12 mmol) and 5-iodopyridin-2-amine (885 mg, 3.9 mmol) were successively added to the zinc reagent **44** prepared by **TP6** (15 mL, 0.2 M in THF, 3 mmol). After stirring at 50 °C for 24 h, the reaction mixture was quenched by the addition of $NH_4Cl_{(sat)}$ (15 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, EtOAc) afforded 5-(benzo[*c*][1,2,5]thiadiazol-4-yl)pyridin-2-amine (**52c**, 360 mg, 53%) as a red solid.

mp (°C): 195-197.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3451 (w), 3292 (w), 3158 (w), 1640 (s), 1628 (s), 1605 (m), 1594 (m), 1554 (w), 1545 (w), 1506 (m), 1482 (s), 1414 (s), 1382 (m), 1355 (w), 1316 (m), 1272 (m), 1146 (w), 1131 (w), 1020 (w), 895 (w), 852 (w), 827 (m), 805 (s), 755 (vs).

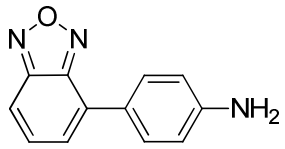
^{1}H-NMR (400 MHz, d6-DMSO): δ = 8.60 (dd, *J* = 2.5, 0.7 Hz, 1H), 8.03 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.98-7.93 (m, 1H), 7.75-7.70 (m, 2H), 6.59 (dd, *J* = 8.7, 0.7 Hz, 1H), 6.25 ppm (br s, 2H).

^{13}C-NMR (100 MHz, d6-DMSO): δ = 159.6, 155.1, 152.6, 148.2, 137.4, 131.4, 130.3, 125.5, 120.7, 119.0, 107.5 ppm.

MS (70 eV, EI): m/z (%) = 229 (11), 228 (100), 227 (21), 201 (11), 200 (7), 69 (8), 57 (10), 55 (10), 43 (8), 41 (6).

HRMS (EI): m/z calc. for [$C_{11}H_8N_4S$] 228.0470; found: 228.0461.

Synthesis of 4-(benzo[*c*][1,2,5]oxadiazol-4-yl)aniline (54a)

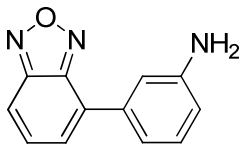


$Pd(OAc)_2$ (7 mg, 2 mol%, 0.03 mmol), SPhos (25 mg, 4 mol%, 0.06 mmol) and 4-iodoaniline (372 mg, 1.7 mmol) were successively added to the zinc reagent prepared by **TP8** (5.6 mL,

0.25 M in THF, 1.4 mmol). After stirring at 50 °C for 24 h, the reaction mixture was quenched by the addition of $NH_4Cl_{(sat)}$ (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 4:1) afforded 4-(benzo[*c*][1,2,5]oxadiazol-4-yl)aniline (**54a**, 175 mg, 59%) as an orange solid.

mp (°C): 115-117.
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3453 (w), 3364 (m), 3217 (w), 1626 (m), 1603 (s), 1544 (w), 1510 (s), 1447 (w), 1423 (w), 1373 (w), 1302 (m), 1276 (m), 1178 (w), 1141 (w), 1016 (w), 892 (w), 871 (w), 836 (m), 815 (m), 797 (s), 754 (vs).
^{1}H-NMR (400 MHz, d6-DMSO): δ = 7.82-7.79 (m, 3H), 7.65-7.56 (m, 2H), 6.72-6.69 (m, 2H), 5.58 ppm (brs, 2H).
^{13}C-NMR (100 MHz, d6-DMSO): δ = 150.1, 149.7, 148.2, 133.2, 129.3, 129.1, 125.3, 121.6, 113.8, 112.1 ppm.
MS (70 eV, EI): m/z (%) = 212 (13), 211 (100), 210 (7), 194 (8), 182 (10), 181 (53), 179 (7), 155 (11), 154 (10), 153 (9), 127 (10).
HRMS (EI): m/z calc. for [$C_{12}H_9N_3O$] 211.0746; found: 211.0741.

Synthesis of 3-benzo[*c*][1,2,5]oxadiazol-4-yl)aniline (54b)



$Pd(OAc)_2$ (7 mg, 2 mol%, 0.03 mmol), SPhos (25 mg, 4 mol%, 0.06 mmol) and 3-iodoaniline (372 mg, 1.7 mmol) were successively added to the zinc reagent prepared by **TP8** (5.6 mL, 0.25 M in THF, 1.4 mmol). After stirring at 50 °C for 24 h, the reaction mixture was quenched by the addition of $NH_4Cl_{(sat)}$ (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ EtOAc = 2:1) afforded 3-benzo[*c*][1,2,5]oxadiazol-4-yl)aniline (**54b**, 160 mg, 55%) as an orange solid.

mp (°C): 95.8-97.4.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3400 (w), 3301 (w), 3196 (w), 1738 (w), 1637 (w), 1602 (m), 1583 (m), 1545 (w), 1489 (w), 1459 (w), 1433 (w), 1311 (w), 1297 (w), 1248 (w), 1140 (w), 1018 (w), 994 (w), 988 (w), 889 (w), 870 (m), 859 (m), 784 (s), 746 (vs), 694 (s).

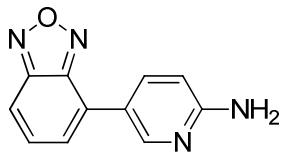
^{1}H-NMR (400 MHz, d6-DMSO): δ = 9.96 (dd, *J* = 8.8, 1.0 Hz, 1H), 7.71-7.64 (m, 2H), 7.23-7.16 (m, 2H), 7.12-7.09 (m, 1H), 6.70-6.67 (m, 1H), 5.30 ppm (br s, 2H).

^{13}C-NMR (100 MHz, d6-DMSO): δ = 149.6, 149.1, 148.2, 135.4, 133.0, 129.7, 129.4, 128.5, 115.6, 114.8, 114.4, 113.4 ppm.

MS (70 eV, EI): m/z (%) = 212 (10), 211 (76), 182 (16), 181 (100), 179 (9), 168 (11), 154 (17), 153 (8), 149 (8), 127 (12).

HRMS (EI): m/z calc. for [$C_{12}H_9N_3O$] 211.0746; found: 211.0737.

Synthesis of 5-(benzo[*c*][1,2,5]oxadiazol-4-yl)pyridin-2-amine (54c)



$Pd(OAc)_2$ (7 mg, 2 mol%, 0.03 mmol), SPhos (25 mg, 4 mol%, 0.06 mmol) and 5-iodopyridin-2-amine (375 mg, 1.7 mmol) were successively added to the zinc reagent prepared by **TP8** (5.6 mL, 0.25 M in THF, 1.4 mmol). After stirring at 50 °C for 24 h, the reaction mixture was quenched by the addition of $NH_4Cl_{(sat)}$ (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, EtOAc) afforded 5-(benzo[*c*][1,2,5]oxadiazol-4-yl)pyridin-2-amine (**54c**, 160 mg, 54%) as a red solid.

mp (°C): 166.9-168.8.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3414 (m), 3322 (w), 3118 (m), 1653 (s), 1612 (m), 1600 (s), 1545 (w), 1505 (vs), 1395 (s), 1372 (m), 1334 (w), 1322 (m), 1298 (m), 1269 (m), 1139 (m), 1081 (w), 1011 (w), 889 (w), 872 (w), 815 (w), 797 (m), 759 (w), 744 (s), 713 (w), 661 (w).

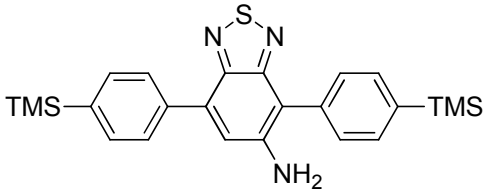
^{1}H-NMR (400 MHz, d6-DMSO): δ = 8.69-8.68. (m, 2H), 8.06 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.87 (dd, *J* = 8.9, 0.7 Hz, 1H), 7.71 (dd, *J* = 6.9, 0.8 Hz, 1H), 7.62 (dd, *J* = 8.9, 6.9 Hz, 1H), 6.60 (dd, *J* = 8.7, 0.7 Hz, 1H), 6.41ppm (br s, 2H).

^{13}C-NMR (100 MHz, d6-DMSO): δ = 160.1, 149.6, 148.0, 147.9, 136.3, 133.2, 126.8, 125.9, 118.6, 113.0, 107.9 ppm.

MS (70 eV, EI): m/z (%) = 213 (15), 212 (100), 196 (9), 185 (8), 182 (11), 155 (17), 142 (8), 128 (8), 57 (8).

HRMS (EI): m/z calc. for [$C_{11}H_8N_4O$] 212.0698; found: 212.0690.

Synthesis of 4,7-bis(4-(trimethylsilyl)phenyl)benzo[*c*][1,2,5]thiadiazol-5-amine (56)



$Pd(OAc)_2$ (5 mg, 4 mol%, 0.04 mmol), SPhos (33 mg, 8 mol%, 0.08 mmol) and 4,7-dibromobenzo[*c*][1,2,5]thiadiazol-5-amine (309 mg, 1.0 mmol) were added successively to a solution of (4-(trimethylsilyl)phenyl)zinc(II) chloride (7.3 mL, 0.55 M in THF, 4.0 mmol) and the resulting reaction mixture was stirred at 40 °C for 13 h. After addition of $NH_4Cl_{(sat)}$ (10 mL), the aqueous layer was extracted with CH_2Cl_2 (4 x 40 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification *via* column chromatography (silicagel, pentane/ CH_2Cl_2 = 4:1) afforded 4,7-bis(4-(trimethylsilyl)phenyl)benzo[*c*][1,2,5]thiadiazol-5-amine (**54**, 220 mg, 49%) as a bright yellow solid.

mp (°C): 235-236.

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3440 (vw), 3344 (w), 2954 (w), 2896 (vw), 1620 (w), 1594 (m), 1548 (w), 1508 (vw), 1416 (w), 1382 (w), 1358 (w), 1336 (vw), 1276 (w), 1248 (m), 1176 (w), 1126 (w), 1090 (w), 884 (w), 834 (vs), 816 (vs), 762 (m), 752 (m), 730 (m), 722 (m), 692 (w), 632 (w.)

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.93-7.89 (m, 2H), 7.75-7.70 (m, 4H), 7.63-7.60 (m, 2H), 7.30 (s, 1H), 4.26 (br s, 2H), 0.35 ppm (s, 18H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 156.5, 149.4, 144.0, 140.9, 140.2, 137.5, 135.2, 134.2, 133.8, 133.6, 129.3, 128.4, 122.9, 111.5, -1.1, -1.1 ppm.

HRMS (ESI): m/z calc. for [$C_{24}H_{29}N_3SSi_2$+H^+] 448.1693; found: 448.1702.

D. APPENDIX

Curriculum Vitae

Personal Informations

Name	Silvia Daniela Zimdars
Date of Birth	July 9th 1982
Place of Birth	Berlin, Germany

Education

June 2002	Abitur: Gymnasium Unterhaching (main subjects: mathematics/ chemistry)
Oct 2002 – Dec 2007	Studies in Chemistry at the Ludwig-Maximilians-Universität, Munich
Sep 2006 – Nov 2006	Internship at Sanofi-Aventis, S&MA Chemical Sciences Germany in Frankfurt/ Main
July 2007 – Dec 2007	Diploma thesis in the group of Prof. Dr. P. Knochel on "Darstellung von polyfunktionalisierten Benzo[*c*][1,2,5]-thiadiazolderivaten unter Verwendung von $TMP_2Mg \cdot 2LiCl$"
Jan 2008 – Jan 2011	PhD thesis in the group of Prof. Dr. P. Knochel

Publications

Barbara Platschek, Nikolay Petkov, Dieter Himsl, Silvia Zimdars, Zhuo Li, Ralf Köhn, Thomas Bein "**Vertical Columnar Block-Copolymer-Templated Mesoporous Silica via Confined Phase Transformation**" *J. Am. Chem. Soc*., **2008**, *130,* 17362-17371.

Heinz Langhals, Paul Knochel, Andreas Esterbauer, Andreas Walter, Silvia Zimdars "**Benzothiadiazoloperylene-amorphe funktionale Materialien**" Patent application DE 10 2009 048 848.0.

Silvia Zimdars, Xavier Mollat du Jourdin, François Crestey, Thomas Carell and Paul Knochel "**Trifunctionalization of the Purine Scaffold using Mg and Zn Organometallic Intermediates**" *Org. Lett.* **2011**, *13,* 792-795.

Silvia Zimdars, Heinz Langhals and Paul Knochel "**Functionalization of the Benzo[*c*][1,2,5]thiadiazole Scaffold *via* Mg-, Zn- and Mn-Intermediates**" *Synthesis*, accepted for publication.

Poster Presentation

Marcel Kienle, Silvia Zimdars, Thomas Kunz, Paul Knochel "**Heterocyclic Building Blocks for Electro-Active Hybrid Systems**" at the 2nd Photovoltaik Symposium in Bitterfeld-Wolfen, 05.–06.11.2009

Symposia

Mar 2009	Symposium of the SFB 749 in Wildbad Kreuth
Nov 2009	2nd Photovoltaik Symposium in Bitterfeld-Wolfen