Univerzita Karlova v Praze

Přírodovědecká fakulta

Studijní program: Organická chemie

Studijní obor: Organická chemie

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Nové C-H aktivace a cross-coupling reakce pro modifikace deazapurinových nukleobází

New C-H activations and cross-coupling reactions for modification of deazapurine nucleobases

Disertační práce

Vedoucí závěrečné práce/Školitel: prof. Ing. Michal Hocek CSc., DSc.

Praha, 2017

Prohlášení:

Prohlašuji, že jsem závěrečnou práci zpracoval samostatně a že jsem uvedl všechny použité informační zdroje a literaturu. Tato práce ani její podstatná část nebyla předložena k získání jiného nebo stejného akademického titulu.

V Praze, 22.09.2017

Podpis

Acknowledgement

I would like to thank my supervisor prof. Michal Hocek for a very interesting research topic, for his excellent guidance and support over the years of my research work. I would also like to acknowledge Dr. Lenka Poštová Slavětínská for measurement and interpretation of NMR spectra and Dr. Blanka Klepetářová for X-Ray analyses. I have to thank all colleagues from Hocek research group for their advices, suggestions and friendly environment. I would especially like to thank my labmates Martin Klečka and Anna Tokarenko for their help, support, many useful advice and ideas. Last but not least, I would like to thank my wife Iryna Sabat, my parents and friends for motivation, inspiration and constant support.

All the synthetic experiments were performed by me as well as the most of the measurements. The measurements and interpretation of NMR spectra of intermediates and all final compounds were done by Dr. Lenka Poštová Slavětínská. Crystal structure analyses were performed by Dr. Blanka Klepetářová. All cytostatic/cytotoxic activity screening and antiviral screening were performed by our collaborators from IOCB, Gilead Sciences and from the group of prof. Hajdúch (Palacky University Olomouc).

This work was supported by the institutional support of the Charles University and Academy of Sciences of the Czech Republic (RVO: 61388963), by the Czech Science Foundation (P207/12/0205, 16-0011785) and by Gilead Sciences, Inc.

Abstract

This PhD thesis reports the development of novel C-H activation strategies and aqueous-phase Suzuki-Miyaura cross-coupling reactions for the synthesis of modified deazapurine nucleobases.

The methodologies of chemo- and regioselective synthesis of highly functionalized deazapurines have been developed by using modern C-H activation chemistry. Various functional groups such as amino-, imido-, silyl- and phosphonyl- were introduced by C-H activation reactions.

Amino deazapurine derivatives were synthesized by developed Pd/Cu-catalyzed direct C-H amination and C-H chloroamination of 6-substituted 7-deazapurines with *N*-chloro-*N*-alkyl-arylsulfonamides. C-H imidation reactions of pyrrolopirimidines were performed under ferrocene catalysis with *N*-succinimido- or *N*-phtalimidoperesters. In order to obtain silylated derivatives, Ir-catalyzed C-H silylations of phenyldeazapurines with alkyl silanes were designed. Highly interesting deazapurine phosphonates were prepared by using Mn-promoted C-H phosphonation method and were further transformed into the corresponding phosphonic acids. All of the developed direct C-H functionalization reactions proceeded regioselectively at position 8 in deazapurine core, except for C-H silylation where reaction undergoes mainly as directed *ortho* C-H silylation on phenyl ring, leading to new interesting nucleobase derivatives.

The second part of this thesis focused on the modification of position 6 and 7 of 7-deazapurine bases by the aqueous Suzuki-Miyaura cross-coupling reactions with diverse (het)aryl boronic acids. A series of 6-(het)aryl-7-deazapurine bases bearing F at position 7 and H, F, Cl, Me or NH_2 at position 2 was prepared. 7-(Het)aryl-7-deazapurine nucleobases were synthesized from SEM-protected-7-iodo-7-deazapurines by using a protecting group strategy. After cleavage of the SEM group, the 6-methoxy derivatives were transformed into 7-deazahypoxanthines and 7-deazaguanines by *O*-demethylation reactions.

C-H functionalization strategies in combination with aqueous Suzuki-Miyaura cross-coupling reactions were shown to be a powerful tool for the modification of the deazapurine scaffold. Diverse functional groups were introduced directly by C-H activation reactions, whereas for (het)aryl substituents aqueous Suzuki-Miyaura cross-couplings were used. This approach allowed multifunctionalization of deazapurine all around the heterocycle system.

Abstrakt

Tato práce se zabývá vývojem nových C-H aktivačních reakcí a Suzuki-Miyaura reakcí ve vodné fázi využitelných pro syntézu modifikovaných deazapurinových nukleobází.

Byla vyvinuta metodologie pro chemo- a regioselektivní syntézu vysoce funkcionalizovaných deazapurinů založená na moderních metodách C-H aktivace, které umožňují do molekuly zavést různé funkční skupiny jako např. amino-, imido-, silyl- a fosfonyl-.

Aminodeazapurinové deriváty byly připraveny přímou Pd/Cu katalyzovanou C-H aminací a C-H chloroaminací z 6-substituovaných 7-deazapurinů pomocí *N*-chlor-*N*-alkyl-arylsulfonamidů. C-H imidační reakce pyrrolopyrimidinů pomocí *N*-sukcinimido- a N-ftalimidoperesterů byly provedeny za katalýzy ferrocenem. Dále byly navrženy iridiem katalyzované C-H silylační reakce 6-fenyldeazapurinů pomocí alkyl silanů. Pomocí manganem iniciované C-H fosfonace byly připraveny velmi zajímavé deazapurinové fosfonáty, které byly dále převedeny na příslušné fosfonové kyseliny.

Všechny vyvinuté přímé C-H aktivační reakce probíhají regioselektivně v poloze 8 na deazapurinovém jádře s výjimkou C-H silylací, které přednostně probíhají v ortho poloze na fenylu, což nicméně vede k zajímavým sloučeninám.

Druhá část této práce je zaměřena na modifikaci 7-deazapurinových bází v polohách 6 a 7 pomocí Suzuki-Miyaura reakcí s různými (hetero)aryl boronovými kyselinami ve vodném prostředí. Byla připravena série 6-(het)aryl-7-deazapurinových bází nesoucích F v poloze 7 a dále H, F, Cl, Me nebo NH_2 skupinu v poloze 2. 7-(Het)aryl-7-deazapurinové báze byly syntetizovány ze 7-jod-7-deazapurinu nesoucího SEM chránicí skupinu. Po odstranění SEM skupiny byly 6-methoxyderiváty převedeny na 7-deazahypoxanthiny a 7-deazaguaniny pomocí *O*-demethylačních reakcí.

Kombinace C-H aktivačních reakcí a vodných Suzuki-Miyaura reakcí se ukázala jako mocný nástroj pro modifikaci deazapurinového skeletu a umožnila zavedení různých funkčních skupin a hetarylových substituentů do všech možných poloh.

List of abbreviations

Ac	acetyl
acac	acetylacetone
Ar	aryl
bpy	2,2'-bipyridine
Bn	benzyl
B_2pin_2	bis(pinacolato)diboron
BSA	*N*,*O*-bis(trimethylsilyl)acetamide
Bz	benzoyl
COE	cyclooctene
COD	1,5-cyclooctadiene
Cp	cyclopentadienyl
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DCE	1,2-dichloroethane
DMF	*N*,*N*-dimethylformamide
DIAD	diisopropyl azodicarboxylate
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
dppf	1,1'-bis(diphenylphosphino)ferrocene
dcpe	bis(dicyclohexylphosphino)ethane
dtbpy	4,4′-di-tert-butyl-2, 2′ bipyridyl
DTBP	di-(*tert*-butyl) peroxide
equiv.	equivalent
Et	ethyl
HPFC	high performance flash chromatography
*i*Pr	isopropyl
[M]	transition metal
M.p.	melting point
Me	methyl
Ms	methylsulfonyl
NMP	*N*-methylpyrrolidone
NSP	*N*-succinimidyl perester

*o*Ns	*o*-nitrobenzenesulfonyl
[O]	oxidant
Ph	phenyl
Phen	1,10- phenanthroline
r.t.	room temperature
SEM	[2-(trimethylsilyl)ethoxy]methyl
SET	single electron transfer
TBAF	tetrabutylamonium fluoride
*t*Bu	*tert*-butyl
TBE	1,1,2,2-tetrabromoethane
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMS	trimethylsilyl
TPPTS	triphenylphosphine-3,3′,3″-trisulfonic acid trisodium salt
Ts	*p*-toluenesulfonyl

List of publications of the author related to the thesis

1. Sabat, N.; Klečka, M.; Slavětínská, L.; Klepetářová, B.; Hocek, M.: "Direct C–H amination and C–H chloroamination of 7-deazapurines" *RSC Adv.* **2014**, 4, 62140 – 62143.

2. Sabat, N.; Slavětínská, L.; Hocek, M.: "Ir-catalyzed C–H silylations of phenyldeazapurines" *Tetrahedron Lett.* **2015**, 49, 6860 – 6862.

3. Sabat, N.; Nauš, P.; Matyašovský, J.; Dziuba, D.; Poštová Slavetínská, L.; Hocek, M.: "Synthesis of Fluorescent 2-Substituted 6-(Het)aryl-7-deazapurine Bases {4-(Het)aryl-pyrrolo[2,3-*d*]pyrimidines} by Aqueous Suzuki–Miyaura Cross-Coupling Reactions" *Synthesis.* **2016**, 48, 1029 – 1045.

4. Sabat, N.; Poštová Slavětínská, L.; Klepetářová, B.; Hocek, M.: "C-H phosphonation of pyrrolopyrimidines. Synthesis of substituted 7- and 9-deazapurine-8-phosphonate derivatives" *J. Org. Chem.* **2016**, 81, 9507 – 9514.

5. Sabat, N.; Smolén. S.; Nauš, P.; Perlíková. P.; Cebová. M.; Poštová Slavětínská, L.; Hocek, M.: "Synthesis of 2,6-Substituted-7-(Het)aryl-7-deazapurine Nucleobases (2,4-Disubstituted-5-(het)aryl-pyrrolo[2,3-*d*]pyrimidines" *Synthesis.* **2017**, in press. DOI: 10.1055/s-0036-1588443.

Contents

1 Introduction

1.1 Purines and their analogues

Purine is a heterocyclic aromatic compound which consists of a pyrimidine ring fused to an imidazole ring. Due to the fact that this heterocycle was synthesized for the first time from uric acid, it was given the name purine (pure urine). There are many classes of naturally occurring molecules bearing a substituted purine moiety and all of them are generally called purines. The most important representatives include the purine nucleobases: adenine, guanine and hypoxanthine (Figure 1). Together with pyrimidine nucleobases they constitute the key components of RNA and DNA. Another notable class consists of xanthine alkaloids including caffeine and theobromine with their central nervous system stimulant effects.[1] It is important to emphasize that purine derivatives play an important role in various processes of living cells. Many of them are involved in enzymatic reactions as enzyme co-factors (ATP, GTP, Acetyl-CoA, cAMP, cGMP, NAD, FAD). For instance, adenosine triphosphate (ATP) (Figure 2) is a crucial nucleotide compound responsible for chemical energy transportation that is required for metabolic processes. It is worth mentioning yet another adenine-containing biomolecule Acetyl coenzyme A (Figure 2), the main function of which is to deliver acyl groups into the Krebs energy cycle. Such nucleotides as nicotinamide adenine dinucleotide (NAD) (Figure 2) and flavin adenine dinucleotide (FAD) are involved in redox/oxidation reactions, since they transfer electrons from one reactant to another. Based on the aforementioned examples of bioactive derivatives, it is difficult to exaggerate the importance of purine containing compounds.

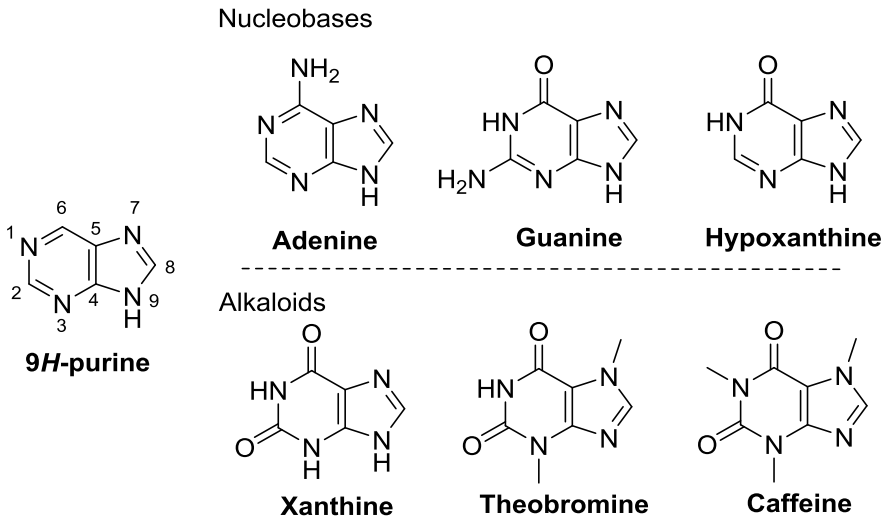


Figure 1 Purine and its analogues

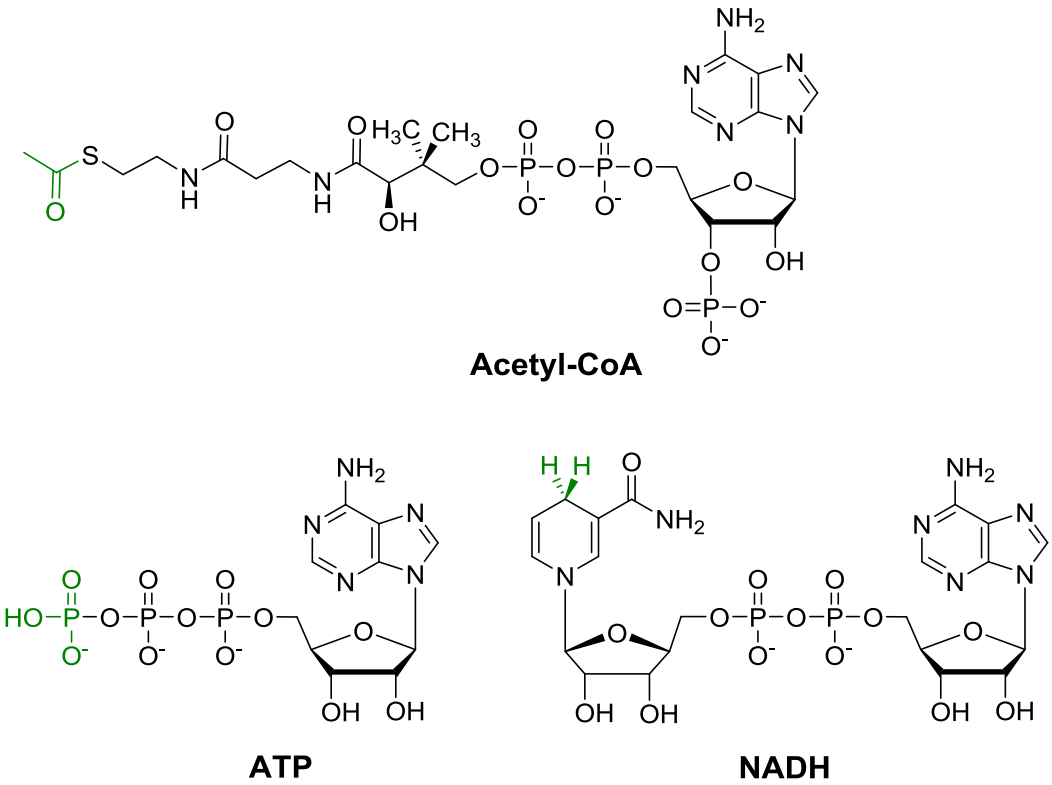


Figure 2 Adenine-containing nucleotide derivatives

In addition to many naturally occurring purine derivatives with a wide range of biological functions, dozens of new synthetic analogues have been synthesized. Different classes of synthetic purine derivatives have been discovered and a large number of them have resulted in medicines against many diseases. In light of this, it is important to mention the anti-HIV drug Tenofovir disoproxil fumarate[2] (trade name Viread, Truvada, Atripla) (Figure 3) and anti-HBV Adefovir dipivoxil[3] (trade name Hepsera) developed by a well-known Czech scientist Antonín Holý. Other reverse transcriptase inhibitor analogues are also known, for instance, Abacavir[4] and Entecavir[5] (Figure 3).

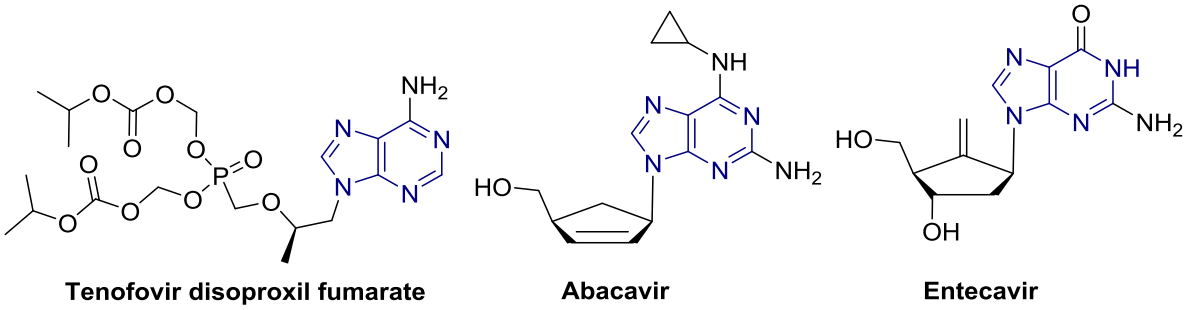


Figure 3 Purine Anti-HIV drugs

Scientific groups all around the world have been working on the synthesis and design of multisubstituted[6] purine bases. A lot of these bases display a broad spectrum of biological effects, mainly as inhibitors of various kinases, which are involved in many cellular processes. For example, the class of CDK inhibitors such as Roscovitine and its analogues has been well studied.[7] There are also other types of substituted purine derivatives that are TNNI3K inhibitors,[8] inhibitors of trypanosomal cysteine proteases,[9] reversible kinase inhibitors,[10] selective cannabinoid receptor agonists,[11] adenosine A_{2A} receptor antagonists (used for the treatment of Parkinson's disease),[12] Hsp90 protein inhibitors (as potent antitumor agents)[13] (Figure 4).

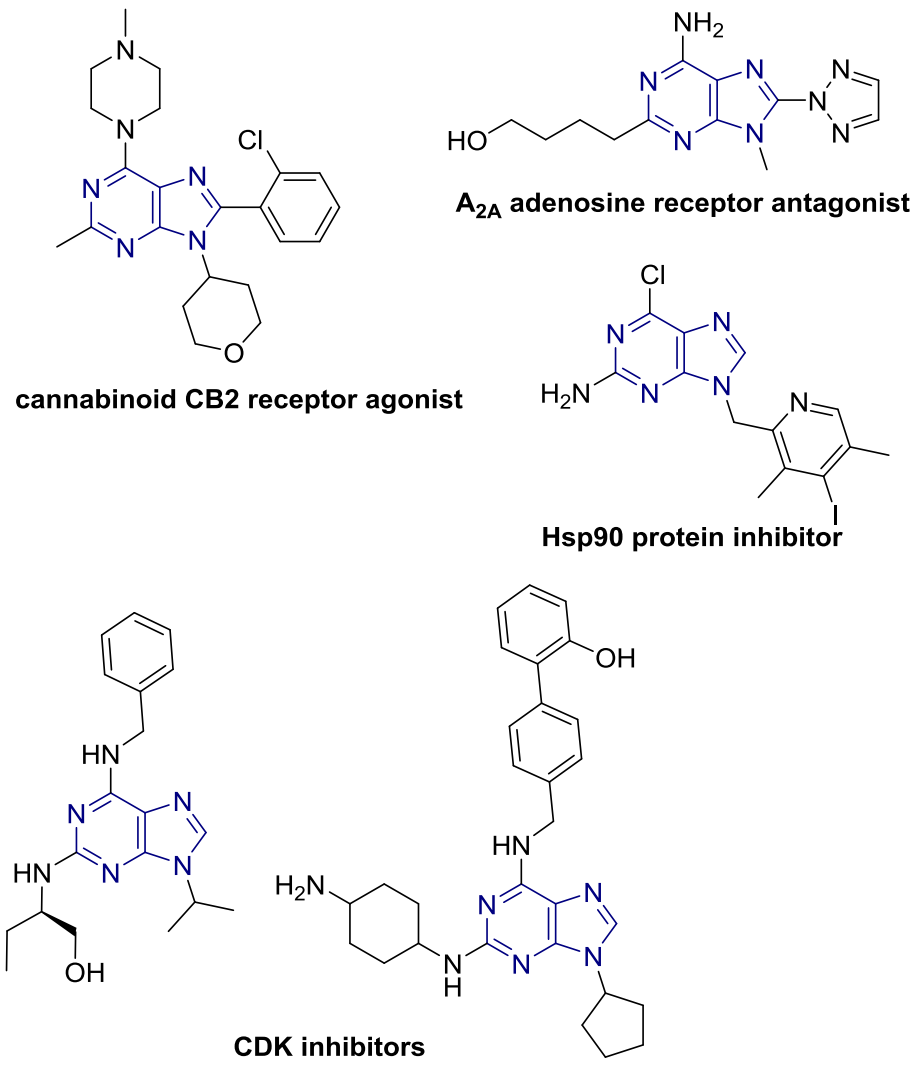


Figure 4 Biologically active purine derivatives with diverse modes of action

1.2 Deazapurine nucleobases and their derivatives

Having addressed purines and their derivatives, it is now worthwhile to consider deazapurine analogues. To begin with, deazapurine is a purine carba-analogue, where the nitrogen atom is replaced with a carbon atom. Based on this, there are several possible deazapurine analogues with imidazopyridine heterocycle (1- and 3-deazapurines) or pyrrolopyrimidine heterocycle (7- and 9-deazapurines) (Figure 5). According to the "purine" nomenclature, the number indicating a particular nitrogen atom in the purine system is replaced by carbon, followed by the prefix deaza. For clarity and to maintain homology when discussing natural purine bases, the purine nomenclature will be used throughout the thesis, while the correct IUPAC (pyrrolopyrimidine) nomenclature with the full names is used in the experimental section.

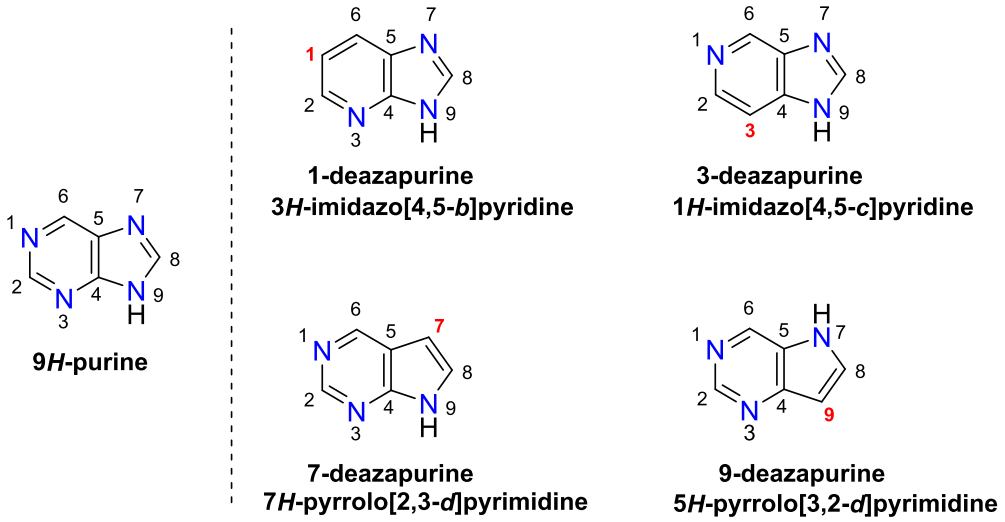


Figure 5 Structures of deazapurine nucleobases

With the additional carbon atom in deazapurine heterocycle compared to purine system, there is an extra space for modification. The chemistry of functionalized deazapurines and their efficient synthesis is a very interesting research area, which has provided motivation for further investigations.

1.2.1 Biological activity of substituted deazapurines

The literature overview resulted in many examples of multisubstituted deazapurines with diverse biological effects. Hence, it is worth addressing each group of deazapurine analogues and describe some structures of these bioactive compounds.

1.2.1.1 Biologically active 1-deazapurines

One of the oldest 1-deazapurine analogues, is cardiotonic drug Sulmazol discovered in 1984.[14] Sulmazol and its analogues are inhibitors of the cGMP phosphodiesterase (Figure 6).[15] Other interesting 8-coumarine-1-deazapurine derivatives are anti-HCV agents[16] and 8-pyridinylethyl derivatives which are selective nitric oxide (iNOS) inhibitors (Figure 6).[17] Some 2,3-disubstituted[18] and series of 2,6,8-trisubstituted[19] 1-deazapurines are known adenosine receptor antagonists (Figure 6). A new class of antiparasitic compounds for human African trypanosomiasis treatment bearing the 1-deazapurine moiety has been developed recently.[20] Several papers about 3,6,8-trisubsituted 1-deazapurines as inhibitors of TBK1/IKK$_{\varepsilon}$[21] and Aurora kinases[22] have been also published (Figure 6).

Thus, substituted 1-deazapurine derivatives undoubtedly display a broad spectrum of biological activities.

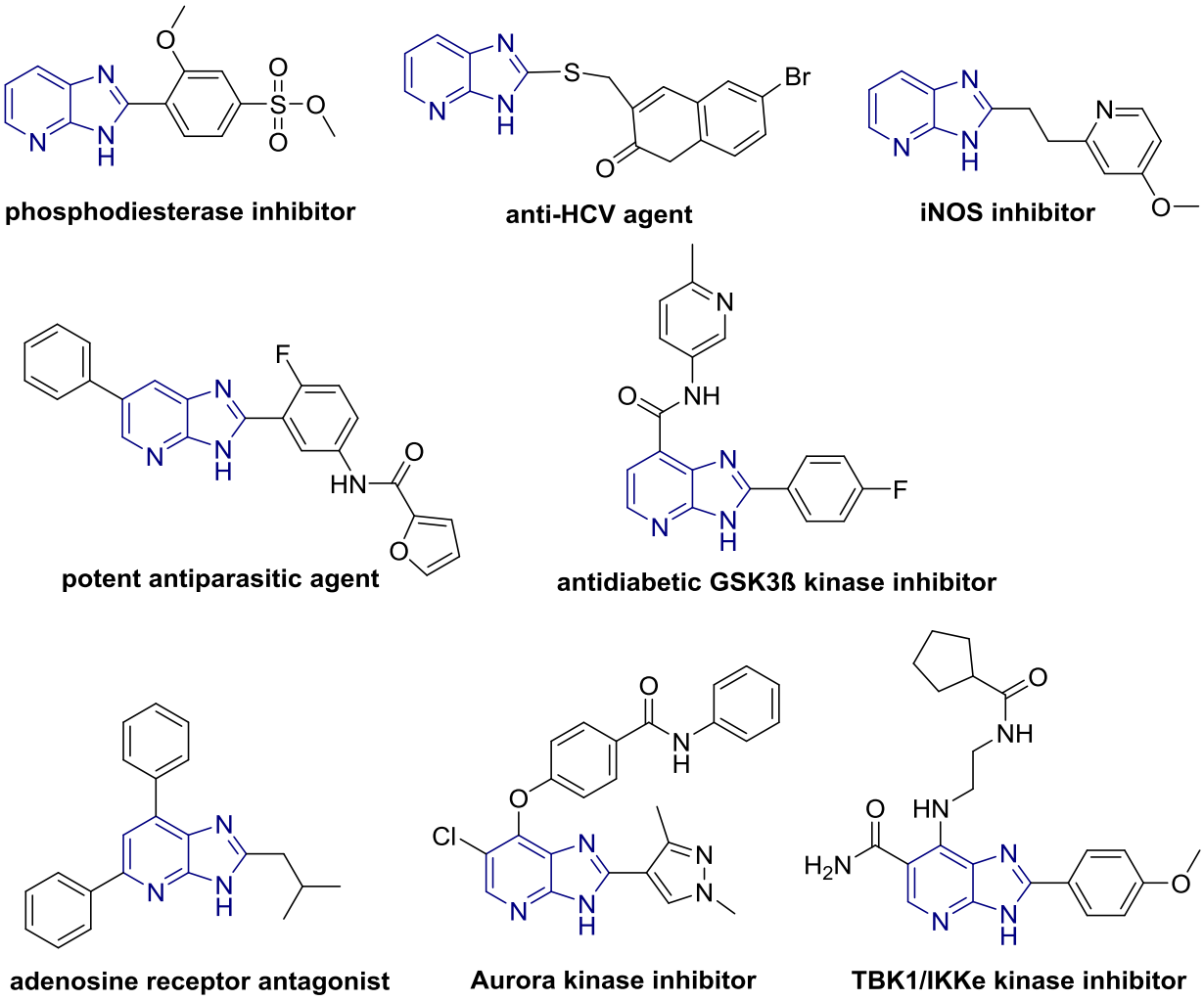


Figure 6 Substituted 1-deazapurine derivatives with diverse biological effects

1.2.1.2 Biologically active 3-deazapurines

Another structural modification of purine that has proven to be effective is 3-deazapurine. Several authors have reported the antiviral and anticancer activity of 3-deazaadenosine in 1978 and 1981.[23] The first attempts towards the synthesis of substituted 3-deazapurine bases were made in 1982 and 1987 in search of potential anticancer agents.[24] Later, 2,6,8-trisubstituted 3-deazapurines were synthesized and proved to be antimitotic agents.[25] Several other 2,6-substituted and 3,6,8-trisubstituted 3-deazapurines are known, such as cathepshin S inhibitors[26] and antimicrobial agents[27] (Figure 7). The research around 3-deazapurines definitely has room for further investigations, since there are only limited examples of their preparation and biological activity studies.

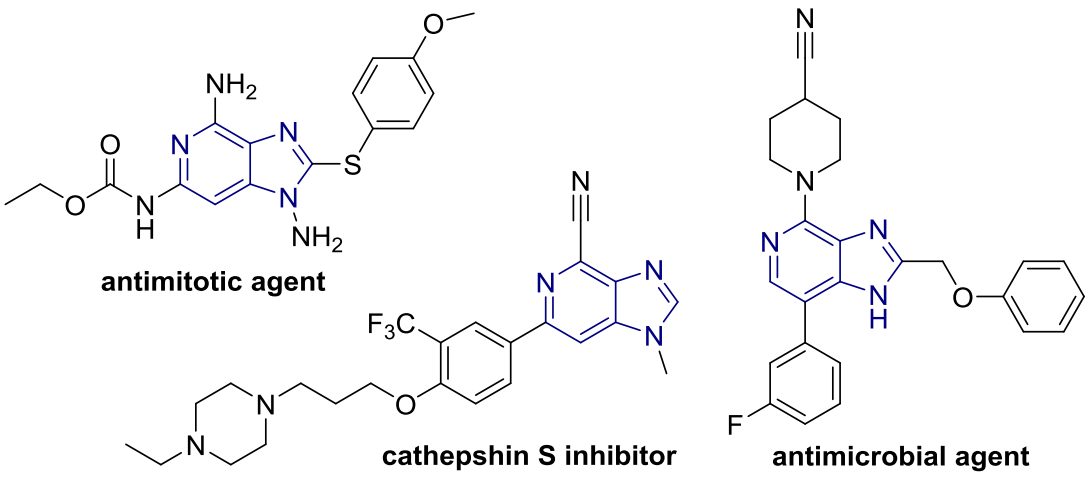


Figure 7 Examples of biologically active 3-deazapurines

1.2.1.3 Biologically active 7-deazapurines

Turning to 7- and 9-deazapurine analogues (pyrrolopyrimidines), it is worth mentioning that they are more interesting due to the close resemblance to purines, which is why they are often used in drug discovery as purine isosteres.

7-Deazapurines occur in nature both as a nucleobase and as a nucleoside. For example, echiguanines A and B (Figure 8) were isolated from the *Streptomyces* strain and were found to be potent inhibitors of phosphatidylinositol kinase, an enzyme that regulates cell growth, differentiation and development.[28] Hypermodified 7-deazapurine nucleosides queuosine and archaeosine (Figure 8) were found in the anticodon loop and D-loop of tRNA, respectively.[29]

Queuosine is distributed broadly in both prokaryotes and eukaryotes,[30] whereas archaeosine is widely distributed in archaeal species.[31]

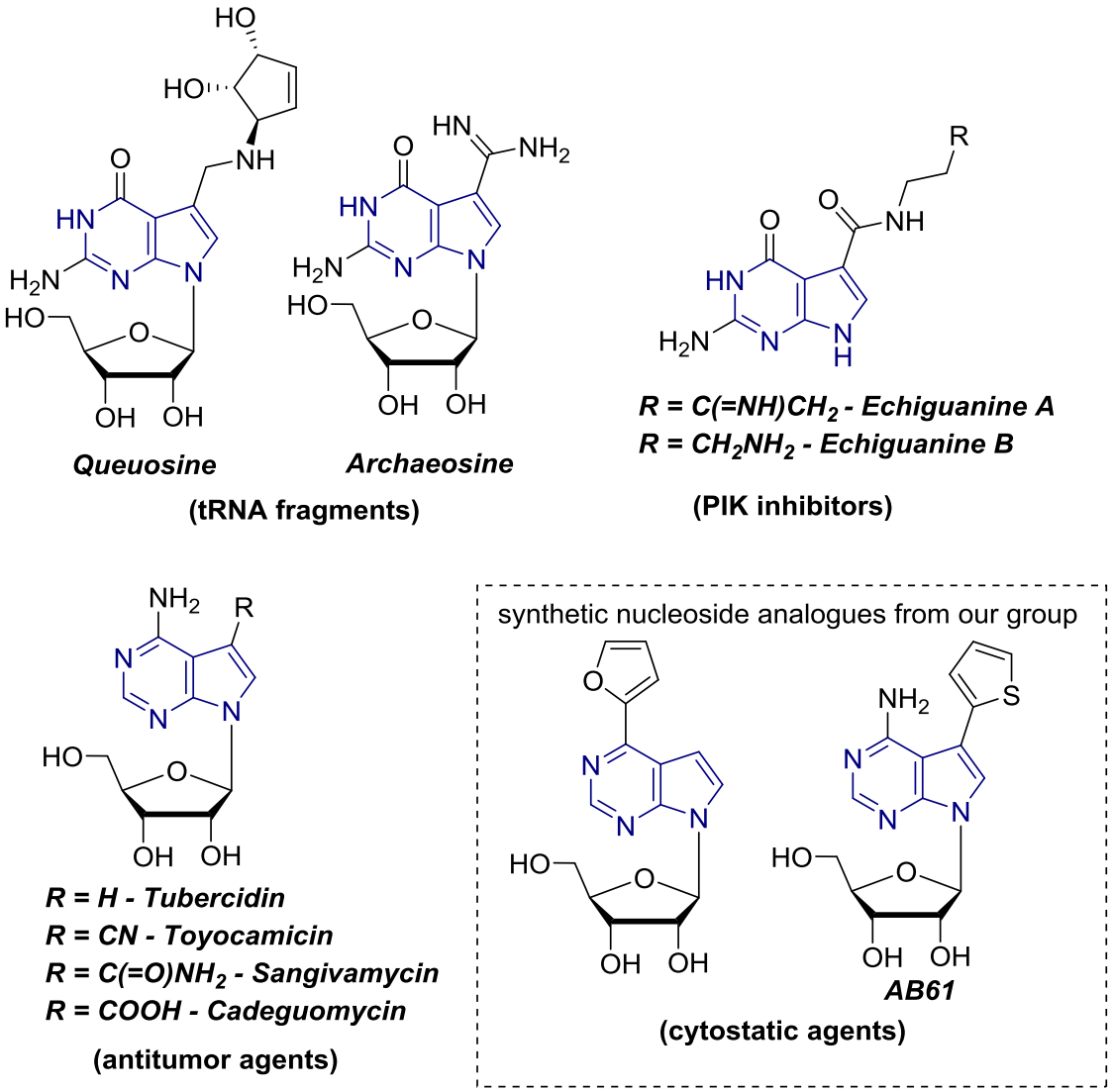


Figure 8 Natural 7-deazapurine derivatives and synthetic ones from our group

Structurally related 7-deazapurine ribonucleosides tubercidin, toyocamycin and sangivamycin (Figure 8) were all isolated from *Streptomyces* cultures. Toyocamycin is a powerful anti-tumor agent both *in vitro* and *in vivo*, however, it also shows high levels of host toxicity.[32] Tubercidin exhibits potent antibiotic activity against *Candida albicans* and *Mycobacterium tuberculosis* but does not inhibit the growth of Gram-positive bacteria, and fungi. It is also shows cytotoxic activity towards NF-mouse sarcoma cells in culture,[32] cultured mouse fibroblasts,[33] and human tumor specimens.[34] Antiviral activity toward Vaccinia, Reovirus III, and Mengiovirus,[33] which contain genomes composed of DNA,

double-stranded RNA, and single-stranded RNA, respectively, have also been noted. Sangivamycin is highly cytotoxic to HeLa cells in culture and leukemia L1210 in mice.[35]

In our scientific group several papers were published about the synthesis, cytostatic, antimicrobial and anti-HCV activity of substituted 7-deazapurine nucleosides (Figure 8).[36,37] We have described the synthesis and biological activity screening of 6-(het)aryl purine and different types of deazapurine nucleosides. According to the biological activity profile, purine nucleosides showed potent cytostatic activity against a number of cancer cell lines.[38] Later on, 7-deazapurine nucleosides proved to be strong cytostatics as well,[36] whereas known 1-deazapurine analogues displayed only a weak activity,[39] and 3-deazapurine nucleosides were completely inactive.[40] Apparently, the exchange of the N-1 or N-3 nitrogen for a carbon (in purines) results in weaker activity. This phenomenon could be explained by the importance of N-1 and N-3-nitrogens in specific interactions between the nucleobase side and target biological environment.

Based on these sdudies presented, the 7-deazapurine nucleobase analogue is a perfect object for investigation due to its close similarity to purine and free room for modification at the C-7 position. In comparison to 9-deazapurine, where the pyrimidine side of the molecule is the same, 7-deazapurine is more essential and closer to natural purines because of its propensity to be glycosylated in the same manner.

According to the numbers of reported publications, diversely substituted 7-deazapurine nucleobases belong to one of the main areas of research interest. In a number of publications Gangjee and co-authors reported the design, synthesis and antitumor activity of substituted 7-deazapurines as inhibitors of thymidylate synthase and dihydrofolate reductase.[41] Other derivatives with 7-deazapurine moiety are selective inhibitors of various kinases with different biological effects. They are inhibitors of Axl kinase (anticancer),[42] LRRK2 kinase (Parkinson's disease treatment),[43] Akt kinase (antitumor),[44] EGFR kinase (anticancer),[45] LIMK kinase (ocular hypertension treatment),[46] TNNI3K kinase (heart failure treatment),[47] JAK3 kinase (autoimmune diseases treatment),[48] ACK1 kinase (anticancer),[49] PTR1 kinase (antiparasitic),[50] GyrB and ParE kinases (antibiotic),[51] RTKs kinase (anticancer),[52] BTK kinase (anticancer), etc.[53] Some of 7-deazapurines are Heat Shock Protein 90 inhibitors with promising anti-cancer activity.[54] Examples of Cathepsine S inhibitors[55] and sodium channels antagonists[56] are also known.

Evidently, substituted 7-deazapurines attract significant attention as synthetic targets due to their wide range of biological effects. Many of them are used in clinical trials and have strong potential to become drugs (Figure 9).

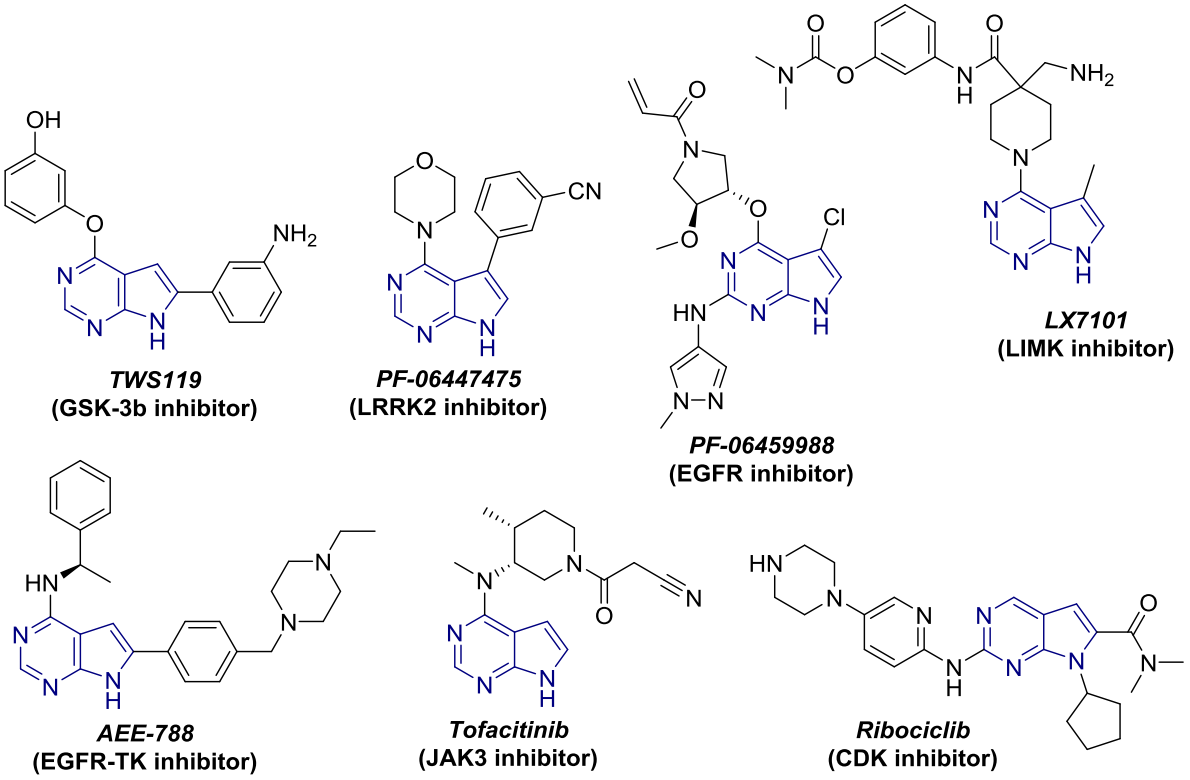


Figure 9 Examples of experimental drugs containing the 7-deazapurine moiety

Additionally, the corresponding 7-deazapurine nucleoside triphosphates are also widely used in biochemical incorporations into the DNA. Previously, our research group reported on the competitive incorporations of 7-substituted 7-deazaadenine dNTPs (in the presence of natural adenine deoxyribonucleoside triphosphates) into DNA by several DNA polymerases. Analysis based on the cleavage by restriction endonucleases was used for that purpose. 7-Aryl-7-deazaadenine dNTPs were more efficient substrates than dATP because of their higher affinity for the active site of the enzyme, as proved by kinetic measurements and calculations.[57]

1.2.1.4 Biologically active 9-deazapurines

In contrast to 7-deazapurines, no 9-deazapurines occur naturally and, thus need to be prepared synthetically. In a series of substituted 9-deazapurine derivatives many biologically active examples were found (Figure 10). Several papers were published about the antiproliferative activity of aminobenzylated[58] and halogenated 9-deazapurines against many cell lines.[59] Other 9-deazapurine compounds are known as antitumor agents.[60] Interesting

papers were published about 9-deazapurines as glucocorticoid receptor agonists and neuropeptide Y5 receptor antagonists.[61] Several substituted 9-deazapurines inhibit different kinds of kinases. They are potent inhibitors of phosphatidylinositol 3-kinase[62] (with the potential in human breast cancer treatment) dual thymidylate and dihydrofolate reductase[63] and epidermal growth factor receptor (HER2/EGFR), that were studied for the treatment of different cancer types, including breast, lung, gastric and others.[64]

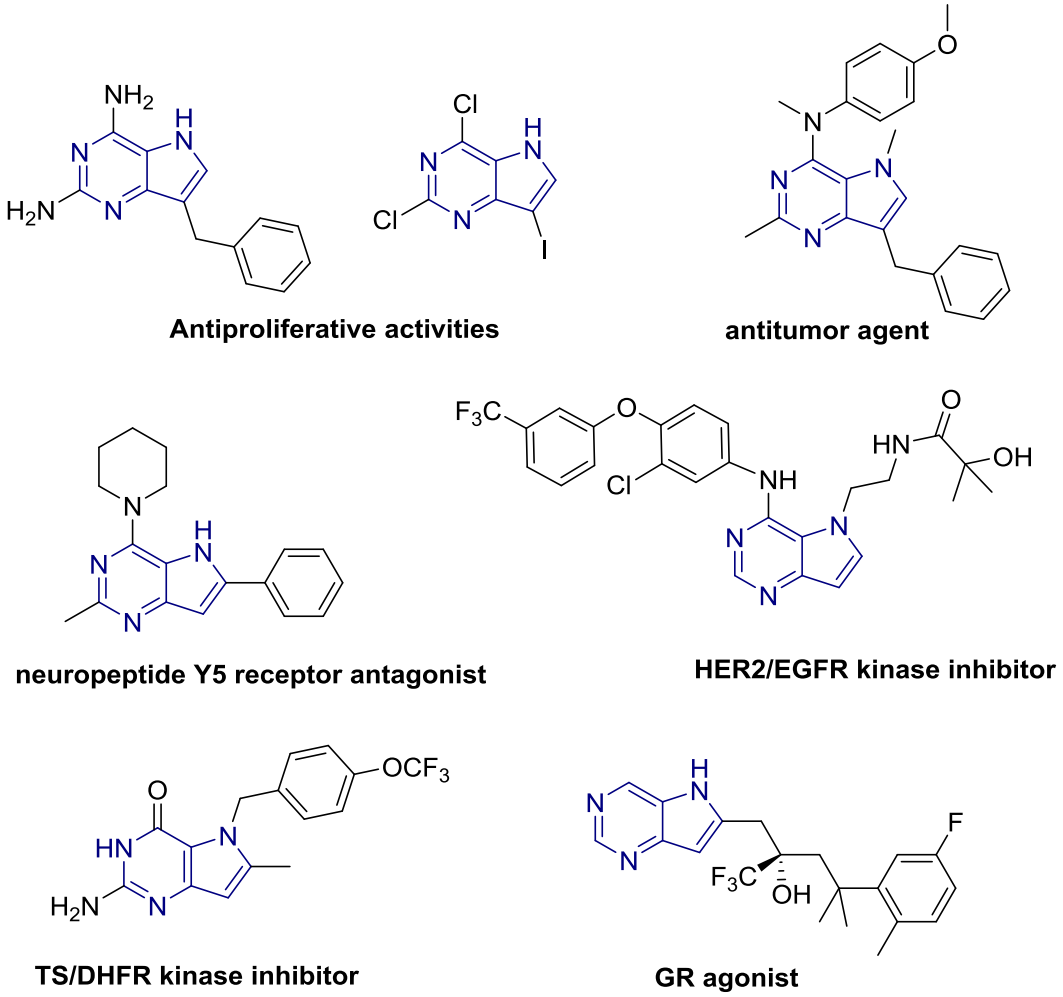


Figure 10 Biological activities of 9-deazapurines

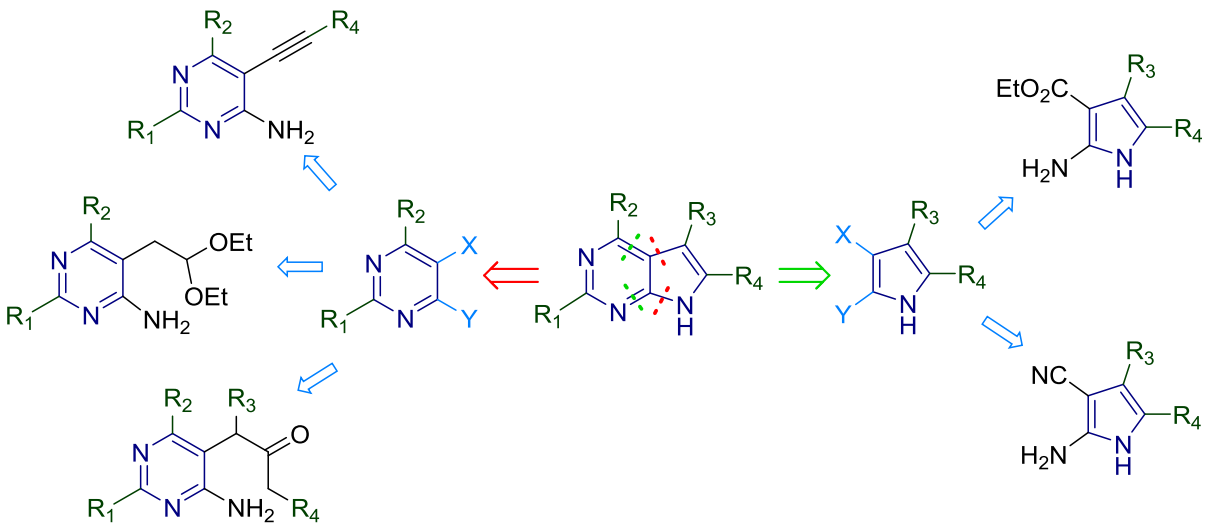
To systematize the literature review, a large number of deazapurine nucleobases with diverse biological effects have been discussed. The most interesting of them are 7-deazapurine analogues due to their close resemblance to biogenic purine bases, the extra space for skeleton modification and many other important properties, as mentioned above.

1.3 Synthesis of substituted 7-deazapurines

1.3.1 Heterocyclization methods

7-Deazapurines (pyrrolo[2,3-*d*]pyrimidines) have been clearly demonstrated to be an important class of heterocycles because of their interesting scaffold structure and various biological effects.[29-56] Hence, the development of a chemo- and regioselective synthesis of highly functionalized 7-deazapurines is a worthwhile goal. According to the literature, preparation of substituted 7-deazapurines is usually performed using a traditional approach based on heterocyclization reactions.

Heterocyclization methods are based on the sequence of multicomponent reactions where the key step is cyclization of a pyrrole or pyrimidine intermediate (Scheme 11).

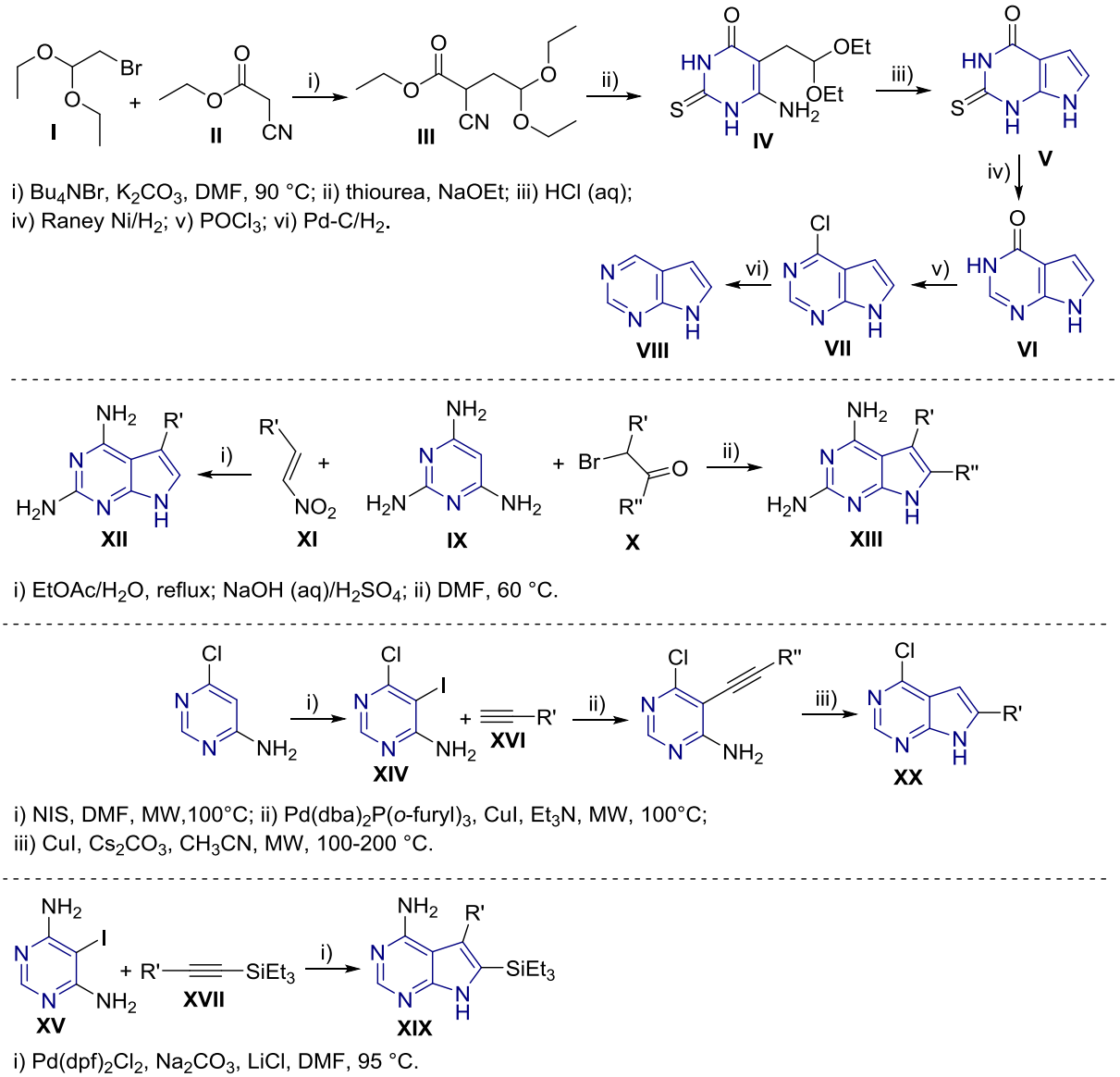


Scheme 11 Retrosynthetic scheme for the preparation of 7-deazapurines

The synthesis of 7-deazapurines through a pyrimidine intermediate could be explored from several synthetic angles. Many pyrimidine precursors are commercially available or need to be prepared through multistep synthesis. The following schemes demonstrate some examples of reported protocols dealing with the synthesis of substituted 7-deazapurine bases via pyrimidine intermediates (Scheme 12). The general synthesis of 7-deazapurines has been provided by several authors.[54b,65] The synthesis starts from the reaction of ethyl cyanoacetate **I** with bromoacetaldehyde diethyl acetal **II**. In the next step, intermediate **III** reacts with thiourea resulting in dihydropyrimidinone **IV**, which further undergoes cyclization to **V** under acidic conditions. Pyrrolopyrimidinone **V** is then reduced to hypoxanthine **VI**, which in turn is chlorinated by phosphorus oxychloride to yield a very useful 6-chloro-7-deazapurine

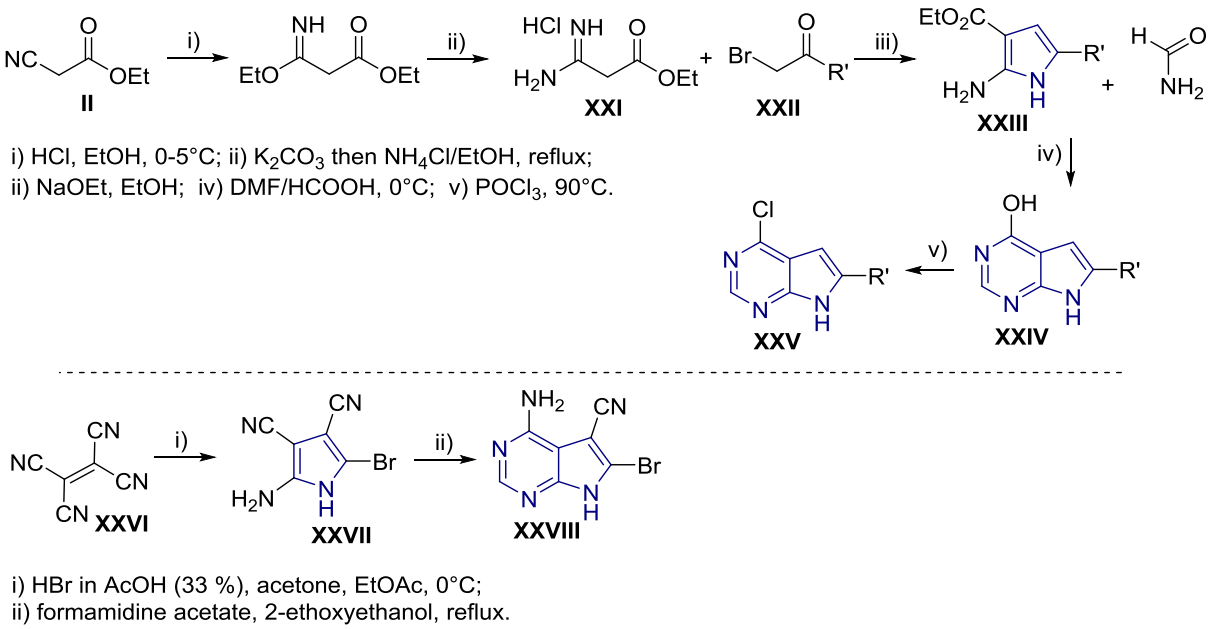
derivative **VII**. Chlorine substituent could be further reduced by hydrogenolysis to fully unsubstituted 7-deazapurine **VIII**.

Other methods for the preparation of 7-deazapurines are based on reactions of functionalized pyrimidines **IX** with substituted ketones **X** or nitroalkenes **XI** resulting in 7- or 7,8-disubstituted 7-deazapurines **XII-XIII**.[50] Another approach involves Sonogashira cross-coupling reactions of 5-iodoprimidine derivatives **XIV-XV** with appropriately substituted alkynes **XVI-XVII**.[49,55,66] Intramolecular cyclization under catalytic conditions occurs , that in turn gives substituted 7-deazapurines **XIX-XX**.



Scheme 12 Synthesis of 7-deazapurines from pyrimidines

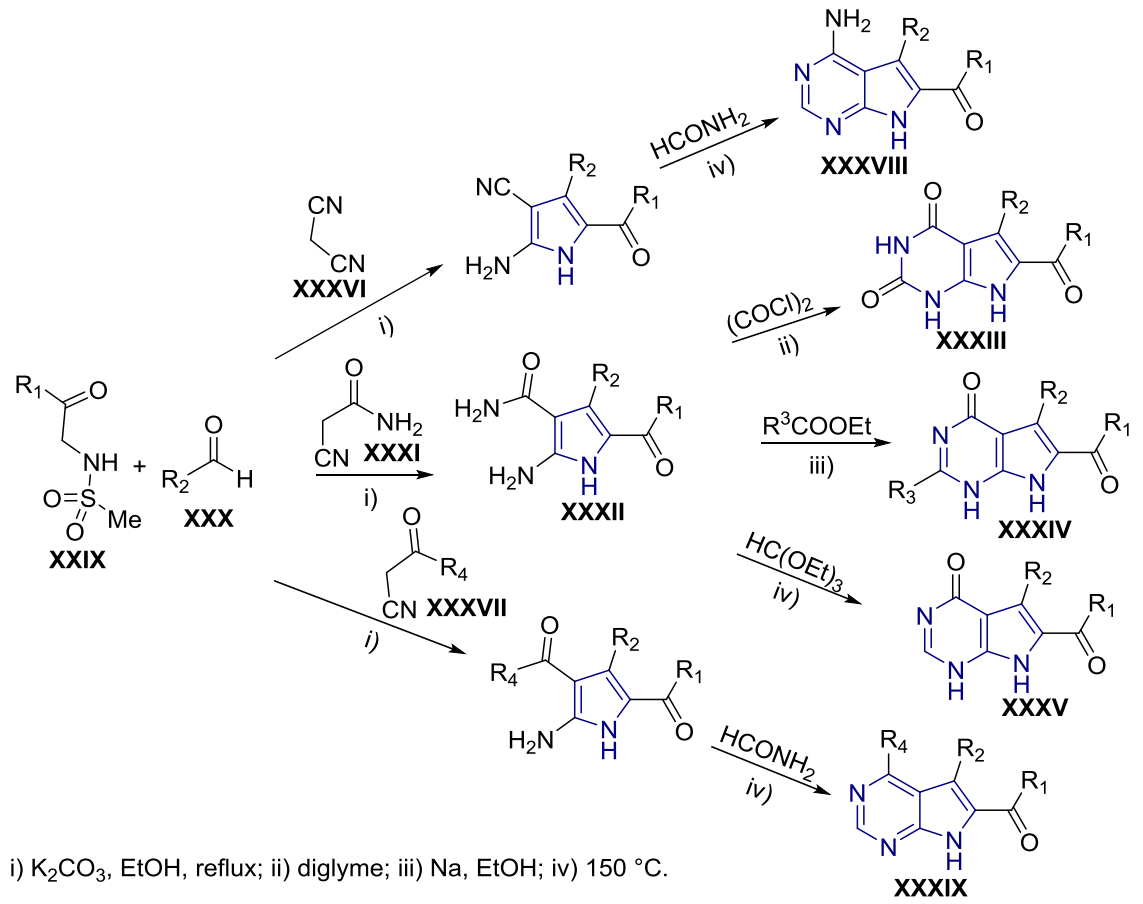
The second strategy towards 7-deazapurines is based on the intramolecular cyclization of pyrrole intermediates. In a usual approach, synthesis starts from ethyl cyanoacetate **II** which is transformed into intermediate **XXI** (Scheme 13). Cyclization of **XXI** with bromoketone **XXII** under basic conditions results in pyrrole precursor **XXIII**. After the intramolecular condensation of **XXIII** with formamide, obtained deazahypoxanthine derivative **XXIV** could be chlorinated to 8-substituted 6-chloro-7-deazapurine **XXV**.[67] Another reported type of pyrrole precursor **XXVII** was obtained from tetracyanoethylene **XXVI** by condensation in the presence of hydrogen bromide. Final cyclization with formamidine acetate gave 7-cyano-8-bromo deazaadenine **XXVIII**.[68]



Scheme 13 Synthesis of 7-deazapurines from pyrroles

In 2013, yet another approach using multicomponent reactions to prepare substituted 7-deazapurine analogues was published.[69] According to this method, various sulfoneamides **XXIX** reacted in a three-component reaction with aromatic aldehydes **XXX** and cyanoacetamide **XXXI** in the presence of potassium carbonate in refluxing methanol to give aminopyrroles **XXXII** (Scheme 14). Cyclization with oxalyl chloride, carboxylic acid ester or orthoester resulted in substituted 7-deazaxanthines **XXXIII** or 7-deazahypoxanthine derivatives **XXXIV-XXXV** respectively. Further studies of three-component reactions led to the discovery of a four-component reaction where formamide was used as a solvent and cyanoacetamide **XXXI** was replaced with malononitrile **XXXVI** or cyanomethylketones

XXXVII. As a result, a series of substituted 7-deazaadenines **XXXVIII** and 7-deazapurines **XXXIX** were prepared.



Scheme 14 Synthesis of 7-deazapurine analogues by multicomponent reactions via pyrroles

Heterocyclization methods are definitely a strong tool for the preparation of substituted 7-deazapurines. Nevertheless, these methods have their limitations. Heterocyclizations require multiple steps throughout the synthesis and reactions are often problematic because of selectivity, harsh conditions, low yields, etc. Thus, to simplify the preparation of functionalized 7-deazapurines there is an actual need for alternative approaches.

1.3.2 Substitution reactions of 7-deazapurines

The synthesis of 7-deazapurine nucleobases bearing different substituents and functional groups is the most important goal of this work. In order to achieve this aim it is necessary to efficiently use all possible instruments for the preparation of 7-deazapurines. Traditional approaches based on heterocyclizations turned out to be quite complicated, and very often it is very dificult to put the designed substituent at the particular position of the 7-deazapurine skeleton. Nevertheless, synthetic organic chemistry offers very flexible tools and there always might be an alternative approach towards the synthesis of complex molecules. Indeed, there are several alternative methods that could be applied to the preparation of diversely substituted 7-deazapurines. These methods are based on the modification of 7-deazapurine bearing the halogen or other functional group at position 6. The most common starting substrate for such modification is commercially available 6-chloro-7-deazapurine (Figure 15).

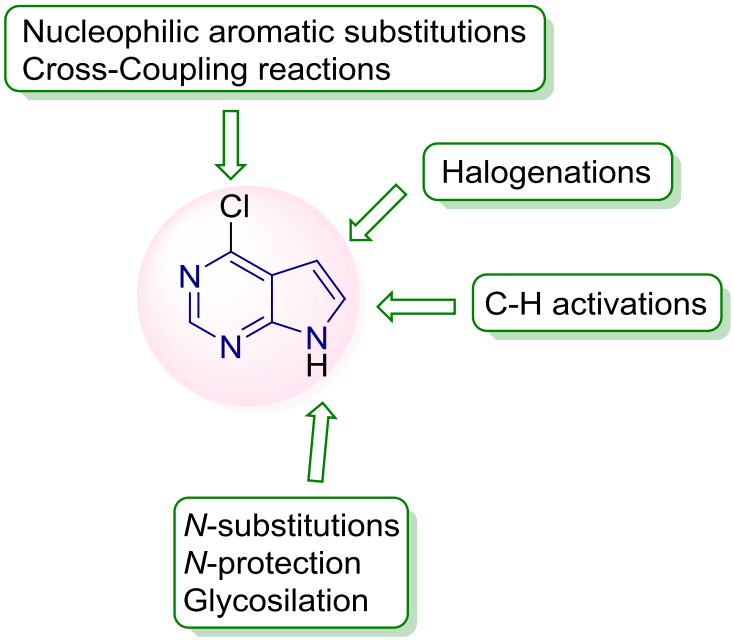
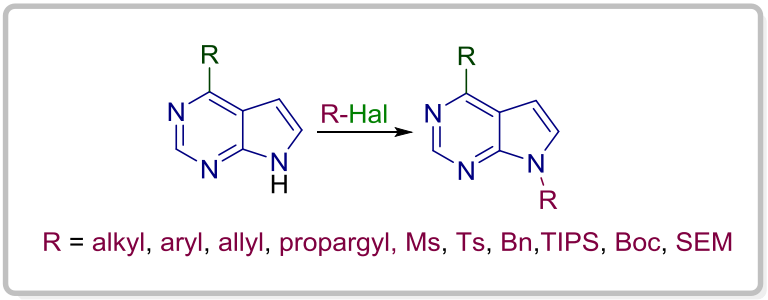


Figure 15 Alternative methods for the preparation of substituted 7-deazapurines

1.3.2.1 *N*-substitutions of 7-deazapurines

In order to modify the N-9 position of 7-deazapurines, nucleophilic substitution reactions have proven to work nicely, and diverse substituents and protecting groups can be introduced this way (Scheme 16). This approach tolerates various alkyl groups such as small Me[70a,b] or Et,[70c] as well as bulkier i-Pr,[70b,c] cyclopentyl,[70b,d] etc.[70] Examples of aryl,[71] allyl[72] and propargyl[73] N9-substituted 7-deazapurines are also known.

Since the free 9-NH group of 7-deazapurines is quite reactive and often can be involved in undesirable reactions, it is necessary to use a protecting group strategy. Typically, installation of sulfonyl (Ms, Ts),[74] triisopropyl (TIPS),[75] tert-butyloxycarbonyl (Boc),[76] benzyl (Bn)[77] and [2-(trimethylsilyl)ethoxy]methyl (SEM)[78] protecting groups have been used.

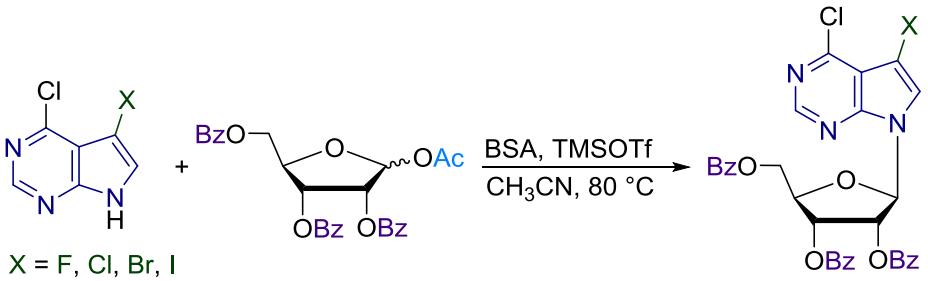


Scheme 16 N-9 substitutions of 7-deazapurines

1.3.2.2 Glycosylation of 6-halo-7-deazapurines

In the synthesis β-ribofuranosyl nucleosides, the most commonly used approach is Vorbrüggen variant[79] of the silyl-Hilbert-Johnson reaction. In this reaction, perbenzoylated ribofuranoside in the presence of a Lewis acid, usually TMSOTf or $SnCl_4$, generates a benzoxonium ion that blocks the α face of the molecule *in situ* from nucleophilic attack, known as a neighboring group effect. A silylated nucleobase is then added, and after extensive heating the desired protected β-nucleoside analogue can be prepared.

Thus, in the regio- and stereo- selective synthesis of 7-deazapurine ribonucleosides the presence of an acyl group at position 2 of ribose (neighboring group participation) and a halogen at position 7 of 7-deazapurine (to avoid formation of N-1 and C-7 products) is crucial (Scheme 17).[80,81]

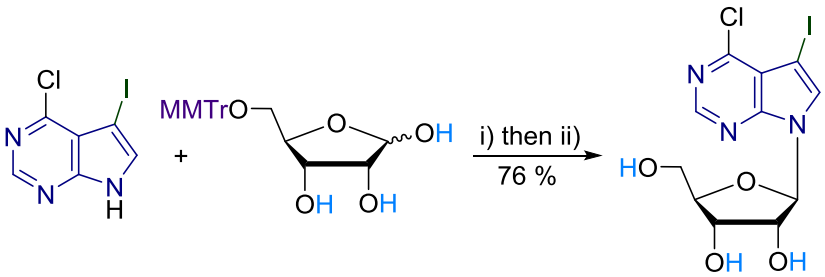


Scheme 17 Synthesis of 7-deazapurine ribonucleosides by Vobrüggen reaction

The typical protocol for this reaction is to generate silylated 7-halo-7-deazapurine by treating starting deazapurine with *N*,*O*-bis(trimethylsilyl)acetamide (BSA) in MeCN at room

temperature. Then, after addition of ribofuranose derivative and TMSOTf the reaction mixture is heated to 80 °C.

Very recently, our scientific group reported a direct one-pot synthesis of nucleosides starting from unprotected or *5-O*-monoprotected D-ribose.[82] This approach is based on modified Mitsunobu conditions, and 7-deazapurine β-ribonucleoside can be prepared from *5-O*-methoxytrityl protected ribofuranose and 7-deazapurine nucleobase (Scheme 18).

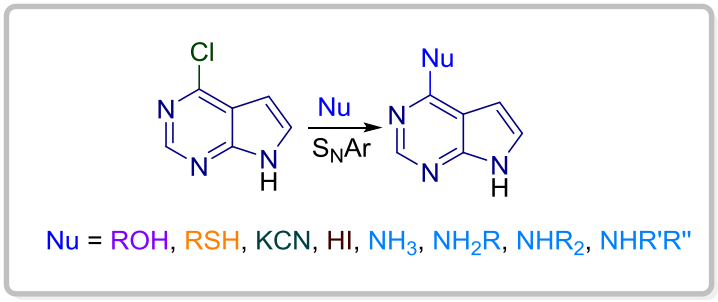


i) Deazapurine (1 equiv) and DBU (1 equiv) in MeCN, 15 min at rt;
then DIAD (2.1 equiv), P(n-Bu)$_3$ (2 equiv), 0 °C to rt, 12h;
ii) 1M HCl (aq), pH = 1, 60 °C, 15 min.

Scheme 18 Synthesis of 7-deazapurine ribonucleoside by modified Mitsunobu conditions

1.3.2.3 Nucleophilic aromatic substitutions of 6-chloro-7-deazapurine

One of the most important methods for modification at 6-chloro position in 7-deazapurines is nucleophilic aromatic substitution. This approach allows for the introduction of various substituents such as alkoxy, arylloxy,[83] sulfanyl,[84] cyano,[85] iodo[86] as well as different amino groups[43,45] (Scheme 19).



Scheme 19 Nucleophilic aromatic substitutions of 6-chloro-7-deazapurine

Many biologically active 7-deazapurine derivatives were prepared by using nucleophilic displacement of chlorine with groups bearing other heteroatoms (Figure 9).

1.3.3 Cross-coupling reactions of 6-halo-7-deazapurines

Nowadays, transition metal-catalyzed cross-couplings have been studied and have proven to be highly selective and a straightforward method for the functionalization of organic molecules. The Suzuki reaction is especially reliable with a great assortment of commercially available boronic acids, boronic esters or trifluoroborates. Nevertheless, there are still some limitations related to the use of cross-coupling reactions due to the stability of organic reagents, chemoselectivity of some reactions, harsh reaction conditions, etc. This fact shows that there is still reasonable interest in the development of new methodologies or improvement of the existing ones.

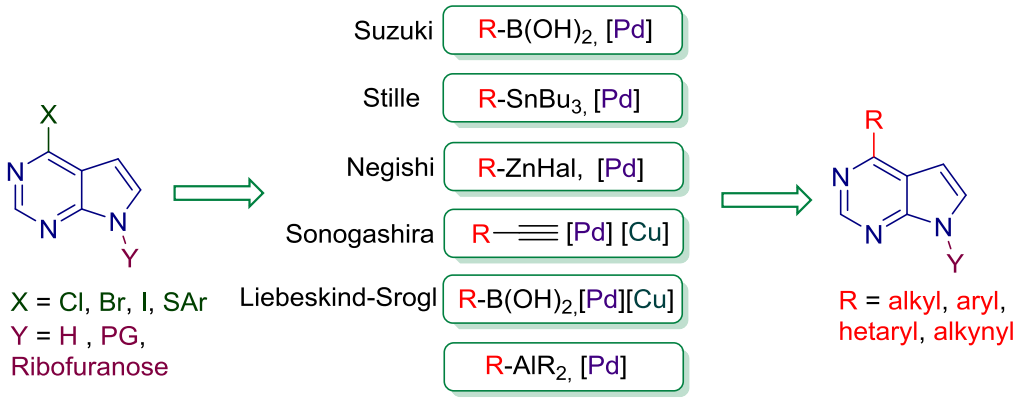


Figure 20 Cross-coupling reactions at position 6 of 7-deazapurines

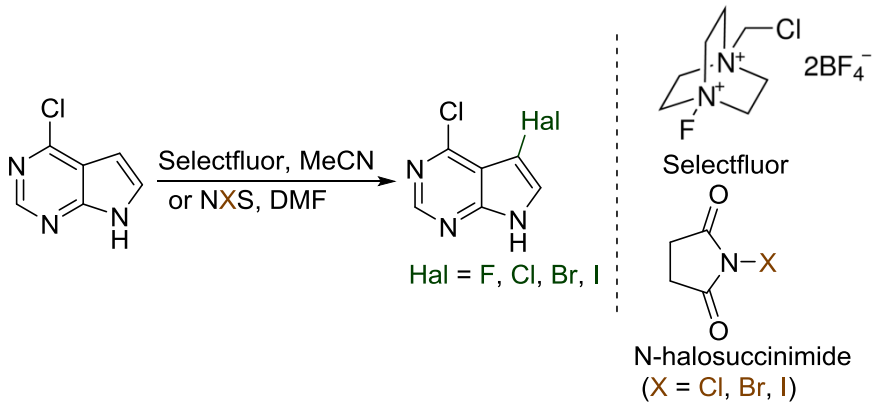
Diversely substituted 7-deazapurines could be synthesized by using various cross-coupling approaches (Figure 20). In the past, our group reported Pd-catalyzed cross-coupling reactions of protected 6-chloro-7-deazapurine nucleosides.[36] Various cross-coupling reactions were performed with the alkyl- or (het)arylboronic acids (Suzuki), tributylstannanes (Stille), organozinc (Negishi) and aluminium reagents. The research related to the modification of 7-deazapurine nucleobases by cross-coupling reactions is rather scarce. Several authors reported Suzuki cross-couplings of 6-chloro or 6-bromo-7-deazapurines by using tetrakis(tryphenylphosphine)palladium ($Pd(PPh_3)_4$) as a catalyst and potassium carbonate as a base in different solvent systems.[48,87] Examples of Sonogashira coupling reactions starting either from 6-chloro or 6-iodo-7-deazapurine have also been described.[86,88] For the reaction, a common protocol was applied, where bis(triphenylphosphine)palladium chloride ($Pd(PPh_3)_2Cl_2$) was used in combination with Cu(I) iodide and trimethylamine. Gundersen and co-authors reported Stille coupling of N-protected 6-chloro-7-deazapurines with several (het)aryltributylstannanes in DMF under ($Pd(PPh_3)_2Cl_2$) catalysis.[89] In addition to classical coupling reactions, there is known Liebeskind-Srogl cross-coupling of thioethers with boronic

acids.[90] Moreover, publication by our group demonstrated a chemoselective synthesis of 6,7-diaryl-7-deazapurines by consecutive Suzuki and Liebeskind-Srogl cross-couplings.[91]

According to the literature, Suzuki cross-couplings showed to be the most useful and versatile approach for the modification of position 6 in 7-deazapurine substrates. A particular interest of this thesis was attracted by altered Suzuki-Miyaura coupling reactions under mild aqueous conditions, previously applied to purines and deazapurine nucleosides.[37,92] However, this variation of coupling reaction has never been used in 7-deazapurine nucleobases themselves and remains a very interesting research topic. Thus, it is worth modifying position 6 and 7 of 7-deazapurines by using these aqueous-phase Suzuki-Miyaura reaction conditions, that will be pursued within the framework of this thesis.

1.3.4 Halogenation reactions of 6-chloro-7-deazapurine

Another important approach towards variously substituted 7-deazapurines is the introduction of halogens onto their scaffold (Scheme 21). The most known protocol for the fluorination of 6-chloro-7-deazapurine is uses Selectfluor as a fluorine donor.[93] Chlorination, bromination and iodination commonly occur by reaction of 6-chloro-7-deazapurine with a stoichiometric amount of *N*-halosuccinimide in DMF.[80] All the halogenation reactions proceed regioselectively at position 7 of 7-deazapurine. A fluorine atom at position 7 is very important due to its influence on the biological activity of deazapurine nucleosides.[36] As it was mentioned before, chlorine, bromine and iodine at position 7 are play a crucial role in the selectivity of Vorbrüggen glycosylation (Scheme 17).[80] As a result, only β-nucleosides are formed, whereas without a halogen atom at position 7 the reaction does not give the desired product. Another meaningful application of halogens at this particular position is their utility in cross-coupling reactions.[37,91]



Scheme 21 Halogenations of 6-chloro-7-deazapurine

1.3.5 C-H activation strategies

Transition metal-catalyzed/mediated C-H bond activation and functionalization represent one of the most straightforward and powerful tools in modern organic synthetic chemistry. Direct and selective replacement of carbon-hydrogen (C-H) bond with a new carbon-heteroatom bond (C-N, C-B, C-S, C-Si, C-P) has drawn tremendous research attention during the past decades.

In comparison with classical cross-coupling reactions that require preparation of organometallic reagents and (het)aryl halides, C-H activation is a more straightforward approach (Figure 22).[94]

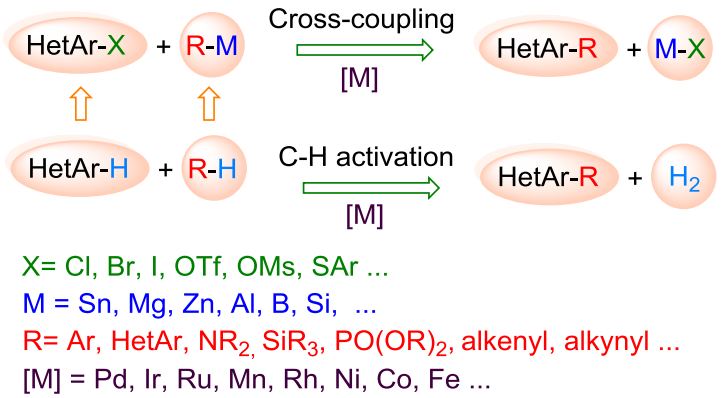


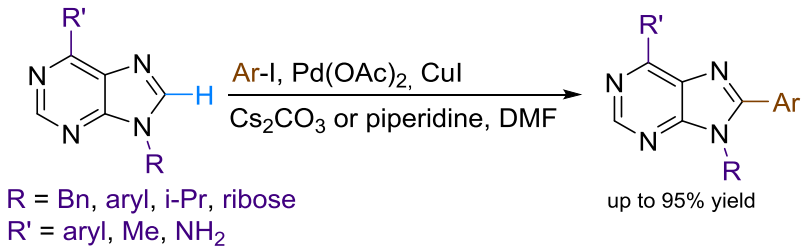
Figure 22 Cross-coupling and C-H activation reactions

Undoubtedly, this approach has strong potential for modification of several positions on the 7-deazapurine scaffold. Despite the versatility of C-H activation strategies, one should expect challenges regarding the architecture of the molecule. The 7-deazapurine heterocycle bears two types of reactive C-H bonds at position 7 and 8. Therefore, studying the reactivity and regioselectivity of these bonds is worthwhile research.

Potentially various functional groups such as amino, boronate, sulfanyl, silyl, phosphonyl could be introduced. Development of such methodologies for the efficient synthesis of substituted 7-deazapurine nucleobases is an important goal from many perspectives, from a synthetic point of view as well as for medicinal chemistry or biochemistry applications.

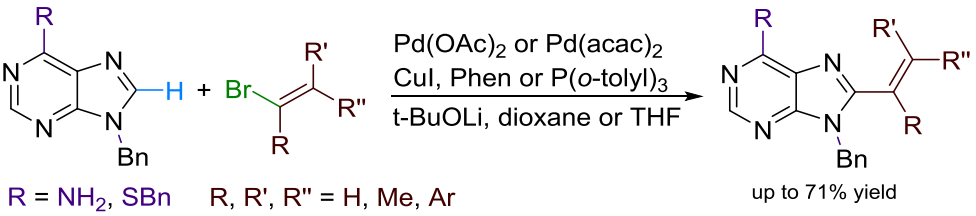
1.3.5.1 C-H activations of purines and deazapurines

Development of new methodologies for the modification of purine and deazapurine nucleobases using C-H activation reactions is a unique research topic and originates from our scientific group. First attempts were performed by Igor Černa, who developed Pd-catalyzed direct C-H arylation of purines and purine ribonucleosides (Scheme 23).[95] C-H arylation methodologies in combination with cross-coupling reactions allowed preparation of multisubstituted purine bases,[95a-b] 8-modified purine nucleosides[95c] and fused purines.[95d]



Scheme 23 Direct C-H arylation of purines and purine nucleosides

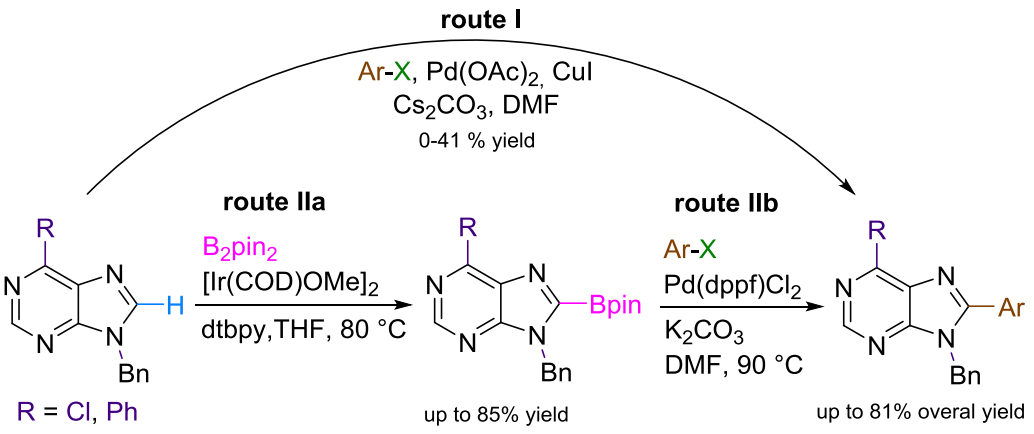
Several other authors also reported direct C-H arylation[96] and C-H alkenylation[97] of adenines and xanthines (Scheme 24).



Scheme 24 Direct C-H alkenylation of purines

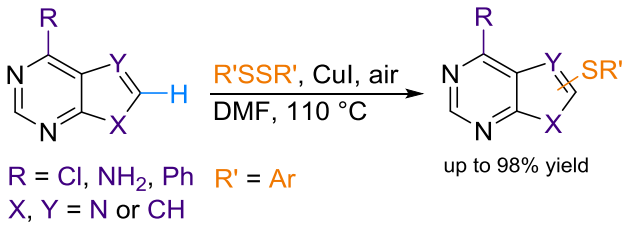
Later on, our group expanded this project by testing the reactivity of deazapurine analogues in C-H activation reactions.

At first, C-H arylation protocol for purines was applied on 7-deazapurines, however, this approach did not proceed well and resulted in very low yields (Scheme 25, route I). Alternatively, Ir-catalyzed direct C-H borylation was developed and resulting deazapurine boronates were subsequently transformed into arylated deazapurines by Suzuki cross-coupling reactions (Scheme 25, route IIa-b).[98] This C-H borylation/arylation approach in combination with other transformations was successfully used for the synthesis of 8-substituted deazaadenines and deazaguanines.[99]



Scheme 25 Direct C-H borylation/C-H arylation

Several years later, a new Cu-catalyzed direct C-H sulfenylation of purines, 7- and 9-deazapurines has been developed (Scheme 26).[100]



Scheme 26 Direct C-H sulfenylation of purines and deazapurines

Obtained 8-arylsulfanylpurines can undergo Liebesking–Srogl coupling with arylstannanes and boronic acids, whereas the (arylsulfanyl)deazapurines were unreactive under the same reaction conditions. Furthermore, C-H sulfenylation methodology was used for the efficient synthesis of 6-substituted-7-(het)arylsulfanyl-7-deazapurine bases and ribonucleosides.[101]

Undoubtedly, development of new reactions for the modification of purines and deazapurines with various functional groups and substituents remains a worthwhile goal. C-H arylation, borylation and sulfenylation reactions have proven to be reliable synthetic strategies towards multifunctionalization of purine and deazapurine nucleobases.

Next, it is worth designing new practical methods for the introduction of amines, imides, silanes and phosphonates. Moreover, according to the literature, there were no examples of direct C-H amination/imidation, silylation or phosphonation of purines or deazapurines reported prior to the beginning of this PhD project.

1.3.5.2 C-H activation of other aromatic and heteroaromatic compounds

To investigate and predict the reactivity of 7-deazapurines, a comprehensive overview of the important aspects of transition metal-catalyzed/mediated C-H activation reactions of arenes and related heterocycles should be highlighted. Over the years of work in this research area, a number of C-H functionalization methods for arenes and heteroarenes have been developed. A variety of functional groups were introduced by using a diverse combinations of transition-metal catalysts, ligands, bases, additives, solvent systems, temperature modes, etc. Considering the wide range of C-H activation methods, a particular interest of this thesis is focused on C-H amination/imidation, C-H silylation and C-H phosphonation reactions as the most attractive and promising strategies for the modification of 7-deazapurine nucleobases.

1.3.5.2.1 C-H amination/imidation

Transformation of arenes and heteroarenes into corresponding amines or imides through C-H bond functionalization represents one of the most efficient methods for the synthesis of aryl- or hetarylamine compounds. To describe the progress in C-N bond formation over the last few decades, a brief literature overview was performed and demonstrated on several examples (Figure 27).

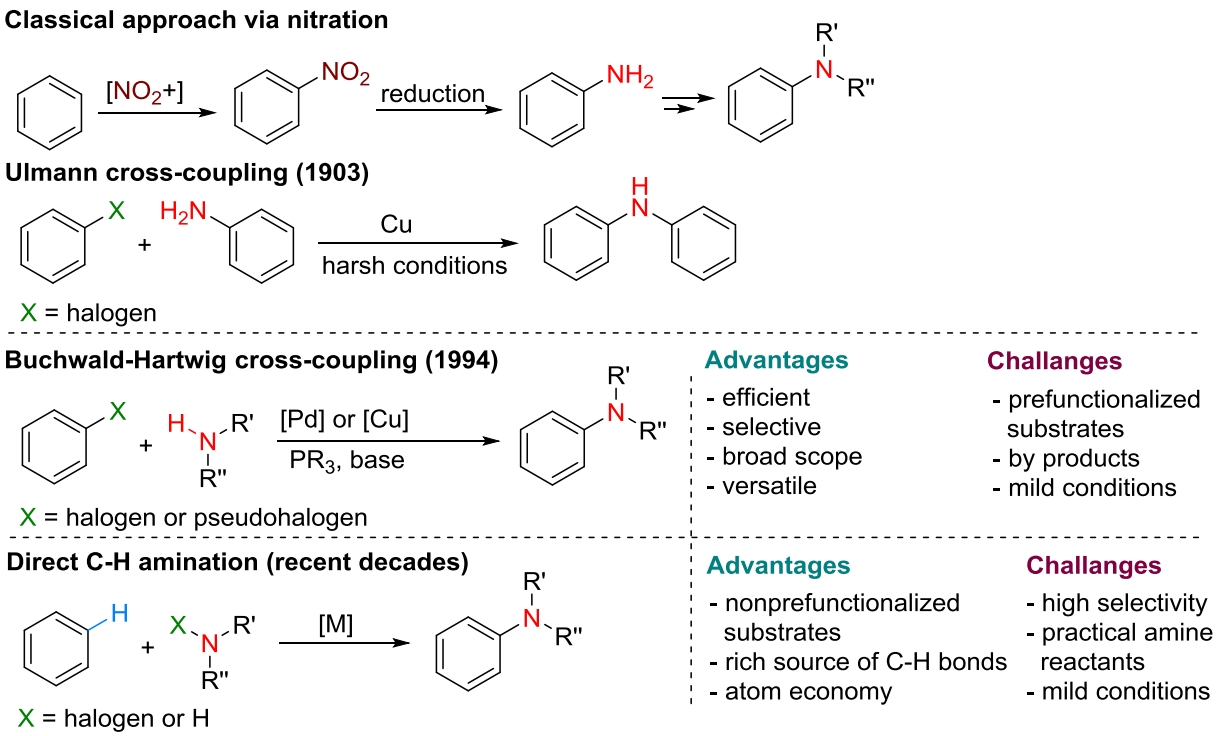


Figure 27 Synthetic strategies towards arylamines

The first example of amination of aryl halides was reported by Ullman in 1903. In 1994, Buchwald and Hartwig reported Pd-catalyzed amination of aryl halides with simple amines that allowed straightforward access to various arylamines. Although Buchwald-Hartwig cross-coupling is efficient and reliable there are many drawbacks. One of the biggest challenges is prefunctionalization of the starting substrate prior to the amination. Many chemists have been working to improve and simplify methods towards C-N bond construction. In the past decade, C-H aminations of simple arenes and related heterocyles have been intensively studied. This alternative approach allows direct functionalization of the hydrocarbon substrate.

It is crucial to emphasize that the C-H amination strategy is only viable under efficient catalytic conditions, where the desired C-H bonds in the molecule can be selectively targeted. From a fundamental perspective, it is important to analyze possible mechanisms and pathways of the C-H amination reaction. Transition metal-catalyzed C-H amination/imidaton reactions can be classified into three categories: C-H activation catalysis, C-H insertion catalysis and single electron transfer (SET) or photoredox catalysis (Figure 28a-b).

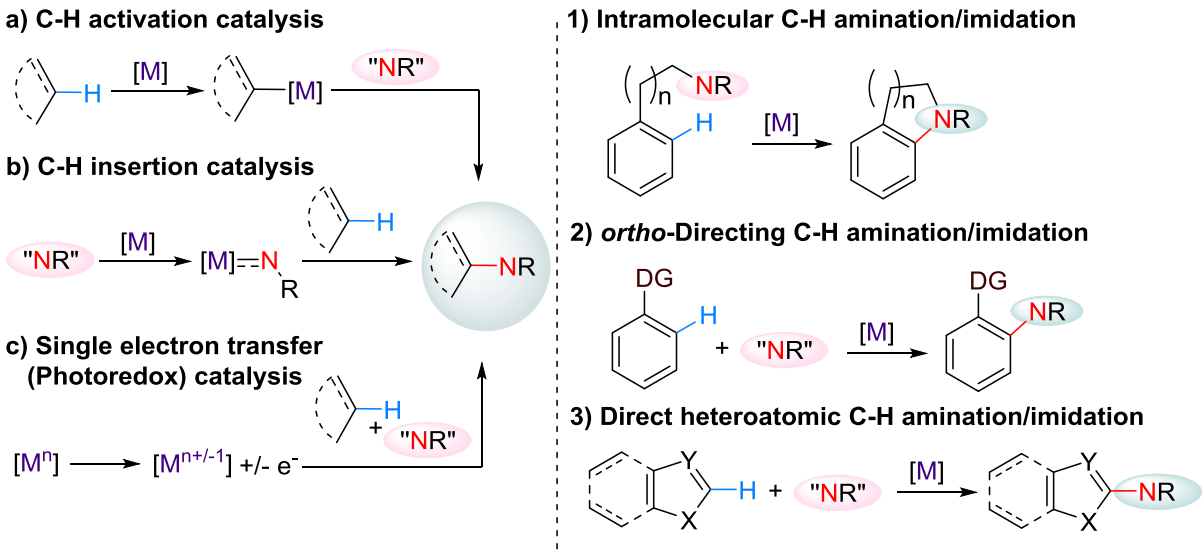


Figure 28 General C-H amination/imidation mechanisms and reaction types

The first reaction pathway is classical C-H activation catalysis a metal-carbon bond forms as a result of carbon-hydrogen bond activation (Figure 28a).[94] Cleavage of the C-H bond is facilitated by a close interaction between a metal and the C-H bond of the hydrocarbon substrate. The corresponding metallocyclic complexes enable a nitrogen source to afford an aminated product.[102] In order to achieve significant catalyst turnover under this

mechanistic pathway, the C-H metalation and subsequent C-N bond-forming step must be highly efficient and selective.

The second mechanism involves C-H insertion catalysis, where instead of direct C-H activation of the hydrocarbons by a metal catalyst, the initially generated metal-amino species reacts with a substrate to result in C-N bond formation (Figure 28b).[103] C-H bond cleavage mostly takes place at the coordinated amino moiety, and the starting hydrocarbon substrate does not bind to the metal complex. In this mechanism, C-H insertion is highly dependent on the stereoelectronic nature of the metal-amino complex.

The third strategy in direct C-H amination is to use SET by a transition metal or photoredox catalysis (Figure 28c).[104] Upon reaction, the catalyst mediates the formation of amino/imido radicals that react with the starting substrate to furnish aminated/imidated products.

Based on the substrate architecture, C-H amination reactions are classified as intramolecular, *ortho*-directing and direct heteroatomic types (Figure 28, types 1-3). Many examples of the intramolecular reactions (Figure 28, type 1) and reactions of aromatics bearing a catalyst-directing group with diverse aminating agents and catalysts (Figure 28, type 2) can be found in the literature.[105-106] The biggest interest of this thesis is drawn by the direct heteroatomic C-H amination/imidation reaction type due to its potential applicability to 7-deazapurines (Figure 28, type 3). These reactions are well studied for arenes and related heterocycles with various amine precursors (Figure 29).

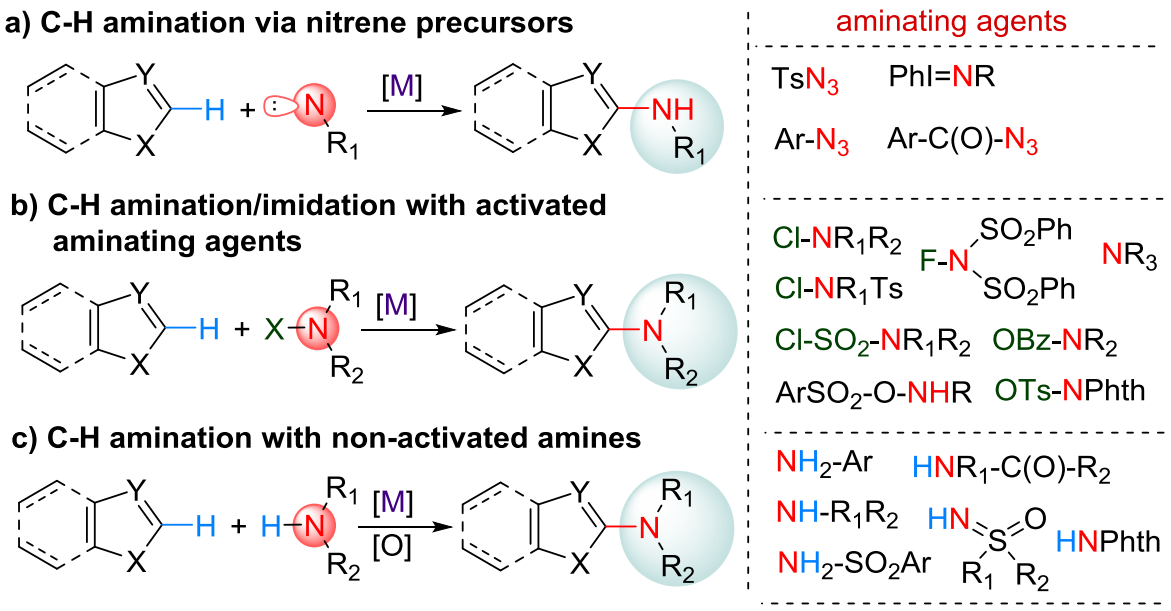


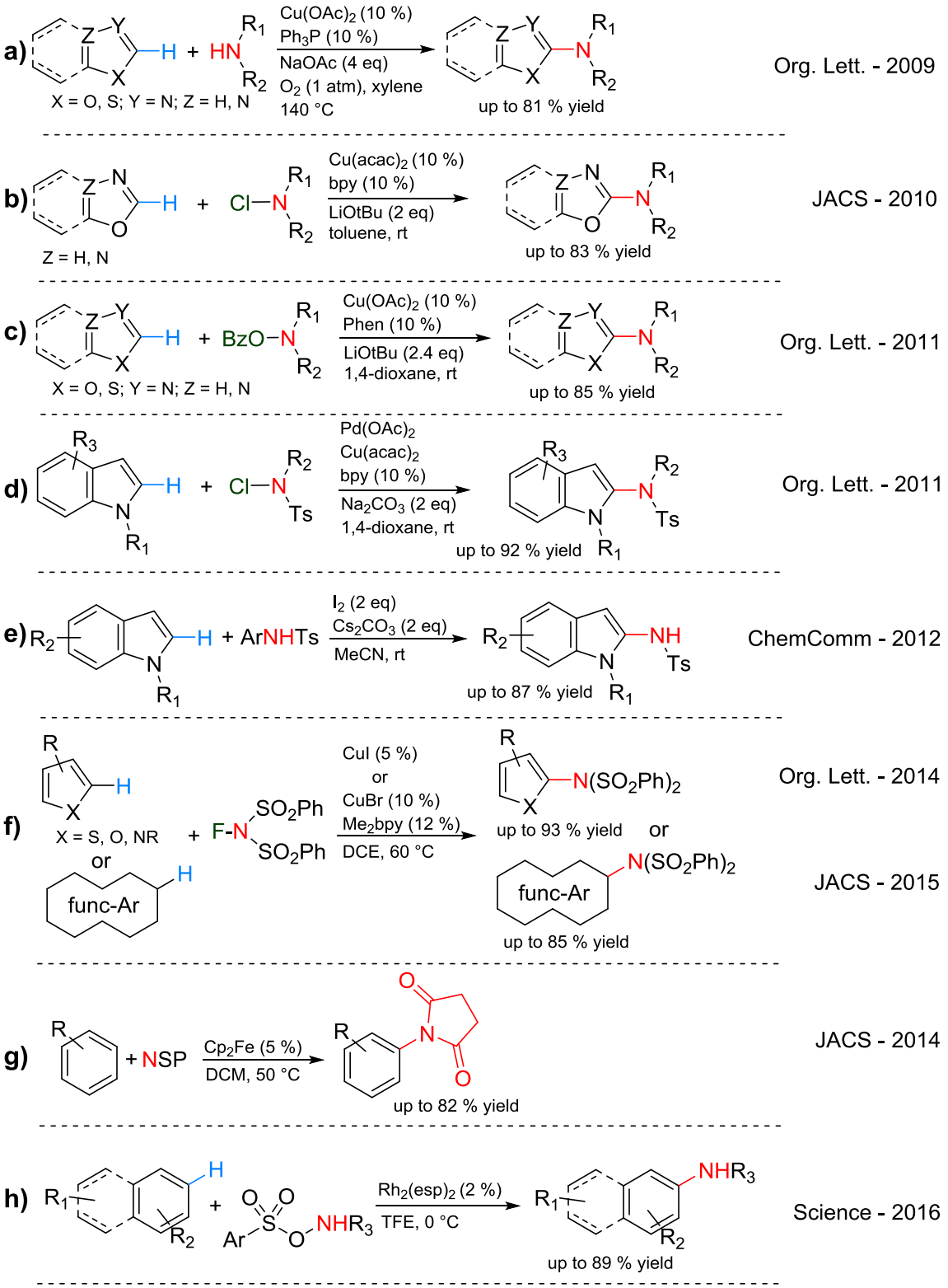
Figure 29 Variations of nitrogen sources for direct C-H amination/imidation reactions

Amination via nitrene precursors is an attractive strategy and is widely used for the directing group reaction. However, there are also several examples of Ru-catalyzed C-H aminations of furans, thiophenes, pyrroles and indoles with aryl azides (Ar-N_3), benzoyl azides (Ar-C(O)-N_3) or N-(*p*-toluenesulfonyl)-iminophenyliodinane (PhI=NTs) as nitrogen sources (Figure 29a).[107] The most robust C-H amination approach employs activated amines, such as N-haloamines or N-oxyamines, and can be applied to different heteroaromatic substrates (Figure 29b). Several authors reported Cu-catalyzed aminations of azoles with N-chloroamines,[108a] Pd/Cu-catalyzed aminations of indoles with *N*-chloro-*N*-alkyl-arylsulfonamides[108b] and of benzoxazoles with sulfamoyl chlorides (Scheme 30b,d).[108c] Copper-catalyzed conditions were also applicable to the reactions of electron deficient pentafluoroarenes, azoles and *N*-quinoline oxides with *N*-carboxyamines.[109] In recent years, N-fluorobenzenesulfonimide (NFSI) has received increasing attention, and several reports of Cu- or Pd/Ag-catalyzed imidation of furans, thiophenes, pyrrols or simple arenes with NFSI have been disclosed (Scheme 30f).[110] Another novel approach towards imidated arenes is the use of SET. Imidations of arenes with *N*-chlorophtalimide[111a] or *N*-bromosaccharin[111b] were reported. In 2014, Baran and co-authors developed ferrocene-catalyzed aromatic C-H imidation with *N*-succinimidyl perester (NSP) (Scheme 30g).[111c]

Aromatic C-H amination through direct transformation of the N-H bond of free amines is ideal because prefunctionalization of nitrogen source is unnecessary. Although reactions of different heteroaromatic systems with nonactivated amines are desired but difficult to conduct, most of them require external oxidants (Figure 29c). Recent research has reported the use of molecular oxygen as the most abundant and environmentally friendly oxidant in combination with copper catalysts. Under such reaction conditions various arenes and heteroarenes such as benzoxazoles, benzothiazoles, benzimidazoles, oxadiazoles, quinolone N-oxides, indoles were aminated by using alkylamines, arylamines, sulfoximines, phtalimide etc.[112] There are also known examples of using of other types of oxidants such as *tert*-butyl hydroperoxide,[113a] manganese (IV) oxide,[113b] $PhI(OAc)_2$,[114] TEMPO,[115] combinations of peroxides with iodine sources, etc.[116] A very recent publication by Falck describing mild dirhodium-catalyzed C-H arene amination using hydroxylamines wa published (Scheme 30h).[117]

Some examples of the reaction protocols are demonstrated in chronological order to show the evolution of C-N bond formation (Scheme 30).

Indeed, over the last decade C-N bond functionalization has drawn the significant attention of many research groups and their work has resulted in the development of various interesting methodologies for C-H amination/imidation of arenes and related heteroarenes.



Scheme 30 Examples of C-H amination/imidation reactions of arenes and heteroarenes

1.3.5.2.2 C-H silylation

Silylation of the C-H bond is a very important transformation because of the diverse application of organosilanes. Over the years, a number of researchers have been working on developing transition metal-catalyzed C-Si bond construction methods. Traditionally, synthetic methods for the introduction of silyl groups to organic molecules involved reactions of organolithium or -magnesium reagents with silicon electrophiles (Figure 31a).[118a] In these reactions, functional groups are often very sensitive and, therefore, protecting groups are necessary. To overcome this challange, transition metal-catalyzed Hiyama cross-couplings[118b] of aryl halides with disilanes or hydrosilanes have been successfully developed (Figure 31b). Nevertheless, the direct C-H activation/functionalization remains the most efficient approach for the synthesis of organosilanes and does not need preactivation of the substrate (Figure 31c).[119]

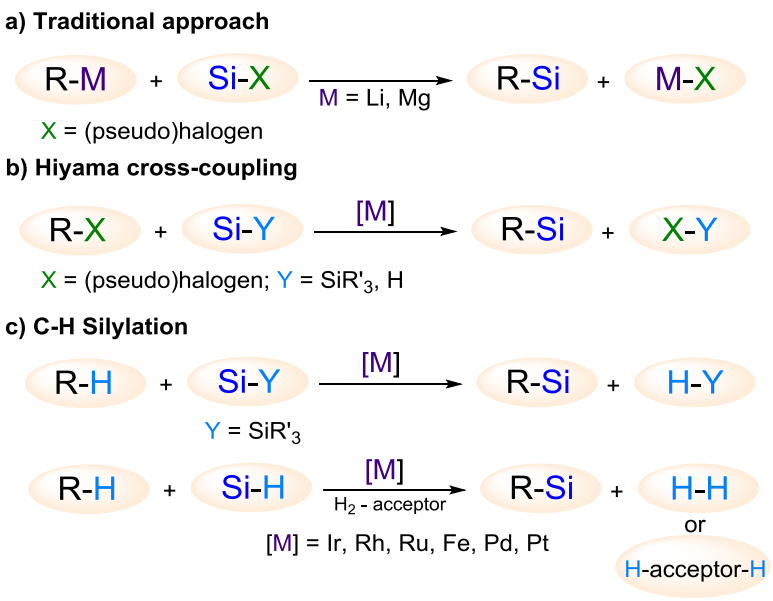


Figure 31 General methods for the preparation of organosilicon compounds

In recent years, direct C-H silylation has achieved enormous success and various transition metal complexes including Ir,[120-122] Ru,[123-125] Rh,[126-128] Pd,[129] Fe,[130] Pt,[131], Ni[132] and Sc[133] have been used as efficient catalysts in the silylation reactions. The biggest challenge in C-Si bond formation from aromatic C-H bonds is the regioselectivity of the process. In light of this issue, it is reasonable to outline several major strategies to control the regioselectivity of C-H silylation. Firstly, it is possible to utilize a directing group for the activation of the adjacent C-H bonds, such as the nitrogen atom from amines, heterocycles, and amides, or the

oxygen atom from carbonyls and heterocycles. Secondly, building up a crowded environment to activate the most sterically accessible C-H bonds may be apllied. Thirdly, activation of the most reactive C-H bonds under optimized reaction conditions (transition metal catalyst, ligand, temperature, additives, silylating agents) can be useful.

For better understanding, a reasonable mechanism for the transition metal-catalyzed silylation of C-H bonds is provided in Figure 32. Cleavage of the C-H bonds of the substrate by a metal-silyl fragment, followed by reductive elimination furnishes the silylated product (Figure 32, step A-B). Addition of the H-Si bond (or Si-Si bond when a disilane is the silicon source) to the metal regenerates the metal-silyl species (Figure 32, step C). The hydrogen by-product of the reaction (or $HSiR_3$ when a disilane is used) is either eliminated directly from the metal center or transferred to a hydrogen acceptor (Figure 32, step D). The exact sequence of events and the oxidation state of the metal during each reaction can vary. When a directing group is present, the catalyst can bind to the directing group (forming a five-membered transition state) before or after oxidative addition of the Si-H bond to the metal center.

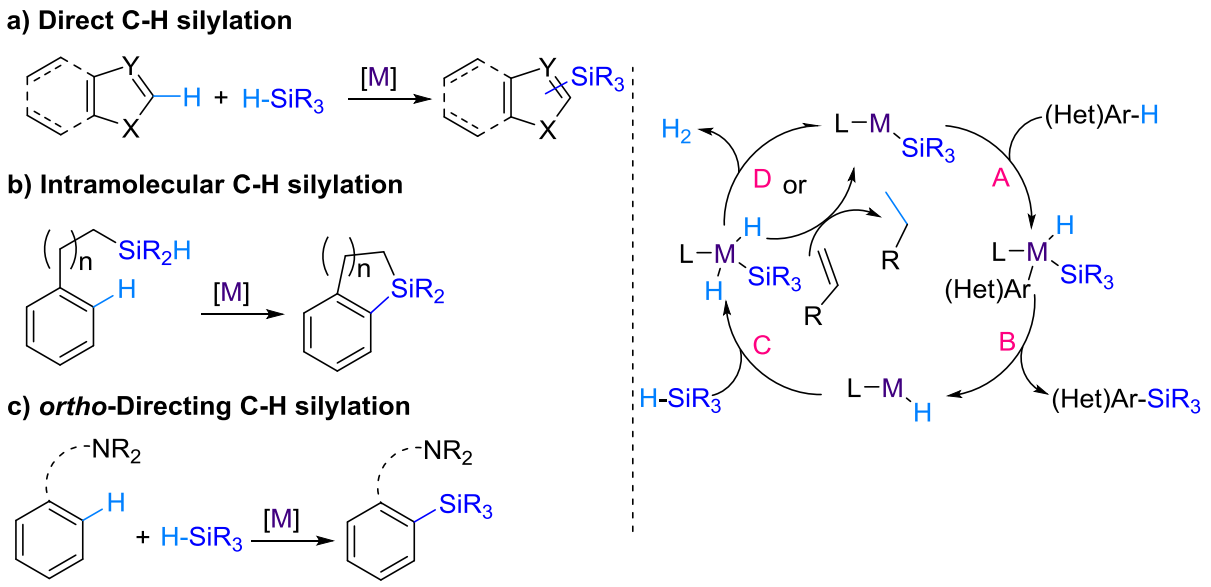


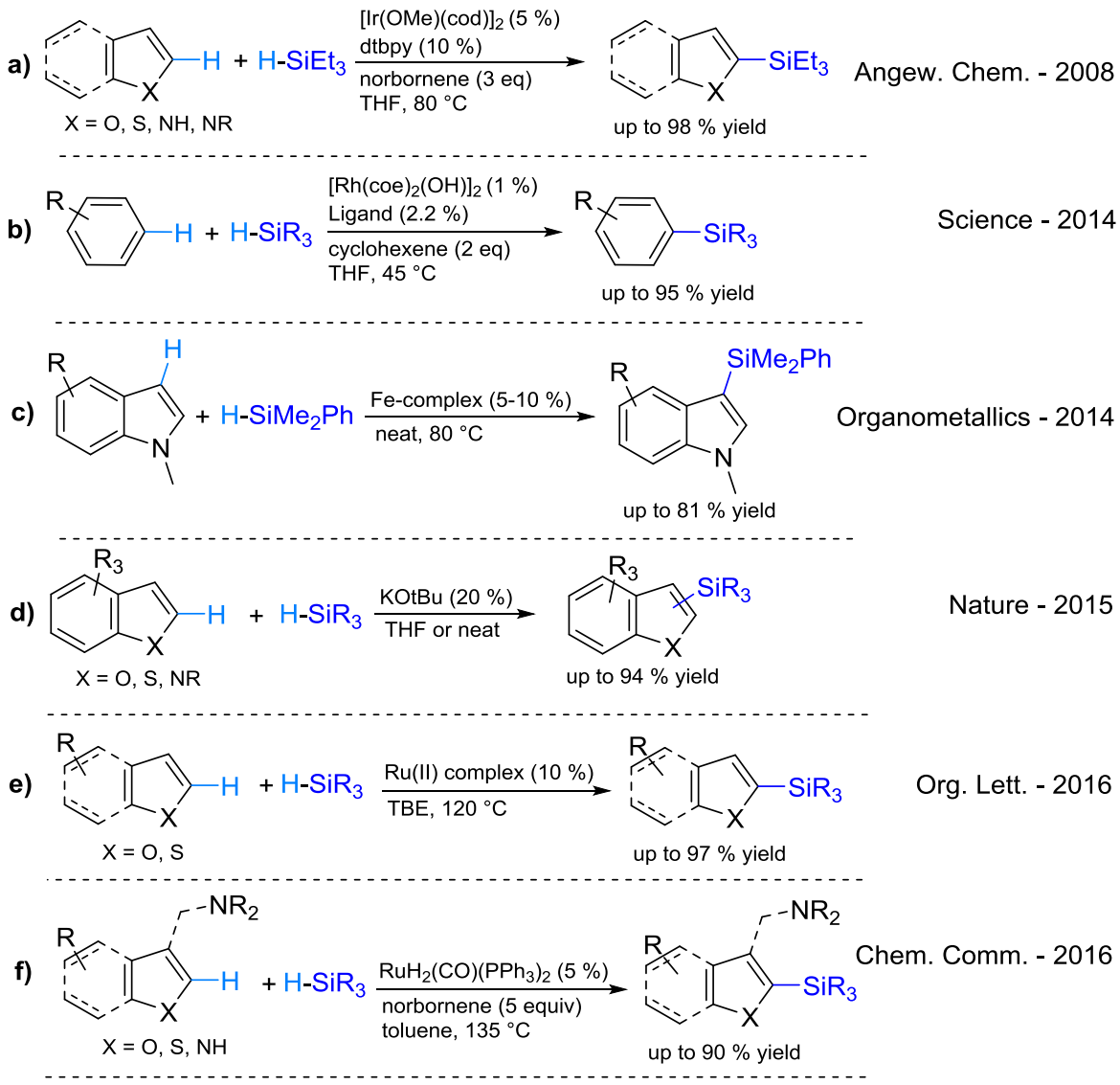
Figure 32 General mechanism and reaction types of C-H silylation

C-H silylation reactions can be categorized into three main reaction types (Figure 32a-c). The first approach is direct silylation of heteroatomic C-H bonds (Figure 32a). Several examples of this reaction type are demonstrated in Figure 33. Many authors have reported Ir-catalyzed C-H silylations of arenes and heteroarenes[120a-g] mostly by using $[Ir(OMe)(cod)]_2$ as a catalyst, bipyridyl or phenanthroline as the ligand and norbornene or cyclohexene as the hydrogen acceptor (Figure 33a). Other common catalysts for this reaction type are

ruthenium[123] complexes such as $RuH_2(CO)(PPh_3)_2$ or rhodium[126] $[Rh(coe)_2(OH)]_2$ (Figure 33b). Recently in 2015, Grubbs and co-workers reported the silylation of aromatic heterocycles by simple potassium *tert*-butoxide,[134] an Earth-abundant catalyst, via radical chain mechanism (Figure 33d).[135]

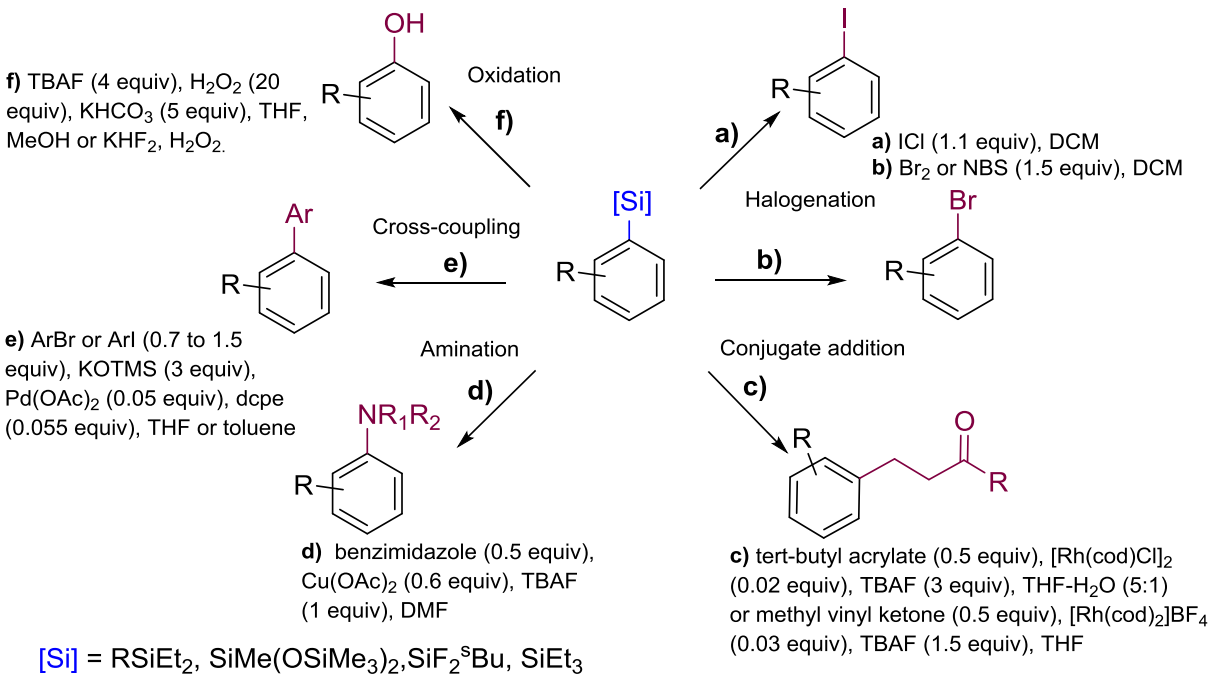
The second class of reactions proceed in an intramolecular fashion (Figure 32b) under Ir,[121a-f] Ru,[125] Pt,[131a] or the most commonly used, Rh[128] catalysis.

The third reaction type, directed by diverse nitrogen or oxygen functional groups have become a useful strategy towards aromatic organosilanes (Figure 32c). Various ruthenium complexes including $Ru_3(CO)_{12}$, $RuH_2(CO)(PPh_3)_2$ and $[Ru(p\text{-cymene})Cl_2]_2$ have proven to be the most suitable catalysts for these reactions (Figure 33f).[124] Nevertheless, catalysts of other transition metals such as Ir,[122a-c] Rh,[127] Pd,[129] and Sc[133] are also known.



Scheme 33 Examples of C-H silylations of arenes and heteroarenes

An important practical application of silylated C-H bonds is further functionalization of the installed silyl groups (Scheme 34).[101g,126c,134] Organosilanes can be halogenated to the corresponding bromo- or iodo- derivatives with NBS or iodine monochloride (Scheme 34a-b). Oxidation of aryl- and alkylsilanes is also known as the Tamao-Fleming oxidation that requires the presence of TBAF or KHF_2 (Scheme 34f). Hiyama cross-coupling of organosilicon reagents allows the construction of complex biaryl motifs and can be used as an alternative to the Suzuki-Miyaura coupling reactions. One of the modified Pd-catalyzed Hiyama reaction is based on the use of silanolates in reaction with a strong base such as KOTMS (Scheme 34e). This reaction belongs to the fluoride-free type and is called Hiyama-Denmark cross-coupling. Aryl silanes also undergo Cu-mediated amination and 1,4-addition to enones and acrylates (Scheme 34c-d).



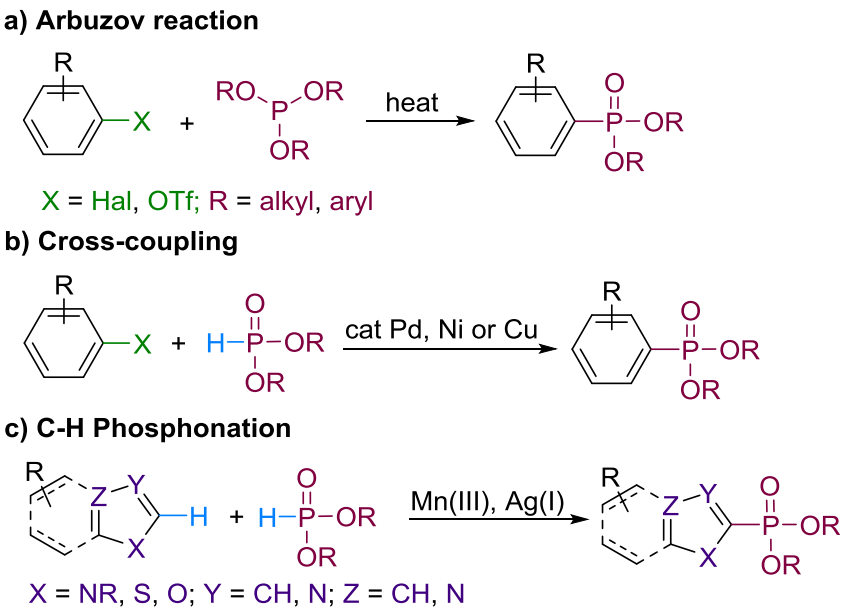
Scheme 34 Functionalization of arylsilanes

C-H silylation of arenes and heteroarenes is a relatively young research field. However, it has received significant research attention over recent years (Scheme 33). It follows from the aforementioned literature overview that the development of practical methods for the C-H silylation of desired 7-deazapurine nucleobases is a worthwhile research topic to be pursued.

1.3.5.2.3 C-H phosphonation

In comparison to other C-H activation strategies, functionalization of aromatic C-H bonds directly into C-P bonds has not been studied systematically. Phosphonation reactions have been a very interesting research topic over the last several years because of the promising applications of hetaryl phosphonates.

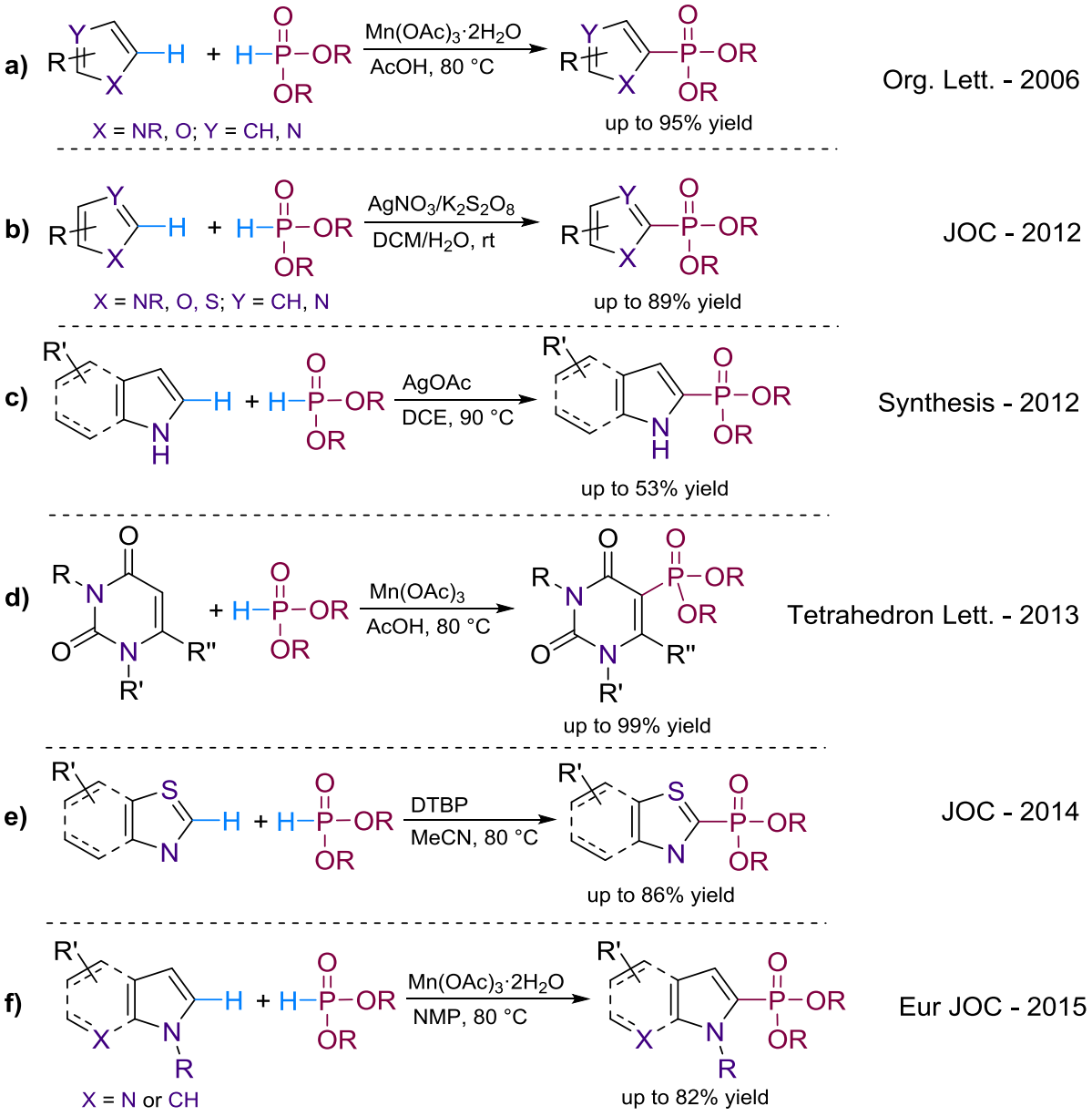
Traditional methods of the preparation of various hetaryl phosphonate derivatives are based on Arbuzov type reactions or cross-couplings of aryl halides with trialkyl phosphates or dialkyl phosphites (Scheme 35a-b).[136]Alternatively, phosphonate group can be introduced through oxidative C-H phosphonation mostly by using Mn(III) and Ag(I) salts as single electron promoters (Scheme 35c).[137-138] Literature reviews have revealed examples of peroxide mediated,[139a] oxygen induced autooxidative[139b] and photocatalytic phosphonation reactions.[139c] Over the recent years, several authors have reported Rh- and Pd-catalyzed *ortho*-directing C-H phosphonations of various arenes.[140]



Scheme 35 Synthetic strategies towards (het)aryl phosphonates

Strategically, the main interest of this thesis was focused on direct C-H phosphonation reactions of heterocycles related to deazapurines. The most reliable methods for the functionalization of various heteroarenes with the phosphonate group were those based on the use of Mn(III) acetate[137] and Ag(I) nitrate or acetate in combination with potassium persulfate as the reaction oxidants.[138] By using $Mn(OAc)_3$ as the promoter in reactions with dialkylphosphites, a number of substituted heterocycles such as furan,[137a] pyrrole,[137a]

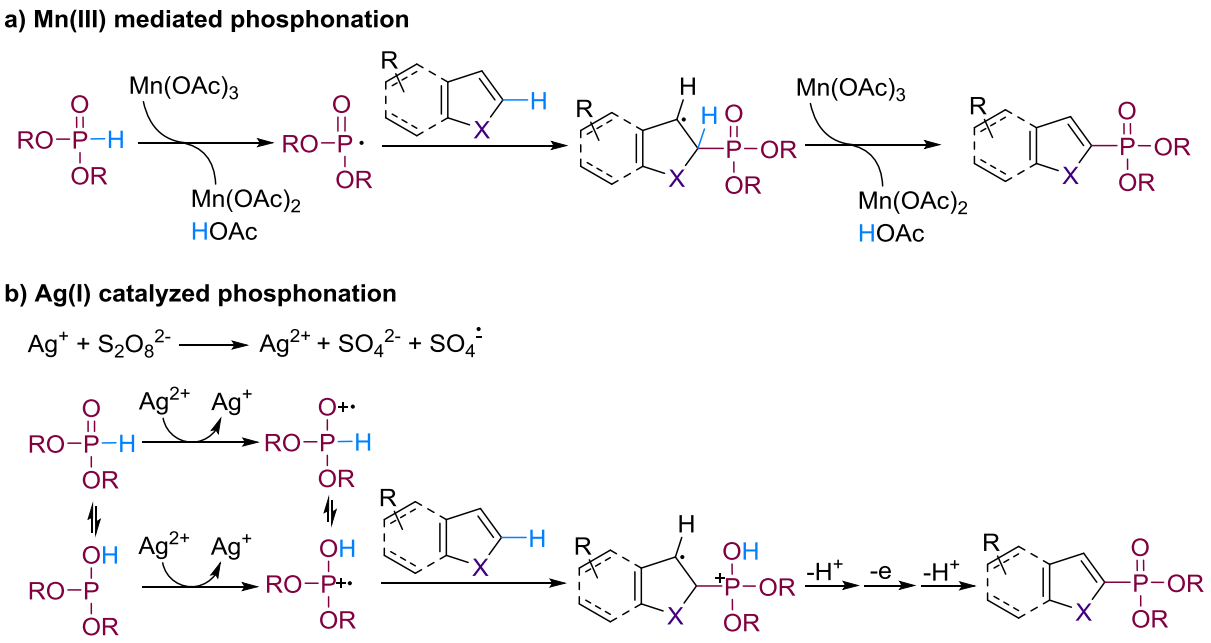
thiazole,[137a,d] benzothiazole,[137d] imidazopyridine,[137c] azaindole,[137c] indole,[137c] uracil derivatives[137e] and caffeine[137e] have been successfully phosphonated (Scheme 36a,f,d). Diversely substituted furans, thiophenes, thiazoles, pyrroles and pyridines were also synthesized using a combination of $AgNO_3$ and $K_2S_2O_8$.[138a] Silver(I) acetate was used in the preparation of substituted indoles[138b] and thiazolotriazoles (Scheme 36b,c).[138c]



Scheme 36 Examples of C-H phosphonations of heteroarenes

Interestingly, attempts at the C-H phosphonation of adenine derivatives have failed,[137e] and this can possibly be explained by a reaction mechanism that may require C-H bond at position 7 next to the reacting C-H bond at position 8 of the purine (Scheme 37). Therefore,

this indicates an advantage of deazapurine nucleobases, which potentially could be reactive in this reaction in contrast to purines.



Scheme 37 Plausible mechanism of heteroarene C-H phosphonation

The mechanism of the formation of hetaryl phosphonate could be proposed as shown in Scheme 37. In the Mn(III) acetate-mediated mechanism, oxidation of diethyl phosphite generates an electrophilic diethyl phosphonyl radical which reacts with heteroarene to form the heteroarene radical intermediate that subsequentely oxidizes to desired phosphonate (Sccheme 37a). In the silver(I) catalytic mechanism, the Ag^{+} cation is oxidized to the Ag^{2+} cation by peroxodisulfate (Scheme 37b). Then, diethyl phosphite deprived of an electron by the Ag(II) ion forms the cation radical. Its electrophilic addition to heteroarene leads to the intermediate, which may lose a hydrogen cation, an electron, and another hydrogen cation successively, giving desired heteroarene phosphonate.

Summarizing, a literature review on C-H phosphonation has shown that reactions tolerate various heterocyclic systems similar to deazapurines (Scheme 36). Since this research topic is not well-explored in general, it is worth developing new phosphonation methods. Phosphonated heteroarenes are attractive targets in general due to a broad spectrum of their biological activity. It will be of particular interest to prepare deazapurine nucleobase phosphonates with potential applications in medicinal chemistry and biochemistry.

2 Specific aims of the project

1. Development of direct C-H amination/imidation of deazapurines
2. Development of direct C-H silylation of deazapurines
3. Development of direct C-H phosphonation of deazapurines
4. Synthesis of substituted 6-(het)aryl 7-deazapurines by aqueous Suzuki-Miyaura cross-coupling reactions
5. Synthesis of substituted 7-(het)aryl 7-deazapurines by aqueous Suzuki-Miyaura cross-coupling reactions

Rationale of the Specific Aims

Efficient synthesis of a library of 7-deazapurines with different combinations of substituents for biological activity screening was my primary goal. To fulfil this aim, there was a need for the development of new methodologies for chemo- and regioselective introduction of diverse substituents and functional groups into the deazapurine scaffold. Transition metal catalyzed/mediated C-H functionalization has proven to be one of the most straightforward and powerful tools in modern synthetic organic chemistry.[94] Previously in our group, methods for the direct C-H arylation of purines, C-H borylation and sulfenylation of deazapurines were developed.[95,98,100] The main interest of this work focused on the development of novel protocols for the selective C-H amination, C-H imidation, C-H silylation and C-H phosphonation of deazapurine nucleobases. Installation of amino-, silyl- or phosphonate groups to arenes and related heterocycles through C-H bond activation has been studied intensively over the last decade.[102,119,137] However, there were no literature examples of these types of reactions on deazapurines, what in turn proves that this is a worthwhile research topic to be pursued.

Potentially, the newly designed C-H activation reactions in combination with cross-couplings and nucleophilic aromatic substitutions can be a strong synthetic approach towards multifunctionalized deazapurine nucleobases.

In addition, inspired by the potent nucleoside cytostatics previously synthesized in our group,[36-37] I was interested in the preparation of the parent deazapurine nucleobases with the same substitution patterns. For the preparation of the series of 6- and 7-(het)aryl 7-deazapurines bearing H, NH_2, CH_3, F, Cl substituents at position 2, the aqueous Suzuki-Miyaura cross-coupling reaction was chosen as the most reliable method.[92]

3 Results and discussion

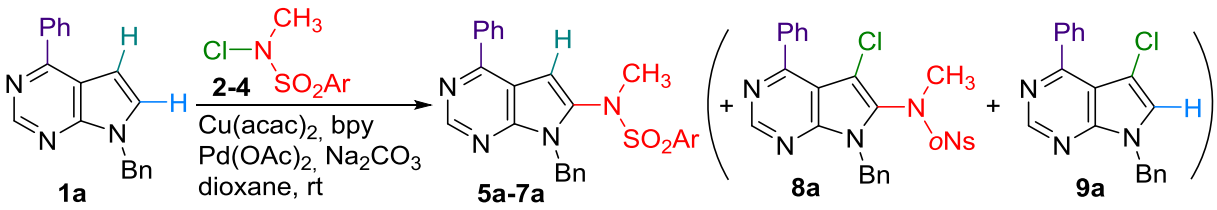
3.1 C-H functionalization of deazapurine nucleobases

In order to introduce various functional groups onto the deazapurine heterocycle, I started by studying of novel methodologies for direct C-H amination, C-H imidation, C-H silylation and C-H phosphonation reactions. My interest also focused on further transformations of installed functionality onto deazapurine nucleobases.

3.1.1 Direct C-H amination and C-H chloroamination of 7-deazapurines

Transition metal-catalyzed direct C-H aminations are increasingly popular reactions for modification of arenes and heterocycles as confirmed by the literature.[102] Thus, this is where the motivation for the investigation of C-H aminations originates from.

For the initial study, I selected easily accessible 6-phenyl-9-benzyl-7-deazapurine **1a** which was prepared from commercially available 6-chloro-7-deazapurine. Next, I started testing its reaction with one of the most efficient reagents *N*-chloro-*N*-methyl-tosylamide **2** using the corresponding literature[108b] conditions in the presence of $Pd(OAc)_2$, $Cu(acac)_2$, 2,2'-bipyridine (bpy) and Na_2CO_3 in 1,4-dioxane (Scheme 1, Table 1). The reaction with 2 equivalents of **2** in the presence of 2 equivalents of Na_2CO_3 gave the desired 8-tosylamino product **5a** in 13 % yield only (Table 1, entry 1). The use of larger excesses of the base (5-7 equiv.) and of reagent **2** (3 equiv.) led only to a low increase in yields (18-29 %). Only the use of a large excess (5 equiv.) of **2** gave product **5a** in acceptable preparative yields of 68 % (Table 1, entry 5).



Scheme 1 C-H aminations of 6-phenyl-9-benzyl-7-deazapurine **1a**

In order to have a choice of some more easily cleavable *N*-protecting groups,[141] I also tested 4-nitrophenylsulfonyl (*p*-nosyl, *p*Ns) and 2-nitrophenylsulfonyl (*o*-nosyl, *o*Ns) chloroamides **3** and **4**. The reaction of **1a** with *p*Ns reagent **3** (3 equiv.) gave the 8-*p*-nosylamino product **6a** in acceptable 47 % yield (Table 1, entry 6). The reactions of **1a** with

*o*Ns chloroamide **4** (1.5-2 equiv.) resulted in very low conversions (Table 2, entries 1-7), whereas the reaction with 5 equiv. of **4** produced a mixture of the desired product of 8-amination **7a** (28 %), 7-chloro-8-amino **8a** and 7-chloro-7-deazapurine **9a** as side-products (Table 1, entry 7).

Table 1 Optimization of C-H aminations of 7-deazapurine **1a** with *N*-chloro-*N*-methyl-arylsulfoneamides **2-4**[a]

Entry	Ar	**2-4** (equiv.)	Na_2CO_3 (equiv.)	Product(s) (yield)
1	4-MePh	**2** (2)	2	**5a** (13 %)
2	4-MePh	**2** (2)	5	**5a** (18 %)
3	4-MePh	**2** (3)	5	**5a** (25 %)
4	4-MePh	**2** (3)	7	**5a** (29 %)
5[b]	4-MePh	**2** (5)	7	**5a** (68 %)
6	4-NO_2Ph	**3** (3)	7	**6a** (47 %)
7	2-NO_2Ph	**4** (5)	5	**7a** (28 %) + **8a** (33 %) + **9a** (25 %)
8	2-NO_2Ph	**4** (3)	7	**7a** (60 %)

[a] Reagents and conditions: $Pd(OAc)_2$ (5 %), $Cu(acac)_2$ (10 %), bpy (10 %), Na_2CO_3, 1,4-dioxane, Ar, rt, 24 h; [b] reaction time 72 h.

Apparently, chloroamide **4** in larger excess can act as an electrophilic chlorination reagent which halogenates the deazapurine at position 7. This was confirmed later by the reaction of deazapurine **1a** with **4** under non catalytic conditions, resulting in a chlorinated product **9a** (Scheme 2, Table 3, entry 11). Therefore, I performed a comprehensive optimization of the C-H amination reaction using different ratios of chloroamide **4** (from 1.5 to 5 equiv.), bases (from stronger Cs_2CO_3 to weaker Ag_2CO_3), catalysts (combinations of $Pd(OAc)_2$ with Cu catalysts), ligands (bpy, dtbpy) and additives (LiCl) in various solvents (THF, toluene, 1,4-dioxane) at ambient temperature or by heating to higher temperatures (Table 2). The optimum protocol for amination used 3 equiv. of **4** in the presence of a large excess of Na_2CO_3 (7 equiv.) to give the desired product **7a** in 60 % yield (Table 1, entry 8; Table 2, entry 12). Later, the yield was slightly improved to 62 % when 3.5 equiv. of **4** was used without compromising the selectivity of reaction (Table 3, entry 1; Table 2, entry 13).

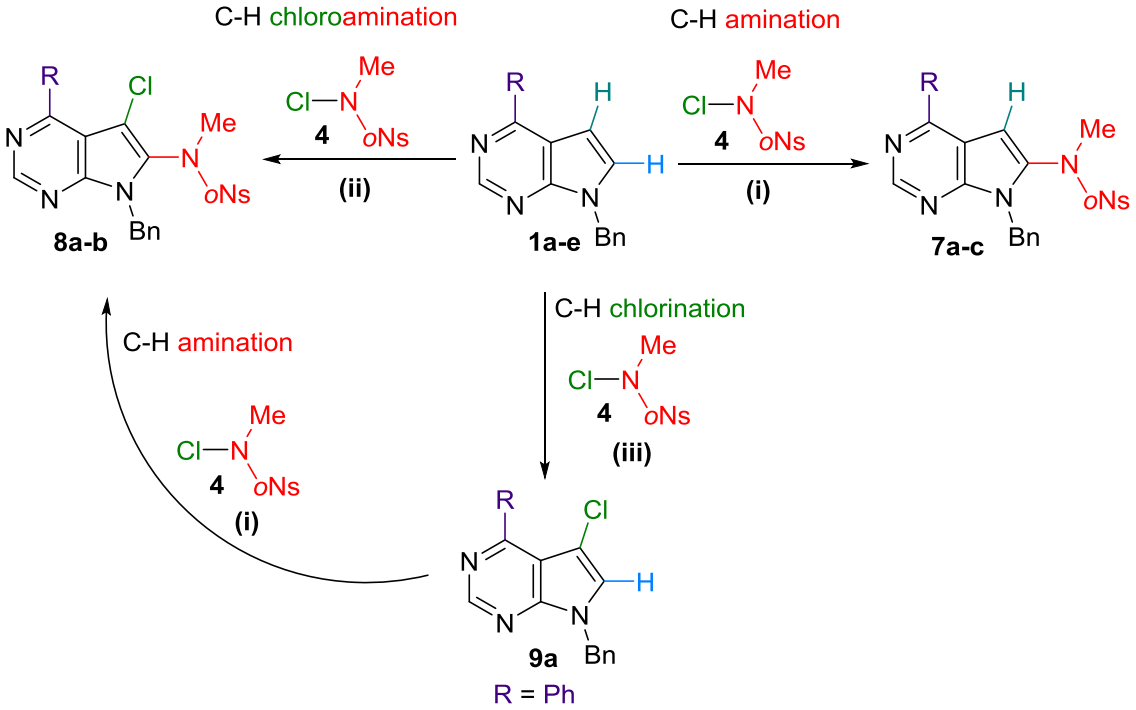
Table 2 Optimization of Pd/Cu-catalyzed C-H amination and C-H chloroamination of 6-phenyl-9-benzyl-7-deazapurine **1a** with *N*-chloro-*N*-methyl-2-nitrobenzenesulfonamide **4**

Entry	**4** (equiv.)	$Pd(OAc)_2$	Cu source (equiv.)	Additive (equiv.)	Base, (equiv.)	NMR conversion, (%)	
						7a	**8a**
1	1.5	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (2)	10	-
2	2	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (2)	15	-
3[a]	2	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (2)	12	-
4	2	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (5)	32	-
5	2	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Cs_2CO_3 (2)	17	-
6	2	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Cs_2CO_3 (5)	22	-
7	2	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	LiOtBu (5)	16	-
8	3.5	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (5)	53	12
9	5	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (5)	30	36
10	2	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (10)	38	-
11	2	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (7)	42	-
12	3	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (7)	62	-
13	**3.5**	**5 %**	**$Cu(acac)_2$ (0.1)**	**bpy (0.1)**	**Na_2CO_3 (7)**	**65**	**-**
14	5	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (7)	34	33
15[b]	3.5	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (7)	40	-
16[c]	3.5	5 %	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (7)	25	35
17	3.5	5 %	$Cu(acac)_2$ (0.1)	dtbpy (0.1)	Na_2CO_3 (7)	46	-
18	3.5	7.5 %	$Cu(acac)_2$ (0.15)	bpy (0.15)	Na_2CO_3 (7)	49	-
19	3.5	5 %	-	bpy (0.1)	Na_2CO_3 (7)	19	16
20	3.5	-	$Cu(acac)_2$ (0.1)	bpy (0.1)	Na_2CO_3 (7)	48	-
21	3.5	-	$Cu(acac)_2$ (0.2)	bpy (0.2)	Na_2CO_3 (7)	45	-
22	3.5	-	$Cu(acac)_2$ (0.4)	bpy (0.4)	Na_2CO_3 (7)	42	-
23	3.5	5	$Cu(acac)_2$ (0.2)	bpy (0.2)	Na_2CO_3 (7)	63	-
24	3.5	5	$Cu(acac)_2$ (0.4)	bpy (0.4)	Na_2CO_3 (7)	48	-
25	3.5	5 %	$Cu(acac)_2$ (0.1)	-	Na_2CO_3 (2)	31	19
26	3.5	5 %	$Cu(acac)_2$ (0.1)	-	Ag_2CO_3 (2)	28	23
27	3.5	5 %	CuCl (0.1)	-	Ag_2CO_3 (2)	12	33
28	3	2.5 %	CuCl (0.1)	-	Ag_2CO_3 (2)	14	38
29	3.5	2.5 %	CuCl (0.1)	-	Ag_2CO_3 (2)	10	39
30	3.5	2.5 %	CuCl (0.1)	LiCl (1)	Ag_2CO_3 (2)	6	47
31	**3.5**	**2.5 %**	**CuCl (0.1)**	**LiCl (2)**	**Ag_2CO_3 (2)**	**-**	**53**
32	3.5	-	CuCl (0.1)	LiCl (2)	Ag_2CO_3 (2)	13	45
33	3.5	-	CuCl (0.2)	LiCl (2)	Ag_2CO_3 (2)	17	40
34	3.5	2.5 %	CuCl (0.2)	LiCl (2)	Ag_2CO_3 (2)	8	50

[a] 70 °C; [b] in THF; [c] in toluene.

The detailed optimization also revealed some ratios of reagents and conditions under which the chloroamination proceeded. I employed CuCl as the copper source, Ag_2CO_3 as the base and LiCl as the additive (Table 2, entries 27-34) to find the optimum protocol leading exclusively to chloroamination. As a result, the optimal reaction conditions were reached by using **4** (3.5 equiv.) in the presence of $Pd(OAc)_2$ (2.5 %), CuCl (10 %), LiCl (2 equiv.) and Ag_2CO_3 (2 equiv.) (Table 2, entry 31; Table 3, entry 6).

The next step was the study of the scope and limitations of the methods. A series of five 9-benzyl-7-deazapurine derivatives **1a-e** bearing a phenyl, methoxy, methyl, chloro or amino group at position 6 was tested in the amination and chloroamination reactions (Scheme 2, Table 3).



Reagents and reaction conditions:
(i) 4 (3.5 equiv), $Pd(OAc)_2$ (5 %), $Cu(acac)_2$ (10 %), bpy (10 %), Na_2CO_3 (7 equiv), 1,4-dioxane, Ar, rt, 24h;
(ii) 4 (3.5 equiv), $Pd(OAc)_2$ (5 %), CuCl (10 %), LiCl (2 equiv), Ag_2CO_3 (2 equiv), 1,4-dioxane, Ar, rt, 24h;
(iii) 4 (1.5 equiv), 1,4-dioxane, Ar, rt, 45h.

Scheme 2 C-H amination, chloroamination and chlorination of 7-deazapurines

Preparative aminations were performed with chloroamide **4** (3.5 equiv.) in the presence of $Pd(OAc)_2$, $Cu(acac)_2$, bpy and 7 equiv. of Na_2CO_3. The reactions of 6-phenyl, -methoxy and -methyl deazapurines proceeded smoothly to give desired 8-(*o*-nosyl)methylamino-7-deazapurines **7a-7c** in acceptable yields of 41-62 % (Table 3, enries 1-3). Conversely, analogous reaction of 6-chloro- and 6-amino-derivatives **1d** and **1e** led to very

complex inseparable mixtures. Next I tested the chloroamination protocol on the same series of deazapurines **1a-1e**. The reactions with **4** (3.5 equiv.) were performed in the presence of $Pd(OAc)_2$, CuCl, LiCl and Ag_2CO_3. The reactions of 6-phenyl and 6-methoxy derivatives **1a** and **1b** proceeded well to obtain desired 7-chloro-8-(*o*Ns)MeNH-7-deazapurines **8a** and **8b** in acceptable yields of 51 and 42 % respectively (Table 3, entries 6-7), whereas the reaction of 6-methyl derivative **1c** gave low conversion to an inseparable mixture containing products of chlorination and chloroamination. Similarly, reactions of 6-chloro- and 6-aminodeazapurines **1d** and **1e** gave complex inseparable mixtures. It was interesting that reaction of **1a** with **4** (1.5 equiv.) under non-catalytic reaction conditions resulted in chlorinated product **9a** in 78 % yield due to the strong chlorinating nature of *N*-chlorosulfonamide (analogous to *N*-chlorosuccinimide) (Table 3, entry 11). Finally, 6-phenyl-7-chloro-7-deazapurine **9a** was also converted to 7-chloro-8-aminated derivative **8a** in 41 % yield (Table 3, entry 12) and this shows the chlorine at position 7 is better tolerated (as it is less reactive toward nucleophiles) than the chlorine at position 6.

Table 3 Preparative C-H aminations, chloroaminations and chlorination of 7-deazapurines

Entry	Starting compound	R	Product (yield)
1	**1a**	Ph	**7a** (62 %)
2	**1b**	OMe	**7b** (60 %)
3	**1c**	Me	**7c** (41 %)
4	**1d**	Cl	complex mixture
5	**1e**	NH_2	complex mixture
6	**1a**	Ph	**8a** (51 %)
7	**1b**	OMe	**8b** (42 %)
8	**1c**	Me	low conversion, complex mixture
9	**1d**	Cl	complex mixture
10	**1e**	NH_2	complex mixture
11	**1a**	Ph	**9a** (78 %)
12	**9a**	Ph	**8a** (41 %)

In addition, to confirm the regioselectivity of reactions, single-crystal X-ray diffraction analysis was performed with compounds **5a**, **7a**, **7b** and **8a**. The crystal structures of these aminated and chloroaminated products are presented in Figure 1.

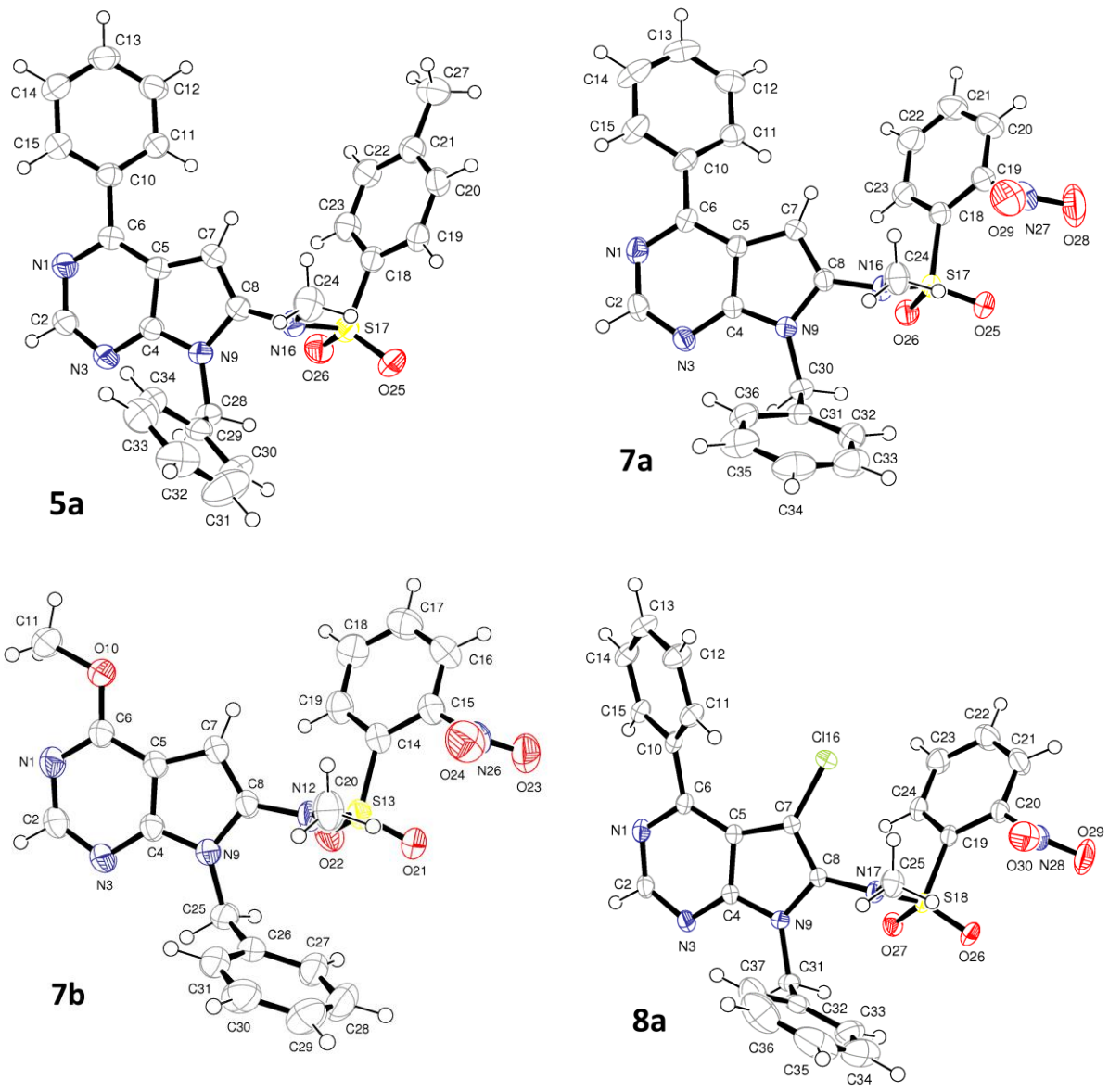
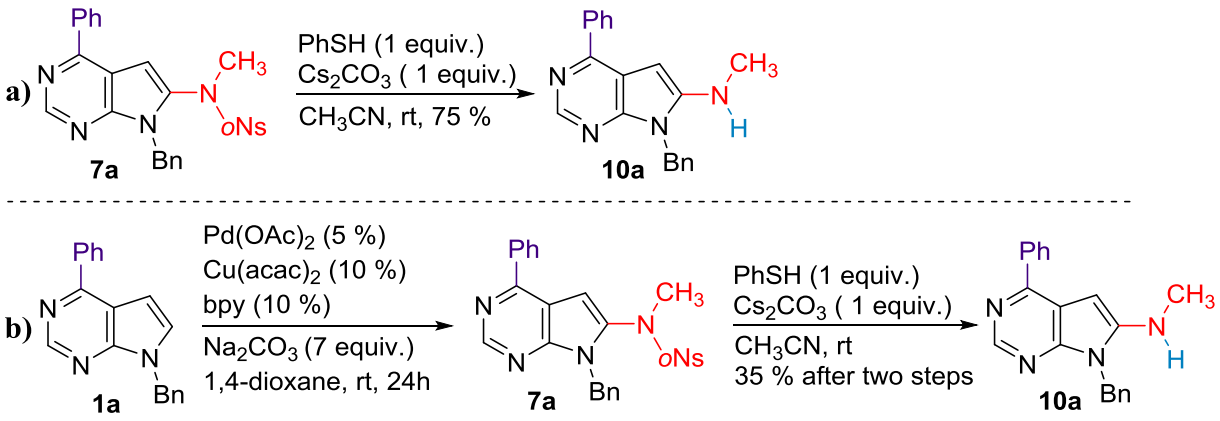


Figure 1 An ORTEP[142] view of compounds **5a** (CCDC 1014819), **7a** (CCDC 1014820), **7b** (CCDC 1014818) and **8a** (CCDC 1014817) shown with 50 % probability displacement ellipsoids.

The last goal of this study was to test the deprotection of the sulfonamides and the stability of the corresponding 8-amino-7-deazapurines (2-aminoindoles are prone to tautomerization and oxidation).[143a,b] Any attempts to cleave the Ts- or *p*Ns-groups in compounds **5a** or **6a** according to the literature[141] either did not work or led to decomposition of the heterocycles. Therefore, a major part of this study was performed with the *o*Ns-group which is more easily cleavable.[141] Deprotection of compound **7a** was successfully performed using thiophenol and cesium carbonate[141d] to afford 8-methylamino-7-deazapurine **10a** in 75

% yield (Scheme 3a). Additionally, I performed one-pot C-H amination/deprotection sequence to furnish the desired compound **10a** directly in 35 % after two steps (Scheme 3b).



Scheme 3 a) Deprotection of 6-phenyl-8-(*o*-nosyl)methylamino-7-deazapurine **7a**; b) C-H amination/deprotection sequence towards 8-methylamino-7-deazapurine **10a**.

The 8-(methylamino)-7-deazapurine **10a** was next studied for further applications. Interestingly, it showed nicer fluorescence in comparison to starting deazapurine **1a** and aminated product **7a** (Figure 2) which was weakly fluorescent (probably the fluorescene was quenched by the electron withdrawing nitro group from the sulfonamide moiety).

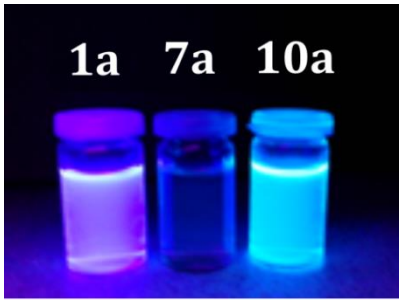


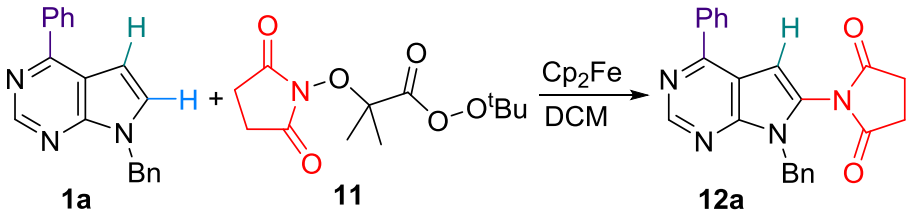
Figure 2 Starting deazapurine **1a** aminated product **7a** and 8-(methylamino)-7-deazapurine **10a** in methanol under UV-light (366 nm).

I was also interested in the preparation of a series of 8-amido derivatives and started testing the reactivity of **10a** by its reaction with carboxylic acids. Unfortunately, 8-(methylamino)-7-deazapurine **10a** quickly decomposed when exposed to even traces of acid (e.g. in chlorinated solvents). The instability of **10a** could be explained by its tendency to protonation and in principal, it can be oxidized with the degradation of deazapurine molecule. Analogous 2-aminoindoles are prone to protonation, tautomerization and autooxidation.[143a,b] However, there are reported examples of stable 1 and/or 3-substituted 2-aminoindoles.[143c,d,e]

3.1.2 Direct C-H imidation of 7-deazapurines

Direct intermolecular imidation is another interesting transformation to effect C-N bond construction. C-H imidation strategies have been attracting more and more scientific attention over the recent years.[110-111] This study draws its inspiration from the reported work regarding mild ferrocene-catalyzed C-H imidation of heteroarenes with *N*-succinimidyl perester (NSP).[111c]

I began the study of the C-H imidation reaction of deazapurines by testing the reactivity of model 6-phenyl-9-benzyl-7-deazapurine **1a** with previously prepared *N*-succinimidyl perester **11** under ferrocene catalysis (Scheme 4, Table 4).



Scheme 4 C-H imidation of 6-phenyl-9-benzyl-7-deazapurine **1a**

The reaction of **1a** with 2 equiv of NSP **11** in the presence of ferrocene catalyst (5 %) gave imidated product **12a** in 22 % yield and unreacted starting material (Table 4, entry 1).

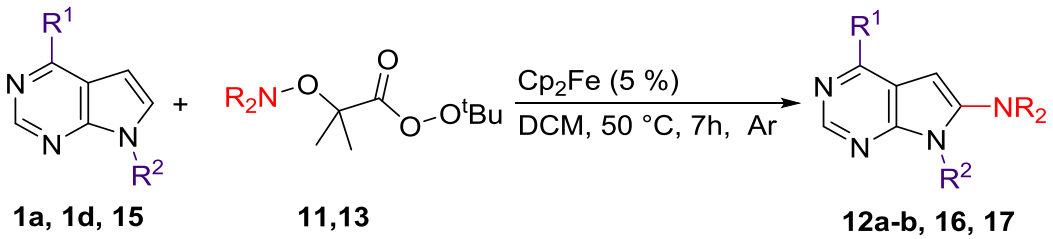
Table 4 Optimization of C-H imidation of 6-phenyl-9-benzyl-7-deazapurine **1a** with *N*-succinimidyl perester (NSP) **11**[a]

Entry	NSP **11**, equiv	Catalyst	Yield (%)
1	2.0	Cp_2Fe (5 %)	12
2	2.5	Cp_2Fe (5 %)	28
3	**2.75**	**Cp_2Fe (5 %)**	**32**
4	3.0	Cp_2Fe (5 %)	32
5	5.0	Cp_2Fe (5 %)	32
6	2.75	Cp_2Fe (10 %)	30
7	2.75	CuOAc (10 %)	11
8	2.75	CuCl (10 %)	9
9	2.75	$Mn(OAc)_3$ (10 %)	5

[a] Reaction conditions: **1a** (0.5 mmol) in DCM, 50 °C, 7h, under Ar.

In order to improve the reaction, a larger excess of NSP **11** was used and 2.75 equivalents was found to be the optimal amount (Table 4, entries 2-5). Increasing of Cp_2Fe catalyst loading (10 %) did not influence the yield (Table 4, entry 6). Next, I screened other potentially suitable catalysts such as Cu(I) and Mn(III) salts for the imidation reaction but, unfortunately, the reactions gave very low conversions (Table 4, entries 7-9). All attempts to improve it by using different solvents (MeCN, THF, 1,4-dioxane), additives, temperature modes (70 °C) or longer reaction time failed.

Despite the fact that conversion was unsatisfactory even after the optimization, I decided to use the best conditions for preparative C-H imidations of 6-substituted-7-deazapurines (Scheme 5, Table 5).



Scheme 5 C-H imidation of 7-deazapurines

The short scope of the method was studied for the series of 6-substituted-7-deazapurines (Table 5). Reaction of 6-Cl- and 6-Ph-9-benzyl-7-deazapurines **1a** and **1d** led to the imidated products **12a-b** in 32 and 27 % yield, respectively (Table 5, entries 1-2). In order to test the tolerance of other protecting groups, reaction of SEM protected 7-deazapurine **15** was carried out resulting in 46 % yield of desired product **16** (Table 5, entry 3). In addition, I was interested in trying another imidyl precursor and, for this purpose, phtaliimidyl perester **13** was prepared similary to NSP. Its reaction with model deazapurine **1a** gave the 8-phtaliimido-7-deazapurine **17** in slightly better 35 % yield in comparison to succinimidyl product **12a** (Table 5, entry 4).

Table 5 Preparative C-H imidations of 7-deazapurines

Entry	Starting compound	NR_2	R^1	R^2	Product (yield)
1	**1a**	succinimidyl	Ph	Bn	**12a** (32 %)
2	**1d**	succinimidyl	Cl	Bn	**12b** (27 %)
3	**15**	succinimidyl	OMe	SEM	**16** (46 %)
4	**1a**	phtalimidyl	Ph	Bn	**17** (35 %)

The regioselectively of the C-H imidation reactions was confirmed by X-ray crystallography for the compound **12a** (Figure 3).

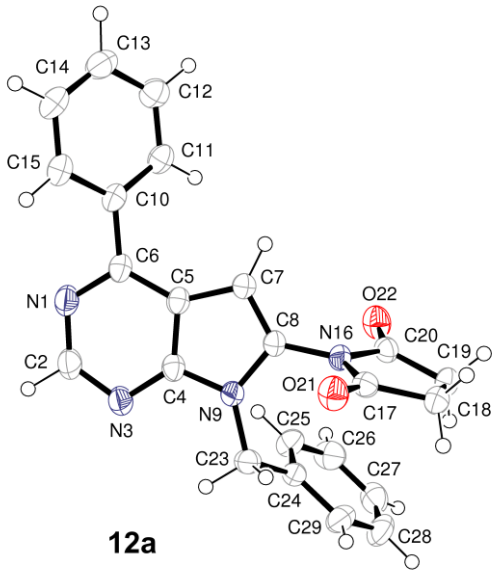


Figure 3 An ORTEP[142] view of **12a** shown with 50 % probability displacement ellipsoids.

In the last step, I tried to obtain deazapurines bearing the primary amino group after hydrolysis of the 8-imidyl derivatives. Unfortunately, after several attempts of acidic hydrolysis or hydrazinolysis I was unable to isolate any amount of the desired 8-amino product, due to the decomposition within reaction. This fact is in accordance with the low stability of similar 8-methylamino-7-deazapurine **10a**. It seems that free amino functionality at position 8 of 7-deazapurine heterocycle makes it very unstable and prone to quick decomposition.

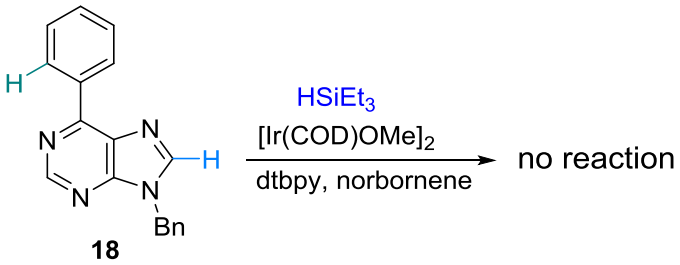
3.1.3 *ortho* C-H silylation of 7- and 9-phenyldeazapurines

Direct C-H silylation is currently widely studied for the functionalization of heteroarenes[119] since the resulting silanes can be further used in Hiyama cross-couplings and other functional group transformations.[126c,134] The most frequently used protocols utilize Ir, Rh and Ru catalysts.[122-128]

In indoles and related five-membered heterocycles, C-H silylation has been reported at the 2-position[120] unless a directing group (coordinating the metal) is present to facilitate *ortho*-silylalation.[121] In 6-aryl-substituted purines and deazapurines, the question arose whether the N-1 atom would direct *ortho*-silylalation of the aryl group or whether the C8

atom reactivity would prevail resulting in substitution at the five-membered ring of the nucleobase.

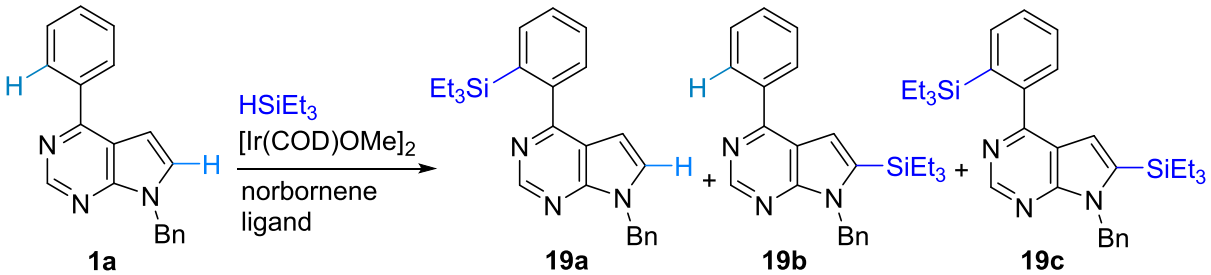
The study of C-H silylation started by testing the reactivity of 9-benzyl-6-phenylpurine **18** and its reaction with $HSiEt_3$ was examined in the presence of $[Ir(COD)OMe]_2$ as the catalyst, dtbpy as the ligand and norbornene as the hydrogen acceptor under literature conditions,[120d-g] but no reaction was observed (Scheme 6).



Scheme 6 Attempted Ir-catalyzed C-H silylation of 6-phenylpurine **18**

This was in accordance with the previous observations regarding the lack of reactivity of purines to Ir-catalyzed C-H borylations[98] that is most likely caused by a strong coordination of the metal to the N7 nitrogen and deactivatation of the catalyst. Therefore, I focused further attention on 7- and 9-deazapurines which were reactive under the reported C-H borylation reactions.[98]

Optimization of the reaction conditions was performed on the model 6-phenyl-9-benzyl-7-deazapurine **1a**. Its reaction with $HSiEt_3$ in the presence of $[Ir(COD)OMe]_2$, dtbpy ligand, and norbornene in THF at r.t. (Scheme 7, Table 6, entry 1) resulted in low conversion (26 %) giving a mixture of three silylated products: compound **19a** (10 %) - a product of *ortho*-silylation at the phenyl group, compound **19b** (9 %) - a product of direct C-H silylation of the deazapurine and compound **19c** (5 %) - a product of silylation at both positions.



Scheme 7 C-H silylations of 6-phenyl-7-deazapurine **1a**

When the same reaction mixture was heated to 80°C for 48 h, conversion increased to 72 %, mostly in favor of the *ortho*-silylated product **19a** (41 % isolated yield), the 8-silyl derivative **19b** in 13 % yield and the bisilylated product **19c** in 5 % yield (Table 6, entry 2). Increasing the excess of the $HSiEt_3$ slightly improved the yield of *ortho*-silylated product **19a** and decreased the formation of **19b** and **19c** (Table 6, entry 3). Replacement of the dtbpy ligand by bpy or Me_3Phen had little effect (Table 6, entries 4-5), whereas the presence of an additional base (Cs_2CO_3 or KO*t*Bu) caused very low conversion (Table 6, entries 6-7). Replacement of norbornene by cyclohexene gave a higher yield of direct C-H silylation (Table 6, entry 8).

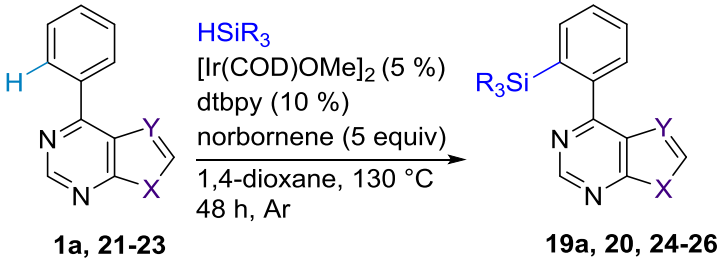
Interestingly, reaction in the absence of norbornene (or cyclohexene) as the hydrogen acceptor predominantly resulted in the direct C-H silylation product **19b** (29 %) along with a minor amount of the bisilylated product **19c**, while no formation of the *ortho*-silylated **19a** was observed (Table 6, entry 10). These reaction conditions were the same as were used for the reported C-H borylations[98] where the reaction proceeded selectively at position 8 of deazapurine **1a**, and no formation of *ortho* C-H borylated product was observed. However, in contrast to efficient C-H borylations, C-H silylation proceeded with a very low conversion under the same conditions. Therefore, I decided to design the reaction to be predominantly an *ortho* C-H silylation method. According to the reported *ortho*-selective C-H silylations of 2-phenylpyridine,[122b,c] which has the same reaction site as 6-phenyl-deazapurines, the presence of the norbornene hydrogen acceptor was crucial. The mechanism for the Ir-catalyzed dehydrogenative silylation of phenyldeazapurines may involve formation of the favored five-membered iridasilacycle over the direct C-H activation. Similarly to 2-phenylpyridine,[122b] for which the next step was insertion of norbornene into the Ir-H bond resulting in a norbornyliridium species, which after heating released norbornane and the Ir-silylated intermediate. Eventually, the Ir-silylated intermediate gave the final *ortho*-silylated product.

Keeping norbornene (5 equiv.), but changing the solvent to 1,4-dioxane and heating to higher reaction temperature (130 °C) further improved the conversion (85 %) and yield of *ortho*-silylated product **19a** (55 %, Table 6, entry 11), whereas the reaction in toluene led to lower conversion (56 %) (Table 6, entry 12). Solvent-free reactions in neat norbornene at 80 °C gave lower conversion but the same reaction at 130 °C again resulted in higher conversion with good selectivity for **19a** (Table 6, entries 13-14). On the other hand, the use of Ru or Rh catalysts led to only very low conversions (Table 6, entries 15-16).

Table 6 Optimization of *ortho* C-H silylation of deazapurine **1a**

Entry	Reagents and conditions	NMR conversion % (isolated yield %)		
		19a	**19b**	**19c**
1	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (3 equiv), norbornene (3 equiv), THF, rt, 48 h	10	9	7
2	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (3 equiv), norbornene (3 equiv), THF, 80 °C , 48 h	45 (41)	18 (13)	9 (5)
3	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), norbornene (5 equiv), THF, 80 °C , 48 h	54 (46)	9 (6)	6 (3)
4	Ir[(COD)OMe]$_2$ (5 %), bpy (10 %), HSiEt$_3$ (5 equiv), norbornene (5 equiv), THF, 80 °C , 48 h	32	6	4
5	Ir[(COD)OMe]$_2$ (5 %), Me$_3$Phen (10 %), HSiEt$_3$ (5 equiv), norbornene (5 equiv), THF, 80 °C , 48 h	44	5	4
6	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), Cs$_2$CO$_3$ (2 equiv), norbornene (5 equiv), THF, 80 °C , 48 h	5	6	2
7	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), KOtBu (1 equiv), norbornene (5 equiv), THF, 80 °C , 48 h	4	3	3
8	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), cyclohexene (5 equiv), THF, 80 °C , 48 h	16	18	8
9	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), norbornene (5 equiv), cyclohexane, 80 °C , 48 h	27	24	12
10	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), THF, 80 °C , 48 h	-	29	8
11	**Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), norbornene (5 equiv), 1,4-dioxane, 130 °C , 48 h**	**61 (55)**	**14 (9)**	**10 (7)**
12	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), norbornene (5 equiv), toluene, 130 °C , 48 h	15	30	11
13	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), norbornene (5 equiv), 80 °C , 48 h	33	27	7
14	Ir[(COD)OMe]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), norbornene (5 equiv), 130 °C , 48 h	57 (51)	9 (5)	7 (4)
15	Rh[(COD)Cl]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), norbornene (5 equiv), THF, 80 °C , 48 h	8	6	4
16	Ru[(p-cymene)Cl$_2$]$_2$ (5 %), dtbpy (10 %), HSiEt$_3$ (5 equiv), norbornene (5 equiv), THF, 80 °C , 48 h	5	6	6

The most synthetically useful protocol was the reaction in dioxane at 130 °C (Table 6, entry 11), that was used for the preparative synthesis of all three products **19a-c** which were separable by column chromatography. The same method was therefore used for silylation reactions of other phenyl-deazapurines (Scheme 8).



Scheme 8 *ortho* C-H silylations of phenyldeazapurines

At first, reaction of **1a** with $HSiMe_2Ph$ was performed under the same conditions, however, the conversion was much lower than in the case of the silylation with $HSiEt_3$. The *ortho*-silylated derivative **17** (Table 7, entry 2) was the only product isolated in 32 % yield (trace amounts of other products were observed but could not be isolated). The reaction with $HSiEt_3$ was applied to 9-unprotected 6-phenyl-7-deazapurine **18** to selectively obtain the *ortho*-silylated 6-phenyl-7-deazapurine base **21** in 47 % yield (Table 7, entry 3) (again, side-products were only observed in trace amounts). The same protocol was then applied to the reaction of 6-phenyl-7-benzyl-9-deazapurine **19**. The reaction proceeded analogously to 7-deazapurine to furnish the *ortho*-silylated derivative **22** in 46 % yield (Table 7, entry 4). Similarly, the reaction of non-benzylated 6-phenyl-9-deazapurine 20 gave the *ortho*-silylated 6-phenyl-9-deazapurine base **23** in 37 % yield (Table 7, entry 5).

Table 7 Preparative *ortho* C-H silylations of phenyldeazapurines

Entry	Starting compound	$HSiR_3$	X	Y	Product (yield)
1	**1a**	$HSiEt_3$	N-Bn	CH	**19a** (55 %)
2	**1a**	$HSiMe_2Ph$	N-Bn	CH	**20** (32 %)
3	**21**	$HSiEt_3$	NH	CH	**24** (47 %)
4	**22**	$HSiEt_3$	CH	N-Bn	**25** (46 %)
5	**23**	$HSiEt_3$	CH	NH	**26** (37 %)

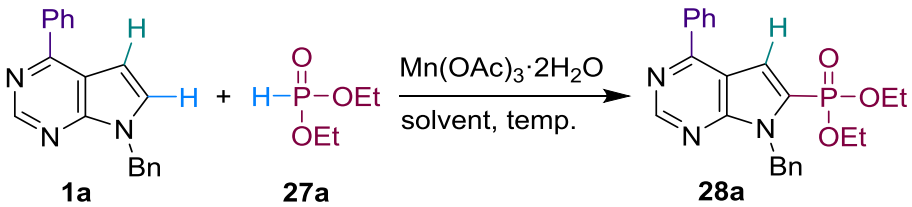
In most cases, I recovered the major part of the unreacted starting compound and observed only trace amounts of other C-H silylated products in the NMR spectra of the crude mixtures. I also tried to apply the conditions in the absence of norbornene (Table 6, entry 10) to other phenyldeazapurines in order to gain access to the corresponding products of direct silylation on the deazapurine, but those reactions ended in negligible conversions.

3.1.4 Direct C-H phosphonation of 7- and 9-deazapurines

Phosphonation of deazapurines is an extremely appealing research topic due to the interesting properties of phosphonate group in heteroaromatic systems in general. Since C-H phosphonation has not been studied intensively, and to the best of my knowledge, no C-H phosphonations of 7- or 9-deazapurines have been reported so far, I endeavored to find such conditions. Motivated by the number of reported oxidative phosphonations of arenes and heteroarenes,[138-140] I began the study of C-H phosphonation reactions on deazapurines.

Typically, I selected 6-phenyl-9-benzyl-7-deazapurine **1a** as a model compound for the study of its C-H phosphonation with diethylphosphite **27a** to screen reagents and reaction conditions. After some initial experiments with Ag(I), Fe(III) and Co(III) salts, which did not work or gave very low conversions, I focused on the use of $Mn(OAc)_3{\cdot}2H_2O$ (Table 8). The reaction using 3 equiv. of $Mn(OAc)_3{\cdot}2H_2O$ in AcOH at room temperature did not proceed, but when the temperature was increased to 50 or 80 °C, I obtained the desired 8-phosphonated 7-deazapurine product **28a** in 23 or 37 % yield, respectively (Table 8, entries 2- 3). Increasing or decreasing the promoter loadings had no positive effect (Table 8, entries 4-5). Next, I tried various solvents (Table 8, entries 6-11) and found out that a mixture of $MeCN/H_2O$ (1:1) resulted in an improved 43 % yield (Table 8, entry 12). Finally, further increasing the temperature to 100 °C and using a larger excess of diethylphosphite (5 equiv.) provided **28a** in 47 % yield (Teble 8, entry 14). None of other efforts to improve the yields were successful, and therefore, I used these conditions as the optimal ones.

Table 8 Optimization of C-H phosphonation reaction of 6-phenyl-9-benzyl-7-deazapurine **1a** with diethylphosphite **27a**[a]

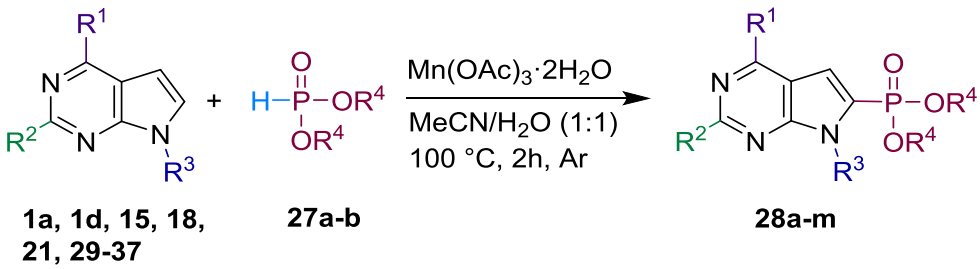


Entry	Solvent	T, °C	Yield (%)
1	AcOH	20	n.r.
2	AcOH	50	23
3	AcOH	80	37
4[b]	AcOH	80	32

5[c]	AcOH	80	38
6	DMSO	80	18
7	MeCN	80	35
8	H_2O	80	34
9	AcOH/H_2O	80	36
10	NMP	80	26
11	MeCN	80	33
12	MeCN/H_2O	80	43
13	MeCN/H_2O	100	45
14[d]	**MeCN/H_2O**	**100**	**47**

[a] General reaction conditions: diethylphosphite (4 equiv.), $Mn(OAc)_3 \cdot 2H_2O$ (3 equiv.), 2 h under Argon atmosphere; [b] $Mn(OAc)_3 \cdot 2H_2O$ (2 equiv.); [c] $Mn(OAc)_3 \cdot 2H_2O$ (4 equiv.); [d] diethylphosphite (5 equiv.).

With optimized reaction conditions in hand, my next step was to study the scope and limitations of the method. A series of diverse substituted 7-deazapurines was tested in preparative C-H phosphonation reactions (Scheme 9, Table 9).



Scheme 9 C-H phosphonations of 7-deazapurines

The reactions of 6-chloro-, 6-substituted-7-benzyl and 7-(2-trimethylsilyl)ethoxymethyl)-protected deazapurines **1a, 1d, 30, 31, 15** proceeded smoothly to provide desired products **28a-b, 28d-f** in acceptable 36-56 % yields (Table 9, entries 1-2, 4-6). Moreover, the C-H phosphonation of benzoyl-protected nucleoside **29** resulted in 25 % yield of the desired phosphono-nucleoside **28c** (Table 9, entry 3**).** Another useful substrate was 6-chloro-7-deazapurine base **32** which was suitable for further functional group transformations at positions 6 and 9. In this case, the C-H phosphonation worked nicely to give the desired 9-unsubstituted 6-chloro-8-phosphono-7-deazapurine **28g** in 41 % yield (Table 9, entry 8). It also showed that no 9-substitution or protection is needed for the C-H

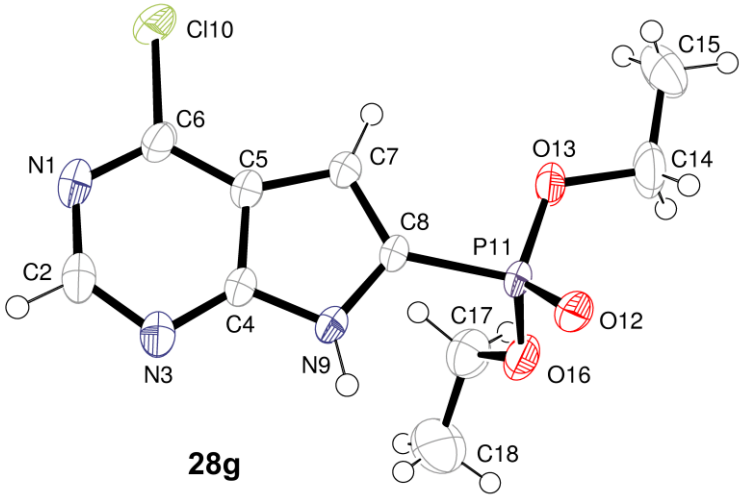
phosphonations. In addition, I tried the reaction of 6-chloro-7-deazapurine **32** with more bulky diisopropyl phosphite **27b** to afford the desired product **28h** in somewhat lower 30 % yield. Then, I decided to explore preparative C-H phosphonations of different 2- and/or 6-substituted-7-deazapurine bases. In all cases, I obtained the desired products **28i-m** in good (37-40 %) yields (Table 9, entries 9-13). On the other hand, attempted C-H phosphonations of 7-fluoro-7-deazapurine **37** and 6-phenylpurine base **18** were unsuccessful (Table 9, entries 14-15).

Table 9 Preparative C-H phosphonations of 7-deazapurines

Entry	Starting compound	R^1	R^2	R^3	R^4	Product (yield)
1	**1a**	Ph	H	Bn	Et	**28a** (47 %)
2	**1d**	Cl	H	Bn	Et	**28b** (36 %)
3	**29**	Ph	H	ribofuranose	Et	**28c** (25 %)
4	**30**	Cl	H	SEM	Et	**28d** (30 %)
5	**31**	SMe	H	SEM	Et	**28e** (56 %)
6	**15**	OMe	H	SEM	Et	**28f** (40 %)
7	**32**	Cl	H	H	iPr	**28h** (30 %)
8	**32**	Cl	H	H	Et	**28g** (41 %)
9	**21**	Ph	H	H	Et	**28i** (40 %)
10	**33**	Cl	NH_2	H	Et	**28k** (38 %)
11	**34**	Cl	Cl	H	Et	**28j** (39 %)
12	**35**	Cl	Me	H	Et	**28l** (37 %)
13	**36**	Cl	F	H	Et	**28m** (37 %)
14[a]	**37**	Cl	H	H	Et	**n.r.**
15[b]	**18**	Ph	H	Bn	Et	**n.r.**

[a] Deazapurine **37** include F substituent at position 7; [b] Compound **18** is a purine analogue.

The structures of phosphonated products **28g** and **28k** were additionally confirmed by X-ray crystallography (Figure 4).



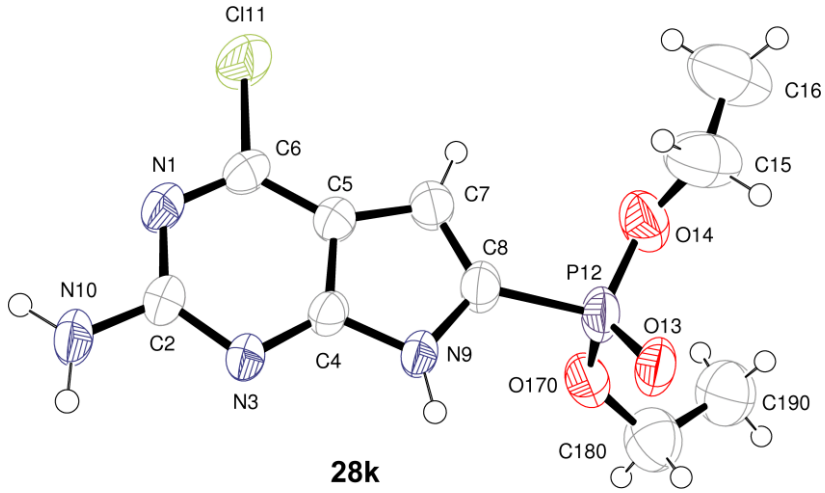
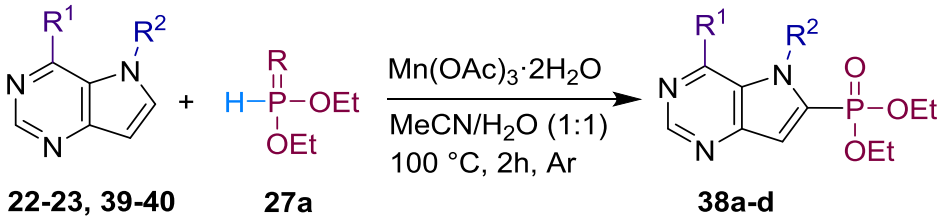


Figure 4 An ORTEP[142] view of **28g** (CCDC 1495148) and **28k** (CCDC 1495150) shown with 50 % probability displacement ellipsoids.

Subsequently, the C-H phosphonation protocol was tested on 9-deazapurines (Scheme 10, Table 10).



Scheme 10 C-H phosphonations of 9-deazapurines

The reactions of 7-benzyl-6-chloro- and 6-phenyl-9-deazapurines **39** and **22** proceeded well to give the 8-phosphonated 9-deazapurine products **38a** and **38b** in 30 and 31 % yield, respectively (Table 10, entries 1-2). The C-H phosphonation of 7-unsubstituted 6-chloro- and 6-phenyl-9-deazapurine **40** and **23** also worked well to afford the corresponding phosphonated 9-deazapurine bases **38c** and **38d** in 37 or 36 % yield, respectively (Table 10, entries 3-4).

Table 10 Preparative C-H phosphonations of 9-deazapurines

Entry	Starting compound	R^1	R^2	Product (yield)
1	**39**	Cl	Bn	**38a** (30 %)
2	**22**	Ph	Bn	**38b** (31 %)
3	**40**	Cl	H	**38c** (37 %)
4	**23**	Ph	H	**38d** (36 %)

The structure of 9-deazapurine phosphonate **38c** was also confirmed by X-ray crystallography (Figure 5).

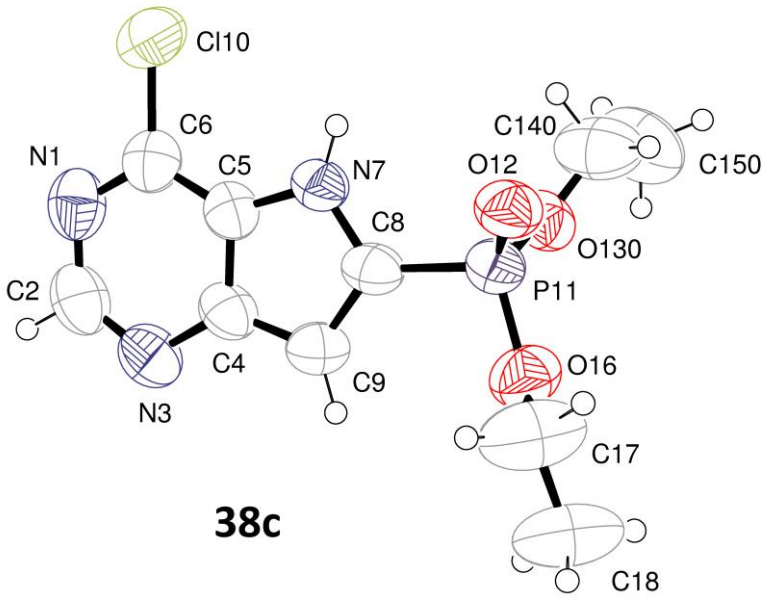
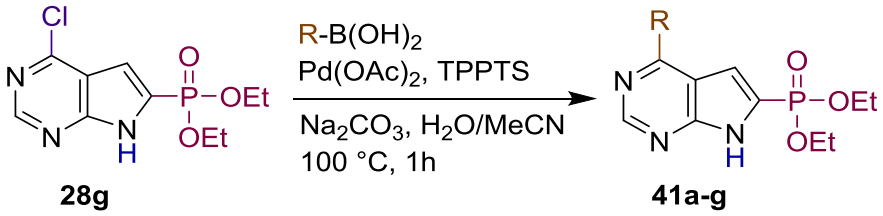


Figure 5 An ORTEP[142] view of **38c** (CCDC 1495149) shown with 50 % probability displacement ellipsoids.

To test synthetic utility of 6-chloro-7-deazapurine phosphonate intermediate **28g**, I performed a series of aqueous-phase Suzuki-Miyaura cross-coupling reactions with different (het)aryl boronic acids (Scheme 11). All of these reactions proceeded smoothly to give a series of 6-substituted-7-deazapurine phosphonate bases **41a-g** in good yields 60-75 % (Table 11).

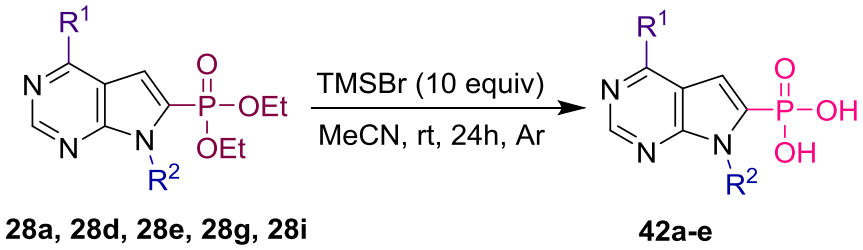


Scheme 11 Suzuki-Miyaura cross-coupling reactions of 7-deazapurine-8-phosphonate **28g**

Table 11 Synthesis of 6-(het)aryl-7-deazapurine phosphonates

Entry	R	Product (yield)
1	furan-2-yl	**41a** (71 %)
2	furan-3-yl	**41b** (65 %)
3	thiophen-2-yl	**41c** (65 %)
4	thiophen-3-yl	**41d** (72 %)
5	phenyl	**41e** (75 %)
6	benzofuran-2-yl	**41f** (67 %)
7	dibenzofuran-4-yl	**41g** (60 %)

My last goal within the framework of this project was to develop a method for phosphodiester bond cleavage in order to obtain interesting free phosphonic acid derivatives. The deprotection was performed in two steps by reaction with bromo(trimethyl)silane in acetonitrile[144] with further aqueous workup (to hydrolyze the silyl-esters after transesterification) (Scheme 12).



Scheme 12 Phosphodiester cleavage of deazapurine phosphonates

I used this protocol for five different 6-chloro- or 6-substituted 7-deazapurine phosphonates either substituted at position 9 with Bn (**28a)** or SEM groups (**28d, 28e)**, or 9-unsubstituted 7-deazapurine phoshphonates (**28g, 28i**). In all cases the reactions proceeded nicely to provide the free phosphonic acids **42a-e** in acceptable yields (55-85 %), which were slightly lowered due to difficulty in isolating the products (Table 12).

Table 12 Synthesis of 7-deazapurine 8-phosphonic acids

Entry	Starting compound	R^1	R^2	Product (yield)
1	**28a**	Ph	Bn	**42a** (75 %)
2	**28d**	Cl	SEM	**42b** (55 %)
3	**28e**	SMe	H	**42c** (85 %)
4	**28g**	Br	H	**42d** (77 %)
5	**28i**	Ph	H	**42e** (63 %)

Interestingly, during the phosphodiester cleavage of 6-SMe-9-SEM-7-deazapurine phosphonate **28e**, the concomitant cleavage of the (2-trimethylsilyl)ethoxymethyl protecting group was observed due to strong acidic conditions (Table 12, entry 3). The deprotection of 6-chloro-7-deazapurine-8-phosphonate **28g** with TMSBr led to a concomitant displacement of chlorine by bromine (likely due to HBr formed during the reaction) to give 6-bromo-7-deazapurine-8-phosphonic acid **42d** (Table 12, entry 4). Despite a rather difficult isolation of the free phosphonic acids, the sequence of C-H phosphonation followed by TMSBr treatment and hydrolysis can be used for efficient synthesis of deazapurine-8-phosphonic acids.

3.2 Synthesis of 2-substituted 6- and 7-(het)aryl-7-deazapurine bases

The second part of this PhD thesis is focused on the synthesis of 2-substituted 6- and 7-(het)aryl-7-deazapurine nucleobases. Previously discovered in our scientific group, 6-(het)aryl-7-deazapurine and 7-fluoro-7-deazapurine ribonucleosides (Figure 6) are potent cytostatics[36] and/or inhibitors of mycobacterial adenosine kinase,[37c] whereas the 2-substituted derivatives[145] as well as sugar-modified nucleosides[146] are less active or inactive. 7-(Het)aryl-7-deazaadenosines (Figure 6) are also potent cytostatics[37a] and/or inhibitors of mycobacterial adenosine kinase.[147] The mechanism of their cytostatic effect involves transformation to nucleoside triphosphates and their incorporation into RNA and DNA.[148] It was also found that 7-(het)aryl-7-deazapurine ribonucleosides bearing other substituents at position 6 (OMe, SMe, Me) (Figure 6) exert cytostatic activities comparable to the 7-(het)aryl deazaadenosines, whereas the 6-oxo and 2-substituted derivatives were inactive (Figure 6).[37b]

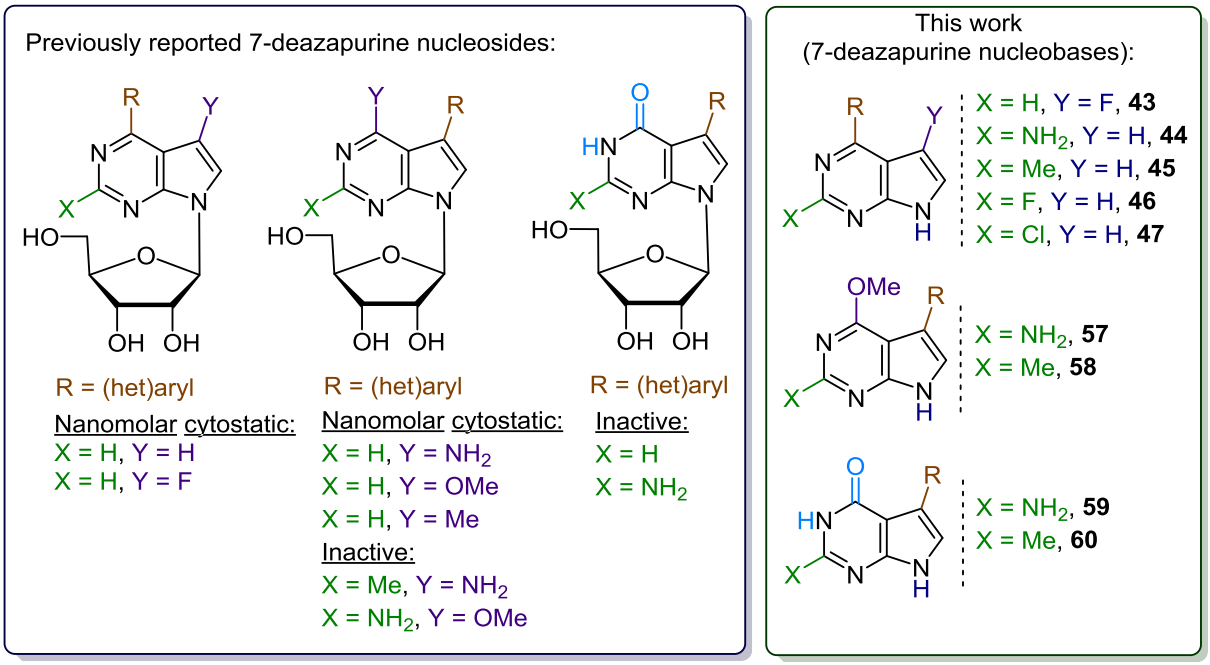


Figure 6 Previously reported biologically active 7-deazapurine nucleosides and 7-deazapurine nucleobases under study

However, the biological activity of the parent 7-deazapurine nucleobases remains unknown. Analysis of this class of compounds is important for determining the structure-activity relationships because, in principle, the nucleobases could be converted into nucleotides by phosphoribosyl transferases of the salvage pathway. This encouraged me to

synthesize and profile several new types of 6- and 7-(het)aryl-7-deazapurine bases and, for this purpose, I chose the reliable Suzuki-Miyaura cross-coupling reaction under aqueous conditions.[37,92] The first group was the 6-(het)aryl-7-deazapurine derivatives **43** bearing F at position 7, the second type was 2-substituted 6-(het)aryl-7-deazapurine bases **44-47**, the third type 2-amino or 2-methyl 6-methoxy-7-hetaryl-7-deazapurines **57-58** and the last group 7-hetaryl-7-deazaguanines **59** and 2-methyl 7-hetaryl-7-deazahypoxanthines **60**. Additionally, I was interested in establishing the photophysical properties of the newly synthesized (het)aryl-7-deazapurines, because introduction of electron-donating (het)aryl substituents can potentially improve the fluorescence.

3.2.1 Synthesis of 2-substituted 6-(het)aryl-7-deazapurines

As mentioned above, 6-(het)aryl-7-deazapurine and 6-(het)aryl-7-fluoro-7-deazapurine ribonucleosides are known for their cytostatic activity,[36] however, there was no information available about the biological activity of their nucleobase analogues. My goal in this project was to synthesize 6-(het)aryl-7-fluoro-7-deazapurine bases **43a-i** and 2-substituted-6-(het)aryl-7-deazapurine bases **44-48** (Figure 7).

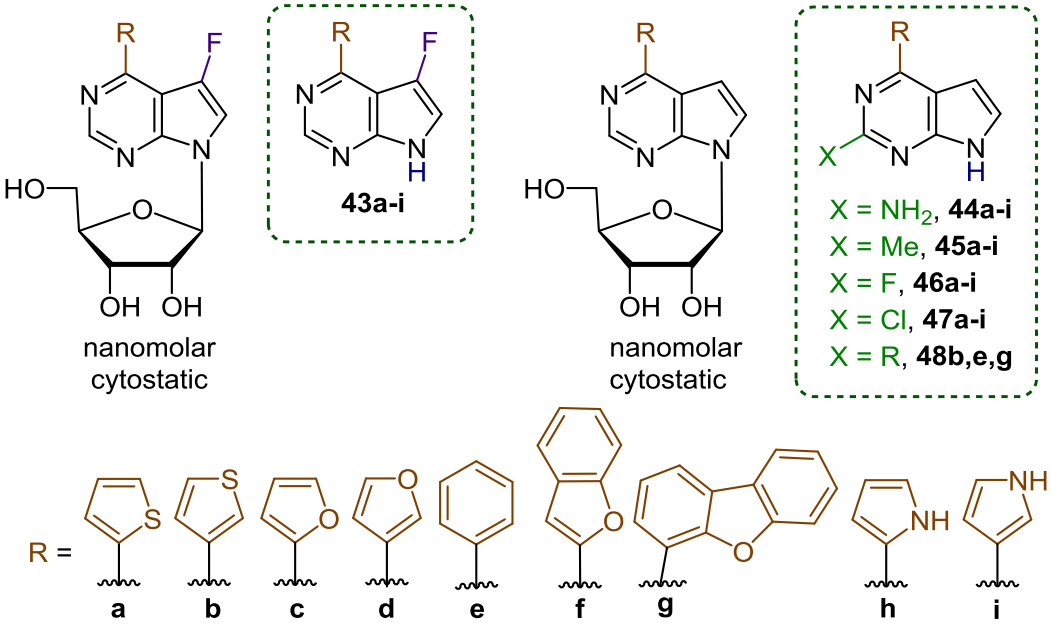
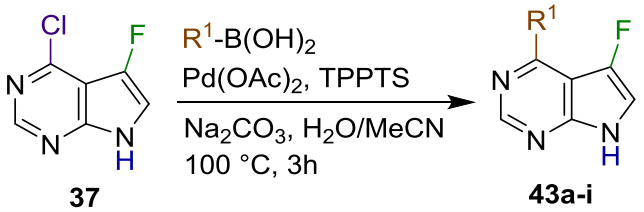


Figure 7 Reported cytostatic 6-(het)aryl-7-deazapurine nucleosides and the 6-(het)aryl-7-deazapurine nucleobases **43-48** under study

Preparation of the target 6-(het)aryl-7-deazapurines started from 6-chloro-7-deazapurines. Thus, 6-chloro-7-fluoro-7-deazapurine **37** reacted with a series of

(het)arylboronic acids to afford the corresponding 6-(het)aryl-7-fluoro-7-deazapurine bases **43a-i** in one step (Table 13). Typically, the substrate was treated with boronic acid (1.5 equiv), Na_2CO_3 (3 equiv) in the presence of $Pd(OAc)_2$ (0.05 equiv) and TPPTS (0.125 equiv) in H_2O/MeCN (2:1) mixture at 100 °C for 3 hours. The reactions proceeded cleanly with full conversion of the starting 6-chloro-7-fluoro-7-deazapurine **37** furnishing products in good yields. The only exceptions were the 2- and 3-pyrrolyl derivatives which were obtained in moderate yields (Table 13, entries 8-9). It should also be noted that the *N*-protecting groups from pyrrolyl boronic acids were cleaved under the reaction conditions. In most cases, the products nicely crystallized from the reaction mixture (except for 2- and 3-pyrrolyl derivatives). However, to obtain even purer products, I performed simple chromatography through a short silica gel column to remove precipitated metallic palladium and organic residue arising from the excess of boronic acid.

Table 13 Synthesis of 6-(het)aryl-7-fluoro-7-deazapurines

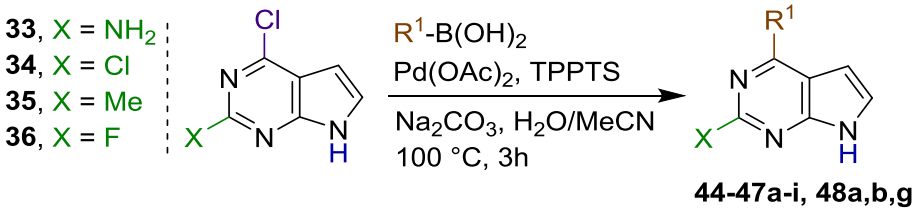


Entry	R^1	Product (yield)
1	thiophen-2-yl	**43a** (75 %)
2	thiophen-3-yl	**43b** (72 %)
3	furan-2-yl	**43c** (69 %)
4	furan-3-yl	**43d** (71 %)
5	phenyl	**43e** (75 %)
6	benzofuran-2-yl	**43f** (69 %)
7	dibenzofuran-4-yl	**43g** (77 %)
8	pyrrol-2-yl[a]	**43h** (32 %)
9	pyrrol-3-yl[a]	**43i** (35 %)

[a] For R^1 = pyrrol-2-yl, *N*-Boc-*1H*-pyrrol-2-yl boronic acid was used; for R^1 = pyrrol-3-yl, *N*-(triisopropylsilyl)-*1H*-pyrrol-3-yl boronic acid was used.

The synthesis of diverse 2-substituted-6-het(aryl)-7-deazapurines **44a-i**, **45a-i**, **46a-i**, **47a-i** was performed by analogous cross-coupling reactions of 2-amino-6-chloro-7-deazapurine **33**, 6-chloro-2-methyl-7-deazapurine **35**, 2-fluoro-6-chloro-7-deazapurine **36** and 2,6-dichloro-7-deazapurine **34** (Table 14). In most cases, the desired 2-substituted-6-hetaryl-7-deazapurine bases were obtained in good to excellent yields (again the pyrrolyl derivatives were prepared less efficiently). It should be noted that no hydrolysis of the relatively reactive 2-fluoro group was observed on 2-fluoro derivatives **46a**-i under basic reaction conditions. In the case of 2,6-dichloro-7-deazapurine **34**, some reactions gave minor amounts of 2,6-diaryl-7-deazapurines **48b**, **48e** and **48g** in addition to the desired major 6-mono-substituted products **47a-i**, which were easily separated by column chromatography.

Table 14 Synthesis of 2-substituted-6-(het)aryl-7-deazapurines



R^1	Product (yield)				
	X = NH_2	X = Me	X = F	X = Cl	X = R^1
thiophen-2-yl	**44a** (86 %)	**45a** (95 %)	**46a** (66 %)	**47a** (93 %)	
thiophen-3-yl	**44b** (90 %)	**45b** (87 %)	**46b** (91 %)	**47b** (60 %)	**48b** (26 %)
furan-2-yl	**44c** (67 %)	**45c** (63 %)	**46c** (84 %)	**47c** (64 %)	
furan-3-yl	**44d** (83 %)	**45d** (84 %)	**46d** (85 %)	**47d** (73 %)	
phenyl	**44e** (80 %)	**45e** (81 %)	**46e** (84 %)	**47e** (50 %)	**48e** (38 %)
benzofuran-2-yl	**44f** (58 %)	**45f** (58 %)	**46f** (65 %)	**47f** (30 %)	
dibenzofuran-4-yl	**44g** (52 %)	**45g** (66 %)	**46g** (43 %)	**47g** (15 %)	**48g** (5 %)
pyrrol-2-yl[a]	**44h** (60 %)	**45h** (70 %)	**46h** (72 %)	**47h** (65 %)	
pyrrol-3-yl[a]	**44i** (43 %)	**45i** (40 %)	**46i** (59 %)	**47i** (56 %)	

[a] For R^1 = pyrrol-2-yl, *N*-Boc-*1H*-pyrrol-2-yl boronic acid was used; for R^1 = pyrrol-3-yl, *N*-(triisopropylsilyl)-*1H*-pyrrol-3-yl boronic acid was used.

Hirao et al. used 6-hetarylpurine nucleosides for the construction of an intrinsically fluorescent unnatural base pair which was efficiently replicated by polymerases in vitro.[149] It was noticed that all final 6-(het)aryl-7-deazapurine bases **43-48** exerted fluorescence properties, and therefore, their photophysical properties were studied in more detail in order to identify new candidates for the development of fluorescent nucleoside analogs.

UV-visible absorption and fluorescence spectra of the synthesized compounds were measured in ethanol as the model protic solvent. The measured spectroscopic characteristics (absorption coefficients, positions of absorption and emission maxima, quantum yields of fluorescence) are summarized in Table 15.

Table 15 UV absorbtion spectra and fluorescence properties

Compd	λ_{abs} [nm] (ε / 10^4 $M^{-1}\times cm^{-1}$)[a]	λ_{em} [nm]	Φ_f
43a	295 (1.2), 334 (1.2)	445	0.17 ± 0.03
43b	260 (1.2), 321 (0.9)	430	0.10 ± 0.03
43c	294 (0.9), 339 (1.1)	440	0.11 ± 0.03
43d	276 (0.6), 316 (0.8)	421	0.07 ± 0.02
43e	250 (1.3), 316 (0.7)	441	0.08 ± 0.03
43f	348 (1.9)	462	0.12 ± 0.03
43g	275 (1.5)	446	0.09 ± 0.03
43h	345 (2.2)	400	0.54 ± 0.03
43i	257 (0.7), 328 (1.2)	395	0.29 ± 0.04
44a	285 (1.0), 363 (0.8)	462	0.54 ± 0.03
44b	344 (0.8)	432	0.52 ± 0.02
44c	282 (1.5), 358 (0.9)	444	0.57 ± 0.02
44d	339 (0.7)	419	0.51 ± 0.02
44e	343 (0.6)	449	0.54 ± 0.02
44f	304 (2.0), 373 (1.2)	468	0.61 ± 0.04
44g	288 (1.3), 343 (0.6)	467	0.51 ± 0.03
44h	301 (1.4), 348 (1.5)	420	0.31 ± 0.02
44i	335 (0.9)	401	0.21 ± 0.02
45a	332 (1.4)	417	0.38 ± 0.03
45b	255 (1.1), 315 (1.1)	403	0.31 ± 0.02
45c	280 (1.0), 328 (1.3)	406	0.44 ± 0.04
45d	269 (0.6), 309 (0.9)	396	0.23 ± 0.03
45e	311 (0.7)	414	0.39 ± 0.04
45f	345 (1.9)	423	0.54 ± 0.02
45g	251 (1.7), 289 (1.5)	427	0.41 ± 0.02
45h	337 (2.4)	383	0.28 ± 0.03
45i	320 (1.5)	372	0.40 ± 0.02
46a	268 (0.8), 336 (1.3)	426	0.57 ± 0.02
46b	258 (1.1), 319 (1.0)	415	0.46 ± 0.01
46c	283 (0.9), 331 (1.2)	443	0.58 ± 0.03
46d	268 (0.5), 312 (0.8)	406	0.44 ± 0.03
46e	249 (1.2), 315 (0.8)	425	0.53 ± 0.03

46f	348 (1.8)	436	0.57 ± 0.03
46g	272 (1.4), 317 (1.2)	435	0.43 ± 0.04
46h	347 (2.3)	388	0.83 ± 0.04
46i	253 (0.8), 325 (1.7)	376	0.63 ± 0.02
47a	288 (0.8), 337 (1.3)	421	0.45 ± 0.03
47b	260 (1.1), 320 (1.0)	409	0.36 ± 0.03
47c	284 (1.1), 332 (1.4)	416	0.48 ± 0.02
47d	273 (0.5), 314 (0.8)	406	0.29 ± 0.04
47e	317 (0.8)	420	0.40 ± 0.03
47f	317 (1.4), 348 (2.0)	433	0.47 ± 0.03
47g	273 (1.4), 289 (1.3), 317 (1.1)	432	0.37 ± 0.03
47h	343 (2.3)	388	0.77 ± 0.02
47i	326 (1.6)	377	0.46 ± 0.02
48b	268 (3.4), 316 (1.0)	399	0.20 ± 0.02
48e	261 (3.4), 313 (1.1)	405	0.40 ± 0.03
48g	246 (4.5), 273 (4.1)	422	0.35 ± 0.02

[a] For every value of ε the confidence interval did not exceed the value of ± 0.1×10^4 [$M^{-1}\times cm^{-1}$]

The aforementioned 7-deazapurine bases bearing aryl and heteroaryl substituents developed a bathochromically shifted band in their UV spectra, which were usually (with a few exceptions) centered between 307 and 363 nm. All studied compounds were substantially fluorescent, exhibiting single-band emission in the long-UV – blue range, centered between 372 nm (**45i**) and 468 nm (**44f**) as shown in Figure 8a.

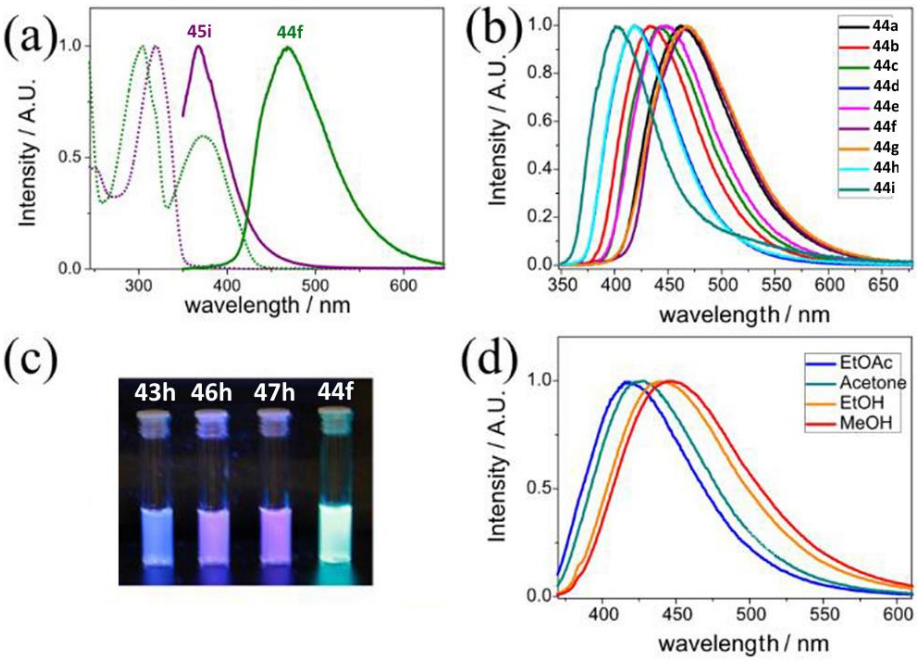


Figure 8 a) Normalized absorption (dotted line) and emission (solid line) of compounds **45i** (violet) and **44f** (green); b) The influence of the substituent at position 6 in the fluorescence spectra; c) Photography of a selected set of compounds in ethanol having the highest values of brightness; d) The influence of the solvent polarity on the emission spectra of compound **43c**.

The fluorescence quantum yield of the synthesized compounds ranged from 0.07 for compound **43d** to 0.83 for compound **46h**, with median of 0.43. The variation of the substituents at positions 2 and 7 of the 7-deazapurine core had no apparent effect on the brightness of fluorescence ($B = \varepsilon_{max} \times \Phi_f$), with the exception of the 7-fluoro series, where the brightness was relatively low (< 4000 $M^{-1} \cdot cm^{-1}$) compared to the other compounds. On the contrary, the variation of the aryl and heteroaryl substituents at the position 6 of the 7-deazapurine core had much stronger effect (Figure 8b).

Typically, the highest brightness of fluorescence was noticed for the benzofuran-2-yl and pyrrol-2-yl derivatives. Within these series the highest value was observed for the compound **46h** (19200 $M^{-1} \cdot cm^{-1}$). The highest overall brightness of the pyrrol-2-yl series was also accomplished by relatively short-wavelength emission, centered at 383–420 nm, whereas the emission of the benzofuran-2-yl series was bathochromically shifted with the longest maximum at 468 nm for **44f** (Figure 8c).

Solvatochromic nucleoside analogues, i.e. those changing the emission color in response to changes in the polarity of microenvironment, are valuable tools for biophysical studies.[150] Emission of the synthesized compounds was examined toward sensitivity to polarity. The best results were obtained for compound **43c**, which changed the emission wavelength from 419 nm in ethyl acetate to 452 nm in methanol (Figure 8d). Potentially, installation of an additional electron donating/withdrawing groups onto this scaffold could further improve the solvatochromism.

All the final 6-(het)aryl-7-deazapurine bases **43-48** were tested for *in vitro* cytostatic activity against a panel of cancer and leukemia cell-lines (A549, HCT116, HCT116p53-/-, CCRF-CEM, CEM-DNR, K562 and K562-TAX) but did not show any significant effect at 10 μM concentrations. The lack of activity of the nucleobases in contrast to the highly potent ribonucleosides[35-37] clearly shows that the salvage pathway does not play an important role in the mechanism of action of the deazapurine nucleoside cytostatics and that these modified nucleobases are probably not substrates for phosphoribosyl transferases that would convert them to bioactive nucleotides.

3.2.2 Synthesis of 2-substituted 7-(het)aryl-7-deazapurines

This particular project was a part of the bigger project in our research group towards preparation of the library of 2,6-disubstituted-7-(het)aryl-7-deazapurine bases, since the above mentioned 7-(het)aryl-7-deazapurine ribonucleosides bearing different substituents at position 6 (NH_2, OMe, SMe, Me) exerted cytostatic activities.[37a] Within this project my goal was to prepare 2-amino- and 2-methyl-6-methoxy-7-(het)aryl-7-deazapurine bases **57** and **58** and their oxo-analogues **59** and **60** (Figure 9).

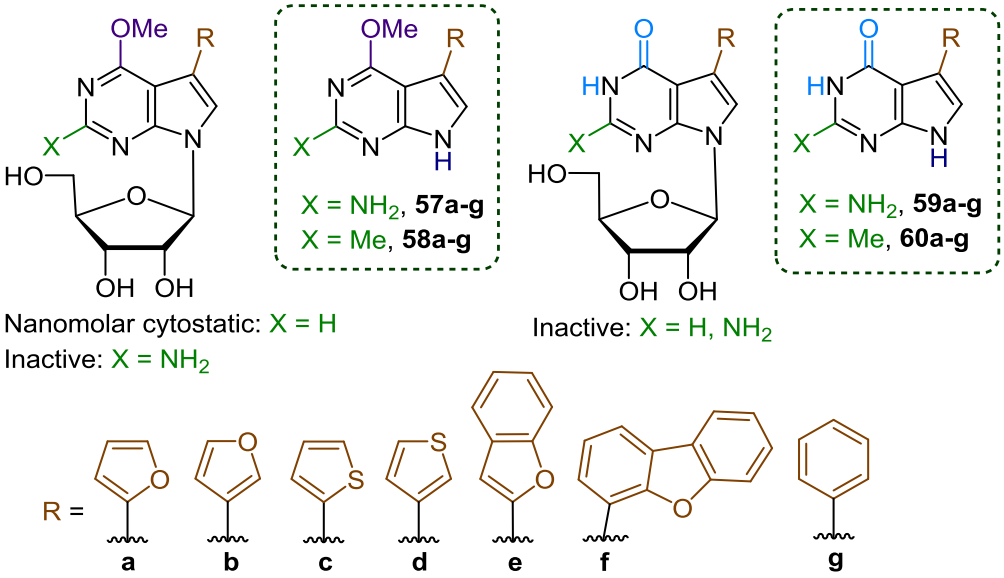
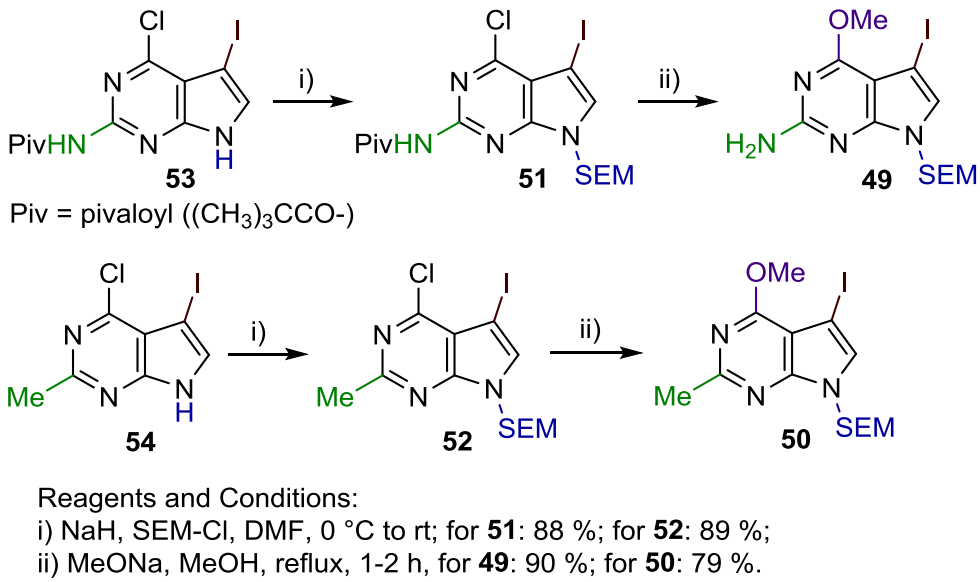


Figure 9 Reported 7-(het)aryl-7-deazapurine nucleosides and 6-methoxy-7-(het)aryl-7-deazapurines **57-58**, 7-(het)aryl-7-deazaguanines **59** and 7-(het)aryl-7-deazahypoxanthines **60** under study.

I intended to synthesize 7-hetaryl-7-deazapurine bases bearing OMe group at position 6 and NH_2 or Me at position 2 through aqueous Suzuki-Miyaura cross-coupling reactions of the corresponding 7-iodo-7-deazapurines with hetarylboronic acids. However, I found out that the aqueous Suzuki-Miyaura cross-couplings of 9-unsubstituted 7-iodo-7-deazapurine bases proceeded less efficiently, and were accompanied by significant deiodinations of the starting heterocycles which lowered the yields and complicated isolation of the products. Therefore, I changed the strategy and decided to introduce a suitable protecting group at the position 9. Previous experience from our laboratory suggested that the 2-(trimethylsilyl)ethoxy]methyl (SEM) group[151] could be suitable for the Suzuki reactions and could be easily removable at the end.

Therefore, the first goal was to synthesize the 9-SEM protected 7-iodo-7-deazapurine intermediates **49** and **50**. They were prepared from the corresponsing 6-chloro-7-iodo-7-deazapurine bases **53** and **54** by alkylation with [2-(trimethylsilyl)ethoxy]methyl chloride (SEM-Cl) under basic conditions,[151] followed by nucleophilic substitution at position 6 with NaOMe (Scheme 13). In the case of 2-amino derivative **53**, orthogonal protection of the amino functionality by the pivaloyl group was introduced to avoid alkylation. These reactions proceeded well to give the key intermediates **49-50** in good overal yields at multigram scale.



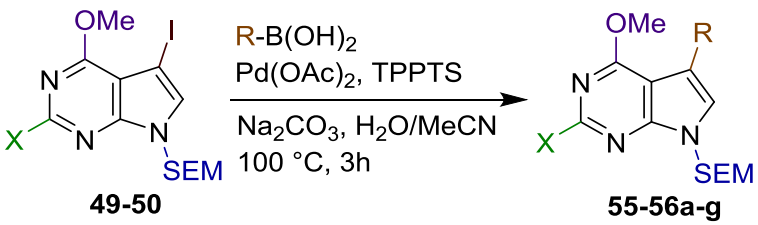
Reagents and Conditions:
i) NaH, SEM-Cl, DMF, 0 °C to rt; for **51**: 88 %; for **52**: 89 %;
ii) MeONa, MeOH, reflux, 1-2 h, for **49**: 90 %; for **50**: 79 %.

Scheme 13 Preparation of starting 7-iodo-7-deazapurine bases **49** and **50**

The 9-SEM-protected 2-amino- and 2-methyl-6-methoxy-7-iodo-7-deazapurines **49** and **50** were then used in aqueous Suzuki-Miyaura reactions with a series of (het)arylboronic acids (Table 16). The choice of the (het)aryl substituents was based on the previous experience with cytostatic nucleosides and involved small furyl or thienyl groups and bulkier benzofuryl, dibenzofuryl and phenyl groups.

The aqueous Suzuki-Miyaura cross-couplings of the SEM-protected 7-iodo-7-deazapurines **49-50** with the (het)aryl boronic acids were performed under standard reaction conditions in the presence of Na_2CO_3 (3 equiv) as a base, $Pd(OAc)_2$ (0.05 equiv) and water soluble sodium triphenylphosphine trisulfonate ligand (TPPTS) (0.125 equiv) in a mixture of H_2O/MeCN (2:1) at 100 °C for 3 hours. The reactions proceeded generally very well and gave the desired SEM-protected 7-(het)aryl-7-deazapurines **55a-g** and **56a-g** in good yields (Table 16). The reactions worked nicely even with 2-thienyl- and 2-furylboronic acids which are usually unstable and prone to protodeboronation during the cross-couplings.

Table 16 Synthesis of SEM-protected 7-(het)aryl-7-deazapurines

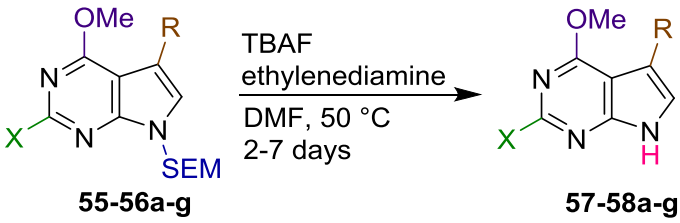


49-50 **55-56a-g**

R	Product (yield)	
	X = NH_2	X = Me
furan-2-yl	**55a** (71 %)	**56a** (68 %)
furan-3-yl	**55b** (73 %)	**56b** (76 %)
thiophen-2-yl	**55c** (73 %)	**56c** (80 %)
thiophen-3-yl	**55d** (76 %)	**56d** (88 %)
phenyl	**55e** (70 %)	**56e** (76 %)
benzofuran-2-yl	**55f** (65 %)	**56f** (71 %)
dibenzofuran-4-yl	**55g** (68 %)	**56g** (64 %)

Later on, SEM-protected 7-(het)aryl-deazapurine intermediates **55a-g** and **56a-g** were deprotected yielding the target free deazapurine bases **57a-g** and **58a-g** (Table 17). The cleavage of 2-(trimethylsilyl)ethoxy]methyl (SEM) group was performed in two steps. In the first step, the SEM-deazapurine derivatives were treated with trifluoroacetic acid resulting in *N*-hydroxymethyl intermediates which were subsequently cleaved in the second step by treatment with aqueous ammonia (urotropine formation). Alternatively, the SEM group was removed using tetrabutylammonium fluoride (TBAF) in the presence of ethylenediamine (to trap the liberated formaldehyde). This procedure was used, in most cases, due to the insufficient stability of target deazapurines under strongly acidic conditions. Deprotection reactions provided the 2-amino-6-methoxy-7-(het)aryl-7-deazapurines **57a-g** and 2-methyl-7-(het)aryl-7-deazapurines **58a-g** in good yields (Table 17).

Table 17 Synthesis of free 7-(het)aryl-7-deazapurines



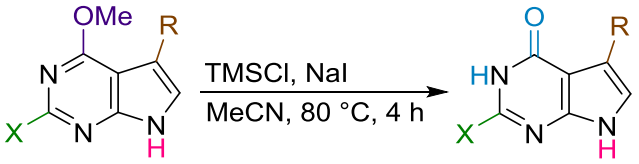
55-56a-g **57-58a-g**

R	Product (yield)	
	X = NH_2	X = Me
furan-2-yl	**57a** (69 %)	**58a** (91 %)[a]
furan-3-yl	**57b** (78 %)	**58b** (61 %)
thiophen-2-yl	**57c** (72 %)	**58c** (87 %)[a]
thiophen-3-yl	**57d** (61 %)	**58d** (58 %)
phenyl	**57e** (56 %)	**58e** (77 %)[a]
benzofuran-2-yl	**57f** (51 %)	**58f** (83 %)[a]
dibenzofuran-4-yl	**57g** (54 %)	**58g** (62 %)

[a] Reaction conditions used: 1) TFA, DCM, 4 h, r.t.; 2) NH_3 aq (25% [w/w]), r.t., 12 h

In order to get the 6-oxo derivatives, I could not use the direct cross-coupling reactions (they did not proceed efficiently). Therefore I prepared the 6-oxo derivatives by demethylation of 6-methoxy-7-deazapurines **57-58**. The 6-methoxy deazapurines **57a-g** and **58a-g** were transformed into 7-substituted 7-deazaguanines **59a-g** and 7-deazahypoxanthines **60-g** (Table 18) which are 7-substituted 7-deaza analogues of natural purine bases guanine and hypoxanthine. The *O*-demethylation reaction[152] was performed by treatment with iodotrimethylsilane (generated *in situ* from TMSCl and NaI in MeCN) furnishing the desired products **59-60a-g** in good yields (Table 18).

Table 18 Synthesis of 7-(het)aryl 7-deazaguanines and 7-deazahypoxanthines



57-58a-g **59-60a-g**

R	Product (yield)	
	X = NH_2	X = Me
furan-2-yl	**59a** (64 %)	**60a** (91 %)
furan-3-yl	**59b** (58 %)	**60b** (61 %)
thiophen-2-yl	**59c** (65 %)	**60c** (87 %)
thiophen-3-yl	**59d** (68 %)	**60d** (58 %)
phenyl	**59e** (77 %)	**60e** (77 %)
benzofuran-2-yl	**59f** (73 %)	**60f** (83 %)
dibenzofuran-4-yl	**59g** (62 %)	**60g** (52 %)

I also performed UV-vis and fluorescence spectroscopy characterization of 7-substituted 7-deazaguanines **59a-g** which are the closest analogues of natural nucleobases (Table 19). They generally exerted absorption maxima at 289-332 nm and some of them showed rather weak fluorescence. The only brighter fluorophores were 7-benzofuryl and 7-dibenzofuryl 7-deazaguanines **59e** and **59f** which might have potential for fluorescent labeling of nucleic acids.

Table 19 UV Absorbtion Spectra and Fluorescence Properties of 7-deazaguanines

Compd	λ_{abs} [nm] (ε / 10^4 $M^{-1}\times cm^{-1}$)[a]	λ_{em} [nm]	Φ_f
59a	304 (1.1)	-	-
59b	292 (1.6)	-	-
59c	310 (1.1)	380	0.03
59d	300 (1.6)	-	-
59e	318 (3.0), 332 (2.6)	360	0.13
59f	289 (2.4)	430	0.36
59g	293 (0.9)	-	-

[a] Position in nm of the absorption maxima (absorption coefficient) measured in EtOH.
[b] Position in nm of the emission maximum in EtOH.
[c] Fluorescence quantum yield in EtOH measured using quinine sulfate in 0.5 M H_2SO_4 (Φ_f = 0.55) as reference.

All final free 7-(het)aryl 7-deazapurine bases **57-60a-g** were evaluated against six cell lines derived from human solid tumors including lung (A549 cells) and colon (HCT116 and HCT116p53−/−) carcinomas, as well as leukemia cell lines (CCRF-CEM, CEM-DNR, K562, and K562-TAX) and, for comparison, non-malignant BJ and MRC-5 fibroblasts. None of the compounds showed any considerable cytotoxic or cytostatic activity at concentrations up to 15 μM. This is an important result in comparison with the corresponding ribonucleosides having the same substituents at the heterocyclic aglycon. This indicates that the salvage pathway (which would allow for formation of the cytotoxic nucleosides from these nucleobases) does not play a role in the metabolism of nucleosides.

4 Conclusion

Novel methodologies for direct C-H functionalization of deazapurine nucleobases have been developed. The newly modified deazapurines bearing amino, imido or phosphonate groups at position 8 and silyl group at *ortho* position of the phenyl ring were synthesized using C-H activation reactions. A series of 2-substituted 6- and 7-(het)aryl-7-deazapurine bases were prepared by aqeous-phase Suzuki-Miyaura cross-couplings.

The Pd/Cu-catalyzed direct C-H amination of 6-substituted-7-deazapurines with *N*-chloro-*N*-alkyl arylsulfonamides proceeded regioselectively at position 8 under mild reaction conditions. Since *N*-chloro-*N*-alkyl arylsulfonamides react both as aminating and chlorinating agents, additional protocols for direct C-H chloroamination and C-H chlorination of 6-substituted-7-deazapurines were developed. The most suitable *ortho*-nitrobenzenesulfonyl group was chosen for the protection of amine, and after protecting group removal, 8-methylamino-7-deazapurine derivative was obtained. Unfortunately, while testing the reactivity of 8-methylaminodeazapurine, it turned out to be unstable, what in principal could be caused by its tendency to protonation and oxidation.

C-H imidation reaction of 6-substituted 9-benzyl or 9-SEM protected 7-deazapurines was performed with *N*-succinimido- or *N*-phtalimidoperesters under ferrocene catalysis. Reactions proceeded selectively at position 8 to give 8-succinimido or 8-phtalimido-7-deazapurines. Any attempts of the acidic hydrolysis or hydrazinolysis of the imide group led to decomposition of the desired 8-amino-7-deazapurine analogously to 8-(methylamino)-7-deazapurine derivative.

Previously reported Ir-catalyzed C-H borylation[98] proceeded directly at position 8 in deazapurines. The same Ir catalyst and dtbpy ligand with the addition of norbornene as a hydrogen acceptor were used for C-H silylations of phenyldeazapurines with alkylsilanes. Interestingly, all reactions proceeded preferentially as *ortho* C-H silylation of the phenyl group, due to the directing effect of the N-1 atom of deazapurine heterocycle, to give a series of 7- and 9-phenyldeazapurine silylated derivatives.

The phosphonate group was introduced into the deazapurine scaffold by Mn(III) acetate-promoted C-H phosphonation with dialkylphosphites. The reactions proceeded regioselectively at position 8 of 7- and 9-deazapurines resulting in novel deazapurine-8-phosphonate derivatives. The method showed no limitations and wide scope of substrates bearing different substituents and protecting groups. In order to test the synthetic utility of 6-chloro-7-deazapurine phosphonate, I applied aqueous Suzuki-Miyaura cross-coupling

reactions with various (het)aryl boronic acids. All of these reactions proceeded smoothly to give a series of 6-substituted-7-deazapurine 8-phosphonate bases. Deazapurine phosphonates were also used for the preparation of a small series of deazapurine 8-phosphonic acids by developed phosphodiester cleavage protocol.

Modifications of position 6 and 7 in 7-deazapurines with different (het)aryl substituents were performed by aqueous Suzuki-Miyaura cross-coupling reactions of corresponding 6-chloro and 7-iodo 7-deazapurine substrates. A large set of 6-(het)aryl-7-deazapurine bases bearing F at the position 7 and H, F, Cl, Me or NH_2 at the position 2 was prepared by aqueous Suzuki-Miyaura cross-coupling reactions from 6-chloro-7-fluoro or 2-amino, 2-chloro, 2-fluoro and 2-methyl 6-chloro-7-deazapurines in high yields. The same aqueous Suzuki-Miyaura cross-coupling conditions did not work efficiently for the preparation of 7-(het)aryl-7-deazapurines due to significant deiodination of starting 7-iodo-7-deazapurines. Alternatively, the protecting group strategy deemed to be most suitable and easily removable by using 2-[(trimethylsilyl)ethoxy]methyl (SEM) group. Indeed, after cleavage of the SEM group, a series of free 6-methoxy-7-(het)aryl deazapurines bearing NH_2 and Me group at position 2 were obtained. The 6-methoxy-7-(het)aryl-deazapurine derivatives were further transformed into 7-(het)aryl 7-deazahypoxanthines and 7-deazaguanines (new substituted analogues of natural hypoxanthine and guanine bases) by *O*-demethylation reactions.

Summarizing, a library (more than 100) of new modified deazapurine nucleobases bearing multiple substituents and functional groups was synthesized by C-H activations and aqueous Suzuki-Miyaura cross-coupling reactions. Unfortunately, biological activity screening of target deazapurine bases did not show any significant cytostatic or antiviral activity in contrast to many of their nucleoside analogues. Nevertheless, a number of newly modified deazapurines exerted good fluorescent properties (quantum yields up to 0.83) with potential as labels for nucleic acids.

Finally, developed C-H functionalization methods and further transformations of installed functional groups nicely complement the current toolbox of reactions (cross couplings, substitutions, halogenations, glycosylation) for modification of privileged deazapurine heterocycles. This clearly has further practical potential in the generation of new libraries of modified deazapurine nucleobases.

5 Experimental section

5.1 General remarks

All reactions with organometalic reagents and transition metal catalysts were carried out in flame-dried glassware under argon atmosphere. 4-Chloro-*7H*-pyrrolo[2,3-*d*]pyrimidine **32**, 2-amino-4-chloro-*7H*-pyrrolo[2,3-*d*]pyrimidine **33,** 2,4-dichloro-*7H*-pyrrolo[2,3-*d*]pyrimidine **34**, alkylsilanes, boronic acids, dialkylphosphites were purchased from commercial suppliers and used without any further purification. Dry solvents were used as received from supplier. All compounds were fully characterized by NMR and spectra were recorded on a 600 MHz (^{1}H at 600.1 MHz, ^{13}C at 150.9 MHz), a 500 MHz (499.8 or 500.0 MHz for ^{1}H and 125.7 MHz for ^{13}C) or a 400 MHz (^{1}H at 400 MHz, ^{13}C at 100.6 MHz) spectrometers. ^{1}H and ^{13}C resonances were assigned using H,C-HSQC and H,C-HMBC spectra. The samples were measured in $CDCl_3$, DMSO-d_6 or D_2O-d_2 and chemical shifts (in ppm, δ-scale) are referenced to solvent signal in $CDCl_3$ [δ (^{1}H) = 7.26 ppm, δ (^{1}H) = 77.0 ppm] in DMSO [δ (^{1}H) = 2.50 ppm, δ (^{1}H) = 39.43 ppm] or in D_2O [δ (^{1}H) = 4.79 ppm]. Coupling constants (J) are given in Hz. High performance flash column chromatography purifications (HPFC) were performed with Biotage SP1 or Teledynne ISCO CombiFlash Rf+ apparatus on KP-Sil columns. Reverse phase - high performance flash chromatography (RP-HPFC) purifications were performed with Biotage SP1 apparatus on KP-C18-HS columns. High resolution mass spectra were measured on a LTQ Orbitrap XL (Thermo Fisher Scientific) spectrometr using electrospray (ESI) or electron impact (EI) ionization technique. IR spectra were recorded on Nicolet Avatar 370 FT-IR spectra using the KBr method or were recorded on Bruker Alpha FT-IR spectrometer using ATR technique (wavenumbers are given in cm^{-1}). Melting points were determined on a Kofler block and are uncorrected. Elemental analyses were measured on PE 2400 Series II CHNS/O (Perkin Elmer, USA, 1999). X-ray diffraction experiment of single crystals was carried out on an Xcalibur X-ray diffractometer by monochromatized CuK_{α} radiation (λ=1.54180 Å) at 180 K and on a Bruker D8 VENTURE system employing Mo(*Kα*) radiation (λ=0.71073 Å) at 293 K.

5.2 Preparation of starting compounds

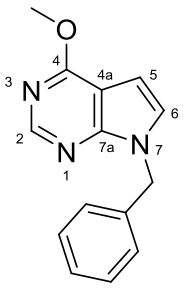
Starting compounds (**1a, 1d, 1e, 21-23**),[98,100] (**15**, **31**),[99] (**18**, **39-40**),[154] (**29**, **36**),[37b,81] **30**,[87a] **35**,[153] **37**,[92] **53**,[155] **54**[156] were prepared according to the literature.

Aminating reagents **2-4** were prepared according the published protocol[157] from corresponding *N*-methyl-arylsulfonamides.[158]

N-succinimidyl perester (NSP) **11** was prepared according to the literature[111c] and *N*-phtalimidyl perester **13** was prepared analoguesly.

7-Benzyl-4-methoxy-*7H*-pyrrolo[2,3-*d*]pyrimidine

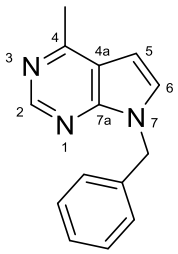
(6-methoxy-9-benzyl-7-deazapurine) (1b)



6-Chloro-9-benzyl-7-deazapurine **1d** (729 mg, 3 mmol) dissolved in MeOH (9 ml) and NaOMe 25 % (~4.4 M) solution in MeOH was added dropwise. The mixture was stirred for 3h at r.t. then quenched with H_2O (9 mL), extracted with EtOAc (20 ml), dried over anhydrous sodium sulphate, filtered and evaporated under reduced pressure. Product was isolated as a white solid (705 mg, 98 %). M.p. 78-79 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 4.13 (s, 3H, CH_3O); 5.43 (s, 2H, CH_2-Ph); 6.55 (d, 1H, $J_{5,6}$ = 3.5 Hz, H-5); 7.00 (d, 1H, $J_{6,5}$ = 3.5 Hz, H-6); 7.19 (m, 2H, H-*o*-Bn); 7.25 – 7.34 (m, 3H, H-*m*,*p*-Bn); 8.51 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 48.19 (CH_2-Ph); 53.62 (CH_3O); 98.78 (CH-5); 105.37 (C-4a); 125.71 (CH-6); 127.45 (CH-*o*-Bn); 127.83 (CH-*p*-Bn); 128.79 (CH-*m*-Bn); 137.08 (C-*i*-Bn); 151.05 (CH-2); 151.94 (C-7a); 163.10 (C-4). IR(KBr): 3120, 3093, 1582, 1459, 1256, 1026, 698. HRMS (ESI) calculated for $C_{14}H_{14}ON_3$: 240.1131; found 240.1131.

7-Benzyl-4-methyl-*7H*-pyrrolo[2,3-*d*]pyrimidine

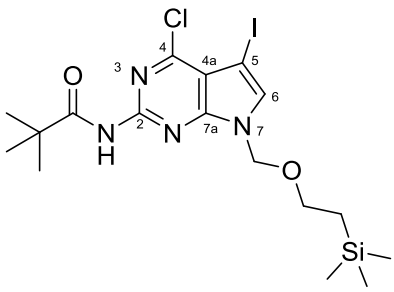
(6-methyl-9-benzyl-7-deazapurine) (1c)



6-Chloro-9-benzyl-7-deazapurine **1d** (972 mg, 4 mmol) $Pd(PPh_3)_4$ (0.2 mmol) were placed in an argon-purged vial and then THF (80 mL) was added. To the stirred reaction mixture, Me_3Al (2M solution in toluene, 4 mL, 8 mmol) was added dropwise at r.t. The mixture was then stirred at 75 °C for 8 h. After cooling to room temperature, the reaction mixture was poured onto a mixture of H_2O (400 mL), NH_4Cl (4g), Na_2EDTA (1g) and extracted with chloroform (3×400 mL). The collected organic layers were dried with anhydrous $MgSO_4$, filtered and evaporated under

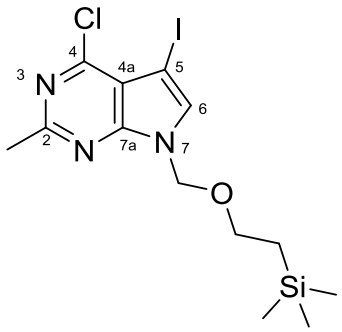
reduced pressure. The crude product was purified by column chromatography on silica gel, eluting with hexanes/EtOAc 5:1 to 1:2. Product was isolated as orange oil (760 mg, 85 %). ^{1}H NMR (500 MHz, $CDCl_3$): 2.75 (s, 3H, CH_3); 5.46 (s, 2H, CH_2-Ph); 6.57 (d, 1H, $J_{5,6}$ = 3.6 Hz, H-5); 7.13 (d, 1H, $J_{6,5}$ = 3.6 Hz, H-5); 7.21 (m, 2H, H-*o*-Bn); 7.27 – 7.35 (m, 3H, H-*m*,*p*-Bn); 8.80 (s, 1H, H-2). ^{13}C NMR (150.9 MHz, $CDCl_3$): 21.43 (CH_3); 47.92 (CH_2-Ph); 99.70 (CH-5); 117.80 (C-4a); 127.55 (CH-*o*-Bn); 127.63 (CH-6); 127.94 (CH-*p*-Bn); 128.85 (CH-*m*-Bn); 136.88 (C-*i*-Bn); 150.35 (C-7a); 151.40 (CH-2); 159.31 (C-4). IR(KBr): 3120, 3090, 1577, 1452, 1260, 1060, 630. HRMS (ESI) calculated for $C_{14}H_{14}N_3$: 224.1191; found 224.1191.

4-Chloro-5-iodo-2-pivalamido-7-{[2-(trimethylsilyl)ethoxy]methyl}-7*H*-pyrrolo[2,3-*d*]pyrimidine (51)



Deazapurine **53** (5 g, 13.2 mmol) was added in portions to a stirred suspension of sodium hydride (0.58 g, 60% dispersion, 44 mmol) in dry dimethylformamide (50 mL) at 0 °C. After the effervescence ceased, SEM-Cl (2.5 mL, 14.1 mmol) was added at 0 °C and the mixture was stirred overnight at ambient temperature, diluted with ethyl acetate (250 mL) and washed with water (200 mL). Organic phase was washed with 10% brine (4 x 100 mL), dried over $MgSO_4$ and evaporated. The residue was recrystallized from acetonitrile to afford the title compound (5.92 g, 88 %) as a pinkish solid. M. p. 145-146 °C. ^{1}H NMR (500 MHz, DMSO-d_6): -0.1 (s, 9H, $Si(CH_3)_3$); 0.87 (m, 2H, CH_2-3´); 1.22 (s, 9H, CH_3-*t*Bu); 3.52 (m, 2H, CH_2-2´); 5.52 (s, 2H, CH_2-1´); 7.93 (s, 1H, CH-6); 10.24 (bs, 1H, NH).^{13}C NMR (125.7 MHz, DMSO-d_6): -1.31 ($Si(CH_3)_3$); 17.16 (CH_2-3´); 26.98 (CH_3-*t*Bu); 39.84 (C-2´´); 53.20 (C-5); 66.24 (CH_2-2´); 72.46 (CH_2-1´); 112.60 (C-4a); 135.50 (CH-6); 151.30 (C-2/4); 152.15 (C-2/4); 152.44 (C-7a); 175.88 (C-1´´). HRMS (ESI) calculated for $C_{17}H_{26}N_4O_2ClISiNa$ [M+Na]: 531.0450; found: 531.0450.

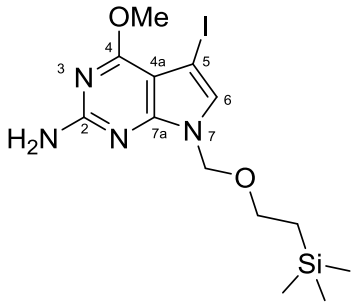
4-Chloro-5-iodo-2-methyl-7-{[2-(trimethylsilyl)ethoxy]methyl}-7*H*-pyrrolo[2,3-*d*]pyrimidine (52)



Deazapurine **54** (11.74 g, 40 mmol) was added in portions to a stirred suspension of sodium hydride (1.76 g, 60% dispersion, 44 mmol) in dry dimethylformamide (100 mL) at 0 °C. After the effervescence ceased, SEM-Cl (7.82 ml, 44 mmol) was added at 0 °C and the mixture was stirred overnight at ambient

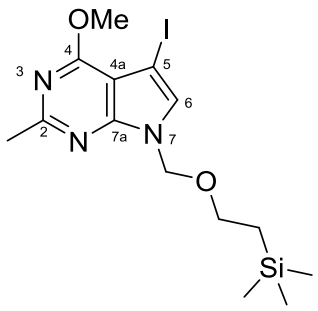
temperature, diluted with ethyl acetate (250 mL) and washed with water (200 mL). Organic phase was washed with 10% brine (4 x 100 mL) and dried over $MgSO_4$. Purification by column chromatography (SiO_2, hexane/dichloromethane 1:1) provided title compound (15.08 g, 89 %) as a redish oil. ^{1}H NMR (500 MHz, $CDCl_3$): -0.05 (s, 9H, CH_3Si); 0.92 (m, 2H, OCH_2CH_2Si); 2.73 (s, 3H, CH_3-2); 3.52 (m, 2H, OCH_2CH_2Si); 5.57 (s, 2H, NCH_2O); 7.43 (s, 1H, H-6). ^{13}C NMR (125.7 MHz, $CDCl_3$): -1.49 (CH_3Si); 17.63 (OCH_2**C**H_2Si); 25.51 (CH_3-2); 52.30 (C-5); 66.89 (O**C**H_2CH_2Si); 72.90 (NCH_2O); 114.28 (C-4a); 133.54 (CH-6); 152.10 (C-7a); 152.34 (C-4); 161.49 (C-2). HRMS (ESI) calculated for $C_{13}H_{20}N_3OClISi$ [M+H]: 424.0103; found: 424.0104.

2-Amino-5-iodo-4-methoxy-7-{[2-(trimethylsilyl)ethoxy]methyl}-7*H*-pyrrolo[2,3-*d*]pyrimidine (49)



A mixture of **51** (4.585 g, 9 mmol) and sodium methoxide (6.2 mL, 25% w/w solution, 27 mmol) in methanol (20 mL) was stirred at 100 °C for 1 h. After cooling the volatiles were evaporated and the residue was partitioned between ethyl acetate (50 mL) and water (50 mL). Organic phase was dried over $MgSO_4$ and evaporated. The residue was recrystallized from hexane to furnish title compound (3.42 g, 90 %) as a white solid. M. p. 92-93 °C. ^{1}H NMR (500 MHz, DMSO-d_6): -0.08 (s, 9H, $Si(CH_3)_3$); 0.80 (t, 2H, $J_{3',2'}$= 8.1 Hz, CH_2-3´); 3.46 (t, 2H, $J_{2',3'}$= 8.1 Hz, CH_2-2´); 3.93 (s, 3H, CH_3O-4); 5.30 (s, 2H, CH_2-1´); 6.37 (bs, 2H, NH_2); 7.18 (s, 1H, CH-6). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.18 ($Si(CH_3)_3$); 17.32 (CH_2-3´); 51.28 (C-5); 53.24 (CH_3O-4); 65.45 (CH_2-2´); 72.15 (CH_2-1´); 98.76 (C-4a); 127.78 (CH-6); 154.74 (C-7a); 159.85 (C-2); 163.10 (C-4). HRMS (ESI) calculated for $C_{13}H_{22}N_4O_2ISi$ [M+H]: 421.0551; found: 421.0551.

5-Iodo-4-methoxy-2-methyl-7-{[2-(trimethylsilyl)ethoxy]methyl}-7*H*-pyrrolo[2,3-*d*]pyrimidine (50)



A mixture of **52** (15 g, 35.4 mmol) and sodium methoxide (16 mL, 25% w/w solution, 70 mmol) in methanol (30 mL) was stirred at 100 °C for 2 h. After cooling the volatiles were evaporated and the residue was partitioned between ethyl acetate (100 mL) and 10% brine (100 mL). Organic phase was dried over

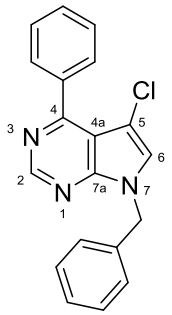
$MgSO_4$ and evaporated. The residue was purified by column chromatography (SiO_2, dichloromethane/hexane 1:1) to give title compound (11.74 g, 79 %) as an orange oil. ^{1}H NMR (500 MHz, DMSO-d_6): -0.11 (s, 9H, CH_3Si); 0.81 (m, 2H, OCH_2CH_2Si); 2.54 (s, 3H, CH_3-2); 3.48 (m, 2H, OCH_2CH_2Si); 4.01 (s, 3H, CH_3O-4); 5.47 (s, 2H, NCH_2O); 7.60 (s, 1H, H-6). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.32 (CH_3Si); 17.21 (OCH_2CH_2Si); 25.73 (CH_3-2); 50.88 (C-5); 53.60 (CH_3O-4); 65.76 (OCH_2CH_2Si); 72.44 (NCH_2O); 104.16 (C-4a); 131.60 (CH-6); 152.75 (C-7a); 160.53 (C-2); 162.17 (C-4). IR(KBr): 3119, 2950, 2895, 1673, 1595, 1340, 1250, 1085, 918, 861, 696. HRMS (ESI) calculated for $C_{14}H_{23}N_3O_2ISi$ [M+H]: 420.0599; found: 420.0600.

Chlorination of 6-phenyl-9-benzyl-7-deazapurine 1a

Method A: A mixture of 6-phenyl-7-deazapurine **1a** (285 mg, 1 mmol) and NCS (141 mg, 1.05 mmol) in DMF (1.5 mL) was stirred at r.t. for 90 h and then the mixture was evaporated under vacuum. The residue was purified by column chromatography on silica gel eluting with hexanes/EtOAc 5:1 to 2:1 to give the product **9a** (272 mg, 85 %) as a colourless solid.

Method B: A mixture of 6-phenyl-7-deazapurine **1a** (285 mg, 1 mmol) and arylsulfonamide **4** (376, 1.5 mmol) in 1,4-dioxane (4 mL) was stirred at r.t. for 45 h and then evaporated under vacuum. The residue was purified by column chromatography on silica gel eluting with hexanes/EtOAc 5:1 to 2:1 to give product **9a** (250 mg, 78 %) as a colourless solid.

7-Benzyl-5-chloro-4-phenyl-7H-pyrrolo[2,3-d]pyrimidine
(6-phenyl-7-chloro-9-benzyl-7-deazapurine) (9a)



M. p. 117-118 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 5.49 (s, 2H, CH_2-Ph); 7.19 (s, 1H, H-6); 7.29 (m, 2H, H-*o*-Bn); 7.30 – 7.39 (m, 3H, H-*m*,*p*-Bn); 7.49 – 7.54 (m, 3H, H-*m*,*p*-Ph); 7.83 (m, 2H, H-*o*-Ph); 9.00 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 48.05 (CH_2-Ph); 104.27 (C-5); 113.14 (C-4a); 125.88 (C-6); 127.86 and 127.87 (CH-*o*-Bn, CH-*m*-Ph); 128.30 (CH-*p*-Bn); 129.00 (CH-*m*-Bn); 129.72 (CH-*p*-Ph); 130.30 (CH-*o*-Ph); 136.09 (C-*i*-Bn); 136.71 (C-*i*-Ph); 150.39 (C-7a); 151.92 (CH-2); 159.70 (C-4). IR(KBr): 3099, 3058, 1550, 1465, 1145, 976, 704. HRMS (ESI) calculated for $C_{20}H_{19}N_4$ [M+H]: 315.1604; found 315.1603.

5.3 C-H amination and C-H chloroamination of 7-deazapurines

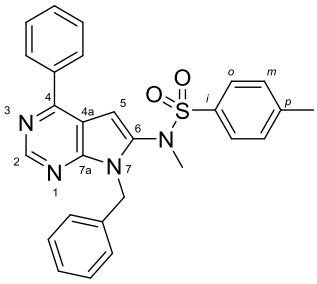
General procedure for C-H amination of 7-deazapurines:

7-Deazapurine **1a-1e** (0.5 mmol), $Pd(OAc)_2$ (0.025 mmol), $Cu(acac)_2$ (0.05 mmol), bpy (0.05 mmol), Na_2CO_3 (3.5 mmol) and chlorsulfonamide (1.0-1.75 mmol) were placed in a vial which was purged with an argon. Then 1,4-dioxane (2 mL) was added and the reaction mixture was stirred for 24 h at r.t., quenched with H_2O (2 mL), extracted with ethyl acetate (3x20 mL) and washed with brine (2 mL). The organic phases were combined and dried over anhydrous sodium sulphate, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel, eluting with hexanes/EtOAc (5:1 to 1:2) to afford the corresponding products.

General procedure for C-H chloroamination of 7-deazapurines:

7-Deazapurine **1a-1e** (0.5 mmol), $Pd(OAc)_2$ (0.0125 mmol), CuCl (0.05 mmol), LiCl (1.0 mmol), Ag_2CO_3 (1.0 mmol) and chlorosulfonamide (1.5-1.75 mmol) were placed in a vial which was purged with an argon. Then 1,4-dioxane (2 mL) was added and the reaction mixture was stirred for 24 h at r.t., quenched with H_2O (2 mL), extracted with ethyl acetate (3 x 20 mL) and washed with brine (2 mL). The organic phases were combined and dried over sodium anhydrous sulphate, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel, eluting with hexanes/EtOAc (5:1 to 1:2) to afford the corresponding products.

_N_-(7-Benzyl-4-phenyl-_7H_-pyrrolo[2,3-_d_]pyrimidin-6-yl)-_N_-methyl-4-methylbenzenesulfonamide
(6-phenyl-8-[_N_-(4-methylbenzenesulfonyl)-_N_-(methyl)amino]-9-benzyl-7-deazapurine)
(5a)

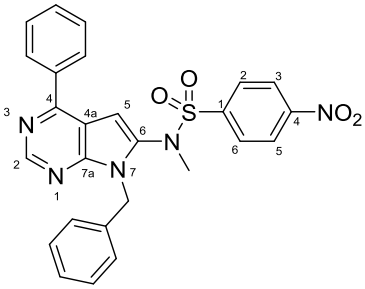


6-Phenyl-9-benzyl-7-deazapurine **1a** (285 mg, 1 mmol) and *N*-chloro-*N*-methyl-4-methylbenzenesulfonamide **2** (1098 mg, 5.0 mmol) were used as starting compounds to give product **5a** (334 mg, 68 %) as white needles after chromatography with hexanes/EtOAc 5:1 to 1:1 and crystallization from EtOAc/hexane. M. p. 226-227 °C. ^{1}H NMR (500.0 MHz, $CDCl_3$): 2.51 (s 3H, CH_3-Ts); 2.78 (s, 3H, CH_3N); 5.73 (bs, 2H, CH_2Ph); 6.04 (s, 1H, H-5); 7.23-7.33 (m, 5H, H-

o,m,p-Bn); 7.38 (m, 2H, H-*m*-Ts); 7.46-7.51 (m, 3H, H-*m,p*-Ph); 7.66 (m, 2H, H-*o*-Ts); 7.92 (m, 2H, H-*o*-Ph); 9.06 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.67 (CH_3-Ts); 39.77 (CH_3N); 45.25 (CH_2Ph); 96.99 (CH-5); 114.12 (C-4a); 127.65 (CH-*p*-Bn); 127.90 (CH-*o*-Bn); 128.57 (CH-*o*-Ts); 128.68 (CH-*m*-Bn); 128.76 (CH-*o,m*-Ph); 129.57 (CH-*m*-Ts); 130.20 (CH-*p*-Ph); 132.67 (C-*i*-Ts); 136.84 (C-*i*-Bn); 137.16 (C-*i*-Ph); 138.65 (C-6); 144.73 (C-*p*-Ts); 150.20 (C-7a); 152.45 (CH-2); 157.37 (C-4). IR(KBr): 2976, 2930, 2817, 1470, 1382, 1355, 1341, 1322, 1186, 1164, 1314, 852, 823, 691. HRMS (ESI) calculated for $C_{27}H_{24}N_4O_2S$ [M+H]: 469.1692; found 469.1691.

_N_-(7-benzyl-4-phenyl-7_H_-pyrrolo[2,3-_d_]pyrimidin-6-yl)-_N_-methyl-4-nitrobenzenesulfonamide

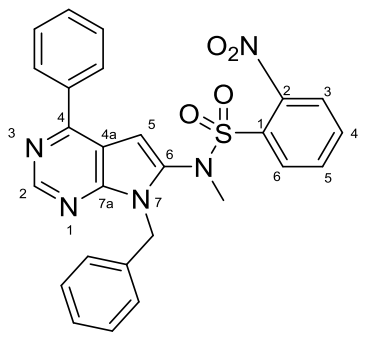
(9-benzyl-8-[_N_-(4-nitrophenylsulfonyl)-_N_-(methyl)amino]-6-phenyl-7-deazapurine) (6a)



1a (285 mg, 1 mmol) and *N*-chloro-*N*-methyl-4-nitrobenzenesulfonamide **3** (877 mg, 3.0 mmol) were used as starting compounds to give product **6a** (235 mg, 47 %) as yellowish needles after chromatography with hexanes/EtOAc 5:1 to 1:1 and crystallization from EtOAc/hexane. M. p. 231-232 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.97 (s, 3H, CH_3N); 5.74 (bs, 2H, CH_2-Ph); 6.04 (s, 1H, H-5); 7.28 (m, 2H, H-*o*-Bn); 7.28 – 7.35 (m, 3H, H-*p,m*-Bn); 7.46 – 7.52 (m, 3H, H-*m,p*-Ph); 7.90 (m, 2H, H-*o*-Ph); 7.97 (m, 2H, H-*o*-$C_6H_4NO_2$); 7.41 (m, 2H, H-*m*-$C_6H_4NO_2$); 9.08 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 39.91 (CH_3-N); 45.34 (CH_2-Ph); 97.21 (CH-5); 113.95 (C-4a); 124.21 (CH-*m*-$C_6H_4NO_2$); 127.86 (CH-*o,p*-Bn); 128.61(CH-*o*-Ph); 128.81 (CH-*m*-Bn); 128.92 (CH-*m*-Ph); 129.64 (CH-*o*-$C_6H_4NO_2$); 130.46 (CH-*p*-Ph); 136.85 (C-*i*-Bn); 137.24 (C-6); 137.48 (C-*i*-Ph); 141.52 (C-*i*-$C_6H_4NO_2$); 150.37 (C-7a); 150.67 (C-*p*-$C_6H_4NO_2$); 152.98 (CH-2); 158.02 (C-4).IR(KBr): 2825, 1537, 1374, 1366, 1362, 1340, 1317, 1305, 1177, 1158, 921. HRMS (ESI) calculated for $C_{26}H_{22}N_5O_4S$ [M+H]: 500.1387; found 500.1386.

_N_-(7-benzyl-4-phenyl-7_H_-pyrrolo[2,3-_d_]pyrimidin-6-yl)-_N_-methyl-2-nitrobenzenesulfonamide

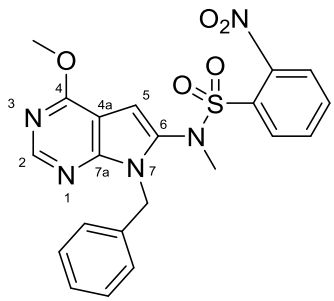
(9-benzyl-8-[_N_-(2-nitrophenylsulfonyl)-_N_-(methyl)amino]-6-phenyl-7-deazapurine) (7a)



1a (285 mg, 1 mmol) and *N*-chloro-*N*-methyl-2-nitrobenzenesulfonamide **4** (877 mg, 3.5 mmol) were used as starting compounds to give product **7a** (310 mg, 62 %) as colourless crystals after chromatography with hexanes/EtOAc 5:1 to 1:1 and crystallization from EtOAc/hexane. M. p. 102-103 °C. ^{1}H NMR (500.0 MHz, $CDCl_3$): 2.94 (s, 3H, CH_3N); 5.67 (bs, 2H, CH_2Ph); 6.45 (s, 1H, H-5); 7.22 (m, 2H, H-*o*-Bn); 7.27 (m, 1H, H-*p*-Bn); 7.30 (m, 2H, H-*m*-Bn); 7.50-7.53 (m, 3H, H-*m*,*p*-Ph); 7.61 (ddd, 1H, $J_{5,6}$ = 8.1, $J_{5,4}$ = 7.5, $J_{5,3}$ = 1.3, H-5-$C_6H_4NO_2$); 7.67 (ddd, 1H, $J_{3,4}$ = 8.0, $J_{3,5}$ = 1.3, $J_{3,6}$ = 0.5, H-3-$C_6H_4NO_2$); 7.76 (ddd, 1H, $J_{6,5}$ = 8.1, $J_{6,4}$ = 1.4, $J_{6,3}$ = 0.5, H-6-$C_6H_4NO_2$); 7.77 (ddd, 1H, $J_{4,3}$ = 8.0, $J_{4,5}$ = 7.5, $J_{4,6}$ = 1.4, H-4-$C_6H_4NO_2$); 7.97 (m, 2H, H-*o*-Ph); 9.10 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 40.53 (CH_3N); 45.29 (CH_2Ph); 96.40 (CH-5); 113.91 (C-4a); 124.12 (CH-3-$C_6H_4NO_2$); 127.65 (CH-*o*-Bn); 127.89 (CH-*p*-Bn); 128.85 (CH-*m*-Ph, CH-*o*-Bn); 128.94 (CH-*m*-Ph); 130.16 (C-1-$C_6H_4NO_2$); 130.64 (CH-*p*-Ph); 131.26 (CH-5-$C_6H_4NO_2$); 132.23 (CH-6-$C_6H_4NO_2$); 134.62 (CH-4-$C_6H_4NO_2$); 136.54 (C-*i*-Bn); 136.86 (C-*i*-Ph); 137.04 (C-6); 148.55 (C-2-$C_6H_4NO_2$); 150.56 (C-7a); 152.40 (CH-2); 157.48 (C-4). IR(KBr): 2821, 1545, 1376, 1368, 1360, 1343, 1318, 1309, 1180, 1163, 924. HRMS (ESI) calculated for $C_{26}H_{22}N_5O_4S$ [M+H]: 500.1387; found 500.1387.

_N_-(7-benzyl-4-methoxy-7_H_-pyrrolo[2,3-_d_]pyrimidin-6-yl)-_N_-methyl-2-nitrobenzenesulfonamide

(9-benzyl-6-methoxy-8-[_N_-(2-nitrophenylsulfonyl)-_N_-(methyl)amino]-7-deazapurine) (7b)

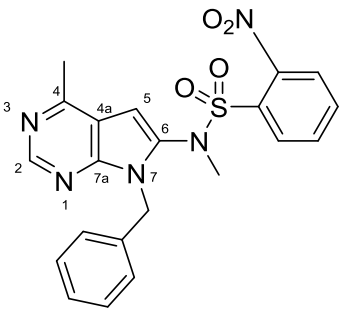


6-methoxy-9-Bn-7-deazapurine **1b** (240 mg, 1 mmol) and *N*-chloro-*N*-methyl-2-nitrobenzenesulfonamide **4** (501 mg, 2 mmol) were used as starting compounds to give product **7b** (274 mg, 60 %) as white needles after chromatography with hexanes/EtOAc 5:1 to 1:1 and crystallization from EtOAc/hexane. M. p. 219-220 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.88 (s, 3H, CH_3N); 4.09 (s, 3H, CH_3O); 5.59 (bs, 2H, CH_2-Ph); 6.13 (s, 1H, H-5); 7.17 (m, 2H, H-*o*-Bn); 7.21 - 7.30 (m, 3H, H-*m*,*p*-Bn); 7.61 (ddd, 1H, $J_{5,6}$ = 8.0 Hz, $J_{5,4}$ = 7.4 Hz, $J_{5,3}$ = 1.3 Hz, H-5-$C_6H_4NO_2$); 7.64 (bdd, 1H, $J_{3,4}$ = 8.0 Hz, $J_{3,5}$ = 1.3 Hz, H-3-$C_6H_4NO_2$); 7.71 (bdd, 1H, $J_{6,5}$ = 8.0 Hz, $J_{6,4}$ = 1.4 Hz, H-6-$C_6H_4NO_2$); 7.75 (ddd, 1H, (ddd, 1H, $J_{4,3}$ = 8.0 Hz, $J_{4,5}$ = 7.4 Hz, $J_{4,6}$ = 1.4 Hz, H-4-

$C_6H_4NO_2$); 8.57 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 40.61 (CH_3-N); 45.32 (CH_2-Ph); 53.77 (CH_3-O); 97.07 (CH-5); 103.94 (C-4a); 123.96 (CH-3-$C_6H_4NO_2$); 127.55 (CH-*o*-Bn); 127.68 (CH-*p*-Bn); 128.74 (CH-*m*-Bn); 130.29 (C-1-$C_6H_4NO_2$); 131.26 (CH-5-$C_6H_4NO_2$); 132.22 (CH-6-$C_6H_4NO_2$); 133.50 (C-6); 134.39 (CH-4-$C_6H_4NO_2$); 136.99 (C-*i*-Bn); 148.57 (C-2-$C_6H_4NO_2$); 150.54 (C-7a); 152.42 (CH-2); 163.04 (C-4). IR(KBr): 3090, 1580, 1549, 1377, 1352, 1262, 1160, 1030, 824, 516. HRMS (ESI) calculated for $C_{21}H_{20}N_5O_5S$ [M+H]: 454.1180; found 454.1179.

_N_-(7-benzyl-4-methyl-7_H_-pyrrolo[2,3-d]pyrimidin-6-yl)-_N_-methyl-2-nitrobenzenesulfonamide

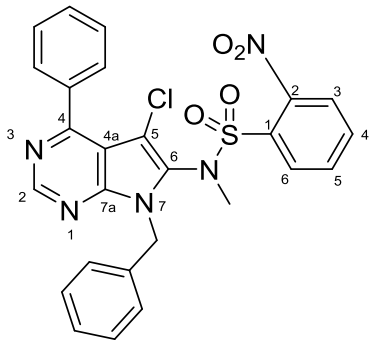
(9-benzyl-6-methyl-8-[_N_-(2-nitrophenylsulfonyl)-_N_-(methyl)amino]-7-deazapurine) (7c)



6-methyl-9-Bn-7-deazapurine **1c** (223 mg, 1 mmol) and *N*-chloro-*N*-methyl-2-nitrobenzenesulfonamide **4** (501 mg, 2 mmol) were used as starting compounds to give product **7c** (180 mg, 41 %) as yellowish crystals after chromatography with hexanes/EtOAc 5:1 to 1:1 and crystallization from EtOAc/hexane. M. p. 186-187 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.65 (s, 3H, CH_3-4); 2.92 (s, 3H, CH_3N); 5.59 (bs, 2H, CH_2-Ph); 6.18 (s, 1H, H-5); 7.17 (m, 2H, H-*o*-Bn); 7.21 – 7.30 (m, 3H, H-*p*,*m*-Bn); 7.61 (ddd, 1H, $J_{5,6}$ = 8.0 Hz, $J_{5,4}$ = 7.4 Hz, $J_{5,3}$ = 1.3 Hz, H-5-$C_6H_4NO_2$); 7.66 (dd, 1H, $J_{3,4}$ = 8.0 Hz, $J_{3,5}$ = 1.3 Hz, H-3-$C_6H_4NO_2$); 7.72 (dd, 1H, $J_{6,5}$ = 8.0 Hz, $J_{6,4}$ = 1.4 Hz, H-6-$C_6H_4NO_2$); 7.76 (ddd, 1H, $J_{4,3}$ = 8.0 Hz, $J_{4,5}$ = 7.4 Hz, $J_{4,6}$ = 1.4 Hz, H-4-$C_6H_4NO_2$); 8.87 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.48 (CH_3-4); 40.57 (CH_3-N); 45.06 (CH_2-Ph); 97.91 (CH-5); 116.18 (C-4a); 124.07 (CH-3-$C_6H_4NO_2$); 127.58 (CH-*o*-Bn); 127.77 (CH-*p*-Bn); 128.79 (CH-*m*-Bn); 130.38 (C-1-$C_6H_4NO_2$); 131.22 (CH-5-$C_6H_4NO_2$); 132.24 (CH-6-$C_6H_4NO_2$); 134.51 (CH-4-$C_6H_4NO_2$); 135.44 (C-6); 136.80 (C-*i*-Bn); 148.56 (C-2-$C_6H_4NO_2$); 149.15 (C-7a); 152.80 (CH-2); 159.85 (C-4).IR(KBr): 3063, 1891, 1550, 1377, 1359, 1237, 1201, 1069, 1165, 893, 600. HRMS (ESI) calculated for $C_{21}H_{20}N_5O_4S$ [M+H]: 438.1232; found 438.1230.

_N_-(7-benzyl-5-chloro-4-phenyl-7_H_-pyrrolo[2,3-_d_]pyrimidin-6-yl)-_N_-methyl-2-nitrobenzenesulfonamide

(9-benzyl-7-chloro-8-[_N_-(2-nitrophenylsulfonyl)-_N_-(methyl)amino]-6-phenyl-7-deazapurine) (8a)

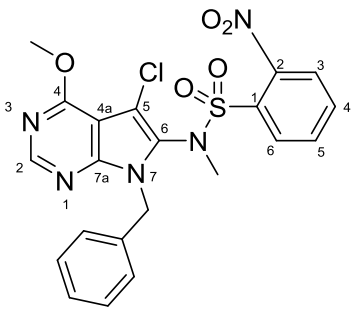


Method A, C-H chloroamination: **1a** (285 mg, 1 mmol) and **4** (877 mg, 3.5 mmol) were used as starting compounds to give product **8a** (273 mg, 51 %) as white crystals after chromatography with hexanes/EtOAc 5:1 to 1:1 and crystallization from EtOAc/hexane.

Method B, C-H amination: **9a** (285 mg, 1 mmol) and **4** (752 mg, 3.0 mmol) were used as starting compounds to give product **8a** (225 mg, 41 %) as white crystals after chromatography with hexanes/EtOAc 5:1 to 1:1 and crystallization from EtOAc/hexane. M. p. 215-216 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.91 (s, 3H, CH_3N); 5.42 (d, 1H, J_{gem} = 15.3 Hz, CH_2a-Ph); 6.16 (d, 1H, J_{gem} = 15.3 Hz, CH_2b-Ph); 7.26 – 7.31 (m, 3H, H-*o*,*p*-Bn); 7.33 (m, 2H, H-*m*-Bn); 7.42 – 7.50 (m, 3H, H-*m*,*p*-Ph); 7.58 – 7.63 (m, 2H, H-3,5-$C_6H_4NO_2$); 7.71 (m, 2H, H-*o*-Ph); 7.73 (ddd, 1H, $J_{4,3}$ = $J_{4,5}$ = 7.7 Hz, $J_{4,6}$ = 1.4 Hz, H-4-$C_6H_4NO_2$); 7.84 (m, 1H, H-6-$C_6H_4NO_2$); 9.09 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 38.28 (CH_3-N); 45.68 (CH_2-Ph); 103.08 (C-5); 112.02 (C-4a); 124.00 (CH-3-$C_6H_4NO_2$); 127.84 (CH-*m*-Ph); 128.09 (CH-*p*-Bn); 128.11 (CH-*o*-Bn); 128.95 (CH-*m*-Bn); 129.86 (CH-*p*-Ph); 130.20 (CH-*o*-Ph); 131.45 (CH-5-$C_6H_4NO_2$); 131.62 (C-1-$C_6H_4NO_2$); 131.65 (CH-6-$C_6H_4NO_2$); 131.89 (C-6); 134.49 (CH-4-$C_6H_4NO_2$); 136.48 (C-*i*-Bn); 136.62 (C-*i*-Ph); 148.56 (C-2-$C_6H_4NO_2$); 148.78 (C-7a); 153.18 (CH-2); 160.20 (C-4). IR(KBr): 3050, 1583, 1545, 1374, 1345, 1165, 826, 558. HRMS (ESI) calculated for $C_{26}H_{21}N_5O_4SCl$ [M+H]: 534.0998; found: 534.0997.

_N_-(7-benzyl-5-chloro-4-methoxy-7_H_-pyrrolo[2,3-_d_]pyrimidin-6-yl)-_N_-methyl-2-nitrobenzenesulfonamide

(9-benzyl-7-chloro-6-methoxy-8-[_N_-(2-nitrophenylsulfonyl)-_N_-(methyl)amino]-7-deazapurine) (8b)



1b (240 mg, 1 mmol) and **4** (752 mg, 3.5 mmol) were used as starting compounds to give a product **8b** (205 mg, 42 %) as white crystals after chromatography with hexanes/EtOAc 5:1 to 1:1 and crystallization from EtOAc/hexane. M. p. 177-179 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.87 (s, 3H, CH_3N); 4.11 (s, 3H, CH_3O); 5.36 (d, 1H, J_{gem} = 15.4 Hz, CH_2a-Ph); 5.99 (d, 1H, J_{gem} = 15.4 Hz, CH_2b-Ph); 7.21 (m, 2H, H-*o*-Bn); 7.24 – 7.33 (m, 3H, H-*p*,*m*-Bn); 7.61 (m, 1H, H-3-$C_6H_4NO_2$); 7.62 (m, 1H, H-5-$C_6H_4NO_2$); 7.74 (bt, 1H, $J_{4,3}$ = $J_{4,5}$ = 7.8 Hz, H-4-$C_6H_4NO_2$);

7.81 (bd, 1H, $J_{6,5}$ = 7.9 Hz, H-6-$C_6H_4NO_2$); 8.57 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 38.30 (CH_3-N); 45.74 (CH_2-Ph); 54.07 (CH_3O); 102.24 (C-4a); 102.49 (C-5); 123.91 (CH-3-$C_6H_4NO_2$); 127.89 (CH-*o*-Bn); 127.94 (CH-*p*-Bn); 128.71 (C-6); 128.85 (CH-*m*-Bn); 131.51 (C-1-$C_6H_4NO_2$); 131.69 (CH-5-$C_6H_4NO_2$); 131.76 (CH-6-$C_6H_4NO_2$); 134.38 (CH-4-$C_6H_4NO_2$); 136.70 (C-*i*-Bn); 148.40 (C-2-$C_6H_4NO_2$); 148.66 (C-7a); 153.06 (CH-2); 163.08 (C-4). IR(KBr): 3068, 1580, 1374, 1352, 1262, 1160, 1030, 853, 517. HRMS (ESI) calculated for $C_{21}H_{19}N_5O_5SCl$ [M+H]: 488.0789; found 488.0790.

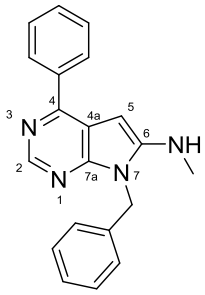
Deprotection of 2-nitrobenzenesulfonamide group (*o*Ns):

Compound **7a** (250 mg, 0.5 mmol) and Cs_2CO_3 (163 mg, 0.5 mmol) were dissolved in dry MeCN (4 mL) under argon atmosphere. Then, thiophenol (55 mg, 0.051 ml, 0.5 mmol) was added dropwise to the stirred reaction mixture at r.t. and the stirring was continued for 1 hour. Then the mixture was filtered and evaporated under vacuum. The residue was purified by column chromatography on silica gel eluting with hexanes/EtOAc 5:1 to 1:1 to obtain product **10a** (118 mg, 75 %) as yellowish solid.

One pot C-H amination/deprotection:

6-Phenyl-9-benzyl-7-deazapurine **1a** (285 mg, 1 mmol), $Pd(OAc)_2$ (0.05 mmol), $Cu(acac)_2$ (0.05 0.1 mmol), bpy (0.1 mmol), Na_2CO_3 (7 mmol) and *N*-chloro-*N*-methyl-2-nitrobenzenesulfonamide **4** (877 mg, 3.5 mmol) were placed in an argon-purged vial and then 1,4-dioxane (4 mL) was added. The reaction mixture was then stirred for 24 h at r.t., quenched with H_2O (4 mL), extracted with ethyl acetate (3 x 40 mL) and washed with brine (4 mL). The organic phases were combined and dried over sodium sulphate, filtered, and evaporated under vacuum. The crude intermediate was combined with Cs_2CO_3 (326 mg, 1 mmol) in an argon-purged vial and dissolved in dry MeCN (8 mL). Thiophenol (110 mg, 0.102 ml, 1 mmol) was added dropwise through septum to the stirred reaction mixture at r.t. and the stirring was continued for 1 h. The mixture was then quenched with H_2O (4 mL), extracted with ethyl acetate (3 x 40 mL) and washed with brine (4 mL). The organic phases were combined and dried over sodium sulphate, filtered, and evaporated under vacuum. The residue was purified by column chromatography on silica gel eluting with hexanes/EtOAc 5:1 to 1:1 to get product **10a** (110 mg, 35 % in two steps) as yellowish solid.

7-Benzyl-*N*-methyl-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-amine (9-benzyl-8-methylamino-6-phenyl-7-deazapurine) (10a)



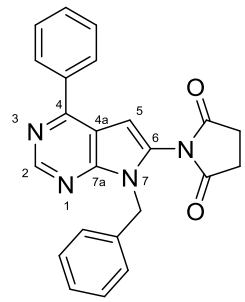
M.p. 154-155 °C. ^{1}H NMR (500.0 MHz, acetone-d_6): 2.94 (d, 3H, J = 5.0, CH_3N); 5.48 (s, 2H, CH_2Ph); 5.68 (bq, 1H, J = 5.0, MeNH); 5.82 (d, 1H, J = 0.6, H-5); 7.20 (m, 2H, H-*o*-Bn); 7.24 (m, 1H, H-*p*-Bn); 7.30 (m, 2H, H-*m*-Bn); 7.44 (m, 1H, H-*p*-Ph); 7.53 (m, 2H, H-*m*-Ph); 8.25 (m, 2H, H-*o*-Ph); 8.57 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, acetone-d_6): 30.97 (CH_3N); 43.94 (CH_2Ph); 74.20 (CH-5); 117.98 (C-4a); 127.65 (CH-*o*-Bn); 128.13 (CH-*p*-Bn); 129.00 (CH-*o*-Ph); 129.22 (CH-*m*-Ph); 129.37 (CH-*m*-Bn); 129.54 (CH-*p*-Ph); 138.14 (C-*i*-Bn); 140.35 (C-*i*-Ph); 148.33 (CH-2); 149.71 (C-4); 150.64 (C-6); 152.97 (C-7a). IR(KBr): 3416, 3220, 3061, 3031, 2820, 1604, 1583, 1570, 1495, 1452, 1344, 1181. HRMS (ESI) calculated for $C_{20}H_{19}N$ [M+H]: 315.1604; found 315.1604.

5.4 C-H imidation of 7-deazapurines

General procedure for C-H imidation of 7-deazapurines:

7-Deazapurine **1a, 1d, 15** (1.0 mmol), ferrocene (9.3 mg, 0.05 mmol) and perester **11, 13** (2.75 mmol) were placed in a vial which was purged with an argon. Then degassed DCM (20 mL) was added, the reaction mixture was heated to 50 °C and stirred for 7 hours. Upon cooling, saturated Na_2CO_3 (25 mL) was added, followed by extraction with EtOAc (3x25 mL). Combined organic layers were dried over anhydrous sodium sulphate, filtered, and evaporated under vacuum. The crude material was purified by column chromatography on silica gel, eluting with hexanes/EtOAc to afford the corresponding products.

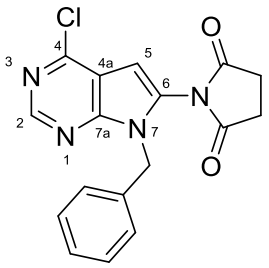
1-(7-benzyl-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)pyrrolidine-2,5-dione (6-phenyl-9-benzyl-8-succinimido-7-deazapurine) (12a)



1a (285 mg, 1 mmol) and **11** (752 mg, 2.75 mmol) were used as starting compounds to give a product **12a** (122 mg, 32 %) as brownish crystals after chromatography with hexanes/EtOAc 2:1 to 1:4 and crystallization from EtOAc/hexane. M. p. 176-177 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.56 (vbs, 4H, CH_2-$C_4H_4O_2N$); 5.52 (s, 2H, CH_2-Ph); 6.84 (s, 1H, H-5); 7.10 (m, 2H, H-*o*-Bn); 7.26 – 7.34 (m, 3H, H-*p*,*m*-Bn); 7.49 – 7.58 (m, 3H, H-*m*,*p*-Ph); 8.10 (m, 2H, H-*o*-Ph); 9.06 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 28.19 (CH_2-$C_4H_4O_2N$); 46.11 (CH_2-Ph); 100.59 (CH-5); 114.43 (C-4a); 126.94 (CH-*o*-Bn);

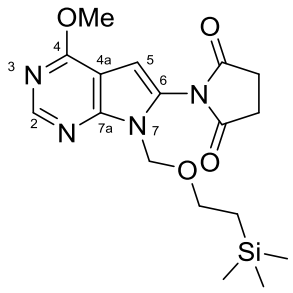
127.71 (C-6); 128.10 (CH-*p*-Bn); 128.81 (CH-*m*-Ph); 128.89 (CH-*o*-Ph); 128.92 (CH-*m*-Bn); 130.29 (CH-*p*-Ph); 135.82 (C-*i*-Bn); 137.66 (C-*i*-Ph); 151.39 (C-7a); 152.55 (CH-2); 158.34 (C-4); 174.76 (CO-$C_4H_4O_2N$). IR(KBr): 3132, 2950, 1724, 1589, 1538, 1336, 1156, 946, 728, 692. HRMS (ESI) calculated for $C_{23}H_{19}N_4O_2$ [M+H]: 383.1502; found 383.1501.

1-(7-benzyl-4-chloro-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)pyrrolidine-2,5-dione (6-chloro-9-benzyl-8-succinimido-7-deazapurine) (12b)



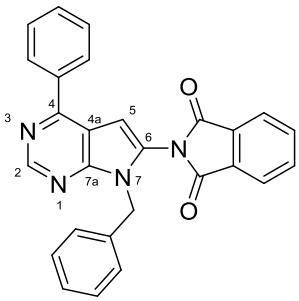
1a (243 mg, 1 mmol) and **11** (752 mg, 2.75 mmol) were used as starting compounds to give a product **12b** (92 mg, 27 %) as yellowish crystals after chromatography with hexanes/EtOAc 2:1 to 1:4 and crystallization from EtOAc/hexane. M. p. 229-230 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.57 (vbs, 4H, CH_2-$C_4H_4O_2N$); 5.46 (s, 2H, CH_2-Ph); 6.64 (s, 1H, H-5); 7.06 (m, 2H, H-*o*-Bn); 7.27 – 7.34 (m, 3H, H-*p*,*m*-Bn); 8.74 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 28.21 (CH_2-$C_4H_4O_2N$); 46.64 (CH_2-Ph); 99.66 (CH-5); 116.23 (C-4a); 126.89 (CH-*o*-Bn); 127.93 (C-6); 128.31 (CH-*p*-Bn); 129.01 (CH-*m*-Bn); 135.25 (C-*i*-Bn); 150.71 (C-7a); 151.79 (CH-2); 152.83 (C-4); 174.50 (CO-$C_4H_4O_2N$). IR(KBr): 3114, 3058, 1724, 1553, 1464, 1338, 1162, 940, 701, 597. HRMS (ESI) calculated for $C_{17}H_{14}N_4O_2Cl$ [M+H]: 341.0799; found 341.0799.

1-(4-methoxy-7-((2-(trimethylsilyl)ethoxy)methyl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)pyrrolidine-2,5-dione (6-methoxy-9-[2-(trimethylsilyl)ethoxymethyl]-8-succinimido-7-deazapurine) (16)



15 (279 mg, 1 mmol) and **11** (752 mg, 2.75 mmol) were used as starting compounds to give a product **16** (173 mg, 46 %) as brownish oil after chromatography with hexanes/EtOAc 2:1 to 1:2. ^{1}H NMR (500 MHz, DMSO-d_6): -0.12 (s, 9H, CH_3Si); 0.76 (m, 2H, OCH_2CH_2Si); 2.90 (s, 4H, CH_2CO); 3.33 (m, 2H, OCH_2CH_2Si); 4.07 (s, 3H, CH_3O); 5.42 (s, 2H, NCH_2O); 6.58 (s, -H, H-5); 8.53 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.30 (CH_3Si); 17.30 (OCH_2CH_2Si); 28.97 (CH_2CO); 54.03 (CH_3O); 65.48 (OCH_2CH_2Si); 70.46 (NCH_2O); 98.45 (CH-5); 103.79 (C-4a); 126.27 (C-6); 151.29 (C-7a); 152.02(CH-2); 162.52 (C-4); 176.81 (CH_2CO). IR(KBr): 2951, 1728, 1559, 1479, 1364, 1169, 1081, 837, 696. HRMS (ESI) calculated for $C_{17}H_{24}N_4O_4NaSi$ [M+Na]: 399.1459; found 399.1460.

2-(7-benzyl-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)isoindoline-1,3-dione (6-phenyl-9-benzyl-8-phtalimido-7-deazapurine) (17)



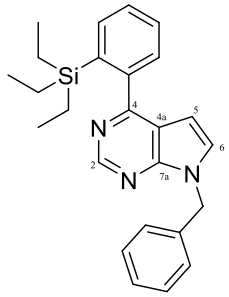
1a (285 mg, 1 mmol) and **13** (884 mg, 2.75 mmol) were used as starting compounds to give a product **17** (151 mg, 35 %) as brownish crystals after chromatography with hexanes/EtOAc 2:1 to 1:4 and crystallization from EtOAc/hexane. M. p. 139-140 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 5.47 (s, 2H, CH_2Ph); 7.03 (m, 2H, *o*-Bn); 7.12-7.16 (m, 3H, *m*-Bn, *p*-Bn); 7.23 (s, 1H, H-5); 7.56-7.64 (m, 3H, *m*-Ph, *p*-Ph); 7.93-8.01 (m, 4H, H-4´,H-5´,H-6´,H-7´); 8.16 (m, 2H, *o*-Ph); 9.01 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 45.43 (CH_2Ph); 100.96 (CH-5); 113.98 (C-4a); 124.31 (CH-4´,CH-7´); 127.21 (CH-*o*-Bn); 127.75 (CH-*p*-Bn); 128.69 (CH-*m*-Bn); 128.98 (CH-*o*-Ph); 129.29 (C-6); 129.34 (CH-*m*-Ph); 131.02 (CH-*p*-Ph); 131.63 (C-3a´,C-7a´); 135.60 (CH-5´,CH-6´); 136.71 (C-*i*-Bn); 137.02 (C-*i*-Ph); 150.89 (C-7a); 152.11 (CH-2); 156.71 (C-4); 166.75 (C=O). HRMS (ESI) calculated for $C_{27}H_{19}N_4O_2$ [M+H]: 431.1502; found 431.1503.

5.5 *ortho* C-H silylation of 7- and 9-phenyldeazapurines

General procedure for C-H *ortho*-silylation of phenyldeazapurines:

Deazapurine (0.5 mmol), [Ir(COD)OMe]$_2$ (0.025 mmol), dtbpy (0.05 mmol) and norbornene (2.5 mmol) were placed in a vial which was purged with argon. Then 1,4-dioxane (1.5 mL) was added. After stirring for 5 minutes, silane (2.5 mmol) was added dropwise and the reaction mixture was heated at 130 °C and stirred for 48 hours. The solvent was concentrated under reduced pressure and the crude mixture was then purified by flash column chromatography eluting with hexanes/EtOAc to afford the corresponding product.

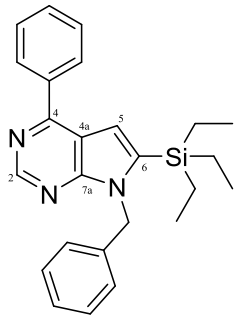
7-Benzyl-4-[2-(triethylsilyl)phenyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (6-[2-(triethylsilyl)phenyl)]-9-benzyl-7-deazapurine) (19a)



6-Phenyl-9-benzyl-7-deazapurine **1a** (143 mg, 0.5 mmol) and triethylsilane (291 mg, 0.4 mL, 2.5 mmol) were used as starting compounds to give product **19a** (110 mg, 55 %) as yellow solid after chromatography with hexanes/EtOAc. M. p. 77-78 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 0.56 (bq, 6H, $J_{CH2,CH3}$ = 7.9 Hz, CH_3CH_2Si); 0.79 (bt, 9H, $J_{CH3,CH2}$ = 7.9 Hz, CH_3CH_2Si); 6.53 (s, 2H, CH_2-Ph); 6.53 (d, 1H, $J_{5,6}$ =

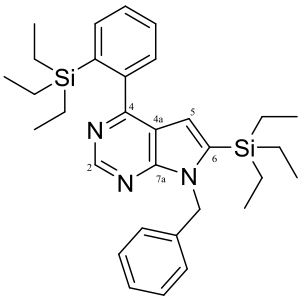
3.6 Hz, H-5); 7.17 (d, 1H, $J_{6,5}$ = 3.6 Hz, H-6); 7.21 (m, 2H, H-*o*-Bn); 7.30 (m, 1H, H-*p*-Bn); 7.33 (m, 2H, H-*m*-Bn); 7.43 – 7.48 (m, 2H, H-4,5-Ph); 7.61 (m, 1H, H-6-Ph); 7.73 (m, 1H, H-3-Ph); 8.93 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 4.38 (CH_3**C**H_2Si); 7.59 (**C**H_3CH_2Si); 47.93 (CH_2-Ph); 100.88 (CH-5); 117.09 (C-4a); 127.43 (CH-*o*-Bn); 127.91 (CH-*p*-Bn, CH-4-Ph); 128.25 (CH-5-Ph); 128.41 (CH-6); 128.84 (CH-*m*-Bn); 129.39 (CH-6-Ph); 136.71 (CH-3-Ph); 136.89 and 136.91 (CH-2-Ph, C-*i*-Bn); 144.62 (C-1-Ph); 151.97 (CH-2); 151.25 (C-7a); 161.50 (C-4). IR(KBr): 3040, 2947, 2869, 1571, 1509, 1347, 1224, 946, 719, 611. HRMS (ESI) calculated for $C_{25}H_{30}N_3Si$ [M+H]: 400.2204; found 400.2203.

7-Benzyl-4-phenyl-6-(triethylsilyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (6-phenyl-8-(triethylsilyl)-9-benzyl-7-deazapurine) (19b)



6-Phenyl-9-benzyl-7-deazapurine **1a** (143 mg, 0.5 mmol) and triethylsilane (291 mg, 0.4 mL, 2.5 mmol) were used as starting compounds to give product **19b** (19 mg, 8 %) as a brown oil after chromatography with hexanes/EtOAc. ^{1}H NMR (500 MHz, $CDCl_3$): 0.72 (m, 6H, CH_3CH_2Si); 087 (m, 9H, CH_3CH_2Si); 5.67 (s, 2H, CH_2-Ph); 6.88 (m, 2H, H-*o*-Bn); 7.07 (s, 1H, H-5); 7.19 – 7.29 (m, 3H, H-*m*,*p*-Bn); 7.53 (m, 1H, H-*p*-Ph); 7.59 (m, 2H, H-*m*-Ph); 8.17 (m, 2H, H-*o*-Ph); 8.95 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 3.28 (CH_3**C**H_2Si); 7.18 (**C**H_3CH_2Si); 47.72 (CH_2-Ph); 112.33 (CH-5); 115.58 (C-4a); 125.69 (CH-*o*-Bn); 127.30 (CH-*p*-Bn); 128.57 (CH-*m*-Bn); 128.79 (CH-*m*-Ph); 128.96 (CH-*o*-Ph); 129.95 (CH-*p*-Ph); 137.71 (C-*i*-Bn); 138.38 (C-*i*-Ph); 140.80 (C-6); 151.95 (CH-2); 155.00 (C-7a); 157.05 (C-4). IR(KBr): 3051, 2950, 2869, 1574, 1497, 1327, 1199, 922, 719, 605. HRMS (ESI) calculated for $C_{25}H_{30}N_3Si$ [M+H]: 400.2204; found 400.2203.

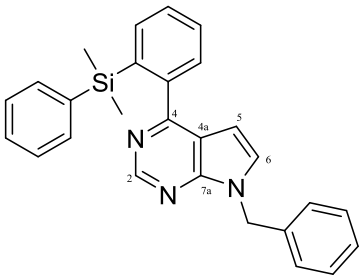
7-Benzyl-6-(triethylsilyl)-4-[2-(triethylsilyl)phenyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (6-[2-(triethylsilyl)phenyl]-8-(triethylsilyl)-9-benzyl-7-deazapurine) (19c)



6-Phenyl-9-benzyl-7-deazapurine **1a** (143 mg, 0.5 mmol) and triethylsilane (291 mg, 0.4 mL, 2.5 mmol) were used as starting compounds to give product **19c** (18 mg, 7 %) as white solid after chromatography with hexanes/EtOAc. M. p. 83-84 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 0.52 (m, 6H, CH_3CH_2Si-Ph); 0.66 (m, 6H, CH_3CH_2Si-6); 0.79 (m, 9H, CH_3CH_2Si-Ph); 0.82 (m, 9H, CH_3CH_2Si-6); 5.68 (s, 2H, CH_2-Ph); 6.73 (s, 1H, H-5); 6.81 (m, 2H, H-*o*-Bn); 7.19 – 7.28 (m,

3H, H-*m*,*p*-Bn); 7.45 – 7.53 (m, 2H, H-4,5-Ph); 7.64 (m, 1H, H-6-Ph); 7.73 (m, 1H, H-3-Ph); 8.86 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 3.22 (CH_3**C**H_2Si-6); 4.32 (CH_3**C**H_2Si-Ph); 7.11 (**C**H_3CH_2Si-6); 7.57 (**C**H_3CH_2Si-Ph); 47.68 (CH_2-Ph); 112.57 (CH-5); 117.24 (C-4a); 125.56 (CH-*o*-Bn); 127.28 (CH-*p*-Bn); 127.84 (CH-4-Ph); 128.33 (CH-5-Ph); 128.57 (CH-*m*-Bn); 129.25 (CH-6-Ph); 136.62 (CH-3-Ph); 136.76 (CH-2-Ph); 137.84 (C-*i*-Bn); 140.30 (C-6); 144.84 (C-1-Ph); 151.27 (CH-2); 154.36 (C-7a); 161.10 (C-4). IR(KBr): 3046, 2956, 2866, 1568, 1455, 1359, 1245, 1009, 737, 594. HRMS (ESI) calculated for $C_{31}H_{44}N_3Si_2$ [M+H]: 514.3068; found 514.3068.

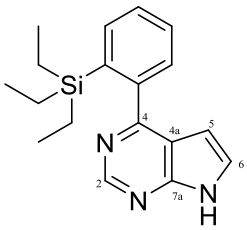
7-Benzyl-4-{2-[dimethyl(phenyl)silyl]phenyl}-7*H*-pyrrolo[2,3-*d*]pyrimidine (6-{2-[dimethyl(phenyl)silyl]phenyl}-9-benzyl-7-deazapurine) (20)



6-Phenyl-9-benzyl-7-deazapurine **1a** (143 mg, 0.5 mmol) and dimethylphenylsilane (341 mg, 0.38 mL, 2.5 mmol) were used as starting compounds to give product **20** (66 mg, 31 %) as a brown oil after chromatography with hexanes/EtOAc. ^{1}H NMR (500 MHz, DMSO-d_6): 0.37 (s, 6H, CH_3Si); 5.45 (s, 2H, CH_2-Ph); 6.53 (d, 1H, $J_{5,6}$ = 3.6 Hz, H-5); 7.00 – 7.06 (m, 3H, H-*m*,*p*-Ph); 7.19 – 7.24 (m, 4H, H-*o*-Bn, H-*o*-Ph); 7.28 (m, 1H, H-*p*-Bn); 7.34 (m, 2H, H-*m*-Bn); 7.50 (td, 1H, $J_{4,5}$ = $J_{4,3}$ = 7.4 Hz, $J_{4,6}$ = 1.4 Hz, H-4-Ph); 7.56 (td, 1H, $J_{5,6}$ = $J_{5,4}$ = 7.5 Hz, $J_{5,3}$ = 1.5 Hz, H-5-Ph); 7.65 (d, 1H, $J_{6,5}$ = 3.6 Hz, H-6); 7.70 (ddd, 1H, $J_{3,4}$ = 7.4 Hz, $J_{3,5}$ = 1.5 Hz, $J_{3,6}$ = 0.7 Hz, H-3-Ph); 7.72 (ddd, 1H, $J_{6,5}$ = 7.6 Hz, $J_{6,4}$ = 1.4 Hz, $J_{6,3}$ = 0.7 Hz, H-6-Ph); 8.67 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 0.20 (CH_3Si); 47.37 (CH_2-Ph); 99.98 (CH-5); 115.86 (C-4a); 127.19 (CH-*m*-Ph); 127.59 (CH-*o*-Bn); 127.79 (CH-*p*-Bn); 128.16 (CH-*p*-Ph); 128.62 (CH-4-Ph); 128.81 (CH-*m*-Bn); 129.40 and 129.42 (CH-5,6-Ph); 130.46 (CH-6); 133.17 (CH-*o*-Ph); 136.97 (CH-3-Ph); 137.86 (C-*i*-Bn); 138.19 (C-2-Ph); 139.62 (C-*i*-Ph); 144.27 (C-1-Ph); 150.27 (CH-2); 150.80 (C-7a); 159.17 (C-4). IR(KBr): 3066, 3049, 2650, 1571, 1512, 1344, 1248, 1114, 925, 818, 779, 725, 591. HRMS (ESI) calculated for $C_{27}H_{26}N_3Si$ [M]: 420.1890; found 420.1890.

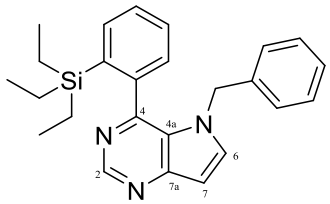
4-[2-(Triethylsilyl)phenyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (6-[2-(Triethylsilyl)phenyl]-7-deazapurine) (24)

6-Phenyl-9-NH-7-deazapurine **21** (98 mg, 0.5 mmol) and triethylsilane (291 mg, 0.4 mL, 2.5 mmol) were used as starting compounds to give product **24** (73 mg, 47 %) as white solid after chromatography with hexanes/EtOAc. M. p. 164-165 °C. ^{1}H NMR (500 MHz, DMSO-d_6):



0.51 (bq, 6H, $J_{CH2,CH3}$ = 7.9 Hz, CH_3CH_2Si); 0.72 (bt, 9H, $J_{CH3,CH2}$ = 7.9 Hz, CH_3CH_2Si); 6.50 (dd, 1H, $J_{5,6}$ = 3.5 Hz, $J_{5,NH}$ = 1.7 Hz, H-5); 7.48 – 7.55 (m, 2H, H-4,5-Ph); 7.59 (dd, 1H, $J_{6,5}$ = 3.5 HZ, $J_{6,NH}$ = 2.3 Hz, H-6); 7.64 – 7.71 (m, 2H, H-3,6-Ph); 8.78 (s, 1H, H-2); 12.23 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 4.30 (CH_3CH_2Si); 7.77 (CH_3CH_2Si); 99.94 (CH-5); 116.07 (C-4a); 127.49 (CH-6); 128.23 (CH-4-Ph); 128.88 (CH-5-Ph); 129.56 (CH-6-Ph); 136.03 (C-2-Ph); 136.69 (CH-3-Ph); 144.92 (C-1-Ph); 150.33 (CH-2); 152.13 (C-7a); 159.83 (C-4). IR(KBr): 3126, 2953, 2869, 1574, 1353, 1260, 1009, 851, 737, 609. HRMS (ESI) calculated for $C_{18}H_{23}N_3Si$ [M]: 309.1660; found 309.1661.

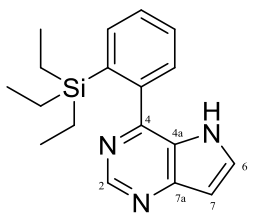
5-Benzyl-4-[2-(triethylsilyl)phenyl]-5*H*-pyrrolo[3,2-d]pyrimidine (6-[2-(triethylsilyl)phenyl]-7-benzyl-9-deazapurine) (25)



6-Phenyl-7-benzyl-9-deazapurine **22** (143 mg, 0.5 mmol) and triethylsilane (291 mg, 0.4 mL, 2.5 mmol) were used as starting compounds to give product **25** (92 mg, 46 %) as yellow solid after chromatography with hexanes/EtOAc. M.p. 106-107 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 0.21 (m, 6H, CH_3CH_2Si); 0.63 (t, 9H, $J_{CH3,CH2}$ = 7.9 Hz, CH_3CH_2Si); 4.94 (m, 1H, CH_2-Pha); 5.09 (m, 1H, CH_2-Phb); 6.47 (m, 2H, H-*o*-Bn); 6.82 (d, 1H, $J_{7,6}$ = 3.3 Hz, H-7); 7.11 – 7.17 (m, 3H, H-*m*,*p*-Bn); 7.18 (ddd, 1H, $J_{6,5}$ = 7.6 Hz, $J_{6,4}$ = 1.3 Hz, $J_{6,3}$ = 0.6 Hz, H-6-Ph); 7.33 (td, 1H, $J_{5,6}$ = $J_{5,4}$ = 7.5 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Ph); 7.50 (td, 1H, $J_{4,3}$ = $J_{4,5}$ = 7.5 Hz, $J_{4,6}$ = 1.3 Hz, H-4-Ph); 7.64 (ddd, 1H, $J_{3,4}$ = 7.5 Hz, $J_{3,5}$ = 1.4 Hz, $J_{3,6}$ = 0.6 Hz, H-3-Ph); 8.03 (d, 1H, $J_{6,7}$ = 3.3 Hz, H-6); 8.83 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 3.30 (CH_3**C**H_2Si); 7.46 (**C**H_3CH_2Si); 51.44 (CH_2-Ph); 101.89 (CH-7); 125.10 (C-4a); 126.12 (CH-*o*-Bn); 127.56 (CH-*p*-Bn); 128.11 (CH-4-Ph); 128.21 (CH-5-Ph); 128.54 (CH-*m*-Bn); 129.55 (CH-6-Ph); 135.75 (CH-3-Ph); 136.33 (C-2-Ph); 137.60 (C-*i*-Bn); 138.39 (CH-6); 143.05 (C-1-Ph); 149.41 (CH-2); 151.37 (C-7a); 151.90 (C-4). IR(KBr): 3108, 2962, 2869, 1586, 1509, 1395, 1344, 1117, 1003, 818, 725, 597. HRMS (ESI) calculated for $C_{25}H_{29}N_3Si$ [M]: 399.2133; found 399.2131.

4-[2-(Triethylsilyl)phenyl]-5*H*-pyrrolo[3,2-*d*]pyrimidine (6-[2-(triethylsilyl)phenyl]-7-NH-9-deazapurine) (26)

6-Phenyl-7-NH-9-deazapurine **23** (98 mg, 0.5 mmol) and triethylsilane (291 mg, 0.4 mL, 2.5 mmol) were used as starting compounds to give product **26** (58 mg, 37 %) as white solid after chromatography with hexanes/EtOAc. M. p. 164-165 °C. ^{1}H NMR (500 MHz, DMSO-d_6):



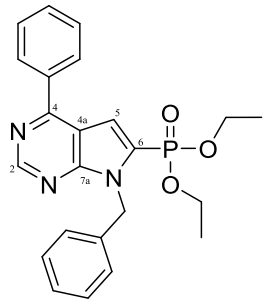
0.45 (bq, 6H, $J_{CH2,CH3}$ = 7.9 Hz, CH_3CH_2Si); 0.70 (bt, 9H, $J_{CH3,CH2}$ = 7.9 Hz, CH_3CH_2Si); 6.68 (dd, 1H, $J_{7,6}$ = 3.1 Hz, $J_{7,NH}$ = 1.6 Hz, H-7); 7.52 – 7.59 (m, 2H, H-4,5-Ph); 7.62 (m, 1H, H-6-Ph); 7.72 (m, 1H, H-3-Ph); 7.82 (t, 1H, $J_{6,7}$ = $J_{6,NH}$ = 3.0 Hz, H-6); 8.83 (s, 1H, H-2); 11.81 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 4.01 (CH_3**C**H_2Si); 7.59 (**C**H_3CH_2Si); 101.59 (CH-7); 124.86 (C-4a); 128.43 (CH-4-Ph); 129.05 (CH-5-Ph); 129.40 (CH-6-Ph); 133.82 (CH-6); 136.22 (C-2-Ph); 136.67 (CH-3-Ph); 143.03 (C-1-Ph); 149.56 (CH-2); 150.55 (C-7a); 151.34 (C-4). IR(KBr): 3069, 2956, 2872, 1607, 1535, 1482, 1368, 1114, 890, 737, 600. HRMS (ESI) calculated for $C_{18}H_{23}N_3Si$ [M]: 309.1660; found 309.1661.

5.6 C-H phosphonation of 7- and 9-deazapurines

General procedure for C-H phosphonation of deazapurines:

A suspension of deazapurine **1a, 1d, 15, 21, 29-36** or **22-23, 39-40** (0.5 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (1.5 mmol, 3 equiv.) and dialkylphosphite (0.34 mL, 2.5 mmol,) in a mixture of acetonitrile-water (1:1, 2 mL) was stirred at 100 °C for 2 h. After cooling to room temperature, mixed with water and extracted with ethyl acetate (3 × 20 mL). Combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel using hexanes/ethyl acetate to give the pure product.

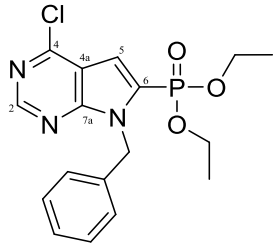
Diethyl (7-benzyl-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-phenyl-9-benzyl-7-deazapurine 8-diethyl phosphonate) (28a)



Deazapurine **1a** (143 mg, 0.5 mmol) and diethylphosphite **27a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **28a** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28a** was obtained as yellowish oil (100 mg, 47 %) after chromatography (70 to 80 % of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6): 1.09 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 3.89 - 4.06 (m, 4H, CH_3CH_2O); 5.75 (s, 2H, CH_2-Ph); 7.11 (m, 2H, H-*o*-Bn); 7.24 (m, 1H, H-*p*-Bn); 7.29 (m, 2H, H-*m*-Bn); 7.50 (d, 1H, $J_{5,P}$ = 5.3 Hz, H-5); 7.59 – 7.67 (m, 3H, H-*m*,*p*-Ph); 8.21 (m, 2H, H-*o*-Ph); 9.04 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.0 (d, $J_{C,P}$ = 6.4 Hz, CH_3CH_2O); 46.9 (CH_2-Ph); 63.0 (d, $J_{C,P}$ = 5.6 Hz, CH_3CH_2O); 112.2 (d, $J_{C,P}$ = 15.9 Hz, CH-5); 113.6 (d, $J_{C,P}$ = 14.1 Hz, C-4a); 126.8 (CH-*o*-

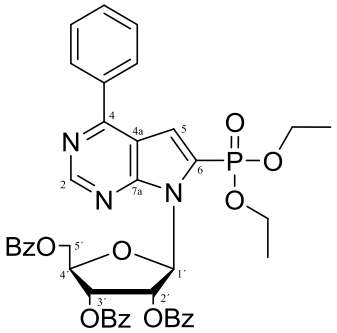
Bn); 127.5 (CH-*p*-Bn); 128.6 (CH-*m*-Bn); 129.1 (d, $J_{C,P}$ = 213.6 Hz, C-6); 129.1 (CH-*o*-Ph); 129.3 (CH-*m*-Ph); 131.1 (CH-*p*-Ph); 137.0 (C-*i*-Ph); 137.5 (C-*i*-Bn); 153.8 (d, $J_{C,P}$ = 13.7 Hz, C-7a); 153.9 (CH-2); 158.9 (C-4). IR(KBr): 3476, 2977, 1553, 1462, 1260, 1018, 770, 695, 564. HRMS (ESI) calculated for $C_{23}H_{24}O_3N_3P$ [M]: 421.1559; found 421.1555.

Diethyl (7-benzyl-4-chloro-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-chloro-9-benzyl-7-deazapurine 8-diethyl phosphonate) (28b)



Deazapurine **1d** (122 mg, 0.5 mmol) and diethylphosphite **27a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **28b** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28b** was obtained as a yellowish oil (69 mg, 36 %) after chromatography (50 to 60 % of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6): 1.09 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 3.90 - 4.06 (m, 4H, CH_3CH_2O); 5.72 (s, 2H, CH_2-Ph); 7.09 (m, 2H, H-*o*-Bn); 7.21 - 7.31 (m, 4H, H-*m*,*p*-Bn, H-5); 8.81 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.0 (d, $J_{C,P}$ = 6.4 Hz, CH_3CH_2O); 47.4 (CH_2-Ph); 63.2 (d, $J_{C,P}$ = 5.6 Hz, CH_3CH_2O); 110.5 (d, $J_{C,P}$ = 15.7 Hz, CH-5); 115.7 (d, $J_{C,P}$ = 15.0 Hz, C-4a); 126.8 (CH-*o*-Bn); 127.6 (CH-*p*-Bn); 128.6 (CH-*m*-Bn); 130.0 (d, $J_{C,P}$ = 213.1 Hz, C-6); 137.0 (C-*i*-Bn); 153.1 (d, $J_{C,P}$ = 13.9 Hz, C-7a); 153.3 (CH-2); 153.4 (d, $J_{C,P}$ = 1.3 Hz, C-4). IR(KBr): 3494, 2980, 1586, 1544, 1452, 1254, 1180, 1018, 776, 558. HRMS (ESI) calculated for $C_{17}H_{19}O_3N_3ClNaP$ [M+Na]: 402.0751; found 402.0744.

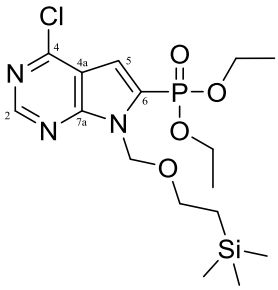
Diethyl (4-phenyl-7-(2,3,5-tri-O-benzoyl-*β*-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-phenyl-9-(O-benzoyl-ribofuranosyl)-7-deazapurine 8-diethyl phosphonate) (28c)



Deazapurine **29** (192 mg, 0.3 mmol) and diethylphosphite **27a** (307 mg, 0.21 mL, 1.5 mmol) were used as starting compounds for the preparation of **28c** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28c** was obtained as a brownish oil (59 mg, 25 %) after chromatography (50 to 60 % of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6): 1.14 and 1.19 (2×t, 2×3H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.00 – 4.18 (m, 2×2H, CH_3CH_2O); 4.67 (bdd, 1H, J_{gem} = 11.8 Hz, $J_{5'a,4'}$ = 4.4 Hz, H-5′a); 4.86 (bdd, 1H, J_{gem} = 11.8 Hz, $J_{5'b,4'}$ = 3.2 Hz, H-5′b); 4.88 (m, 1H, H-4′); 6.38 (t, 1H, $J_{3',2'}$ = $J_{3',4'}$ = 6.4 Hz, H-

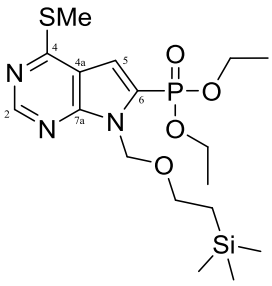
3'); 6.69 (d, 1H, $J_{1',2'}$ = 4.5 Hz, H-1'); 6.89 (dd, 1H, $J_{2',3'}$ = 6.4 Hz, $J_{2',1'}$ = 4.5 Hz, H-2'); 7.40 – 7.55 (m, 7H, H-5, H-*m*-Bz); 7.61 – 7.69 (m, 6H, H-*m*,*p*-Ph, H-*p*-Bz); 7.87, 7.94 and 8.00 (3×m, 3×2H, H-*o*-Bz); 8.15 (m, 2H, H-*o*-Ph); 8.87 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.1 and 16.2 (2×d, $J_{C,P}$ = 6.2 Hz, CH_3CH_2O); 63.2 (CH_2-5´); 63.5 (d, $J_{C,P}$ = 5.3 Hz, CH_3CH_2O); 70.6 (CH-3´); 72.7 (CH-2´); 79.0 (CH-4´); 88.7 (CH-1´); 114.0 (d, $J_{C,P}$ = 15.1 Hz, CH-5); 114.9 (d, $J_{C,P}$ = 14.5 Hz, C-4a); 128.5 and 128.8 (C-*i*-Bz); 129.0, 129.0 and 129.1 (CH-*m*-Bz); 129.2 (CH-*o*-Ph); 129.4 (d, $J_{C,P}$ = 210.8 Hz, C-6); 129.4 (CH-*m*-Ph); 129.4 (C-*i*-Bz); 129.5, 129.5 and 129.6 (CH-*o*-Bz); 131.3 (CH-*p*-Ph); 133.8, 134.2 and 134.3 (CH-*p*-Bz); 136.7 (C-*i*-Ph); 153.6 (CH-2); 153.8 (d, $J_{C,P}$ = 12.2 Hz, C-7a); 159.6 (C-4); 164.8, 165.0 and 165.6 (CO). IR(KBr): 3064, 2928, 2851, 1727, 1564, 1267, 1121, 1025, 972, 711, 559. HRMS (ESI) calculated for $C_{42}H_{38}N_3O_{10}PNa$ [M+Na]: 798.2188; found 798.2187.

Diethyl (4-chloro-7-[2-(trimethylsilyl)ethoxymethyl]-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate
(6-chloro-9-[2-(trimethylsilyl)ethoxymethyl]-7-deazapurine 8-diethyl phosphonate) (28d)



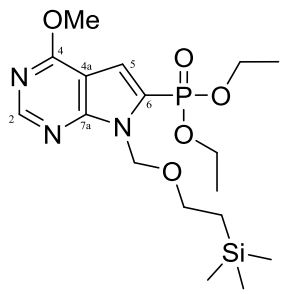
Deazapurine **30** (383 mg, 1.35 mmol) and diethylphosphite **27a** (932 mg, 0.93 mL, 6.75 mmol) were used as starting compounds for the preparation of **28d** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28d** was obtained as a brownish oil (170 mg, 30 %) after chromatography (20 to 30 % of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6): -0.09 (s, 9H, CH_3Si); 0.84 (m, 2H, OCH_2CH_2Si); 1.28 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 3.55 (m, 2H, OCH_2CH_2Si); 4.08 – 4.19 (m, 4H, CH_3CH_2O); 5.81 (s, 2H, NCH_2O); 7.26 (d, 1H, $J_{5,P}$ = 5.2 Hz, H-5); 8.84 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.3 (CH_3Si); 16.3 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2O); 17.4 (OCH_2CH_2Si); 63.3 (d, $J_{C,P}$ = 5.6 Hz, CH_3CH_2O); 66.2 (OCH_2CH_2Si); 71.2 (NCH_2O); 111.3 (d, $J_{C,P}$ = 15.2 Hz, CH-5); 115.8 (d, $J_{C,P}$ = 15.0 Hz, C-4a); 130.0 (d, $J_{C,P}$ = 212.2 Hz, C-6); 153.4 (C-4); 153.4 (CH-2); 153.6 (d, $J_{C,P}$ = 13.9 Hz, C-7a). IR(KBr): 2983, 2951, 2900, 1584, 1541, 1356, 1250, 1085, 1028, 835, 781, 562. HRMS (ESI) calculated for $C_{16}H_{27}N_3O_4ClSiPNa$ [M+Na]: 442.1089; found 442.1089.

Diethyl (4-(methylsulfanyl)-7-[2-(trimethylsilyl)ethoxymethyl]-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate
(6-methylsulfanyl-9-[2-(trimethylsilyl)ethoxymethyl]-7-deazapurine 8-diethyl phosphonate) (28e)



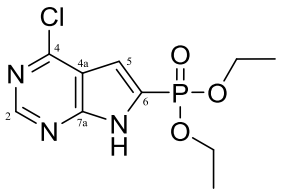
Deazapurine **31** (591 mg, 2.0 mmol) and diethylphosphite **27a** (1381 mg, 1.37 mL, 10.0 mmol) were used as starting compounds for the preparation of **28e** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28e** was obtained as a colorless oil (483 mg, 56 %) after chromatography (20 to 30 % of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6): -0.11 (s, 9H, CH_3Si); 0.82 (m, 2H, OCH_2CH_2Si); 1.26 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 2.67 (s, 3H, CH_3S); 3.52 (m, 2H, OCH_2CH_2Si); 4.04 – 4.16 (m, 4H, CH_3CH_2O); 5.76 (s, 2H, NCH_2O); 7.14 (d, 1H, $J_{5,P}$ = 5.2 Hz, H-5); 8.77 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.3 (CH_3Si); 11.7 (CH_3S); 16.3 (d, $J_{C,P}$ = 6.3 Hz, CH_3CH_2O); 17.4 (OCH_2CH_2Si); 63.0 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 66.0 (OCH_2CH_2Si); 71.6 (NCH_2O); 111.2 (d, $J_{C,P}$ = 15.3 Hz, CH-5); 114.0 (d, $J_{C,P}$ = 14.3 Hz, C-4a); 127.0 (d, $J_{C,P}$ = 214.0 Hz, C-6); 150.0 (d, $J_{C,P}$ = 13.8 Hz, C-7a); 153.2 (CH-2); 163.9 (C-4). IR(KBr): 2980, 2951, 2890, 1549, 1441, 1250, 1079, 1024, 837, 784, 565. HRMS (ESI) calculated for $C_{17}H_{30}N_3O_4SSiPNa$ [M+Na]: 454.1354; found 454.1356.

Diethyl (4-methoxy-7-[2-(trimethylsilyl)ethoxymethyl]-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate
(6-methoxy-9-[2-(trimethylsilyl)ethoxymethyl]-7-deazapurine 8-diethyl phosphonate) (28f)



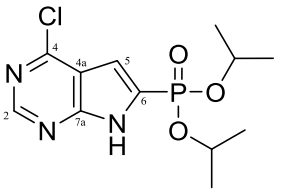
Deazapurine **15** (559 mg, 2.0 mmol) and diethylphosphite **27a** (1381 mg, 1.37 mL, 10.0 mmol) were used as starting compounds for the preparation of **28f** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28f** was obtained as a yellowish oil (333 mg, 40 %) after chromatography (20 to 30 % of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6): -0.10 (s, 9H, CH_3Si); 0.82 (m, 2H, OCH_2CH_2Si); 1.25 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 3.52 (m, 2H, OCH_2CH_2Si); 4.08 (s, 3H, CH_3O); 4.03 – 4.15 (m, 4H, CH_3CH_2O); 5.76 (s, 2H, NCH_2O); 7.13 (d, 1H, $J_{5,P}$ = 5.1 Hz, H-5); 8.59 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.3 (CH_3Si); 16.3 (d, $J_{C,P}$ = 6.4 Hz, CH_3CH_2O); 17.4 (OCH_2CH_2Si); 54.2 (CH_3O); 63.0 (d, $J_{C,P}$ = 5.3 Hz, CH_3CH_2O); 65.9 (OCH_2CH_2Si); 71.8 (NCH_2O); 104.0 (d, $J_{C,P}$ = 14.6 Hz, C-4a); 111.0 (d, $J_{C,P}$ = 15.5 Hz, CH-5); 125.9 (d, $J_{C,P}$ = 215.0 Hz, C-6); 153.8 (CH-2); 154.7 (d, $J_{C,P}$ = 13.8 Hz, C-7a); 163.6 (C-4). IR(KBr): 2980, 2953, 2903, 1595, 1560, 1250, 1079, 1021, 837, 789, 576. HRMS (ESI) calculated for $C_{17}H_{30}N_3O_5SiPNa$ [M+Na]: 438.1583; found 438.1584.

Diethyl (4-chloro-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-chloro-9-NH-7-deazapurine 8-diethyl phosphonate) (28g)



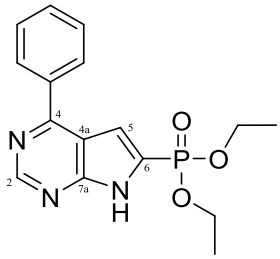
Deazapurine **32** (77 mg, 0.5 mmol) and diethylphosphite **27a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **28g** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28g** was obtained as a white solid (60 mg, 41 %) after chromatography (70 to 80 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 131-132 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.06 - 4.18 (m, 4H, CH_3CH_2O); 7.11 (d, 1H, $J_{5,P}$ = 4.9 Hz, H-5); 8.72 (s, 1H, H-2); 13.34 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.3 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 63.0 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 108.9 (d, $J_{C,P}$ = 17.0 Hz, CH-5); 116.2 (d, $J_{C,P}$ = 15.2 Hz, C-4a); 128.7 (d, $J_{C,P}$ = 215.5 Hz, C-6); 152.9 (C-2); 153.0 (d, $J_{C,P}$ = 1.4 Hz, C-4); 153.6 (d, $J_{C,P}$ = 15.2 Hz, C-7a). IR(KBr): 3055, 2986, 2929, 1589, 1452, 1233, 1036, 967, 851, 570. HRMS (ESI) calculated for $C_{10}H_{14}O_3N_3ClP$ [M+H]: 290.0455; found 290.0455. Anal. Calcd for $C_{10}H_{13}O_3N_3ClP$: C, 41.47; H, 4.52; N, 14.51. Found: C, 41.79; H, 4.62; N, 14.53.

Diisopropyl (4-chloro-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-chloro-9-NH-7-deazapurine 8-diisopropyl phosphonate) (28h)



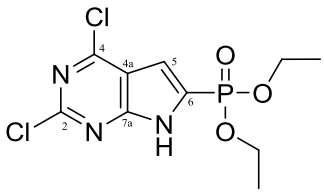
Deazapurine **32** (307 mg, 2.0 mmol) and diisopropylphosphite **27b** (1662 mg, 1.7 mL, 10.0 mmol) were used as starting compounds for the preparation of **28h** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28h** was obtained as a white solid (190 mg, 30 %) after chromatography (70 to 80 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 137-138 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.22 and 1.30 (2×t, 2×6H, $J_{CH3,CH}$ = 6.2 Hz, CH_3-*i*Pr); 4.65 (dsept, 2H, $J_{CH,P}$ = 7.8 Hz, $J_{CH,CH3}$ = 6.2 Hz, CH-*i*Pr); 7.05 (d, 1H, $J_{5,P}$ = 4.9 Hz, H-5); 8.72 (s, 1H, H-2); 13.32 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 23.7 and 24.0 (2×d, $J_{C,P}$ = 4.9 and 4.0 Hz, CH_3-*i*Pr); 71.9 (d, $J_{C,P}$ = 5.4 Hz, CH-*i*Pr); 108.5 (d, $J_{C,P}$ = 16.9 Hz, CH-5); 116.1 (d, $J_{C,P}$ = 15.1 Hz, C-4a); 130.1 (d, $J_{C,P}$ = 215.9 Hz, C-6); 152.8 (CH-2); 152.9 (C-4); 153.6 (d, $J_{C,P}$ = 15.2 Hz, C-7a). IR(KBr): 3059, 2982, 2936, 1592, 1555, 1230, 1095, 1003, 850, 771, 566. HRMS (ESI) calculated for $C_{12}H_{17}N_3O_3ClPNa$ [M+Na]: 340.0588; found 340.0588. Anal. Calcd for $C_{12}H_{17}O_3N_3ClP \cdot 0.1MeOH \cdot 0.05H_2O$: C, 45.16; H, 5.48; N, 13.06. Found: C, 45.11; H, 5.24; N, 12.81.

Diethyl (4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-phenyl-9-NH-7-deazapurine 8-diethyl phosphonate) (28i)



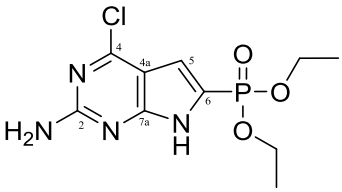
Deazapurine **21** (98 mg, 0.5 mmol) and diethylphosphite **27a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **28i** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28i** was obtained as a white solid (67 mg, 40 %) after chromatography (70 to 80 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 156-157 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.06 - 4.19 (m, 4H, CH_3CH_2O); 7.37 (d, 1H, $J_{5,P}$ = 5.1 Hz, H-5); 7.56 – 7.65 (m, 3H, H-*m*,*p*-Ph); 8.19 (m, 2H, H-*o*-Ph); 8.97 (s, 1H, H-2); 13.02 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.3 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 62.8 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 110.5 (d, $J_{C,P}$ = 17.0 Hz, CH-5); 114.0 (d, $J_{C,P}$ = 14.3 Hz, C-4a); 127.8 (d, $J_{C,P}$ = 215.7 Hz, C-6); 129.0 (CH-*o*-Ph); 129.2 (CH-*m*-Ph); 130.8 (CH-*p*-Ph); 137.4 (C-*i*-Ph); 153.5 (CH-2); 154.4 (d, $J_{C,P}$ = 15.0 Hz, C-7a); 158.4 (d, $J_{C,P}$ = 1.3 Hz, C-4). IR(KBr): 3072, 2986, 2812, 1553, 1428, 1254, 1018, 976, 767, 701, 555. HRMS (ESI) calculated for $C_{16}H_{18}O_3N_3NaP$ [M+Na]: 354.0977; found 354.0978. Anal. Calcd for $C_{16}H_{18}O_3N_3P\cdot0.1$ MeOH: C, 57.81; H, 5.54; N, 12.55. Found: C, 58.06; H, 5.42; N, 12.15.

Diethyl (2,4-dichloro-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (2,6-dichloro-9-NH-7-deazapurine 8-diethyl phosphonate) (28j)



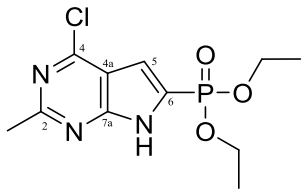
Deazapurine **34** (564 mg, 3 mmol) and diethylphosphite **27a** (2072 mg, 1.92 mL, 15.0 mmol) were used as starting compounds for the preparation of **28j** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28j** was obtained as a brownish solid (379 mg, 39 %) after chromatography (70 to 80 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 190-191 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.07 - 4.17 (m, 4H, CH_3CH_2O); 7.17 (dd, 1H, $J_{5,P}$ = 5.0 Hz, $J_{5,NH}$ = 2.0 Hz, H-5); 13.51 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.3 (d, $J_{C,P}$ = 6.3 Hz, CH_3CH_2O); 63.2 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 109.3 (d, $J_{C,P}$ = 16.8 Hz, CH-5); 115.6 (d, $J_{C,P}$ = 15.3 Hz, C-4a); 129.6 (d, $J_{C,P}$ = 215.0 Hz, C-6); 152.8 and 153.6 (C-2,4); 154.8 (d, $J_{C,P}$ = 15.2 Hz, C-7a). IR(KBr): 2984, 2939, 2806, 1558, 1374, 1235, 1043, 1016, 973, 873, 555. HRMS (ESI) calculated for [M+H]: $C_{10}H_{13}N_3O_3Cl_2P$: 324.0067; found 324.0066. Anal. Calcd for $C_{10}H_{12}O_3N_3Cl_2P\cdot0.05MeOH\cdot0.55H_2O$: C, 35.94; H, 3.66; N, 12.17. Found: C, 35.97; H, 3.99; N, 12.52.

Diethyl (2-amino-4-chloro-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (2-amino-6-chloro-9-NH-7-deazapurine 8-diethyl phosphonate) (28k)



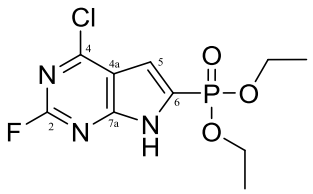
Deazapurine **33** (337 mg, 2 mmol) and diethylphosphite **27a** (1381 mg, 1.37 mL, 10.0 mmol) were used as starting compounds for the preparation of **28k** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28k** was obtained as a yellowish solid (231 mg, 38 %) after chromatography (70 to 80 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 227-228 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.25 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 2.64 (s, 3H, CH_3-2); 4.05 - 4.15 (m, 4H, CH_3CH_2O); 7.04 (d, 1H, $J_{5,P}$ = 4.9 Hz, H-5); 13.09 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.3 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 25.5 (CH_3-2); 63.0 (d, $J_{C,P}$ = 5.3 Hz, CH_3CH_2O); 108.9 (d, $J_{C,P}$ = 16.9 Hz, CH-5); 113.7 (d, $J_{C,P}$ = 15.3 Hz, C-4a); 127.6 (d, $J_{C,P}$ = 216.3 Hz, C-6); 152.6 (C-4); 154.4 (d, $J_{C,P}$ = 15.1 Hz, C-7a); 162.5 (C-2). IR(KBr): 3222, 3091, 2981, 1624, 1557, 1230, 1054, 1028, 960, 791, 562. HRMS (ESI) calculated for $C_{10}H_{14}N_4O_3ClPNa$ [M+Na]: 327.0385; found 327.0384. Anal. Calcd for $C_{10}H_{14}O_3N_4ClP$: C, 39.42; H, 4.63; N, 18.39. Found: C, 39.45; H, 4.43; N, 18.28.

Diethyl (4-chloro-2-methyl-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (2-methyl-6-chloro-9-NH-7-deazapurine 8-diethyl phosphonate) (28l)



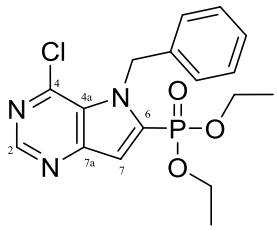
Deazapurine **35** (335 mg, 2 mmol) and diethylphosphite **27a** (1381 mg, 1.37 mL, 10.0 mmol) were used as starting compounds for the preparation of **28l** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28l** was obtained as a white solid (224 mg, 37 %) after chromatography (70 to 80 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 148-149 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.25 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 2.64 (s, 3H, CH_3-2); 4.05 - 4.15 (m, 4H, CH_3CH_2O); 7.04 (d, 1H, $J_{5,P}$ = 4.9 Hz, H-5); 13.09 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.3 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 25.5 (CH_3-2); 63.0 (d, $J_{C,P}$ = 5.3 Hz, CH_3CH_2O); 108.9 (d, $J_{C,P}$ = 16.9 Hz, CH-5); 113.7 (d, $J_{C,P}$ = 15.3 Hz, C-4a); 127.6 (d, $J_{C,P}$ = 216.3 Hz, C-6); 152.6 (C-4); 154.4 (d, $J_{C,P}$ = 15.1 Hz, C-7a); 162.5 (C-2). IR(KBr): 3076, 2984, 2783, 1601, 1397, 1231, 1115, 1016, 983, 886, 553. HRMS (ESI) calculated for $C_{11}H_{15}N_3O_3ClPNa$ [M+Na]: 326.0432; found 326.0431. Anal. Calcd for $C_{11}H_{15}O_3N_3ClP$: C, 43.51; H, 4.98; N, 13.84. Found: C, 43.32; H, 4.84; N, 13.53.

Diethyl (4-chloro-2-fluoro-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (2-fluoro-6-chloro-9-NH-7-deazapurine 8-diethyl phosphonate) (28m)



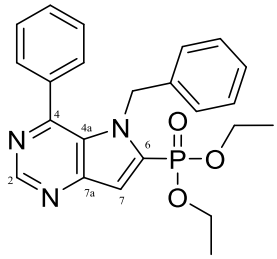
Deazapurine **36** (343 mg, 2 mmol) and diethylphosphite **27a** (1381 mg, 1.37 mL, 10.0 mmol) were used as starting compounds for the preparation of **28m** according to general procedure for C-H phosphonation. Deazapurine phosphonate **28m** was obtained as a white solid (227 mg, 37 %) after chromatography (70 to 80 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 144-145 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.06 - 4.17 (m, 4H, CH_3CH_2O); 7.17 (dd, 1H, $J_{5,P}$ = 5.0 Hz, $J_{5,NH}$ = 2.0 Hz, H-5); 13.48 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.4 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 63.1(d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 109.7 (d, $J_{C,P}$ = 16.9 Hz, CH-5); 115.3 (dd, $J_{C,P}$ = 15.5 Hz, $J_{C,F}$ = 4.2 Hz, C-4a); 129.3 (dd, $J_{C,P}$ = 216.2 Hz, $J_{C,F}$ = 3.4 Hz, C-6); 154.6 (d, $J_{C,F}$ = 18.1 Hz, C-4); 155.0 (dd, $J_{C,F}$ = 17.0 Hz, $J_{C,P}$ = 15.5 Hz, C-7a); 158.0 (d, $J_{C,P}$ = 212.6 Hz, C-2). IR(KBr): 2984, 2942, 2795, 1576, 1410, 1234, 1125, 1016, 974, 920, 561. HRMS (ESI) calculated for [M+H]: $C_{10}H_{13}N_3O_3ClFP$: 308.0360; found 308.0361. Anal. Calcd for $C_{10}H_{12}O_3N_3ClFP{\cdot}0.15MeOH$: C, 38.93; H, 3.81; N, 13.19. Found: C, 39.02; H, 4.00; N, 13.45.

Diethyl (5-benzyl-4-chloro-*5H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phosphonate (6-chloro-7-benzyl-9-deazapurine 8-diethyl phosphonate (38a)



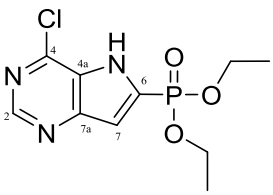
Deazapurine **39** (122 mg, 0.5 mmol) and diethylphosphite **27a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **38a** according to general procedure for C-H phosphonation. Deazapurine phosphonate **38a** was obtained as a brownish oil (57 mg, 30 %) after chromatography (50 to 60 % of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6): 1.10 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 3.95 - 4.10 (m, 4H, CH_3CH_2O); 6.02 (s, 2H, CH_2-Ph); 6.85 (m, 2H, H-*o*-Bn); 7.24 (m, 1H, H-*p*-Bn); 7.29 (m, 2H, H-*m*-Bn); 7.41 (d, 1H, $J_{7,P}$ = 4.5 Hz, H-7); 8.80 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.0 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2O); 50.3 (CH_2-Ph); 63.5 (d, $J_{C,P}$ = 5.7 Hz, CH_3CH_2O); 113.0 (d, $J_{C,P}$ = 16.1 Hz, CH-7); 125.3 (CH-*o*-Bn); 126.7 (d, $J_{C,P}$ = 11.8 Hz, C-4a); 127.4 (CH-*p*-Bn); 128.7 (CH-*m*-Bn); 136.9 (d, $J_{C,P}$ = 209.1 Hz, C-6); 136.4 (C-*i*-Bn); 143.6 (d, $J_{C,P}$ = 2.0 Hz, C-4); 150.0 (d, $J_{C,P}$ = 17.6 Hz, C-7a); 150.5 (C-2). IR(KBr): 2983, 2929, 2848, 1718, 1619, 1455, 1377, 1248, 1015, 734, 564. HRMS (ESI) calculated for $C_{17}H_{19}N_3O_3ClNaP$ [M+Na]: 402.0750; found 402.0744.

Diethyl (5-benzyl-4-phenyl-*5H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phosphonate (6-phenyl-7-benzyl-9-deazapurine 8-diethyl phosphonate (38b)



Deazapurine **22** (143 mg, 0.5 mmol) and diethylphosphite **27a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **38b** according to general procedure for C-H phosphonation. Deazapurine phosphonate **38b** was obtained as a brownish oil (65 mg, 31 %) after chromatography (50 to 60 % of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6): 1.15 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.00 - 4.13 (m, 4H, CH_3CH_2O); 5.46 (s, 2H, CH_2-Ph); 6.17 (m, 2H, H-*o*-Bn); 7.01 (m, 2H, H-*m*-Bn); 7.07 (m, 1H, H-*p*-Bn); 7.28 (m, 2H, H-*o*-Ph); 7.35 (m, 2H, H-*m*-Ph); 7.42 (d, 1H, $J_{7,P}$ = 4.6 Hz, H-7); 7.48 (m, 1H, H-*p*-Ph); 9.01 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.1 (d, $J_{C,P}$ = 6.3 Hz, CH_3CH_2O); 50.6 (CH_2-Ph); 63.4 (d, $J_{C,P}$ = 5.8 Hz, CH_3CH_2O); 112.9 (d, $J_{C,P}$ = 16.1 Hz, CH-7); 125.0 (CH-*o*-Bn); 127.0 (CH-*p*-Bn); 127.8 (d, $J_{C,P}$ = 10.9 Hz, C-4a); 128.0 (CH-*o*-Ph); 128.2 (CH-*m*-Bn); 129.0 (CH-*m*-Ph); 129.5 (CH-*p*-Ph); 136.2 (d, $J_{C,P}$ = 209.9 Hz, C-6); 136.7 (C-*i*-Ph); 137.3 (C-*i*-Bn); 149.6 (d, $J_{C,P}$ = 17.4 Hz, C-7a); 150.9 (CH-2); 153.0 (d, $J_{C,P}$ = 1.9 Hz, C-4). IR(KBr): 3494, 2983, 2923, 1559, 1353, 1248, 1015, 976, 695, 555. HRMS (ESI) calculated for $C_{23}H_{25}O_3N_3P$ [M+H]: 422.1631; found 422.1628.

Diethyl (4-chloro-*5H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phosphonate (6-chloro-7-NH-9-deazapurine 8-diethyl phosphonate (38c)

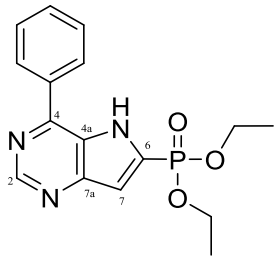


Deazapurine **40** (115 mg, 0.75 mmol) and diethylphosphite **27a** (518 mg, 0.51 mL, 3.75 mmol) were used as starting compounds for the preparation of **38c** according to general procedure for C-H phosphonation. Deazapurine phosphonate **38c** was obtained as a brownish solid (80 mg, 37 %) after chromatography (70 to 80 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. > 200 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6): 1.28 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 4.09 - 4.21 (m, 4H, CH_3CH_2O); 7.22 (d, 1H, $J_{7,P}$ = 4.2 Hz, H-7); 8.75 (s, 1H, H-2); 13.25 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.3 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2O); 63.2 (d, $J_{C,P}$ = 5.5 Hz, CH_3CH_2O); 111.3 (d, $J_{C,P}$ = 17.6 Hz, CH-7); 127.2 (d, $J_{C,P}$ = 13.2 Hz, C-4a); 134.7 (d, $J_{C,P}$ = 211.9 Hz, C-6); 144.1 (d, $J_{C,P}$ = 1.9 Hz, C-4); 149.5 (d, $J_{C,P}$ = 17.6 Hz, C-7a); 150.2 (CH-2). IR(KBr): 3494, 3052, 2995, 1604, 1473, 1233, 1027, 967, 824, 567. HRMS (ESI) calculated for $C_{10}H_{14}O_3N_3ClP$ [M+H]: 290.0457;

found 290.0455. Anal. Calcd for $C_{10}H_{13}O_3N_3ClP$: C, 41.47; H, 4.52; N, 14.51. Found: C, 41.74; H, 4.74; N, 14.13.

Diethyl (4-phenyl-*5H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phosphonate

(6-phenyl -7-NH-9-deazapurine 8-diethyl phosphonate (38d)



Deazapurine **23** (98 mg, 0.5 mmol) and diethylphosphite **27a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **38d** according to general procedure for C-H phosphonation. Deazapurine phosphonate **38d** was obtained as a yellowish solid (60 mg, 36 %) after chromatography (70 to 80 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 149-150 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.28 (2×t, 2×3H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.10 - 4.19 (m, 4H, CH_3CH_2O); 7.21 (d, 1H, $J_{7,P}$ = 4.3 Hz, H-7); 7.56 – 7.66 (m, 3H, H-*m*,*p*-Ph); 8.06 (m, 2H, H-*o*-Ph); 9.01 (s, 1H, H-2); 12.64 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.4 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 63.0 (d, $J_{C,P}$ = 5.5 Hz, CH_3CH_2O); 111.4 (d, $J_{C,P}$ = 17.2 Hz, CH-7); 126.8 (d, $J_{C,P}$ = 12.0 Hz, C-4a); 128.9 (CH-*m*-Ph); 129.4 (CH-*o*-Ph); 130.6 (CH-*p*-Ph); 134.0 (d, $J_{C,P}$ = 212.1 Hz, C-6); 135.7 (C-*i*-Ph); 149.7 (d, $J_{C,P}$ = 17.2 Hz, C-7a); 150.6 (d, $J_{C,P}$ = 1.7 Hz, CH-2); 151.2 (CH-2). IR(KBr): 3144, 3060, 2980, 1550, 1413, 1236, 1024, 800, 701, 537. HRMS (ESI) calculated for $C_{16}H_{18}O_3N_3NaP$ [M+Na]: 354.0977; found 354.0978. Anal. Calcd for $C_{16}H_{18}O_3N_3P$: C, 58.00; H, 5.48; N, 12.68. Found: C, 57.70; H, 5.31; N, 12.51.

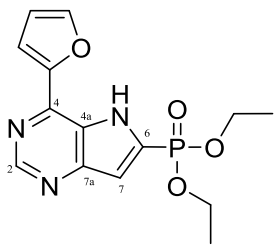
General procedure for synthesis of 6-(het)aryl-7-deazapurine phosphonates by aqueous Suzuki-Miyaura cross-coupling reaction:

A mixture of diethyl (4-chloro-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate **28g** (0.75 mmol), boronic acid (1.5 mmol), Na_2CO_3 (238 mg, 2.25 mmol), $Pd(OAc)_2$ (8.4 mg, 0.038 mmol) and TPPTS (53 mg, 0.094 mmol) in H_2O/MeCN (2:1, 2.25 mL) was stirred at 100 °C for 1 h. After cooling, the reaction mixture was filtered through a layer of celite and silica and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel using hexanes/ethyl acetate to give the pure product.

Diethyl (4-(furan-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate

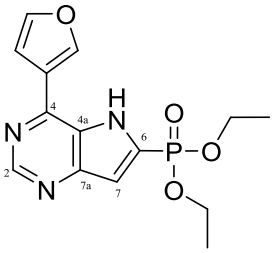
(6-(furan-2-yl)-9-NH-7-deazapurine 8-diethyl phosphonate) (41a)

Substituted deazapurine phosphonate **41a** was prepared according to general procedure for aqeous Suzuki-Miyaura cross-coupling reaction by using **28g** (217 mg, 0.75 mmol) and furan-



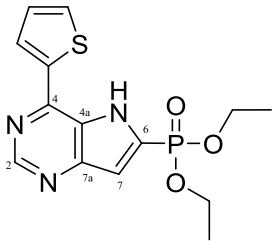
2-boronic acid (168 mg, 1.5 mmol) as starting compounds**.** Product **41a** was obtained as a yellowish solid (171 mg, 71 %) after chromatography (80 to 90 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 141-142 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 4.06 - 4.17 (m, 4H, CH_3CH_2O); 6.80 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 7.47 (dd, 1H, $J_{5,P}$ = 5.0 Hz, $J_{5,NH}$ = 1.4 Hz, H-5); 7.53 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 8.12 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 8.83 (s,1H, H-2); 12.94 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.4 (d, $J_{C,P}$ = 6.6 Hz, CH_3CH_2O); 62.8 (d, $J_{C,P}$ = 5.7 Hz, CH_3CH_2O); 111.0 (d, $J_{C,P}$ = 17.2 Hz, CH-5); 111.1 (d, $J_{C,P}$ = 15.2 Hz, C-4a); 113.0 (CH-4-furyl); 114.1 (CH-3-furyl); 127.7 (d, $J_{C,P}$ = 216.0 Hz, C-6); 147.2 (CH-5-furyl); 148.3 (C-4); 152.5 (C-2-furyl); 153.5 (CH-2); 154.5 (d, $J_{C,P}$ = 15.0 Hz, C-7a). IR(KBr): 3106, 2977, 2814, 1588, 1553, 1257, 1017, 956, 848, 773, 569. HRMS (ESI) calculated for $C_{14}H_{16}O_4N_3PNa$ [M+Na]: 344.0772; found 344.0770. Anal. Calcd for $C_{14}H_{16}O_4N_3P{\cdot}0.2H_2O$: C, 51.76; H, 5.09; N, 12.93. Found: C, 51.99; H, 4.95; N, 12.57.

Diethyl (4-(furan-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-(furan-3-yl)-9-NH-7-deazapurine 8-diethyl phosphonate) (41b)



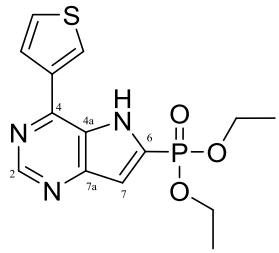
Substituted deazapurine phosphonate **41b** was prepared according to general procedure for aqeous Suzuki-Miyaura cross-coupling reaction by using **28g** (217 mg, 0.75 mmol) and furan-3-boronic acid (168 mg, 1.5 mmol) as starting compounds**.** Product **41b** was obtained as a brownish solid (157 mg, 65 %) after chromatography (80 to 90 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 149-150 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.28 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.08 - 4.17 (m, 4H, CH_3CH_2O); 7.27 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.49 (d, 1H, $J_{5,P}$ = 5.1 Hz, H-5); 7.90 (t, 1H, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, H-5-furyl); 8.85 (s, 1H, H-2); 8.85 (m, 1H, H-2-furyl); 12.91 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.3 (d, $J_{C,P}$ = 6.4 Hz, CH_3CH_2O); 62.8 (d, $J_{C,P}$ = 5.2 Hz, CH_3CH_2O); 109.6 (CH-4-furyl); 110.1 (d, $J_{C,P}$ = 17.2 Hz, CH-5); 113.1 (d, $J_{C,P}$ = 14.3 Hz, C-4a); 124.9 (C-3-furyl); 127.3 (d, $J_{C,P}$ = 216.4 Hz, C-6); 144.9 (CH-5-furyl); 145.7 (CH-2-furyl); 152.2 (d, $J_{C,P}$ = 1.9 Hz, C-4); 153.4 (CH-2); 153.9 (d, $J_{C,P}$ = 14.9 Hz, C-7a). IR(KBr): 3122, 2977, 2812, 1579, 1341, 1239, 1013, 970, 846, 740, 574. HRMS (ESI) calculated for $C_{14}H_{16}O_4N_3PNa$ [M+Na]: 344.0772; found 344.0770. Anal. Calcd for $C_{14}H_{16}O_4N_3P$: C, 52.34; H, 5.02; N, 13.08. Found: C, 52.25; H, 5.01; N, 12.86.

Diethyl (4-(thiophen-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-(thiophen-2-yl)-9-NH-7-deazapurine 8-diethyl phosphonate) (41c)



Substituted deazapurine phosphonate **41c** was prepared according to general procedure for aqeous Suzuki-Miyaura cross-coupling reaction by using **28g** (145 mg, 0.5 mmol) and thiophen-2-boronic acid (128 mg, 1.0 mmol) as starting compounds**.** Product **41c** was obtained as a yellowish solid (110 mg, 65 %) after chromatography (80 to 90 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 156-157 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.28 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.08 - 4.18 (m, 4H, CH_3CH_2O); 7.31 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.8 Hz, H-4-thienyl); 7.55 (d, 1H, $J_{5,P}$ = 5.1 Hz, H-5); 7.90 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.1 Hz, H-5-thienyl); 8.28 (dd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 8.82 (s, 1H, H-2); 13.01 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.4 (d, $J_{C,P}$ = 6.2 Hz, CH_3CH_2O); 62.9 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 110.1 (d, $J_{C,P}$ = 17.0 Hz, CH-5); 111.6 (d, $J_{C,P}$ = 14.5 Hz, C-4a); 127.9 (d, $J_{C,P}$ = 216.0 Hz, C-6); 129.5 (CH-4-thienyl); 130.8 (CH-3-thienyl); 131.6 (CH-5-thienyl); 142.2 (C-2-thienyl); 152.2 (d, $J_{C,P}$ = 1.4 Hz, C-4); 153.3 (CH-2); 154.4 (d, $J_{C,P}$ = 15.0 Hz, C-7a). IR(KBr): 3067, 2982, 2813, 1561, 1440, 1254, 1016, 968, 832, 703, 559. HRMS (ESI) calculated for $C_{14}H_{16}O_3N_3SPNa$ [M+Na]: 360.0542; found 360.0542. Anal. Calcd for $C_{14}H_{16}O_3N_3SP$: C, 49.85; H, 4.78; N, 12.46. Found: C, 49.72; H, 4.54; N, 12.20.

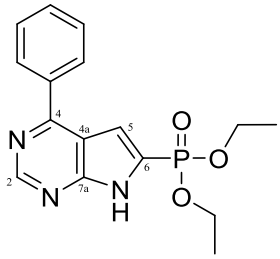
(4-(thiophen-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-(thiophen-3-yl)-9-NH-7-deazapurine 8-diethyl phosphonate) (41d)



Substituted deazapurine phosphonate **41d** was prepared according to general procedure for aqeous Suzuki-Miyaura cross-coupling reaction by using **28g** (217 mg, 0.75 mmol) and thiophen-3-boronic acid (192 mg, 1.5 mmol) as starting compounds**.** Product **41d** was obtained as a brownish solid (182 mg, 72 %) after chromatography (80 to 90 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 158-159 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.28 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.08 - 4.18 (m, 4H, CH_3CH_2O); 7.51 (dd, 1H, $J_{5,P}$ = 5.1 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.75 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.96 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 8.65 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 8.88 (s, 1H, H-2); 12.95 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.4 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2O); 62.8 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 110.4 (d, $J_{C,P}$ = 17.1 Hz, CH-5); 113.1 (d, $J_{C,P}$ = 14.3 Hz, C-4a); 127.5 (CH-5-thienyl); 127.6 (d, $J_{C,P}$ =

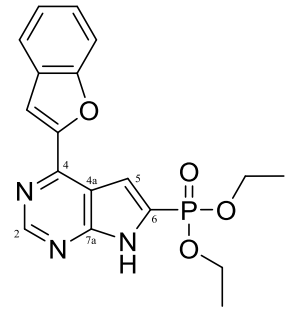
216.0 Hz, C-6); 127.7 (CH-4-thienyl); 129.7 (CH-2-thienyl); 139.7 (C-3-thienyl); 153.4 (CH-2); 153.6 (d, $J_{C,P}$ = 1.4 Hz, C-4); 154.4 (d, $J_{C,P}$ = 14.9 Hz, C-7a). IR(KBr): 3106, 2977, 2814, 1588, 1553, 1257, 1017, 956, 848, 773, 569. HRMS (ESI) calculated for $C_{14}H_{16}O_3N_3SPNa$ [M+Na]: 360.0544; found 360.0542. Anal. Calcd for $C_{14}H_{16}O_3N_3SP \cdot 0.15H_2O$: C, 49.45; H, 4.83; N, 12.36. Found: C, 49.73; H, 4.63; N, 11.97.

Diethyl (4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-phenyl-9-NH-7-deazapurine 8-diethyl phosphonate) (41e)



Substituted deazapurine phosphonate **41e** was prepared according to general procedure for aqeous Suzuki-Miyaura cross-coupling reaction by using **28g** (217 mg, 0.75 mmol) and phenylboronic acid (183 mg, 1.5 mmol) as starting compounds**.** Product **41e** was obtained as a white solid (186 mg, 75 %) after chromatography (80 to 90 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 156-157 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.06 - 4.19 (m, 4H, CH_3CH_2O); 7.37 (d, 1H, $J_{5,P}$ = 5.1 Hz, H-5); 7.56 – 7.65 (m, 3H, H-*m*,*p*-Ph); 8.19 (m, 2H, H-*o*-Ph); 8.97 (s, 1H, H-2); 13.02 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.3 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 62.8 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 110.5 (d, $J_{C,P}$ = 17.0 Hz, CH-5); 114.0 (d, $J_{C,P}$ = 14.3 Hz, C-4a); 127.8 (d, $J_{C,P}$ = 215.7 Hz, C-6); 129.0 (CH-*o*-Ph); 129.2 (CH-*m*-Ph); 130.8 (CH-*p*-Ph); 137.4 (C-*i*-Ph); 153.5 (CH-2); 154.4 (d, $J_{C,P}$ = 15.0 Hz, C-7a); 158.4 (d, $J_{C,P}$ = 1.3 Hz, C-4). IR(KBr): 3072, 2986, 2812, 1553, 1428, 1254, 1018, 976, 767, 701, 555. HRMS (ESI) calculated for $C_{16}H_{18}O_3N_3NaP$ [M+Na]: 354.0977; found 354.0978. Anal. Calcd for $C_{16}H_{18}O_3N_3P \cdot 0.1$ MeOH: C, 57.81; H, 5.54; N, 12.55. Found: C, 58.06; H, 5.42; N, 12.15.

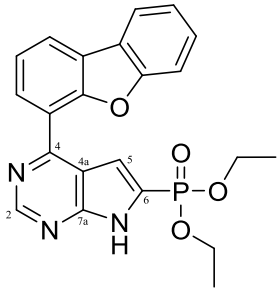
Diethyl (4-(benzofuran-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-(benzofuran-2-yl)-9-NH-7-deazapurine 8-diethyl phosphonate) (41f)



Substituted deazapurine phosphonate **41f** was prepared according to general procedure for aqeous Suzuki-Miyaura cross-coupling reaction by using **28g** (174 mg, 0.6 mmol) and benzofuran-2-boronic acid (194 mg, 1.2 mmol) as starting compounds**.** Product **41f** was obtained as a yellowish solid (149 mg, 67 %) after chromatography (80 to 90 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. > 200 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6): 1.30 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.10 - 4.20 (m, 4H, CH_3CH_2O); 7.37 (ddd, 1H, $J_{5,4}$ = 7.8 Hz, $J_{5,6}$ = 7.2

Hz, $J_{5,7}$ = 1.0 Hz, H-5-benzofuryl); 7.50 (ddd, 1H, $J_{6,7}$ = 8.3 Hz, $J_{6,5}$ = 7.2 Hz, $J_{6,4}$ = 1.3 Hz, H-6-benzofuryl); 7.66 (dd, 1H, $J_{5,P}$ = 5.0 Hz, $J_{5,NH}$ = 2.0 Hz, H-5); 7.83 (ddd, 1H, $J_{4,5}$ = 7.8 Hz, $J_{4,6}$ = 1.3 Hz, $J_{4,7}$ = 0.8 Hz, H-4-benzofuryl); 7.87 (dq, 1H, $J_{7,6}$ = 8.3 Hz, $J_{7,5} = J_{7,4} = J_{7,3}$ = 0.8 Hz, H-7-benzofuryl); 8.01 (d, 1H, $J_{3,7}$ = 1.0 Hz, H-3-benzofuryl); 8.95 (s,1H, H-2); 13.07 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.4 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 62.9 (d, $J_{C,P}$ = 5.3 Hz, CH_3CH_2O); 109.9 (CH-3-benzofuryl); 111.1 (d, $J_{C,P}$ = 17.2 Hz, CH-5); 112.2 (CH-7-benzofuryl); 112.3 (d, $J_{C,P}$ = 15.2 Hz, C-4a); 122.8 (CH-4-benzofuryl); 124.1 (CH-5-benzofuryl); 127.0 (CH-6-benzofuryl); 128.9 (C-3a-benzofuryl); 128.5 (d, $J_{C,P}$ = 215.6 Hz, C-6); 148.3 (C-4); 153.5 (CH-2); 154.0 (C-2-benzofuryl); 154.7 (d, $J_{C,P}$ = 15.2 Hz, C-7a); 155.7 (C-7a-benzofuryl). IR(KBr): 3059, 2985, 2811, 1583, 1337, 1249, 1052, 1022, 973, 856, 750, 550. HRMS (ESI) calculated for $C_{18}H_{18}O_4N_3PNa$ [M+Na]: 394.0927; found 394.0927. Anal. Calcd for $C_{18}H_{18}O_4N_3P \cdot 0.45H_2O$: C, 56.98; H, 5.02; N, 11.07. Found: C, 57.32; H, 4.77; N, 10.75.

Diethyl (4-(dibenzofuran-4-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonate (6-(dibenzofuran-4-yl)-9-NH-7-deazapurine 8-diethyl phosphonate) (41g)



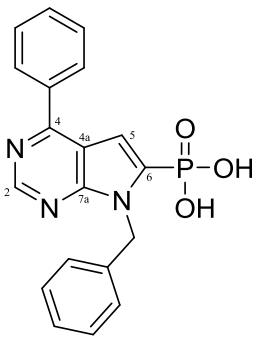
Substituted deazapurine phosphonate **41g** was prepared according to general procedure for aqeous Suzuki-Miyaura cross-coupling reaction by using **28g** (174 mg, 0.6 mmol) and dibenzofuran-4-boronic acid (255 mg, 1.2 mmol) as starting compounds**.** Product **41g** was obtained as a yellowish solid (152 mg, 60 %) after chromatography (80 to 90 % of EtOAc in hexanes) which was crystalized from MeOH-H_2O. M. p. 199-200 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 1.26 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 4.07 - 4.18 (m, 4H, CH_3CH_2O); 7.15 (bd, 1H, $J_{5,P}$ = 5.0 Hz, H-5); 7.48 (bt, 1H, $J_{8,7} = J_{8,9}$ = 7.5 Hz, H-8-$C_{12}H_7O$); 7.58 (dt, 1H, $J_{7,6} = J_{7,8}$ = 7.7 Hz, H-7-$C_{12}H_7O$); 7.64 (t, 1H, $J_{2,1} = J_{2,3}$ = 7.7 Hz, H-2-$C_{12}H_7O$); 7.68 (dm, 1H, $J_{6,7}$ = 8.2 Hz, H-6-$C_{12}H_7O$); 8.04 (dd, 1H, $J_{3,2}$ = 7.6 Hz, $J_{3,1}$ = 1.4 Hz, H-3-$C_{12}H_7O$); 8.27 (ddd, 1H, $J_{9,8}$ = 7.7 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.7 Hz, H-9-$C_{12}H_7O$); 8.39 (dd, 1H, $J_{1,2}$ = 7.7 Hz, $J_{1,3}$ = 1.4 Hz, H-1-$C_{12}H_7O$); 9.09 (s, 1H, H-2); 13.08 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.3 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 62.9 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 111.0 (d, $J_{C,P}$ = 16.7 Hz, CH-5); 111.8 (CH-6-$C_{12}H_7O$); 115.7 (d, $J_{C,P}$ = 14.5 Hz, C-4a); 121.6 (CH-9-$C_{12}H_7O$); 122.3 (C-4-$C_{12}H_7O$); 123.4 (CH-1-$C_{12}H_7O$); 123.4 (C-9a-$C_{12}H_7O$); 123.7 and 123.7 (CH-2,8-$C_{12}H_7O$); 125.0 (C-9b-$C_{12}H_7O$); 127.5 (d, $J_{C,P}$ = 215.6 Hz, C-6); 128.3 (CH-7-$C_{12}H_7O$); 128.8 (CH-3-$C_{12}H_7O$); 152.9 (C-4a-$C_{12}H_7O$); 153.6 (CH-2); 154.0 (d, $J_{C,P}$ = 15.0 Hz, C-7a); 155.6 (C-5a-

$C_{12}H_7O$); 155.8 (C-4). IR(KBr): 3082, 2984, 2815, 1587, 1564, 1253, 1188, 1019, 962, 850, 758, 528. HRMS (ESI) calculated for $C_{22}H_{20}O_4N_3PNa$ [M+Na]: 444.1084; found 444.1083. Anal. Calcd for $C_{22}H_{20}O_4N_3P$: C, 62.71; H, 4.78; N, 9.97. Found: C, 62.66; H, 4.78; N, 9.64.

General procedure for synthesis of 7-deazapurine-8-phosphonic acids:

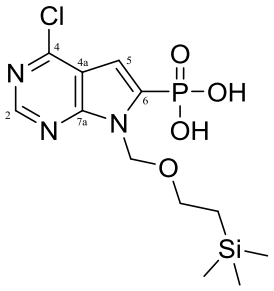
TMSBr (8.25 mmol, 1.09 mL) was added dropwise to the mixture of 7-deazapurine phosphonate **28a, 28d, 28e, 28g** or **28i** (0.825 mmol) in MeCN (5 mL), and the reaction mixture was stirred for 24h at room temperature. After concentration in vacuo and co-distillation with MeCN, crude reaction mixture was treated with water, sonicated, and formed precipitate was filtered off. Purification was done by reverse phase flash column chromatography (C-18, eluting water/MeOH).

(7-Benzyl-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonic acid
(6-phenyl-9-benzyl-7-deazapurine-8-phosphonic acid) (42a)



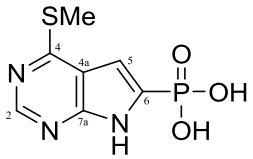
Deazapurine phosphonic acid **42a** was prepared according to general procedure from deazapurine phosphonate **28a** (347 mg, 0.825 mmol) and TMSBr (1263 mg, 1.09 mL, 8.25 mmol). Product **42a** was obtained as a white solid (226 mg, 75 %) which was purified by reverse phase flash column chromatography and crystalized from MeOH-H_2O. M. p. 279-280 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 5.74 (s, 2H, CH_2-Ph); 7.21 (m, 1H, H-*p*-Bn); 7.23 – 7.28 (m, 5H, H-5, H-*o*,*m*-Bn); 7.56 – 7.64 (m, 3H, H-*m*,*p*-Ph); 8.12 (m, 2H, H-*o*-Ph); 8.91 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 47.3 (CH_2-Ph); 108.1 (d, $J_{C,P}$ = 15.3 Hz, CH-5); 114.0 (d, $J_{C,P}$ = 13.2 Hz, C-4a); 127.3 (CH-*p*-Bn); 127.4 (CH-*o*-Bn); 128.4 (CH-*m*-Bn); 128.9 (CH-*o*-Ph); 129.3 (CH-*m*-Ph); 130.9 (CH-*p*-Ph); 136.4 (d, $J_{C,P}$ = 203.0 Hz, C-6); 137.4 (C-*i*-Ph); 137.9 (C-*i*-Bn); 152.8 (CH-2); 153.3 (d, $J_{C,P}$ = 12.6 Hz, C-7a); 157.8 (C-4). IR(KBr): 3064, 3029, 2924, 1600, 1574, 1413, 1036, 917, 779, 607, 577, 472. HRMS (ESI) calculated for $C_{19}H_{15}O_3N_3P$ [M-H]: 364.0852; found 364.0856. Anal. Calcd for $C_{19}H_{16}O_3N_3P{\cdot}0.4H_2O$: C, 61.26; H, 4.55; N, 11.28. Found: C, 60.96; H, 4.15; N, 11.13.

(4-Chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonic acid
(6-chloro-9-[2-(trimethylsilyl)ethoxy)methyl]-7-deazapurine-8-phosphonic acid) (42b)



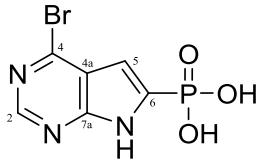
Deazapurine phosphonic acid **42b** was prepared according to general procedure with addition of 2,6-lutidine (429 mg, 0.47 mL, 4.0 mmol) to deazapurine phosphonate **28d** (170 mg, 0.4 mmol) and TMSBr (612 mg, 0.52 mL, 4.0 mmol). Product **42b** was obtained as a yellowish solid (80 mg, 55 %) which was purified by reverse phase flash column chromatography and crystalized from MeOH-H_2O. M. p. > 200 °C (dec). ^{1}H NMR (500 MHz, D_2O): -0.20 (s, 9H, CH_3Si); 0.79 (m, 2H, OCH_2CH_2Si); 3.61 (m, 2H, OCH_2CH_2Si); 5.79 (s, 2H, NCH_2O); 6.97 (d, 1H, $J_{5,P}$ = 4.8 Hz, H-5); 8.31 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, D_2O): -2.0 (CH_3Si); 17.9 (OCH_2CH_2Si); 67.6 (OCH_2CH_2Si); 73.1 (NCH_2O); 108.1 (d, $J_{C,P}$ = 13.9 Hz, CH-5); 117.9 (d, $J_{C,P}$ = 13.4 Hz, C-4a); 140.5 (d, $J_{C,P}$ = 191.0 Hz, C-6); 151.6 (CH-2); 153.4 (C-4); 153.6 (d, $J_{C,P}$ = 11.5 Hz, C-7a). IR(KBr): 3056, 2954, 2893, 1586, 1456, 1251, 1075, 837, 778, 567. HRMS (ESI) calculated for $C_{12}H_{18}O_4N_3ClPSi$ [M-H]: 362.0498; found 362.0498.

(4-(Methylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonic acid (6-(methylsulfanyl)-9-NH-7-deazapurine-8-phosphonic acid) (42c)



Deazapurine phosphonic acid **42c** was prepared according to general procedure from deazapurine phosphonate **28e** (500 mg, 1.15 mmol) and TMSBr (1760 mg, 1.48 mL, 11.5 mmol). Product **42c** was obtained as a white solid (250 mg, 89 %) which was purified by reverse phase flash column chromatography and crystalized from MeOH-H_2O. M. p. 223-224 °C. ^{1}H NMR (500 MHz, D_2O): 2.52 (s, 3H, CH_3S); 6.68 (bd, 1H, $J_{5,P}$ = 3.5 Hz, H-5); 8.24 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, D_2O): 12.1 (CH_3S); 105.2 (d, $J_{C,P}$ = 14.6 Hz, CH-5); 116.1 (d, $J_{C,P}$ = 13.0 Hz, C-4a); 136.1 (d, $J_{C,P}$ = 198.1 Hz, C-6); 149.0 (d, $J_{C,P}$ = 12.2 Hz, C-7a); 151.3 (CH-2); 163.8 (C-4). IR(KBr): 3324, 3252, 2812, 1682, 1410, 1234, 1165, 1021, 869, 621, 594. HRMS (ESI) calculated for $C_7H_7O_3N_3PS$ [M-H]: 243.9946; found 243.9951.

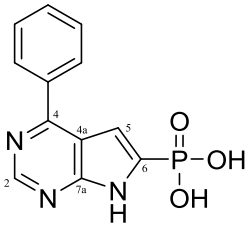
(4-Bromo-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonic acid (6-bromo-9-NH-7-deazapurine-8-phosphonic acid) (42d)



Deazapurine phosphonic acid **42d** was prepared according to general procedure from deazapurine phosphonate **28g** (723 mg, 2.5 mmol) and TMSBr (3827 mg, 3.3 mL, 25.0 mmol). Product **42d** was obtained as a white solid (532 mg, 77 %) which was purified by reverse phase flash column chromatography and crystalized from MeOH-H_2O. M. p. 228-229 °C. ^{1}H NMR

(500 MHz, D_2O): 6.72 (d, 1H, $J_{5,P}$ = 4.5 Hz, H-5); 8.29 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, D_2O): 105.7 (d, $J_{C,P}$ = 14.1 Hz, CH-5); 121.2 (d, $J_{C,P}$ = 13.2 Hz, C-4a); 140.9 (d, $J_{C,P}$ = 186.0 Hz, C-6); 143.9 (C-4); 150.3 (CH-2); 150.8 (d, $J_{C,P}$ = 12.0 Hz, C-7a). IR(KBr): 3075, 2949, 2818, 1565, 1444, 1344, 1150, 1022, 967, 845, 776, 560. HRMS (ESI) calculated for $C_6H_4O_3N_3PBr$ [M-H]: 275.9174; found 275.9179.

(4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)phosphonic acid (6-phenyl-9-NH-7-deazapurine-8-phosphonic acid) (42e)



Deazapurine phosphonic acid **42e** was prepared according to general procedure from deazapurine phosphonate **28i** (133 mg, 0.4 mmol) and TMSBr (612 mg, 0.52 mL, 4.0 mmol). Product **42e** was obtained as a yellowish solid (70 mg, 63 %) which was purified by reverse phase flash column chromatography and crystalized from MeOH-H_2O. M. p. > 200 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6): 7.13 (bd, 1H, $J_{5,P}$ = 3.5 Hz, H-5); 7.57 (m, 1H, H-*p*-Ph); 7.61 (m, 2H, H-*m*-Ph); 8.14 (m, 2H, H-*o*-Ph); 8.89 (s, 1H, H-2); 12.80 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 106.9 (d, $J_{C,P}$ = 16.5 Hz, CH-5); 114.1 (d, $J_{C,P}$ = 12.8 Hz, C-4a); 128.8 (CH-*o*-Ph); 129.2 (CH-*m*-Ph); 130.6 (CH-*p*-Ph); 134.6 (d, $J_{C,P}$ = 203.9 Hz, C-6); 137.7 (C-*i*-Ph); 152.5 (CH-2); 154.1 (d, $J_{C,P}$ = 13.4 Hz, C-7a); 157.3 (C-4). IR(KBr): 3047, 2783, 1595, 1415, 1165, 1066, 956, 765, 605, 557. HRMS (ESI) calculated for $C_{12}H_9O_3N_3P$ [M-H]: 274.0383; found 274.0387.

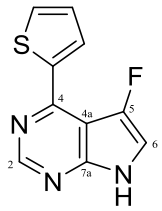
5.7 Synthesis of 2-substituted 6-(het)aryl-7-deazapurines

General procedure for aqeous Suzuki-Miyaura cross-coupling reaction:

An argon-purged mixture of 4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidine derivative (compounds **33-37**, 1 mmol), boronic acid (1.5 mmol), Na_2CO_3 (318 mg, 3 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol) and TPPTS (71 mg, 0.125 mmol) in water/MeCN (2:1, 5 mL) was stirred at 100 °C for 3 h. After cooling, the precipitated product was dissolved by stirring with added CH_2Cl_2 (25 mL) and MeOH (10 mL) and the mixture was loaded onto silica by co-evaporation. Purification by chromatography through a short column of silica (mobile phase is given for individual products) afforded pure solid products, which were crystallized as indicated.

5-Fluoro-4-(thiophen-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine

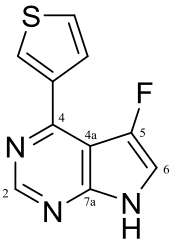
(6-(thiophen-2-yl)-7-fluoro-9-NH-7-deazapurine (43a)



Compound **43a** was prepared from **37** (172 mg, 1 mmol) and thiophene-2-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a brownish solid (165 mg, 75 %), which was crystallized from MeOH/water. R_f = 0.38 ($CHCl_3$-MeOH, 10:1). M.p. 278-279 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 7.30 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,3}$ = 3.8 Hz, H-4-thienyl); 7.69 (t, 1H, $J_{6,F}$ = $J_{6,NH}$ = 2.5 Hz, H-6); 7.86 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,3}$ = 1.1 Hz, H-5-thienyl); 8.07 (dd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,5}$ = 1.1 Hz, H-3-thienyl); 8.71 (s, 1H, H-2); 12.21 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 101.47 (d, $J_{C,F}$ = 14.6 Hz, C-4a); 110.59 (d, $J_{C,F}$ = 30.0 Hz, CH-6); 129.23 (d, $J_{C,F}$ = 2.7 Hz, CH-4-thienyl); 129.80 (d, $J_{C,F}$ = 16.4 Hz, CH-3-thienyl); 131.45 (CH-5-thienyl); 140.92 (d, $J_{C,F}$ = 243.4 Hz, C-5); 142.52 (d, $J_{C,F}$ = 1.6 Hz, C-2-thienyl); 147.69 (d, $J_{C,F}$ = 3.7 Hz, C-7a); 149.80 (d, $J_{C,F}$ = 4.0 Hz, C-4); 151.48 (CH-2). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -158.32 (s, 1F, F-5). IR(KBr): 3105, 2990, 2830, 1565, 1446, 1365, 815, 785, 737, 594 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3FS$ [M+H]: 220.0339; found: 220.0339.

5-Fluoro-4-(thiophen-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine

(6-(thiophen-3-yl)-7-fluoro-9-NH-7-deazapurine (43b)

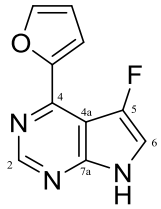


Compound **43b** was prepared from **37** (172 mg, 1 mmol) and thiophene-3-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a brownish solid (170 mg, 72 %), which was crystallized from MeOH/water. R_f = 0.38 ($CHCl_3$-MeOH, 10:1). M. p. 261-262 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 7.66 (t, 1H, $J_{6,F}$ = $J_{6,NH}$ = 2.5 Hz, H-6); 7.72 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.84 (bddd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,2}$ = 1.4 Hz, $J_{4,F}$ = 0.8 Hz, H-4-thienyl); 8.34 (ddd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.4 Hz, $J_{2,F}$ = 0.6 Hz, H-2-thienyl); 8.78 (s, 1H, H-2); 12.15 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 103.14 (d, $J_{C,F}$ = 14.2 Hz, C-4a); 110.26 (d, $J_{C,F}$ = 29.7 Hz, CH-6); 127.08 (d, $J_{C,F}$ = 1.1 Hz, CH-5-thienyl); 127.99 (d, $J_{C,F}$ = 5.9 Hz, CH-4-thienyl); 128.99 (d, $J_{C,F}$ = 11.3 Hz, CH-2-thienyl); 139.53 (d, $J_{C,F}$ = 1.4 Hz, C-3-thienyl); 140.93 (d, $J_{C,F}$ = 243.9 Hz, C-5); 147.66 (d, $J_{C,F}$ = 3.5 Hz, C-4); 151.25 (d, $J_{C,F}$ = 4.1 Hz, C-4); 151.74 (CH-2). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -158.51 (s, 1F, F-5). IR(KBr): 3105, 2983, 2836, 1559, 1467, 1347, 842, 782,

734, 591 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3FS$ [M+H]: 220.0339; found: 220.0339. Anal. Calcd for $C_{10}H_6FN_3S$: C, 54.79; H, 2.76; N, 19.17. Found: C, 55.01; H, 2.97; N, 18.83.

5-Fluoro-4-(furan-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine

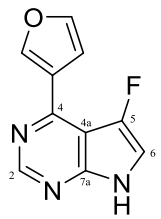
6-(furan-2-yl)-7-fluoro-9-NH-7-deazapurine (43c)



Compound **43c** was prepared from **37** (172 mg, 1 mmol) and furan-2-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a brownish solid (140 mg, 69 %), which was crystallized from MeOH/water. R_f = 0.42 ($CHCl_3$-MeOH, 10:1). M. p. 262-263 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 6.78 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 7.44 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.65 (t, 1H, $J_{6,F}$ = $J_{6,NH}$ = 2.6 Hz, H-6); 8.05 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 8.74 (s, 1H, H-2); 12.15 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 101.19 (d, $J_{C,F}$ = 15.1 Hz, C-4a); 110.62 (d, $J_{C,F}$ = 29.2 Hz, CH-6); 112.98 (CH-4-furyl); 114.31 (d, $J_{C,F}$ = 6.4 Hz, CH-3-furyl); 140.82 (d, $J_{C,F}$ = 246.1 Hz, C-5); 145.68 (d, $J_{C,F}$ = 3.8 Hz, C-4); 146.61 (CH-5-furyl); 147.73 (d, $J_{C,F}$ = 3.3 Hz, C-7a); 151.42 (d, $J_{C,F}$ = 1.7 Hz, C-2-furyl); 151.57 (CH-2). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -159.40 (s, 1F, F-5). IR(KBr): 3105, 2983, 2845, 1592, 1467, 1359, 1245, 836, 755, 737, 597 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3FO$ [M+H]: 204.0568; found: 204.0568. Anal. Calcd for $C_{10}H_6FN_3O$: C, 59.12; H, 2.98; N, 20.68. Found: C, 58.99; H, 3.16; N, 20.37.

5-Fluoro-4-(furan-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine

6-(furan-3-yl)-7-fluoro-9-NH-7-deazapurine (43d)

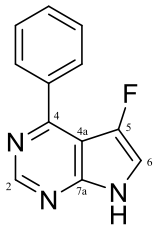


Compound **43d** was prepared from **37** (172 mg, 1 mmol) and furan-3-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a brownish solid (145 mg, 71 %), which was crystallized from MeOH/water. R_f = 0.38 ($CHCl_3$-MeOH, 10:1). M. p. 253-254 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 7.17 (bdt, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,F}$ = $J_{4,2}$ = 0.7 Hz, H-4-furyl); 7.63 (t, 1H, $J_{6,F}$ = $J_{6,NH}$ = 2.5 Hz, H-6); 7.88 (t, 1H, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, H-5-furyl); 8.45 (dt, 1H, $J_{2,5}$ = 1.6 Hz, $J_{2,4}$ = 0.8 Hz, H-2-furyl); 8.75 (s, 1H, H-2); 12.12 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 103.05 (d, $J_{C,F}$ = 15.0 Hz, C-4a); 109.93 (d, $J_{C,F}$ = 6.4 Hz, CH-4-furyl); 110.09 (d, $J_{C,F}$ = 29.6 Hz, CH-6); 124.84 (C-3-furyl); 140.89 (d, $J_{C,F}$ = 243.4 Hz, C-5); 144.74 (d, $J_{C,F}$ = 1.4 Hz, CH-5-furyl); 145.11 (d, $J_{C,F}$ = 13.7 Hz, CH-2-furyl);

147.33 (d, $J_{C,F}$ = 3.6 Hz, C-7a); 149.15 (d, $J_{C,F}$ = 3.8 Hz, C-4); 151.80 (CH-2). ^{19}F NMR (470.3 MHz, DMSO-d$_6$): δ = -160.71 (s, 1F, F-2). IR(KBr): 3117, 2992, 2842, 1571, 1473, 1356, 1219, 827, 788, 731, 594 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3FO$ [M+H]: 204.0568; found: 204.0568.

5-Fluoro-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine

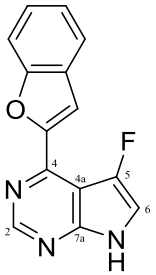
6-phenyl-7-fluoro-9-NH-7-deazapurine (43e)



Compound **43e** was prepared from **37** (172 mg, 1 mmol) and phenylboronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a white solid (160 mg, 75 %), which was crystallized from MeOH/water. R_f = 0.38 ($CHCl_3$-MeOH, 10:1). M. p. 279-280 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 7.53 – 7.60 (m, 3H, H-*m*,*p*-Ph); 7.67 (bt, 1H, $J_{6,NH}$ = $J_{6,F}$ = 2.0 Hz, H-6); 7.97 (m, 2H, H-*o*-Ph); 8.86 (s, 1H, H-2); 12.20 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 104.10 (d, $J_{C,F}$ = 14.0 Hz, C-4a); 110.38 (d, $J_{C,F}$ = 29.0 Hz, CH-6); 128.68 (CH-*m*-Ph); 129.33 (d, $J_{C,F}$ = 4.7 Hz, CH-*o*-Ph); 130.40 (CH-*p*-Ph); 137.36 (d, $J_{C,F}$ = 1.5 Hz, C-*i*-Ph); 140.93 (d, $J_{C,F}$ = 244.5 Hz, C-5); 147.52 (d, $J_{C,F}$ = 3.2 Hz, C-7a); 151.85 (C-2); 156.44 (d, $J_{C,F}$ = 4.4 Hz, C-4). ^{19}F NMR (470.3 MHz, DMSO-d$_6$): δ = -158.57 (s, 1F, F-5). IR(KBr): 3135, 3069, 2920, 1562, 1452, 1323, 1201, 839, 746, 728, 591 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_9N_3F$ [M+H]: 214.0775; found: 214.0775.

4-(Benzofuran-2-yl)-5-fluoro-*7H*-pyrrolo[2,3-*d*]pyrimidine

6-(benzofuran-2-yl)-7-fluoro-9-NH-7-deazapurine (43f)

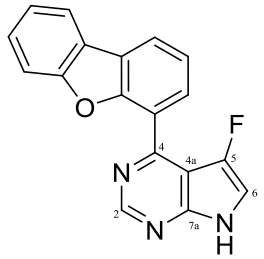


Compound **43f** was prepared from **37** (172 mg, 1 mmol) and benzofuran-2-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a brownish solid (175 mg, 69 %), which was crystallized from MeOH/water. R_f = 0.38 ($CHCl_3$-MeOH, 10:1). M. p. 285-286 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 7.35 (ddd, 1H, $J_{5,4}$ = 7.9 Hz, $J_{5,6}$ = 7.2 Hz, $J_{5,7}$ = 0.9 Hz, H-5-benzofuryl); 7.76 (ddd, 1H, $J_{6,7}$ = 8.3 Hz, $J_{6,5}$ = 7.2 Hz, $J_{6,4}$ = 1.3 Hz, H-6-benzofuryl); 7.71 (dq, 1H, $J_{7,6}$ = 8.3 Hz, $J_{7,5}$ = $J_{7,4}$ = $J_{7,3}$ = 0.9 Hz, H-7-benzofuryl); 7.75 (t, 1H, $J_{6,F}$ = $J_{6,NH}$ = 2.6 Hz, H-6); 7.83 (ddd, 1H, $J_{4,5}$ = 7.8 Hz, $J_{4,6}$ = 1.4 Hz, $J_{4,7}$ = 0.8 Hz, H-4-benzofuryl); 7.87 (d, 1H, $J_{3,7}$ = 1.0 Hz, H-3-benzofuryl); 8.85 (s, 1H, H-2); 12.29 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 102.39 (d, $J_{C,F}$ = 14.8 Hz, C-4a); 110.00 (d, $J_{C,F}$ = 7.1 Hz, CH-3-benzofuryl); 111.52 (d, $J_{C,F}$ = 29.3 Hz, CH-6); 111.88 (CH-7-

benzofuryl); 122.72 (CH-4-benzofuryl); 123.90 (CH-5-benzofuryl); 126.79 (CH-6-benzofuryl); 128.07 (C-3a-benzofuryl); 140.70 (d, $J_{C,F}$ = 246.3 Hz, C-5); 145.63 (d, $J_{C,F}$ = 3.8 Hz, C-4); 147.92 (d, $J_{C,F}$ = 3.3 Hz, C-7a); 151.55 (CH-2); 152.95 (d, $J_{C,F}$ = 2.0 Hz, C-2-benzofuryl); 155.38 (C-7a-benzofuryl). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -158.87 (s, 1F, F-5). IR(KBr): 3108, 2989, 2818, 1586, 1470, 1344, 1242, 845, 794, 734, 591 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_9N_3FO$ [M+H]: 254.0724; found: 254.0724.

4-(Dibenzo[*b,d*]furan-4-yl)-5-fluoro-*7H*-pyrrolo[2,3-*d*]pyrimidine

6-(dibenzofuran-4-yl)-7-fluoro-9-NH-7-deazapurine (43g)

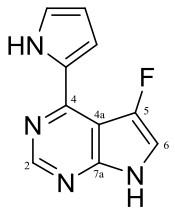


Compound **43g** was prepared from **37** (172 mg, 1 mmol) and dibenzo[*b*,*d*]furan-4-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a white solid (235 mg, 77 %), which was crystallized from MeOH/water. R_f = 0.38 ($CHCl_3$-MeOH, 10:1). M. p. 285-286 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.44 (btd, 1H, $J_{8,7}$ = $J_{8,9}$ = 7.5 Hz, $J_{8,6}$ = 1.0 Hz, H-8-$C_{12}H_7O$); 7.53 (ddd, 1H, $J_{7,6}$ = 8.3 Hz, $J_{7,8}$ = 7.3 Hz, $J_{7,9}$ = 1.4 Hz, H-7-$C_{12}H_7O$); 7.59 (t, 1H, $J_{2,1}$ = $J_{2,3}$ = 7.6 Hz, H-2-$C_{12}H_7O$); 7.66 (bt, 1H, $J_{6,F}$ = $J_{6,NH}$ = 2.3 Hz, H-6); 7.67 (dt, 1H, $J_{6,7}$ = 8.2 Hz, $J_{6,8}$ = $J_{6,9}$ = 0.9 Hz, H-6-$C_{12}H_7O$); 7.85 (ddd, 1H, $J_{3,2}$ = 7.6 Hz, $J_{3,F}$ = 1.9 Hz, $J_{3,1}$ = 1.3 Hz, H-3-$C_{12}H_7O$); 8.24 (ddd, 1H, $J_{9,8}$ = 7.7 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.7 Hz, H-9-$C_{12}H_7O$); 8.34 (dd, 1H, $J_{1,2}$ = 7.7 Hz, $J_{1,3}$ = 1.3 Hz, H-1-$C_{12}H_7O$); 8.97 (s, 1H, H-2); 12.26 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 106.14 (d, $J_{C,F}$ = 14.3 Hz, C-4a); 110.68 (d, $J_{C,F}$ = 27.6 Hz, CH-6); 111.95 (CH-6-$C_{12}H_7O$); 121.57 (CH-9-$C_{12}H_7O$); 122.48 (C-4-$C_{12}H_7O$); 122.91 (CH-1-$C_{12}H_7O$); 123.38 (CH-2-$C_{12}H_7O$); 123.41 (C-9a-$C_{12}H_7O$); 123.55 (CH-8-$C_{12}H_7O$); 124.53 (C-9b-$C_{12}H_7O$); 128.17 (CH-7-$C_{12}H_7O$); 128.58 (CH-3-$C_{12}H_7O$); 141.21 (d, $J_{C,F}$ = 245.5 Hz, C-5); 147.18 (d, $J_{C,F}$ = 2.9 Hz, C-7a); 152.04 (CH-2); 152.60 (d, $J_{C,F}$ = 4.0 Hz, C-4); 153.30 (C-4a-$C_{12}H_7O$); 155.79 (C-5a-$C_{12}H_7O$). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -163.91 (s, 1F, F-5). IR(KBr): 3108, 2989, 2818, 1586, 1470, 1344, 1242, 845, 794, 734, 591 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{11}N_3FO$ [M+H]: 304.0881; found: 304.0881.

5-Fluoro-4-(*1H*-pyrrol-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine

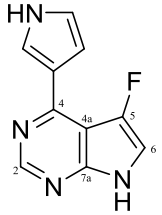
6-(*1H*-pyrrol-2-yl)-7-fluoro-9-NH-7-deazapurine (43h)

Compound **43h** was prepared from **37** (172 mg, 1 mmol) and *N*-boc-pyrrole-2-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a brownish solid



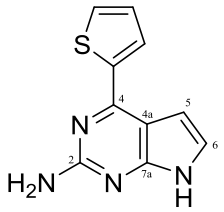
solid (65 mg, 32 %), which was crystallized from MeOH/water. R_f = 0.35 ($CHCl_3$-MeOH, 10:1). M. p. > 200 °C (dec). ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 6.29 (dt, 1H, $J_{4,3}$ = 3.7 Hz, $J_{4,NH}$ = $J_{4,5}$ = 2.4 Hz, H-4-pyrrolyl); 7.04 (btd, 1H, $J_{5,4}$ = $J_{5,NH}$ = 2.7 Hz, $J_{5,3}$ = 1.4 Hz, H-5-pyrrolyl); 7.16 (ddt, 1H, $J_{3,4}$ = 3.7 Hz, $J_{3,NH}$ = 2.5 Hz, $J_{3,5}$ = $J_{3,F}$ = 1.3 Hz, H-3-pyrrolyl); 7.53 (t, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.4 Hz, H-6); 8.64 (s, 1H, H-2); 11.82 (bs, 1H, NH-pyrrolyl); 11.95 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 100.46 (d, $J_{C,F}$ = 14.8 Hz, C-4a); 108.99 (d, $J_{C,F}$ = 30.0 Hz, CH-6); 110.67 (d, $J_{C,F}$ = 2.5 Hz, CH-4-pyrrolyl); 113.58 (d, $J_{C,F}$ = 17.6 Hz, CH-3-pyrrolyl); 123.39 (CH-5-pyrrolyl); 128.67 (C-2-pyrrolyl); 141.21 (d, $J_{C,F}$ = 243.4 Hz, C-5); 147.32 (d, $J_{C,F}$ = 3.8 Hz, C-7a); 148.27 (d, $J_{C,F}$ = 3.7 Hz, C-4); 151.50 (CH-2). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -158.88 (s, 1F, F-5). IR(KBr): 3102, 2983, 2848, 1577, 1455, 1042, 833, 740, 600 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_8N_4F$ [M+H]: 203.0727; found: 203.0728.

5-Fluoro-4-(*1H*-pyrrol-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
6-(*1H*-pyrrol-3-yl)-7-fluoro-9-NH-7-deazapurine (43i)



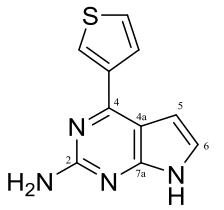
Compound **43i** was prepared from **37** (172 mg, 1 mmol) and 1-(triisopropylsilyl)-1*H*-pyrrole-3-boronic acid. Purification using column chromatography (1 % → 3 % MeOH in $CHCl_3$) provided a brownish solid (75 mg, 35 %), which was crystallized from MeOH/water. R_f = 0.25 ($CHCl_3$-MeOH, 10:1). M. p. > 200 °C (dec). ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 6.88 (m, 1H, H-4-pyrrolyl); 6.91 (td, 1H, $J_{5,NH}$ = $J_{5,4}$ = 2.7 Hz, $J_{5,2}$ = 1.8 Hz, H-5-pyrrolyl); 7.47 (t, 1H, $J_{6,F}$ = $J_{6,NH}$ = 2.5 Hz, H-6); 7.68 (dt, 1H, $J_{2,NH}$ = 2.9 Hz, $J_{2,5}$ = $J_{2,4}$ = 1.6 Hz, H-2-pyrrolyl); 8.60 (s, 1H H-2); 11.36 (bs, 1H, NH-pyrrolyl); 11.83 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 101.81 (d, $J_{C,F}$ = 14.8 Hz, C-4a); 108.45 (d, $J_{C,F}$ = 30.5 Hz, CH-6); 108.47 (d, $J_{C,F}$ = 8.1 Hz, H-4-pyrrolyl); 119.65 (d, $J_{C,F}$ = 1.7 Hz, CH-5-pyrrolyl); 121.69 (d, $J_{C,F}$ = 13.1 Hz, CH-2-pyrrolyl); 121.86 (C-3-pyrrolyl); 141.46 (d, $J_{C,F}$ = 243.2 Hz, C-5); 147.32 (d, $J_{C,F}$ = 4.0 Hz, C-7a); 151.81 (CH-2); 153.05 (d, $J_{C,F}$ = 3.7 Hz, C-4). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -158.93 (s, 1F, F-5). IR(KBr): 3096, 2989, 2878, 1565, 1473, 1054, 794, 734, 597 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_8N_4F$ [M+H]: 203.0727; found: 203.0728.

2-Amino-4-(thiophen-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-amino-6-(thiophen-2-yl)-9-NH-7-deazapurine) (44a)



Compound **44a** was prepared from **33** (337 mg, 2 mmol) and thiophene-2-boronic acid. Purification using column chromatography (2 % MeOH in $CHCl_3$) provided a yellowish solid (370 mg, 86 %), which was crystallized from MeOH/water. R_f = 0.35 ($CHCl_3$-MeOH, 10:1). M. p. 210-211 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 6.10 (s, 2H, NH_2); 6.71 (dd, 1H, $J_{5,6}$ = 3.7 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 7.12 (dd, 1H, $J_{6,5}$ = 3.7 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.23 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.7 Hz, H-4-thienyl); 7.73 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.1 Hz, H-5-thienyl); 7.97 (dd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,5}$ = 1.1 Hz, H-3-thienyl); 11.27 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 100.02 (CH-5); 105.77 (C-4a); 123.47 (CH-6); 128.60 (CH-3-thienyl); 128.70 (CH-4-thienyl); 129.44 (CH-5-thienyl); 143.76 (C-2-thienyl); 150.61 (C-4); 155.63 (C-7a); 159.63 (C-2). IR(KBr): 3425, 3312, 3072, 2854, 1625, 1565, 1467, 1404, 899, 827, 698, 594 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_9N_4S$ [M+H]: 217.0542; found: 217.0543.

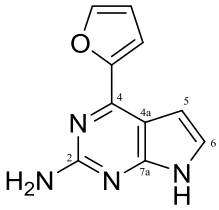
2-Amino-4-(thiophen-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-amino-6-(thiophen-3-yl)-9-NH-7-deazapurine) (44b)



Compound **44b** was prepared from **33** (253 mg, 1.5 mmol) and thiophene-3-boronic acid. Purification using column chromatography (2 % MeOH in $CHCl_3$) provided a yellowish solid (290 mg, 90 %), which was crystallized from MeOH/water. R_f = 0.35 ($CHCl_3$-MeOH, 10:1). M. p. 272-273 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 6.06 (bs, 2H, NH_2); 6.67 (dd, 1H, $J_{5,6}$ = 3.7 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 7.10 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.2 Hz, H-6); 7.66 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.81 (dd, 1H, $J_{4,5}$= 5.0 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 8.30 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 11.23 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 100.24 (CH-5); 107.13 (C-4a); 123.04 (CH-6); 126.62 (CH-5-thienyl); 127.34 (CH-2-thienyl); 127.64 (CH-4-thienyl); 141.07 (C-3-thienyl); 152.14 (C-4); 155.49 (C-7a); 159.89 (C-2). IR(KBr): 3494, 3306, 3093, 2845, 1634, 1568, 1479, 1413, 1275, 896, 827, 698, 594 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_9N_4S$ [M+H]: 217.0542; found: 217.0542.

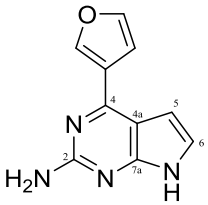
2-Amino-4-(furan-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-amino-6-(furan-2-yl)-9-NH-7-deazapurine) (44c)

Compound **44c** was prepared from **33** (253 mg, 1.5 mmol) and furan-2-boronic acid. Purification using column chromatography (2 % MeOH in $CHCl_3$) provided a yellowish solid (190 mg, 67 %), which was crystallized from MeOH/water. R_f = 0.35 ($CHCl_3$-MeOH, 10:1).



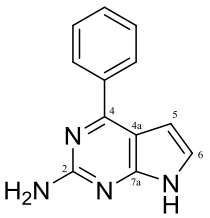
M. p. 269-270 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 6.10 (bs, 2H, NH$_2$); 6.66 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 6.71 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 7.09 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.23 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.95 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 11.22 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 100.47 (CH-5); 105.60 (C-4a); 111.86 (CH-3-furyl); 112.42 (CH-4-furyl); 123.27 (CH-6); 145.32 (CH-5-furyl); 147.14 (C-4); 153.36 (C-2-furyl); 155.60 (C-7a); 159.93 (C-2). IR(KBr): 3449, 3282, 3120, 2833, 1625, 1559, 1476, 1413, 1287, 899, 827, 740, 588 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_8N_4ONa$ [M+Na]: 223.0590; found: 223.0586. Anal. Calcd for $C_{10}H_8N_4O \cdot 0.05CH_3OH$: C, 59.82; H, 4.10; N, 27.76. Found: C, 60.01; H, 4.19; N, 27.43.

2-Amino-4-(furan-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-amino-6-(furan-3-yl)-9-NH-7-deazapurine) (44d)



Compound **44d** was prepared from **33** (253 mg, 1.5 mmol) and furan-3-boronic acid. Purification using column chromatography (2 % MeOH in CHCl$_3$) provided a yellowish solid (250 mg, 83 %), which was crystallized from MeOH/water. R_f = 0.35 (CHCl$_3$-MeOH, 10:1). M. p. 282-283 °C; ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 6.02 (bs, 2H, NH$_2$); 6.63 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 7.06 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.09 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.82 (bt, 1H, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, H-5-furyl); 8.50 (dd, 1H, $J_{2,5}$ = 1.6 Hz, $J_{2,4}$ = 0.9 Hz, H-2-furyl); 11.19 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 100.02 (CH-5); 107.10 (C-4a); 109.64 (CH-4-furyl); 122.68 (CH-6); 125.87 (C-3-furyl); 144.13 (CH-2-furyl); 144.20 (CH-5-furyl); 150.49 (C-4); 155.04 (C-7a); 159.96 (C-2). IR(KBr): 3461, 3297, 3129, 2830, 1625, 1586, 1506, 1404, 1159, 896, 821, 707, 591 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_9N_4O$ [M+H]: 201.0771; found: 201.0769.

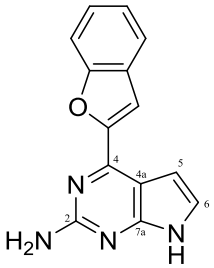
2-Amino-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-amino-6-phenyl-9-NH-7-deazapurine) (44e)



Compound **44e** was prepared from **33** (253 mg, 1.5 mmol) and phenylboronic acid. Purification using column chromatography (2 % MeOH in CHCl$_3$) provided a yellowish solid (250 mg, 80 %), which was crystallized from MeOH/water. R_f = 0.35 (CHCl$_3$-MeOH, 10:1). M. p. 241-

242 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 6.13 (bs, 2H, NH$_2$); 6.55 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 7.11 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.46 – 7.56 (m, 3H, H-*m*,*p*-Ph); 8.04 (m, 2H, H-*o*-Ph); 11.27 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 100.15 (CH-5); 107.78 (C-4a); 123.13 (CH-6); 128.50 (CH-*o*-Ph); 128.72 (CH-*m*-Ph); 129.75 (CH-*p*-Ph); 138.66 (C-*i*-Ph); 155.44 (C-7a); 156.88 (C-4); 160.10 (C-2). IR(KBr): 3500, 3312, 3114, 2869, 1634, 1562, 1482, 1392, 1269, 887, 776, 701, 561 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{10}N_4Na$ [M+Na]: 233.0798; found: 233.0798.

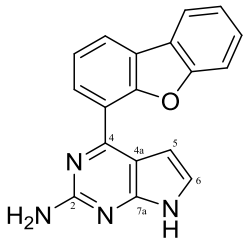
2-Amino-4-(benzofuran-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-amino-6-(benzofuran-2-yl)-9-NH-7-deazapurine) (44f)



Compound **44f** was prepared from **33** (337 mg, 2 mmol) and benzofuran-2-boronic acid. Purification using column chromatography (2 % MeOH in CHCl$_3$) provided a yellowish solid (290 mg, 58 %), which was crystallized from MeOH/water. R_f = 0.35 (CHCl$_3$-MeOH, 10:1). M. p. 261-262 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 6.24 (bs, 2H, NH$_2$); 6.86 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 7.19 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.2 Hz, H-6); 7.33 (ddd, 1H, $J_{5,4}$ = 7.8 Hz, $J_{5,6}$ = 7.2 Hz, $J_{5,7}$ = 1.0 Hz, H-5-benzofuryl); 7.43 (ddd, 1H, $J_{6,7}$ = 8.3 Hz, $J_{6,5}$ = 7.2 Hz, $J_{6,4}$ = 1.3 Hz, H-6-benzofuryl); 7.69 (d, 1H, $J_{3,7}$ = 1.0 Hz, H-3-benzofuryl); 7.75 (dq 1H, $J_{7,6}$ = 8.3 Hz, $J_{7,5}$ = $J_{7,4}$ = $J_{7,3}$ = 0.9 Hz, H-7-benzofuryl); 7.78 (ddd, 1H, $J_{4,5}$ = 7.8 Hz, $J_{4,6}$ = 1.3 Hz, $J_{4,7}$ = 0.7 Hz, H-4-benzofuryl); 11.34 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 100.64 (CH-5); 106.90 (C-4a); 107.76 (CH-3-benzofuryl); 111.85 (CH-7-benzofuryl); 122.33 (CH-4-benzofuryl); 123.70 (CH-5-benzofuryl); 124.05 (CH-6); 126.11 (CH-6-benzofuryl); 128.11 (C-3a-benzofuryl); 146.81 (C-4); 154.97 and 155.02 (C-2,7a-benzofuryl); 155.91 (C-7a); 159.99 (C-2). IR(KBr): 3309, 3156, 2995, 2827, 1628, 1598, 1473, 1413, 1278, 896, 746, 716, 591 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_{10}N_4ONa$ [M+Na]: 273.0747; found: 273.0747.

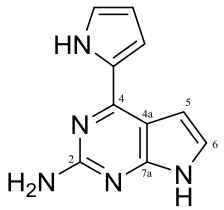
2-Amino-4-(dibenzo[*b*,*d*]furan-4-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-amino-6-(dibenzofuran-4-yl)-9-NH-7-deazapurine) (44g)

Compound **44g** was prepared from **33** (337 mg, 2 mmol) and dibenzo[*b*,*d*]furan-4-boronic acid. Purification using column chromatography (2 % MeOH in CHCl$_3$) provided a yellowish solid (310 mg, 52 %), which was crystallized from MeOH/water. R_f = 0.35 (CHCl$_3$-MeOH, 10:1). M. p. 321-322 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): δ = 6.24 (dd, 1H, $J_{5,6}$ = 3.6 Hz,



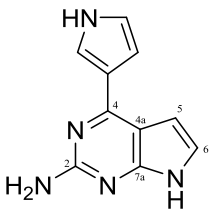
$J_{5,NH}$ = 1.9 Hz, H-5); 6.25 (bs, 2H, NH_2); 7.09 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.2 Hz, H-6); 7.44 (btd, 1H, $J_{8,7}$ = $J_{8,9}$ = 7.5 Hz, $J_{8,6}$ = 1.0 Hz, H-8-$C_{12}H_7O$); 7.54 (ddd, 1H, $J_{7,6}$ = 8.3 Hz, $J_{7,8}$ = 7.3 Hz, $J_{7,9}$ = 1.4 Hz, H-7-$C_{12}H_7O$); 7.55 (t, 1H, $J_{2,1}$ = $J_{2,3}$ = 7.6 Hz, H-2-$C_{12}H_7O$); 7.68 (dt, 1H, $J_{6,7}$ = 8.2 Hz, $J_{6,8}$ = $J_{6,9}$ = 0.9 Hz, H-6-$C_{12}H_7O$); 7.85 (dd, 1H, $J_{3,2}$ = 7.6 Hz, $J_{3,1}$ = 1.3 Hz, H-3-$C_{12}H_7O$); 8.22 (ddd, 1H, $J_{9,8}$ = 7.7 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.7 Hz, H-9-$C_{12}H_7O$); 8.28 (dd, 1H, $J_{1,2}$ = 7.7 Hz, $J_{1,3}$ = 1.3 Hz, H-1-$C_{12}H_7O$); 11.29 (bt, 1H, $J_{NH,6}$ = $J_{NH,5}$ = 2.0 Hz, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 100.65 (CH-5); 109.79 (C-4a); 111.95 (CH-6-$C_{12}H_7O$); 121.48 (CH-9-$C_{12}H_7O$); 122.21 (CH-1-$C_{12}H_7O$); 122.81 (CH-6); 123.32 (CH-2-$C_{12}H_7O$); 123.49 (CH-8-$C_{12}H_7O$); 123.57 and 123.65 (C-4,9a-$C_{12}H_7O$); 124.68 (C-9b-$C_{12}H_7O$); 128.07 (CH-7-$C_{12}H_7O$); 128.43 (CH-3-$C_{12}H_7O$); 152.84 (C-4a-$C_{12}H_7O$); 154.45 (C-4); 155.01 (C-7a); 155.64 (C-5a-$C_{12}H_7O$); 160.31 (C-2). IR(KBr): 3494, 3327, 3150, 2998, 1607, 1571, 1479, 1401, 1189, 839, 740, 588 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{12}N_4ONa$ [M+Na]: 323.0903; found: 323.0903.

2-Amino-4-(*1H*-pyrrol-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-amino-6-(*1H*-pyrrol-2-yl)-9-NH-7-deazapurine) (44h)



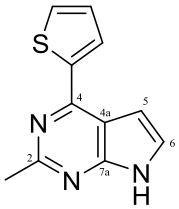
Compound **44h** was prepared from **33** (253 mg, 1.5 mmol) and *N*-boc-pyrrole-2-boronic acid. Purification using column chromatography (1 % → 3 % MeOH in $CHCl_3$) provided as a brownish solid (180 mg, 60 %), which was crystallized from MeOH/water. R_f = 0.28 ($CHCl_3$-MeOH, 10:1). M. p. 289-290 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 5.76 (bs, 2H, NH_2); 6.23 (dt, 1H, $J_{4,3}$ = 3.6 Hz, $J_{4,NH}$ = $J_{4,5}$ = 2.4 Hz, H-4-pyrrolyl); 6.62 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 6.95 (btd, 1H, $J_{5,4}$ = $J_{5,NH}$ = 2.7 Hz, $J_{5,3}$ = 1.4 Hz, H-5-pyrrolyl); 6.97 (ddd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,NH}$ = 2.5 Hz, $J_{3,5}$ = 1.4 Hz, H-3-pyrrolyl); 7.02 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.2 Hz, H-6); 11.12 (bs, 1H, NH); 11.25 (bs, 1H, NH-pyrrolyl). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 100.22 (CH-5); 105.10 (C-4a); 110.00 (CH-4-pyrrolyl); 111.92 (CH-3-pyrrolyl); 121.63 (CH-5-pyrrolyl); 122.21 (CH-6); 129.88 (C-2-pyrrolyl); 149.53 (C-4); 154.95 (C-7a); 159.55 (C-2). IR(KBr): 3458, 3422, 3315, 3171, 1637, 1580, 1458, 1389, 1287, 884, 743, 522 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_{10}N_5$ [M+H]: 200.0931; found: 200.0927.

2-Amino-4-(*1H*-pyrrol-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-amino-6-(*1H*-pyrrol-3-yl)-9-NH-7-deazapurine) (44i)



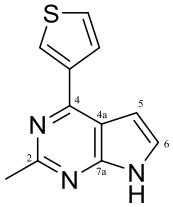
Compound **44i** was prepared from **33** (253 mg, 1.5 mmol) and 1-(triisopropylsilyl)-1*H*-pyrrole-3-boronic acid. Purification using column chromatography (1 % → 5 % MeOH in $CHCl_3$) provided a brownish solid (130 mg, 43 %), which was crystallized from MeOH/water. R_f = 0.15 ($CHCl_3$-MeOH, 10:1). M. p. > 200 °C (dec). ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 5.79 (bs, 2H, NH_2); 6.58 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 6.76 (td, 1H, $J_{4,5}$ = $J_{4,NH}$ = 2.6 Hz, $J_{4,2}$ = 1.6 Hz, H-4-pyrrolyl); 6.85 (td, 1H, $J_{5,4}$ = $J_{5,NH}$ = 2.6 Hz, $J_{5,2}$ = 1.9 Hz, H-5-pyrrolyl); 6.96 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.2 Hz, H-6); 7.57 (dt, 1H, $J_{2,NH}$ = 2.8 Hz, $J_{2,5}$ = $J_{2,4}$ = 1.7 Hz, H-2-pyrrolyl); 10.99 (bs, 1H, NH); 11.21 (bs, 1H, NH-pyrrolyl). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 100.53 (CH-5); 106.17 (C-4a); 107.92 (CH-4-pyrrolyl); 118.98 (CH-5-pyrrolyl); 120.21 (CH-2-pyrrolyl); 121.40 (CH-6); 123.23 (C-3-pyrrolyl); 154.12 (C-4); 154.78 (C-7a); 159.83 (C-2). IR(KBr): 3303, 3144, 2983, 2923, 1697, 1571, 1512, 1476, 1407, 794, 719, 594 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_{10}N_5$ [M+H]: 200.0931; found: 200.0928.

2-Methyl-4-(thiophen-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-(thiophen-2-yl)-9-NH-7-deazapurine) (45a)



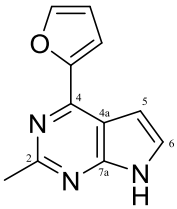
Compound **45a** was prepared from **35** (168 mg, 1 mmol) and thiophene-2-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided as yellowish solid (205 mg, 95 %), which was crystallized from MeOH/water. R_f = 0.40 ($CHCl_3$-MeOH, 10:1). M. p. 248-249 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 2.63 (bs, 3H, CH_3); 6.95 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.27 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.8 Hz, H-4-thienyl); 7.54 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.4 Hz, H-6); 7.80 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.1 Hz, H-5-thienyl); 8.09 (dd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,5}$ = 1.1 Hz, H-3-thienyl); 12.01 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 25.72 (CH_3); 99.82 (CH-5); 108.98 (C-4a); 127.18 (CH-6); 129.00 (CH-4-thienyl); 129.15 (CH-3-thienyl); 130.16 (CH-5-thienyl); 143.32 (C-2-thienyl); 149.73 (C-4); 153.82 (C-7a); 159.35 (C-2). IR(KBr): 3192, 3069, 2980, 2866, 1559, 1398, 1254, 893, 818, 728, 597 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{10}N_3S$ [M+H]: 216.0590; found: 216.0590. Anal. Calcd for $C_{11}H_9N_3S$: C, 61.37; H, 4.21; N, 19.52. Found: C, 61.31; H, 4.36; N, 19.20.

2-Methyl-4-(thiophen-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-(thiophen-3-yl)-9-NH-7-deazapurine)(45b)



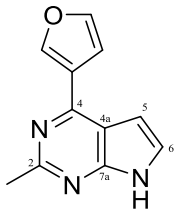
Compound **45b** was prepared from **35** (168 mg, 1 mmol) and thiophene-3-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a white solid (188 mg, 87 %), which was crystallized from MeOH/water. R_f = 0.40 ($CHCl_3$-MeOH, 10:1). M. p. 221-222 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 2.66 (s, 3H, CH_3); 6.92 (d, 1H, $J_{5,6}$ = 3.6 Hz, H-5); 7.52 (d, 1H, $J_{6,5}$ = 3.6 Hz, H-6); 7.71 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.92 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 8.45 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 11.95 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 25.91 (CH_3); 99.98 (CH-5); 111.44 (C-4a); 126.76 (CH-6); 126.96 (CH-5-thienyl); 127.66 (CH-4-thienyl); 127.99 (CH-2-thienyl); 140.72 (C-3-thienyl); 151.08 (C-4); 153.77 (C-7a); 159.47 (C-2). IR(KBr): 3192, 3069, 2980, 2866, 1559, 1398, 1254, 893, 818, 728, 597 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{10}N_3S$ [M+H]: 216.0590; found: 216.0590. Anal. Calcd for $C_{11}H_9N_3S$: C, 61.37; H, 4.21; N, 19.52. Found: C, 61.47; H, 4.35; N, 19.13.

4-(Furan-2-yl)-2-methyl-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-methyl-6-(furan-2-yl)-9-NH-7-deazapurine) (45c)



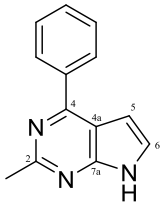
Compound **45c** was prepared from **35** (168 mg, 1 mmol) and furan-2-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a yellowish solid (125 mg, 63 %), which was crystallized from MeOH/water. R_f = 0.40 ($CHCl_3$-MeOH, 10:1). M. p. 229-230 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 2.64 (s, 3H, CH_3); 6.75 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.87 (dd, 1H, $J_{5,6}$ = 3.5 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 7.39 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.51 (dd, 1H, $J_{6,5}$ = 3.5 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 8.01 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 11.95 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 25.82 (CH_3); 100.23 (CH-5); 109.74 (C-4a); 112.62 and 112.65 (CH-3,4-furyl); 126.96 (CH-6); 145.91 (CH-5-furyl); 146.20 (C-4); 153.10 (C-2-furyl); 153.81 (C-7a); 159.60 (C-2). IR(KBr): 3216, 3114, 2989, 2833, 1592, 1326, 1009, 839, 812, 728, 600 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{10}N_3O$ [M+H]: 200.0818; found: 200.0818. Anal. Calcd for $C_{11}H_9N_3O$: C, 66.32; H, 4.55; N, 21.09. Found: C, 65.95; H, 4.68; N, 20.76.

4-(Furan-3-yl)-2-methyl-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-methyl-6-(furan-3-yl)-9-NH-7-deazapurine) (45d)



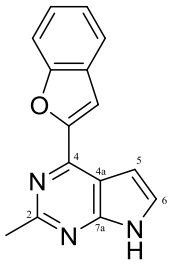
Compound **45d** was prepared from **35** (168 mg, 1 mmol) and furan-3-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a yellowish solid (167 mg, 84 %), which was crystallized from MeOH/water. R_f = 0.38 ($CHCl_3$-MeOH, 10:1). M. p. 207-208 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 2.64 (s, 3H, CH_3); 6.87 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.21 (bd, 1H, $J_{4,5}$ = 2.0 Hz, H-4-furyl); 7.49 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.86 (t, 1H, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, H-5-furyl); 8.64 (dd, 1H, $J_{2,5}$ = 1.4 Hz, $J_{2,4}$ = 0.8 Hz, H-2-furyl); 11.91 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 25.89 (CH_3); 99.78 (CH-5); 109.64 (CH-4-furyl); 111.44 (C-4a); 125.67 (C-3-furyl); 126.42 (CH-6); 144.49 (CH-5-furyl); 144.60 (CH-2-furyl); 149.56 (C-4); 153.31 (C-7a); 159.55 (C-2). IR(KBr): 3210, 3108, 2983, 2875, 1571, 1404, 1162, 830, 791, 716, 600 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{10}N_3O$ [M+H]: 200.0818; found: 200.0819.

2-Methyl-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-methyl-6-phenyl-9-NH-7-deazapurine) (45e)



Compound **45e** was prepared from **35** (168 mg, 1 mmol) and phenylboronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a white solid (170 mg, 81 %), which was crystallized from MeOH/water. R_f = 0.43 ($CHCl_3$-MeOH, 10:1). M. p. 189-190 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 2.70 (s, 3H, CH_3); 6.79 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.49 – 7.59 (m, 4H, H-*m*,*p*-Ph, H-6); 8.15 (m, 2H, H-*o*-Ph); 12.02 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 25.91 (CH_3); 99.92 (CH-5); 112.31 (C-4a); 126.92 (CH-6); 128.72 (CH-*o*-Ph); 128.92 (CH-*m*-Ph); 130.03 (CH-*p*-Ph); 138.31 (C-*i*-Ph); 153.74 (C-7a); 155.66 (C-4); 159.64 (C-4). IR(KBr): 3207, 3108, 3001, 2875, 1601, 1544, 1392, 1254, 878, 806, 689, 594 cm^{-1}. HRMS (ESI) calculated for $C_{13}H_{12}N_3$ [M+H]: 210.1026; found: 210.1026.

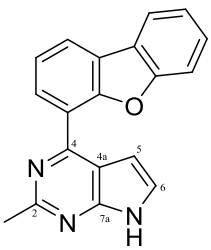
4-(Benzofuran-2-yl)-2-methyl-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-methyl-6-(benzofuran-2-yl)-9-NH-7-deazapurine) (45f)



Compound **45f** was prepared from **35** (168 mg, 1 mmol) and benzofuran-2-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a yellowish solid (140 mg, 58 %), which was crystallized from MeOH/water. R_f = 0.40 ($CHCl_3$-MeOH, 10:1). M. p. 274-275 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 2.70 (s, 3H CH_3); 7.09 (dd, 1H, $J_{5,6}$ = 3.6

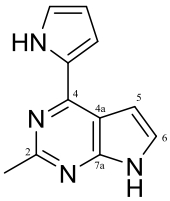
Hz, $J_{5,NH}$ = 1.2 Hz, H-5); 7.09 (ddd, 1H, $J_{5,4}$ = 7.6 Hz, $J_{5,6}$ = 7.2 Hz, $J_{5,7}$ = 1.1 Hz, H-5-benzofuryl); 7.45 (ddd, 1H, $J_{6,7}$ = 8.3 Hz, $J_{6,5}$ = 7.2 Hz, $J_{6,4}$ = 1.3 Hz, H-6-benzofuryl); 7.62 (dd, 1H, $J_{6,5}$ = 3.5 Hz, $J_{6,NH}$ = 1.8 Hz, H-6); 7.77 - 7.81 (m, 2H, H-4,7-benzofuryl); 7.86 (bd, 1H, $J_{3,7}$ = 0.9 Hz, H-3-benzofuryl); 12.08 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 25.83 (CH_3); 100.49 (CH-5); 108.46 (CH-3-benzofuryl); 111.05 (C-4a); 112.00 (CH-7-benzofuryl); 122.45 (CH-4-benzofuryl); 123.83 (CH-5-benzofuryl); 126.36 (CH-6-benzofuryl); 127.78 (CH-6); 128.10 (C-3a-benzofuryl); 145.96 (C-4); 154.12 (C-7a); 154.73 (C-2-benzofuryl); 155.31 (C-7a-benzofuryl); 159.73 (C-2). IR(KBr): 3207, 3102, 3001, 2869, 1589, 1404, 1311, 1254, 857, 806, 722, 603 cm^{-1}. HRMS (ESI) calculated for $C_{15}H_{12}N_3O$ [M+H]: 250.0975; found: 250.0975.

4-(Dibenzo[*b*,*d*]furan-4-yl)-2-methyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-(dibenzofuran-4-yl)-9-NH-7-deazapurine) (45g)



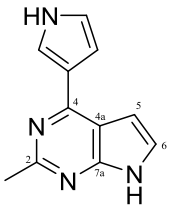
Compound **45g** was prepared from **35** (168 mg, 1 mmol) and dibenzo[*b*,*d*]furan-4-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a yellowish solid (200 mg, 66 %), which was crystallized from MeOH/water. R_f = 0.40 ($CHCl_3$-MeOH, 10:1). M. p. 265-266 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.35 (s, 3H, CH_3); 6.51 (d, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.45 (btd, 1H, $J_{8,7}$ = $J_{8,9}$ = 7.5 Hz, $J_{8,6}$ = 1.1 Hz, H-8-$C_{12}H_7O$); 7.53 (dd, 1H, $J_{6,5}$ = 3.5 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.54 (ddd, 1H, $J_{7,6}$ = 8.3 Hz, $J_{7,8}$ = 7.3 Hz, $J_{7,9}$ = 1.4 Hz, H-7-$C_{12}H_7O$); 7.59 (t, 1H, $J_{2,1}$ = $J_{2,3}$ = 7.6 Hz, H-2-$C_{12}H_7O$); 7.68 (dt, 1H, $J_{6,7}$ = 8.2 Hz, $J_{6,8}$ = $J_{6,9}$ = 0.9 Hz, H-6-$C_{12}H_7O$); 7.94 (dd, 1H, $J_{3,2}$ = 7.5 Hz, $J_{3,1}$ = 1.3 Hz, H-3-$C_{12}H_7O$); 8.24 (ddd, 1H, $J_{9,8}$ = 7.7 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.6 Hz, H-9-$C_{12}H_7O$); 8.33 (dd, 1H, $J_{1,2}$ = 7.7 Hz, $J_{1,3}$ = 1.3 Hz, H-1-$C_{12}H_7O$); 12.05 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 25.92 (CH_3); 100.57 (CH-5); 111.97 (CH-6-$C_{12}H_7O$); 114.34 (C-4a); 121.52 (CH-9-$C_{12}H_7O$); 121.57 (CH-1-$C_{12}H_7O$); 123.26 (C-4-$C_{12}H_7O$); 123.51 (CH-2-$C_{12}H_7O$); 123.53 (C-9a-$C_{12}H_7O$); 123.55 (CH-8-$C_{12}H_7O$); 124.78 (C-9b-$C_{12}H_7O$); 126.61 (CH-6); 128.11 (CH-7-$C_{12}H_7O$); 128.72 (CH-3-$C_{12}H_7O$); 152.94 (C-4a-$C_{12}H_7O$); 153.19 (C-4); 153.29 (C-7a); 155.66 (C-5a-$C_{12}H_7O$); 159.84 (C-2). IR(KBr): 3210, 3126, 3004, 2881, 1574, 1398, 1180, 842, 749, 594 cm^{-1}. HRMS (ESI) calculated for $C_{19}H_{14}N_3O$ [M+H]: 300.1131; found: 300.1132. Anal. Calcd for $C_{19}H_{13}N_3O \cdot 0.35H_2O$: C, 74.69; H, 4.52; N, 13.75. Found: C, 74.60; H, 4.32; N, 13.57.

2-Methyl-4-(*1H*-pyrrol-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-(*1H*-pyrrol-2-yl)-9-NH-7-deazapurine) (45h)



Compound **45h** was prepared from **35** (168 mg, 1 mmol) and *N*-boc-pyrrole-2-boronic acid. Purification using column chromatography (1 % MeOH in $CHCl_3$) provided a greenish solid (145 mg, 70 %), which was crystallized from MeOH/water. R_f = 0.36 ($CHCl_3$-MeOH, 10:1). M. p. 276-277 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 2.63 (s, 3H, CH_3); 6.26 (dt, 1H, $J_{4,3}$ = 3.6 Hz, $J_{4,NH}$ = $J_{4,5}$ = 2.4 Hz, H-4-pyrrolyl); 6.83 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.7 Hz, H-5); 6.99 (btd, 1H, $J_{5,4}$ = $J_{5,NH}$ = 2.7 Hz, $J_{5,3}$ = 1.5 Hz, H-5-pyrrolyl); 7.09 (ddd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,NH}$ = 2.5 Hz, $J_{3,5}$ = 1.4 Hz, H-3-pyrrolyl); 7.40 (dd, 1H, $J_{6,5}$ = 3.5 Hz, $J_{6,NH}$ = 2.2 Hz, H-6); 11.54 (bs, 1H, NH-pyrrolyl); 11.77 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 25.93 (CH_3); 99.95 (CH-5); 109.01 (C-4a); 110.29 (CH-4-pyrrolyl); 112.51 (CH-3-pyrrolyl); 122.18 (CH-5-pyrrolyl); 125.60 (CH-6); 129.59 (C-2-pyrrolyl); 148.52 (C-4); 153.23 (C-7a); 159.22 (C-2). IR(KBr): 3198, 3111, 2980, 2863, 1574, 1410, 1269, 1084, 884, 836, 728, 603 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{11}N_4$ [M+H]: 199.0978; found: 199.0978.

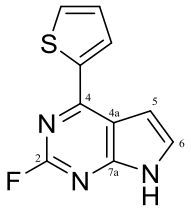
2-Methyl-4-(*1H*-pyrrol-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-(*1H*-pyrrol-3-yl)-9-NH-7-deazapurine) (45i)



Compound **45i** was prepared from **35** (168 mg, 1 mmol) and 1-(triisopropylsilyl)-1*H*-pyrrole-3-boronic acid. Purification using column chromatography (1 % → 3 % MeOH in $CHCl_3$) provided a brownish solid (81 mg, 40 %), which was crystallized from MeOH/water. R_f = 0.22 ($CHCl_3$-MeOH, 10:1). M. p. 321-322 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 2.58 (s, 3H, CH_3); 6.79 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 6.85 (td, 1H, $J_{4,5}$ = $J_{4,NH}$ = 2.7 Hz, $J_{4,2}$ = 1.6 Hz, H-4-pyrrolyl); 6.89 (td, 1H, $J_{5,NH}$ = $J_{5,4}$ = 2.7 Hz, $J_{5,2}$ = 1.9 Hz, H-5-pyrrolyl); 7.35 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.69 (dt, 1H, $J_{2,NH}$ = 2.9 Hz, $J_{2,5}$ = $J_{2,4}$ = 1.7 Hz, H-2-pyrrolyl); 11.31 (bs, 1H, NH-pyrrolyl); 11.65 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 26.02 (CH_3); 100.21 (CH-5); 108.03 (CH-4-pyrrolyl); 110.27 (C-4a); 119.34 (CH-5-pyrrolyl); 120.65 (CH-2-pyrrolyl); 122.90 (C-3-pyrrolyl); 124.91 (CH-6); 153.15 and 153.20 (C-4,7a); 159.32 (C-2). IR(KBr): 3198, 3114, 2983, 2863, 1580, 1404, 1353, 1096, 902, 830, 734, 611 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{11}N_4$ [M+H]: 199.0978; found: 199.0978.

2-Fluoro-4-(thiophen-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine

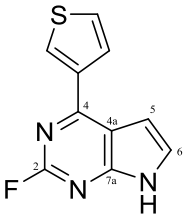
(2-fluoro-6-(thiophen-2-yl)-9-NH-7-deazapurine) (46a)



Compound **46a** was prepared from **36** (172 mg, 1 mmol) and thiophene-2-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a yellowish solid (145 mg, 66 %), which was crystallized from MeOH/water. R_f = 0.62 ($CHCl_3$-MeOH, 10:1). M. p. 212-213 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 7.08 (dd, 1H, $J_{5,6}$ = 3.7 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.31 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.8 Hz, H-4-thienyl); 7.64 (dd, 1H, $J_{6,5}$ = 3.7 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.91 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.0 Hz, H-5-thienyl); 8.20 (dd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,5}$ = 1.0 Hz, H-3-thienyl); 12.41 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 100.84 (CH-5); 111.20 (d, $J_{C,F}$ = 3.6 Hz, C-4a); 128.63 (d, $J_{C,F}$ = 3.3 Hz, CH-6); 129.38 (CH-4-thienyl); 130.72 (CH-3-thienyl); 131.76 (CH-5-thienyl); 141.28 (C-2-thienyl); 152.00 (d, $J_{C,F}$ = 15.5 Hz, C-4); 154.89 (d, $J_{C,F}$ = 16.9 Hz, C-7a); 158.15 (d, $J_{C,F}$ = 204.5 Hz, C-2). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -51.51 (s, 1F, F-2). IR(KBr): 3219, 3147, 3007, 2875, 1574, 1437, 1332, 899, 824, 725, 594 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3FS$ [M+H]: 220.0339; found: 220.0340.

2-Fluoro-4-(thiophen-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine

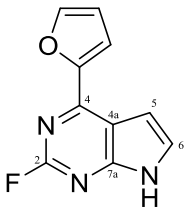
(2-fluoro-6-(thiophen-3-yl)-9-NH-7-deazapurine) (46b)



Compound **46b** was prepared from **36** (172 mg, 1 mmol) and thiophene-3-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a brownish solid (200 mg, 91 %), which was crystallized from MeOH/water. R_f = 0.62 ($CHCl_3$-MeOH, 10:1). M. p. 188-189 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 7.07 (dd, 1H, $J_{5,6}$ = 3.7 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.63 (dd, 1H, $J_{6,5}$ = 3.7 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.76 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.92 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 8.60 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 12.37 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 101.02 (CH-5); 112.60 (d, $J_{C,F}$ = 3.8 Hz, C-4a); 127.49 (CH-5-thienyl); 127.65 (CH-4-thienyl); 128.33 (d, $J_{C,F}$ = 3.4 Hz, CH-6); 129.89 (CH-2-thienyl); 139.11 (C-3-thienyl); 153.37 (d, $J_{C,F}$ = 15.3 Hz, C-4); 154.88 (d, $J_{C,F}$ = 16.7 Hz, C-7a); 158.52 (d, $J_{C,F}$ = 203.9 Hz, C-2). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -51.09 (s, 1F, F-2). IR(KBr): 3210, 3144, 3010, 2884, 1577, 1407, 1350, 899, 851, 779, 594 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3FS$ [M+H]: 220.0339; found: 220.0339.

2-Fluoro-4-(furan-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine

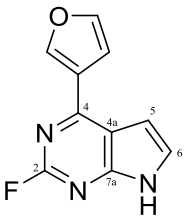
(2-fluoro-6-(furan-2-yl)-9-NH-7-deazapurine) (46c)



Compound **46c** was prepared from **36** (172 mg, 1 mmol) and furan-2-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a yellowish solid (170 mg, 84 %), which was crystallized from MeOH/water. R_f = 0.62 ($CHCl_3$-MeOH, 10:1). M. p. 246-247 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 6.80 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.98 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.50 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.8 Hz, H-3-furyl); 7.61 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 8.08 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.8 Hz, H-5-furyl); 12.36 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 101.18 (CH-5); 110.86 (d, $J_{C,F}$ = 3.4 Hz, C-4a); 113.10 (CH-4-furyl); 114.70 (CH-3-furyl); 128.45 (d, $J_{C,F}$ = 3.3 Hz, CH-6); 147.11 (CH-5-furyl); 147.95 (d, $J_{C,F}$ = 16.2 Hz, C-4); 151.72 (C-2-furyl); 154.95 (d, $J_{C,F}$ = 16.9 Hz, C-7a); 158.57 (d, $J_{C,F}$ = 203.9 Hz, C-2). ^{19}F NMR (470.3 MHz, DMSO-d$_6$): δ = -51.11 (s, 1F, F-2). IR(KBr): 3210, 3147, 2989, 2911, 1604, 1461, 1359, 1018, 893, 839, 743, 588 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3FO$ [M+H]: 204.0568; found: 204.0568. Anal. Calcd for $C_{10}H_6FN_3O \cdot 0.05CH_3OH \cdot 0.15H_2O$: C, 58.18; H, 3.16; N, 20.25. Found: C, 58.12; H, 3.19; N, 20.29.

2-Fluoro-4-(furan-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine

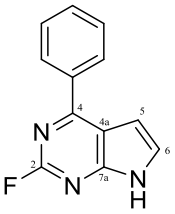
(2-fluoro-6-(furan-3-yl)-9-NH-7-deazapurine) (46d)



Compound **46d** was prepared from **36** (172 mg, 1 mmol) and furan-3-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a yellowish solid (175 mg, 85 %), which was crystallized from MeOH/water. R_f = 0.57 ($CHCl_3$-MeOH, 10:1). M. p. 200-201 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 7.03 (dd, 1H, $J_{5,6}$ = 3.7 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.23 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.60 (dd, 1H, $J_{6,5}$ = 3.7 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.91 (bt, 1H, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, H-5-furyl); 8.77 (dd, 1H, $J_{2,5}$ = 1.5 Hz, $J_{2,4}$ = 0.9 Hz, H-2-furyl); 12.34 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 100.77 (CH-5); 109.45 (CH-4-furyl); 112.59 (d, $J_{C,F}$ = 3.6 Hz, C-4a); 124.57 (C-3-furyl); 128.00 (d, $J_{C,F}$ = 3.3 Hz, CH-6); 145.06 (CH-5-furyl); 145.84 (CH-2-furyl); 152.14 (d, $J_{C,F}$ = 15.7 Hz, C-4); 154.40 (d, $J_{C,F}$ = 16.7 Hz, C-7a); 158.62 (d, $J_{C,F}$ = 203.7 Hz, C-2). ^{19}F NMR (470.3 MHz, DMSO-d$_6$): δ = -51.20 (s, 1F, F-2). IR(KBr): 3213, 3162, 3010, 2920, 1601, 1389, 1350, 1045, 872, 842, 728, 597 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3FO$ [M+H]: 204.0568; found: 204.0568.

2-Fluoro-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine

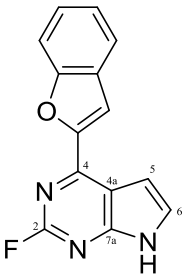
(2-fluoro-6-phenyl-9-NH-7-deazapurine) (46e)



Compound **46e** was prepared from **36** (172 mg, 1 mmol) and phenylboronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a yellowish solid (180 mg, 84 %), which was crystallized from MeOH/water. R_f = 0.64 ($CHCl_3$-MeOH, 10:1). M. p. 205-206 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 6.95 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.4 Hz, H-5); 7.56 – 7.63 (m, 3H, H-*m*,*p*-Ph); 7.65 (dd, 1H, $J_{6,5}$ = 3.7 Hz, $J_{6,NH}$ = 2.1 Hz, H-6); 8.17 (m, 2H, H-*o*-Ph); 12.44 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 101.03 (CH-5); 113.59 (d, $J_{C,F}$ = 3.8 Hz, C-4a); 128.59 (d, $J_{C,F}$ = 3.4 Hz, CH-6); 128.90 (CH-*o*-Ph); 129.19 (CH-*m*-Ph); 131.04 (CH-*p*-Ph); 136.71 (C-*i*-Ph); 154.83 (d, $J_{C,F}$ = 16.5 Hz, C-7a); 158.24 (d, $J_{C,F}$ = 14.6 Hz, C-4); 158.16 (d, $J_{C,F}$ = 204.1 Hz, C-2). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -51.01 (s, 1F, F-2). IR(KBr): 3222, 3138, 3063, 3004, 1586, 1365, 1281, 1039, 887, 752, 698, 600 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_9N_3F$ [M+H]: 214.0775; found: 214.0774. Anal. Calcd for $C_{12}H_8FN_3$: C, 67.60; H, 3.78; N, 19.71. Found: C, 67.64; H, 3.97; N, 19.42.

4-(Benzofuran-2-yl)-2-fluoro-*7H*-pyrrolo[2,3-*d*]pyrimidine

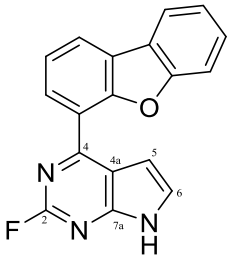
(2-fluoro-6-(benzofuran-2-yl)-9-NH-7-deazapurine) (46f)



Compound **46f** was prepared from **36** (172 mg, 1 mmol) and benzofuran-2-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a yellowish solid (165 mg, 65 %), which was crystallized from MeOH/water. R_f = 0.64 ($CHCl_3$-MeOH, 10:1). M. p. > 200 °C (dec). ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 7.20 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.37 (ddd, 1H, $J_{5,4}$ = 7.8 Hz, $J_{5,6}$ = 7.2 Hz, $J_{5,7}$ = 1.0 Hz, H-5-benzofuryl); 7.50 (ddd, 1H, $J_{6,7}$ = 8.3 Hz, $J_{6,5}$ = 7.2 Hz, $J_{6,4}$ = 1.3 Hz, H-6-benzofuryl); 7.72 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.80 - 7.83 (m, 2H, H-4,7-benzofuryl); 7.95 (d, 1H, $J_{3,7}$ = 1.0 Hz, H-3-benzofuryl); 12.49 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 101.49 (CH-5); 110.29 (CH-3-benzofuryl); 112.14 (CH-7-benzofuryl); 112.29 (d, $J_{C,F}$ = 3.4 Hz, C-4a); 122.80 (CH-4-benzofuryl); 124.10 (CH-5-benzofuryl); 127.12 (CH-6-benzofuryl); 127.83 (C-3a-benzofuryl); 129.25 (d, $J_{C,F}$ = 3.3 Hz, CH-6); 147.74 (d, $J_{C,F}$ = 15.9 Hz, C-4); 153.20 (C-2-benzofuryl); 155.36 (d, $J_{C,F}$ = 16.7 Hz, C-7a); 155.57 (C-7a-benzofuryl); 158.52 (d, $J_{C,F}$ = 204.5 Hz, C-2). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -51.04 (s, 1F, F-2). IR(KBr):

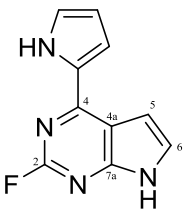
3213, 3144, 3010, 1592, 1383, 1323, 994, 860, 752, 731, 597 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_9N_3FO$ [M+H]: 254.0724; found: 254.07235.

4-(Dibenzo[*b,d*]furan-4-yl)-2-fluoro-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-fluoro-6-(dibenzofuran-4-yl)-9-NH-7-deazapurine) (46g)



Compound **46g** was prepared from **36** (172 mg, 1 mmol) and dibenzo[*b,d*]furan-4-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a yellowish solid (130 mg, 43 %), which was crystallized from MeOH/water. R_f = 0.64 ($CHCl_3$-MeOH, 10:1). M. p. > 200 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 6.71 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.47 (btd, 1H, $J_{8,7}$ = $J_{8,9}$ = 7.5 Hz, $J_{8,6}$ = 1.0 Hz, H-8-$C_{12}H_7O$); 7.57 (ddd, 1H, $J_{7,6}$ = 8.3 Hz, $J_{7,8}$ = 7.3 Hz, $J_{7,9}$ = 1.4 Hz, H-7-$C_{12}H_7O$); 7.62 (t, 1H, $J_{2,1}$ = $J_{2,3}$ = 7.6 Hz, H-2-$C_{12}H_7O$); 7.65 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.72 (dt, 1H, $J_{6,7}$ = 8.3 Hz, $J_{6,8}$ = $J_{6,9}$ = 0.8 Hz, H-6-$C_{12}H_7O$); 8.00 (dd, 1H, $J_{3,2}$ = 7.6 Hz, $J_{3,1}$ = 1.3 Hz, H-3-$C_{12}H_7O$); 8.26 (ddd, 1H, $J_{9,8}$ = 7.7 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.7 Hz, H-9-$C_{12}H_7O$); 8.39 (dd, 1H, $J_{1,2}$ = 7.7 Hz, $J_{1,3}$ = 1.3 Hz, H-1-$C_{12}H_7O$); 12.47 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 101.64 (CH-5); 112.05 (CH-6-$C_{12}H_7O$); 115.58 (d, $J_{C,F}$ = 3.7 Hz, C-4a); 121.61 (CH-9-$C_{12}H_7O$); 121.70 (C-4-$C_{12}H_7O$); 123.34 (C-9a-$C_{12}H_7O$); 123.59 (CH-1-$C_{12}H_7O$); 123.69 and 123.71 (CH-2,8-$C_{12}H_7O$); 125.12 (C-9b-$C_{12}H_7O$); 128.32 (CH-7-$C_{12}H_7O$); 128.33 (m, CH-6); 128.81 (CH-3-$C_{12}H_7O$); 152.82 (C-4a-$C_{12}H_7O$); 154.49 (d, $J_{C,F}$ = 16.5 Hz, C-7a); 155.55 (d, $J_{C,F}$ = 15.3 Hz, C-4); 155.70 (C-5a-$C_{12}H_7O$); 158.61 (d, $J_{C,F}$ = 204.8 Hz, C-2). ^{19}F NMR (470.3 MHz, DMSO-d_6): δ = -50.93 (s, 1F, F-2). IR(KBr): 3204, 3166, 2920, 1592, 1461, 1401, 1314, 1186, 1030, 893, 746, 692, 594 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{11}N_3FO$ [M+H]: 304.0881; found: 304.0880.

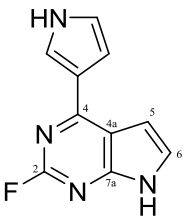
2-Fluoro-4-(*1H*-pyrrol-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-fluoro-6-(*1H*-pyrrol-2-yl)-9-NH-7-deazapurine) (46h)



Compound **46h** was prepared from **36** (172 mg, 1 mmol) and *N*-boc-pyrrole-2-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a brownish solid (145 mg, 72 %), which was crystallized from MeOH/water. R_f = 0.55 ($CHCl_3$-MeOH, 10:1). M. p. > 200 °C (dec); ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 6.31 (dt, 1H, $J_{4,3}$ = 3.7 Hz, $J_{4,NH}$ = $J_{4,5}$ = 2.4 Hz, H-4-pyrrolyl); 6.97 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.07 (btd, 1H, $J_{5,4}$ = $J_{5,NH}$

= 2.7 Hz, $J_{5,3}$ = 1.4 Hz, H-5-pyrrolyl); 7.24 (ddd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,NH}$ = 2.6 Hz, $J_{3,5}$ = 1.4 Hz, H-3-pyrrolyl); 7.49 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.4 Hz, H-6); 11.87 (bs, 1H, NH-pyrrolyl); 12.16 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 100.96 (CH-5); 109.83 (d, $J_{C,F}$ = 3.4 Hz, C-4a); 110.99 (CH-4-pyrrolyl); 114.38 (CH-3-pyrrolyl); 123.85 (CH-5-pyrrolyl); 126.90 (d, $J_{C,F}$ = 3.3 Hz, CH-6); 128.45 (C-2-pyrrolyl); 150.79 (d, $J_{C,F}$ = 15.7 Hz, C-4); 154.10 (d, $J_{C,F}$ = 17.2 Hz, C-7a); 158.70 (d, $J_{C,F}$ = 202.7 Hz, C-2). ^{19}F NMR (470.3 MHz, DMSO-d$_6$): δ = -51.14 (s, 1F, F-2). IR(KBr): 3306, 3255, 3117, 2920, 1604, 1458, 1359, 1120, 1030, 842, 731, 668, 579 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_8N_4F$ [M+H]: 203.0727; found: 203.0727.

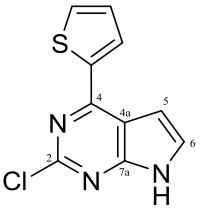
2-Fluoro-4-(*1H*-pyrrol-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-fluoro-6-(*1H*-pyrrol-3-yl)-9-NH-7-deazapurine) (46i)



Compound **46i** was prepared from **36** (172 mg, 1 mmol) and 1-(triisopropylsilyl)-1*H*-pyrrole-3-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a brownish solid (120 mg, 59 %), which was crystallized from MeOH/water. R_f = 0.38 ($CHCl_3$-MeOH, 10:1). M. p. 251-252 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 6.87 (btd, 1H, $J_{4,5}$ = $J_{4,NH}$ = 2.7 Hz, $J_{4,2}$ = 1.6 Hz, H-4-pyrrolyl); 6.94 (m, 1H, H-5-pyrrolyl); 6.95 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.44 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.81 (dt, 1H, $J_{2,NH}$ = 3.0 Hz, $J_{2,5}$ = $J_{2,4}$ = 1.8 Hz, H-2-pyrrolyl); 11.51 (bs, 1H, NH-pyrrolyl); 12.06 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 101.20 (CH-5); 108.23 (CH-4-pyrrolyl); 111.11 (d, $J_{C,F}$ = 3.6 Hz, C-4a); 120.09 (CH-5-pyrrolyl); 121.71 (C-3-pyrrolyl); 122.04 (CH-2-pyrrolyl); 126.31 (d, $J_{C,F}$ = 3.3 Hz, CH-6); 154.04 (d, $J_{C,F}$ = 17.1 Hz, C-7a); 155.94 (d, $J_{C,F}$ = 16.1 Hz, C-4); 158.92 (d, $J_{C,F}$ = 201.8 Hz, C-2). ^{19}F NMR (470.3 MHz, DMSO-d$_6$): δ = -51.15 (s, 1F, F-2). IR(KBr): 3255, 3138, 3004, 2857, 1580, 1455, 1386, 1159, 836, 755, 603 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_8N_4F$ [M+H]: 203.0727; found: 203.0727.

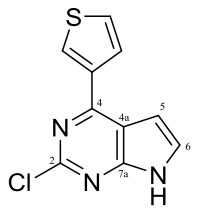
2-Chloro-4-(thiophen-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-chloro-6-(thiophen-2-yl)-9-NH-7-deazapurine) (47a)

Compound **47a** was prepared from **34** (376 mg, 2 mmol) and thiophene-2-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a yellowish solid (440 mg, 93 %), which was crystallized from MeOH/water. R_f = 0.59 ($CHCl_3$-



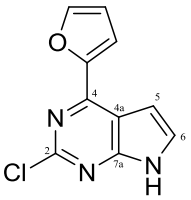
MeOH, 10:1). M. p. 250-251 °C. ^{1}H NMR (500.0 MHz, Acetone-d$_6$): δ = 7.08 (dd, 1H, $J_{5,6}$ = 3.7 Hz, $J_{5,NH}$ = 1.9 Hz, H-5); 7.31 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.8 Hz, H-4-thienyl); 7.68 (dd, 1H, $J_{6,5}$ = 3.7 Hz, $J_{6,NH}$ = 2.4 Hz, H-6); 7.82 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.1 Hz, H-5-thienyl); 8.18 (dd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,5}$ = 1.1 Hz, H-3-thienyl); 11.40 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, Acetone-d$_6$): δ = 101.48 (CH-5); 112.44 (C-4a); 128.84 (CH-6); 129.60 (CH-4-thienyl); 130.89 (CH-3-thienyl); 131.73 (CH-5-thienyl); 142.59 (C-2-thienyl); 153.15 (C-4); 153.55 (C-2); 155.40 (C-7a). IR(KBr): 3183, 3114, 2989, 2845, 1559, 1284, 1159, 961, 824, 772, 591 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3ClS$ [M+H]: 236.0044; found: 236.0044. Anal. Calcd for $C_{10}H_6ClN_3S$: C, 50.96; H, 2.57; N, 17.83. Found: C, 50.63; H, 2.83; N, 17.71.

2-Chloro-4-(thiophen-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-chloro-6-(thiophen-3-yl)-9-NH-7-deazapurine) (47b)



Compound **47b** was prepared from **34** (376 mg, 2 mmol) and thiophene-3-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a white solid (280 mg, 60 %), which was crystallized from MeOH/water. R_f = 0.59 ($CHCl_3$-MeOH, 10:1). M. p. 255-256 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 7.07 (dd, 1H, $J_{5,6}$ = 3.7 Hz, $J_{5,NH}$ = 1.1 Hz, H-5); 7.69 (dd, 1H, $J_{6,5}$ = 3.7 Hz, $J_{6,NH}$ = 1.9 Hz, H-6); 7.76 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.90 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 8.58 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 12.43 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 100.80 (CH-5); 112.92 (C-4a); 127.48 (CH-4-thienyl); 127.66 (CH-5-thienyl); 128.78 (CH-6); 129.79 (CH-2-thienyl); 139.05 (C-3-thienyl); 152.20 (C-2); 153.05 (C-4); 154.28 (C-7a). IR(KBr): 3195, 3138, 2998, 2851, 1592, 1284, 1156, 845, 776, 772, 600 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3SCl$ [M+H]: 236.0044; found: 236.044.

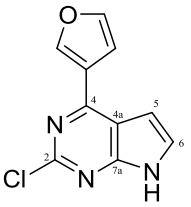
2-Chloro-4-(furan-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-chloro-6-(furan-2-yl)-9-NH-7-deazapurine) (47c)



Compound **47c** was prepared from **34** (376 mg, 2 mmol) and furan-2-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a white solid (280 mg, 64 %), which was crystallized from MeOH/water. R_f = 0.55 ($CHCl_3$-MeOH, 10:1). M. p. 265-266 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 6.80 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.7 Hz, H-4-furyl); 6.98 (dd,

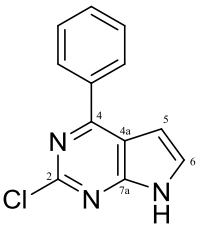
1H, $J_{5,6}$ = 3.5 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.50 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.67 (dd, 1H, $J_{6,5}$ = 3.5 Hz, $J_{6,NH}$ = 2.4 Hz, H-6); 8.09 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 12.43 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 100.97 (CH-5); 111.09 (C-4a); 113.13 (CH-4-furyl); 114.63 (CH-3-furyl); 128.91 (CH-6); 147.10 (CH-5-furyl); 147.78 (C-4); 151.56 (C-2-furyl); 152.25 (C-2); 154.27 (C-7a). IR(KBr): 3195, 3114, 2992, 2857, 1589, 1338, 1281, 928, 836, 737, 594 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3OCl$ [M+H]: 220.0272; found: 220.0273.

2-Chloro-4-(furan-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-chloro-6-(furan-3-yl)-9-NH-7-deazapurine) (47d)



Compound **47d** was prepared from **34** (188 mg, 1 mmol) and furan-3-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a white solid (160 mg, 73 %), which was crystallized from MeOH/water. R_f = 0.54 ($CHCl_3$-MeOH, 10:1). M. p. 256-257 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 7.02 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.7 Hz, H-5); 7.21 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.66 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.3 Hz, H-6); 7.91 (bt, 1H, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, H-5-furyl); 8.75 (dd, 1H, $J_{2,5}$ = 1.5 Hz, $J_{2,4}$ = 0.9 Hz, H-2-furyl); 12.40 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 100.82 (CH-5); 109.69 (CH-4-furyl); 113.14 (C-4a); 124.76 (C-3-furyl); 128.70 (CH-6); 145.29 (CH-5-furyl); 146.00 (CH-2-furyl); 152.05 (C-4); 152.53 (C-2); 154.04 (C-7a). IR(KBr): 3189, 3132, 2998, 2854, 1559, 1281, 1165, 830, 791, 737, 588 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_7N_3OCl$ [M+H]: 220.0272; found: 220.0272.

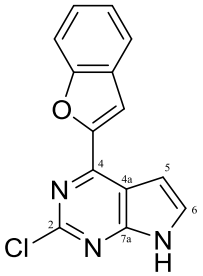
2-Chloro-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-chloro-6-phenyl-9-NH-7-deazapurine) (47e)



Compound **47e** was prepared from **34** (376 mg, 2 mmol) and phenylboronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a white solid (230 mg, 50 %), which was crystallized from MeOH/water. R_f = 0.59 ($CHCl_3$-MeOH, 10:1). M. p. 232-233 °C. ^{1}H NMR (500.0 MHz, DMSO-d$_6$): δ = 6.95 (d, 1H, $J_{5,6}$ = 3.6 Hz, H-5); 7.57 – 7.63 (m, 3H, H-*m*,*p*-Ph); 7.71 (d, 1H, $J_{6,5}$ = 3.7 Hz, H-6); 8.15 (m, 2H, H-*o*-Ph); 12.50 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): δ = 100.81 (CH-5); 113.92 (C-4a); 128.93 (CH-*o*-Ph); 129.06 (CH-6); 129.23 (CH-*m*-Ph); 131.01 (CH-*p*-Ph); 136.71 (C-*i*-Ph); 152.39 (C-2);

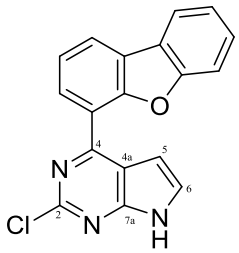
154.24 (C-7a); 157.84 (C-4); IR(KBr): 3189, 3111, 2995, 2851, 1547, 1335, 1275, 869, 749, 698, 597 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_9N_3Cl$ [M+H]: 230.04795; found: 230.0480.

4-(Benzofuran-2-yl)-2-chloro-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-chloro-6-(benzofuran-2-yl)-9-NH-7-deazapurine) (47f)



Compound **47f** was prepared from **34** (376 mg, 2 mmol) and benzofuran-2-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a white solid (160 mg, 30 %), which was crystallized from MeOH/water. R_f = 0.59 ($CHCl_3$-MeOH, 10:1). M. p. 309-310 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 7.20 (d, 1H, $J_{5,6}$ = 3.6 Hz, H-5); 7.38 (btd, 1H, $J_{5,4}$ = $J_{5,6}$ = 7.4 Hz, $J_{5,7}$ = 1.2 Hz, H-5-benzofuryl); 7.50 (ddd, 1H, $J_{6,7}$ = 8.3 Hz, $J_{6,5}$ = 7.2 Hz, $J_{6,4}$ = 1.3 Hz, H-6-benzofuryl); 7.78 (dd, 1H, $J_{6,5}$ = 3.7 Hz, $J_{6,NH}$ = 1.5 Hz, H-6); 7.81 - 7.84 (m, 2H, H-4,7-benzofuryl); 7.97 (d, 1H, $J_{3,7}$ = 1.0 Hz, H-3-benzofuryl); 12.56 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 101.29 (CH-5); 110.31 (CH-3-benzofuryl); 112.18 (CH-7-benzofuryl); 112.49 (C-4a); 122.83 (CH-4-benzofuryl); 124.13 (CH-5-benzofuryl); 127.13 (CH-6-benzofuryl); 127.90 (C-3a-benzofuryl); 129.72 (CH-6); 147.64 (C-4); 152.25 (C-2); 153.07 (C-2-benzofuryl); 154.63 (C-7a); 155.57 (C-7a-benzofuryl). IR(KBr): 3186, 3123, 2989, 2851, 1583, 1350, 1278, 940, 848, 752, 597 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_8N_3OClNa$ [M+Na]: 292.0248; found: 292.0249.

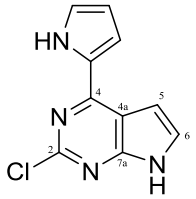
2-Chloro-4-(dibenzo[*b*,*d*]furan-4-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-chloro-6-(dibenzofuran-4-yl)-9-NH-7-deazapurine) (47g)



Compound **47g** was prepared from **34** (376 mg, 2 mmol) and dibenzo[*b*,*d*]furan-4-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a white solid (93 mg, 15 %), which was crystallized from MeOH/water. R_f = 0.59 ($CHCl_3$-MeOH, 10:1). M. p. 309-310 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 6.69 (d, 1H, $J_{5,6}$ = 3.6 Hz, H-5); 7.47 (btd, 1H, $J_{8,7}$ = $J_{8,9}$ = 7.5 Hz, $J_{8,6}$ = 1.0 Hz, H-8-$C_{12}H_7O$); 7.57 (ddd, 1H, $J_{7,6}$ = 8.3 Hz, $J_{7,8}$ = 7.3 Hz, $J_{7,9}$ = 1.4 Hz, H-7-$C_{12}H_7O$); 7.62 (t, 1H, $J_{2,1}$ = $J_{2,3}$ = 7.6 Hz, H-2-$C_{12}H_7O$); 7.71 (d, 1H, $J_{6,5}$ = 3.5 Hz, H-6); 7.72 (dt, 1H, $J_{6,7}$ = 8.3 Hz, $J_{6,8}$ = $J_{6,9}$ = 0.9 Hz, H-6-$C_{12}H_7O$); 7.97 (dd, 1H, $J_{3,2}$ = 7.6 Hz, $J_{3,1}$ = 1.3 Hz, H-3-$C_{12}H_7O$); 8.26 (ddd, 1H, $J_{9,8}$ = 7.7 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.7 Hz, H-9-$C_{12}H_7O$); 8.39 (dd, 1H, $J_{1,2}$ = 7.7 Hz, $J_{1,3}$ = 1.3 Hz, H-1-$C_{12}H_7O$); 12.55 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ =

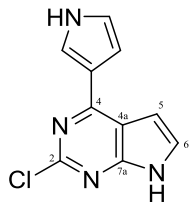
101.45 (CH-5); 112.06 (CH-6-$C_{12}H_7O$); 115.91 (C-4a); 121.63 (CH-9-$C_{12}H_7O$); 121.69 (C-4-$C_{12}H_7O$); 123.37 (C-9a-$C_{12}H_7O$); 123.52 (CH-1-$C_{12}H_7O$); 123.71 (CH-2,8-$C_{12}H_7O$); 125.07 (C-9b-$C_{12}H_7O$); 128.31 (CH-7-$C_{12}H_7O$); 128.75 (CH-6); 128.83 (CH-3-$C_{12}H_7O$); 152.32 (C-2); 152.81 (C-4a-$C_{12}H_7O$); 153.87 (C-7a); 155.22 (C-4); 155.69 (C-5a-$C_{12}H_7O$). IR(KBr): 3189, 3144, 2923, 2851, 1565, 1449, 1278, 1192, 845, 740, 623 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{10}N_3OClNa$ [M+Na]: 342.0405; found: 342.0405.

2-Chloro-4-(*1H*-pyrrol-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-chloro-6-(*1H*-pyrrol-2-yl)-9-NH-7-deazapurine) (47h)



Compound **47h** was prepared from **34** (376 mg, 2 mmol) and *N*-boc-pyrrole-2-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a greenish solid (282 mg, 65 %), which was crystallized from MeOH/water. R_f = 0.50 ($CHCl_3$-MeOH, 10:1). M. p. > 200 °C (dec). ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 6.31 (dt, 1H, $J_{4,3}$ = 3.7 Hz, $J_{4,NH}$ = $J_{4,5}$ = 2.4 Hz, H-4-pyrrolyl); 6.95 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.4 Hz, H-5); 7.07 (btd, 1H, $J_{5,4}$ = $J_{5,NH}$ = 2.7 Hz, $J_{5,3}$ = 1.4 Hz, H-5-pyrrolyl); 7.21 (ddd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,NH}$ = 2.6 Hz, $J_{3,5}$ = 1.4 Hz, H-3-pyrrolyl); 7.53 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.1 Hz, H-6); 11.74 (bs, 1H, NH-pyrrolyl); 12.22 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 100.85 (CH-5); 110.28 (C-4a); 111.11 (CH-4-pyrrolyl); 114.48 (CH-3-pyrrolyl); 124.02 (CH-5-pyrrolyl); 127.46 (CH-6); 128.35 (C-2-pyrrolyl); 150.54 (C-4); 152.38 (C-2); 153.62 (C-7a). IR(KBr): 3401, 3129, 2986, 2851, 1574, 1452, 1377, 1278, 1081, 833, 749 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_8N_4Cl$ [M+H]: 219.0432; found: 219.0430.

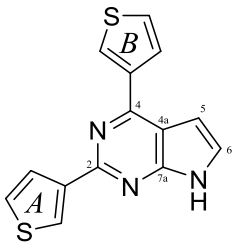
2-Chloro-4-(*1H*-pyrrol-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine
(2-chloro-6-(*1H*-pyrrol-3-yl)-9-NH-7-deazapurine) (47i)



Compound **47i** was prepared from **34** (376 mg, 2 mmol) and 1-(triisopropylsilyl)-1*H*-pyrrole-3-boronic acid. Purification using column chromatography (0 % → 15 % EtOAc in CH_2Cl_2) provided a brownish solid (245 mg, 56 %), which was crystallized from MeOH/water. R_f = 0.34 ($CHCl_3$-MeOH, 10:1). M. p. 137-138 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 6.86 (btd, 1H, $J_{4,5}$ = $J_{4,NH}$ = 2.7 Hz, $J_{4,2}$ = 1.6 Hz, H-4-pyrrolyl); 6.91 – 6.95 (m, 2H, H-5-pyrrolyl, H-5); 7.50 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 1.4 Hz, H-6); 7.79 (dt, 1H, $J_{2,NH}$ = 2.9 Hz, $J_{2,5}$ = $J_{2,4}$ = 1.7 Hz, H-2-pyrrolyl); 11.50 (bs, 1H, NH-pyrrolyl); 12.12 (bs, 1H, NH). ^{13}C NMR (125.7 MHz,

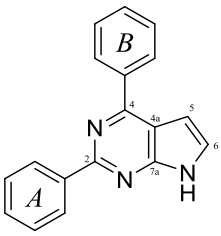
DMSO-d_6): δ = 100.97 (CH-5); 108.20 (CH-4-pyrrolyl); 111.49 (C-4a); 120.08 (CH-5-pyrrolyl); 121.60 (C-3-pyrrolyl); 121.98 (CH-2-pyrrolyl); 126.78 (CH-6); 152.53 (C-2); 153.53 (C-7a); 155.50 (C-4)). IR(KBr): 3186, 3108, 2944, 2869, 1568, 1488, 1263, 1084, 833, 689 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_8N_4Cl$ [M+H]: 219.0432; found: 219.0430.

2,4-Di(thiophen-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2,6-di(thiophen-3-yl)-9-NH-7-deazapurine) (48b)



Compound **48b** was obtained as a less polar byproduct during the preparation of **47b** from **34** (376 mg, 2 mmol) and thiophene-3-boronic acid. Column chromatography (0 % → 15 % EtOAc in CH_2Cl_2, **48b** eluted at 100 % CH_2Cl_2) provided a white solid (145 mg, 26 %), which was crystallized from MeOH/water. R_f = 0.70 ($CHCl_3$-MeOH, 10:1). M. p. 215-216 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 7.01 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.62 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.4 Hz, H-6); 7.65 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 3.1 Hz, H-5-thienyl*A*); 7.76 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl*B*); 7.94 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.2 Hz, H-4-thienyl*A*); 8.09 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl*B*); 8.37 (dd, 1H, $J_{2,5}$ = 3.1 Hz, $J_{2,4}$ = 1.2 Hz, H-2-thienyl*A*); 8.61 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl*B*); 12.19 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 100.52 (CH-5); 112.15 (C-4a); 126.22 (CH-2-thienyl*A*); 126.77 (CH-5-thienyl*A*); 127.06 (CH-5-thienyl*B*); 127.48 (CH-4-thienyl*A*); 127.86 (CH-2-thienyl*B*); 127.91 (CH-6); 128.46 (CH-2-thienyl*B*); 140.70 (C-3-thienyl*B*); 142.83 (C-3-thienyl*A*); 151.21 (C-4); 153.72 (C-7a); 154.21 (C-2). IR(KBr): 3192, 3135, 2995, 2878, 1562, 1350, 1114, 833, 824, 776, 597 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_{10}N_3S_2$ [M+H]: 284.0311; found: 284.0311.

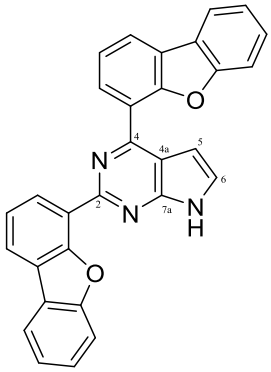
2,4-Diphenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (2,6-diphenyl-9-NH-7-deazapurine) (48e)



Compound **48e** was obtained as a less polar byproduct during the preparation of **47e** from **34** (376 mg, 2 mmol) and phenylboronic acid. Column chromatography (0 % → 15 % EtOAc in CH_2Cl_2, **48e** eluted at 100 % CH_2Cl_2) provided a white solid (205 mg, 38 %), which was crystallized from MeOH/water. R_f = 0.77 ($CHCl_3$-MeOH, 10:1). M. p. 220-221 °C. ^{1}H NMR (500.0 MHz, DMSO-d_6): δ = 6.93 (dd, 1H, $J_{5,6}$ = 3.6 Hz, $J_{5,NH}$ = 1.1 Hz, H-5); 7.48 (m, 1H, H-*p*-Ph*A*); 7.54 (m, 2H, H-*m*-Ph*A*); 7.58 (m, 1H, H-*p*-Ph*B*); 7.63 (m, 2H,

H-*m*-Ph*B*); 7.68 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,NH}$ = 2.0 Hz, H-6); 8.32 (m, 2H, H-*o*-Ph*B*); 8.55 (m, 2H, H-*o*-Ph*A*); 12.31 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 100.46 (CH-5); 113.40 (C-4a); 127.65 (CH-*o*-Ph*A*); 128.45 (CH-6); 128.74 (CH-*m*-Ph*A*); 128.84 (CH-*o*-Ph*B*); 129.09 (CH-*m*-Ph*B*); 129.82 (CH-*p*-Ph*A*); 130.32 (CH-*p*-Ph*B*); 138.34 (C-*i*-Ph*B*); 138.81 (C-*i*-Ph*A*); 153.92 (C-7a); 155.68 (C-4); 156.44 (C-2). IR(KBr): 3198, 3120, 2995, 2875, 1553, 1386, 1326, 863, 764, 695, 591 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{14}N_3$ [M+H]: 272.1182; found: 272.1182.

2,4-Bis(dibenzo[*b*,*d*]furan-4-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2,6-bis(dibenzofuran-4-yl)-9-NH-7-deazapurine) (48g)



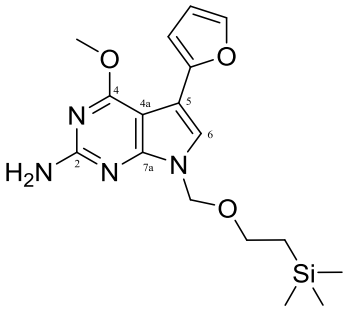
Compound **48g** was obtained as a less polar byproduct at the preparation of **47g** from **34** (376 mg, 2 mmol) and dibenzo[*b*,*d*]furan-4-boronic acid. Column chromatography (0 % → 15 % EtOAc in CH_2Cl_2, **48g** eluted at 100 % CH_2Cl_2) provided a white solid (42 mg, 5 %), which was crystallized from MeOH/water. R_f = 0.77 ($CHCl_3$-MeOH, 10:1). M. p. 301-302 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 6.74 (dd, 1H, $J_{5,6}$ = 3.5 Hz, $J_{5,NH}$ = 1.0 Hz, H-5); 7.46 and 7.48 (2×btd, 2×1H, $J_{8,7}$ = $J_{8,9}$ = 7.5 Hz, $J_{8,6}$ = 1.0 Hz, H-8-$C_{12}H_7O$); 7.58 (2×ddd, 2H, $J_{7,6}$ = 8.3 Hz, $J_{7,8}$ = 7.3 Hz, $J_{7,9}$ = 1.4 Hz, H-7-$C_{12}H_7O$); 7.59 and 7.69 (2×t, 2×1H, $J_{2,1}$ = $J_{2,3}$ = 7.6 Hz, H-2-$C_{12}H_7O$); 7.75 (m, 1H, H-6); 7.74 and 7.77 (2×dt, 2×1H, $J_{6,7}$ = 8.3 Hz, $J_{6,8}$ = $J_{6,9}$ = 0.9 Hz, H-6-$C_{12}H_7O$); 8.23 (dd, 1H, $J_{3,2}$ = 7.7 Hz, $J_{3,1}$ = 1.3 Hz, H-3-$C_{12}H_7O$); 8.25 and 8.29 (2×ddd, 2×1H, $J_{9,8}$ = 7.6 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.7 Hz, H-9-$C_{12}H_7O$); 8.30 and 8.40 (2×dd, 2×1H, $J_{1,2}$ = 7.7 Hz, $J_{1,3}$ = 1.4 Hz, H-1-$C_{12}H_7O$); 8.47 (dd, 1H, $J_{3,2}$ = 7.7 Hz, $J_{3,1}$ = 1.4 Hz, H-3-$C_{12}H_7O$). ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 101.14 (CH-5); 111.94 and 112.04 (CH-6-$C_{12}H_7O$); 115.20 (C-4a); 121.42 and 121.60 (CH-9-$C_{12}H_7O$); 122.30 and 122.95 (CH-1-$C_{12}H_7O$); 123.24 (C-4-$C_{12}H_7O$); 123.31 (CH-2-$C_{12}H_7O$); 123.37 (CH-8-$C_{12}H_7O$); 123.55 and 123.61 (C-9a-$C_{12}H_7O$); 123.65 (CH-8-$C_{12}H_7O$); 123.75 (CH-2-$C_{12}H_7O$); 124.92 and 124.98 (C-9b-$C_{12}H_7O$); 125.27 (C-4-$C_{12}H_7O$); 128.02 and 128.21 (CH-7-$C_{12}H_7O$); 128.42 (CH-6); 129.03 and 129.07 (CH-3-$C_{12}H_7O$); 153.13, 153.33. 153.46 and 153.70 (C-4,7a, C-4a-$C_{12}H_7O$); 155.51 (C-2); 155.76 and 155.94 (C-5a-$C_{12}H_7O$). IR(KBr): 3183, 3135, 2926, 2848, 1562, 1455, 1416, 1198, 839, 743 cm^{-1}. HRMS (ESI) calculated for $C_{30}H_{18}N_3O_2$ [M+H]: 452.13935; found: 452.1393.

5.8 Synthesis of 2-substituted 7-(het)aryl-7-deazapurines

General procedure for aqeous Suzuki-Miyaura cross-coupling reaction:

An argon-purged mixture of SEM protected 7-iodo-deazapurine derivative (compounds **49**-**50** 1 mmol), boronic acid (1.5 mmol), Na_2CO_3 (318 mg, 3 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and TPPTS (28 mg, 0.05 mmol) in water/MeCN (2:1, 5 mL) was stirred at 100 °C for 3 hours. After cooling, the mixture was diluted with water and extracted with chloroform. Organic phase was dried over magnesium sulfate, filtered, evaporated and the residue was purified by column chromatography on silica gel using mobile phase as indicated for individual products. Alernatively, after cooling the reaction mixture was directly loaded on silica by co-evaporation without aqueous work-up.

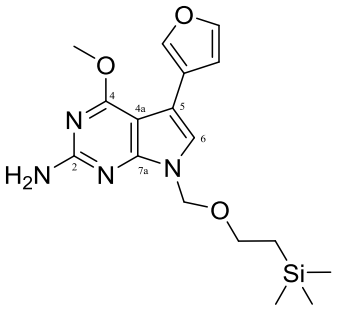
5-(Furan-2-yl)-4-methoxy-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine
(2-amino-6-methoxy-7-(furan-2-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine)
(55a)



Compound **55a** was prepared from **49** (420 mg, 1.0 mmol) and furan-2-boronic acid (168 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (30-40 % EtOAc in hexanes) provided a yellowish oil (256 mg, 71 %). ^{1}H NMR (500 MHz, DMSO-d_6): -0.08 (s, 9H, CH_3Si); 0.83 (m, 2H, OCH_2CH_2Si); 3.50 (m, 2H, OCH_2CH_2Si); 3.99 (s, 3H, CH_3O-4); 5.38 (s, 2H, NCH_2O); 6.37 (bs, 2H, NH_2); 6.50 (dd, 1H, $J_{4,3}$ = 3.3 Hz, $J_{4,5}$ = 1.9 Hz, H-4-furyl); 6.82 (dd, 1H, $J_{3,4}$ = 3.3 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.30 (s, 1H, H-6); 7.58 (dd, 1H, $J_{5,4}$ = 1.9 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.16 (CH_3Si); 17.35 (OCH_2CH_2Si); 53.27 (CH_3O-4); 65.43 (OCH_2CH_2Si); 72.37 (NCH_2O); 93.54 (C-4a); 106.49 (CH-3-furyl); 107.13 (C-5); 111.69 (CH-4-furyl); 119.55 (CH-6); 141.15 (CH-5-furyl); 149.16 (C-2-furyl); 155.37 (C-7a); 160.10 (C-2); 163.37 (C-4). HRMS (ESI) calculated for $C_{17}H_{25}N_4O_3Si$ [M+H]: 361.1690; found 361.1691.

5-(Furan-3-yl)-4-methoxy-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine

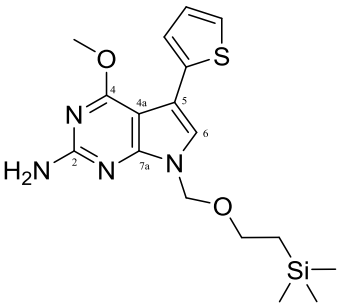
(2-amino-6-methoxy-7-(furan-3-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (55b)



Compound **55b** was prepared from **49** (420 mg, 1.0 mmol) and furan-3-boronic acid (168 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (30-40 % EtOAc in hexanes) provided a yellowish oil (263 mg, 73 %). ^{1}H NMR (500 MHz, DMSO-d$_6$): -0.07 (s, 9H, CH_3Si); 0.84 (m, 2H, OCH_2CH_2Si); 3.49 (m, 2H, OCH_2CH_2Si); 3.98 (s, 3H, CH_3O-4); 5.35 (s, 2H, NCH_2O); 6.30 (bs, 2H, NH_2); 6.84 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.31 (s, 1H, H-6); 7.64 (t, 1H, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, H-5-furyl); 8.02 (m, 1H, H-2-furyl). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): -1.16 (CH_3Si); 17.33 (OCH_2CH_2Si); 53.19 (CH_3O-4); 65.34 (OCH_2CH_2Si); 72.21 (NCH_2O); 94.74 (C-4a); 107.21 (C-5); 109.97 (CH-4-furyl); 119.14 (C-3-furyl); 120.36 (CH-6); 139.53 (CH-2-furyl); 143.51 (CH-5-furyl); 155.57 (C-7a); 159.93 (C-2); 163.37 (C-4). HRMS (ESI) calculated for $C_{17}H_{25}N_4O_3Si$ [M+H]: 361.1690; found 361.1691.

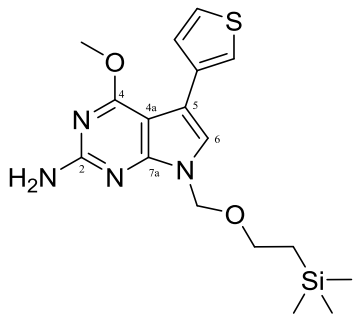
5-(Thiophen-2-yl)-4-methoxy-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine

(2-amino-6-methoxy-7-(thiophen-2-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (55c)



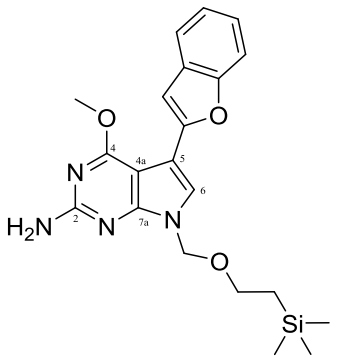
Compound **55c** was prepared from **49** (420 mg, 1.0 mmol) and thiophene-2-boronic acid (192 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (30-40 % EtOAc in hexanes) provided a yellowish oil (275 mg, 73 %). ^{1}H NMR (500 MHz, DMSO-d$_6$): -0.07 (s, 9H, CH_3Si); 0.83 (m, 2H, OCH_2CH_2Si); 3.51 (m, 2H, OCH_2CH_2Si); 3.96 (s, 3H, CH_3O-4); 5.37 (s, 2H, NCH_2O); 6.36 (bs, 2H, NH_2); 7.04 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.6 Hz, H-4-thienyl); 7.27 (s, 1H, H-6); 7.34 (dd, 1H, $J_{5,4}$ = 5.1Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.40 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): -1.17 (CH_3Si); 17.34 (OCH_2CH_2Si); 53.13 (CH_3O-4); 65.43 (OCH_2CH_2Si); 72.25 (NCH_2O); 94.70 (C-4a); 110.01 (C-5); 120.74 (CH-6); 123.57 (CH-5-thienyl); 125.02 (CH-3-thienyl); 127.76 (CH-4-thienyl); 136.79 (C-2-thienyl); 155.42 (C-7a); 159.95 (C-2); 163.44 (C-4). HRMS (ESI) calculated for $C_{17}H_{25}N_4O_2SSi$ [M+H]: 377.1462; found 377.1462.

5-(Thiophen-3-yl)-4-methoxy-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine
(2-amino-6-methoxy-7-(thiophen-3-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (55d)



Compound **55d** was prepared from **49** (420 mg, 1.0 mmol) and thiophene-3-boronic acid (192 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (30-40 % EtOAc in hexanes) provided a yellowish oil (286 mg, 76 %).m ^{1}H NMR (500 MHz, DMSO-d$_6$): -0.07 (s, 9H, CH_3Si); 0.84 (m, 2H, OCH_2CH_2Si); 3.51 (m, 2H, OCH_2CH_2Si); 3.98 (s, 3H, CH_3O-4); 5.37 (s, 2H, NCH_2O); 6.31 (bs, 2H, NH_2); 7.37 (s, 1H, H-6); 7.45 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 7.50 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 3.0 Hz, H-5-thienyl); 7.77 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): -1.16 (CH_3Si); 17.35 (OCH_2CH_2Si); 53.19 (CH_3O-4); 65.39 (OCH_2CH_2Si); 72.27 (NCH_2O); 94.86 (C-4a); 111.76 (C-5); 120.32 (CH-2-thienyl); 121.06 (CH-6); 125.58 (CH-5-thienyl); 127.71 (CH-4-thienyl); 134.93 (C-3-thienyl); 155.53 (C-7a); 159.79 (C-2); 163.43 (C-4). HRMS (ESI) calculated for $C_{17}H_{25}N_4O_2SSi$ [M+H]: 377.1462; found 377.1463.

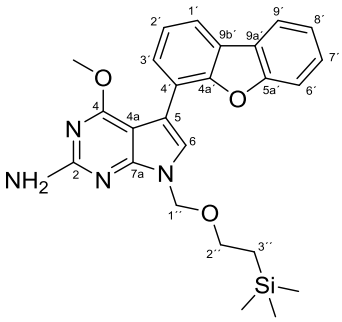
5-(Benzofuran-2-yl)-4-methoxy-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine
(2-amino-6-methoxy-7-(benzofuran-2-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (55e)



Compound **55e** was prepared from **49** (420 mg, 1.0 mmol) and benzofuran-2-boronic acid (243 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (40-50 % EtOAc in hexanes) provided a yellowish oil (287 mg, 70 %). ^{1}H NMR (500 MHz, DMSO-d$_6$): -0.07 (s, 9H, CH_3Si); 0.84 (m, 2H, OCH_2CH_2Si); 3.54 (m, 2H, OCH_2CH_2Si); 4.07 (s, 3H, CH_3O-4); 5.43 (s, 2H, NCH_2O); 6.46 (bs, 2H, NH_2); 7.21 (btd, 1H, $J_{5,4} = J_{5,6}$ = 7.2 Hz, $J_{5,7}$ = 1.2 Hz, H-5-benzofuryl); 7.24 (bddd, 1H, $J_{6,7}$ = 8.2 Hz, $J_{6,5}$ = 7.3 Hz, $J_{6,4}$ = 1.5 Hz, H-6-benzofuryl); 7.31 (d, 1H, $J_{3,7}$ = 1.1 Hz, H-3-benzofuryl); 7.50 (dm, 1H, $J_{7,6}$ = 8.2 Hz, H-7-benzofuryl); 7.60 (s,

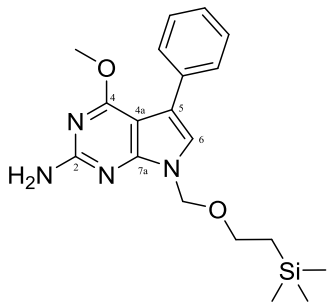
1H, H-6); 7.61 (dm, 1H, $J_{4,5}$ = 7.3 Hz, H-4-benzofuryl). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): -1.16 (CH_3Si); 17.37 (OCH_2CH_2Si); 53.47 (CH_3O-4); 65.57 (OCH_2CH_2Si); 72.56 (NCH_2O); 93.74 (C-4a); 102.39 (CH-3-benzofuryl); 106.39 (C-5); 110.55 (CH-7-benzofuryl); 120.78 (CH-4-benzofuryl); 121.96 (CH-6); 123.04 (CH-5-benzofuryl); 123.89 (CH-6-benzofuryl); 129.60 (C-3a-benzofuryl); 151.62 (C-2-benzofuryl); 153.65 (C-7a-benzofuryl); 155.81 (C-7a); 160.33 (C-2); 163.40 (C-4). HRMS (ESI) calculated for $C_{21}H_{27}N_4O_3Si$ [M+H]: 411.1846; found 411.1848.

5-(Dibenzo[*b,d*]furan-4-yl)-4-methoxy-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine
(2-amino-6-methoxy-7-(dibenzofuran-4-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (55f)



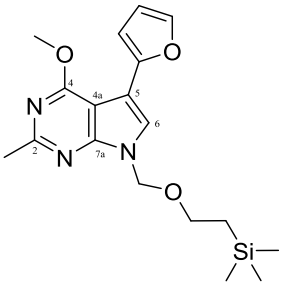
Compound **55f** was prepared from **49** (420 mg, 1.0 mmol) and dibenzo[*b,d*]furan-4-boronic acid (318 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (40-50 % EtOAc in hexanes) provided a colorless oil (299 mg, 65 %). ^{1}H NMR (500 MHz, DMSO-d$_6$): -0.05 (s, 9H, $(CH_3)_3Si$); 0.87 (m, 2H, CH_2-3´´); 3.60 (m, 2H, CH_2-2´´); 3.84 (s, 3H, CH_3O-4); 5.49 (s, 2H, CH_2-1´´); 6.38 (bs, 2H, NH_2-2); 7.40 (m, 1H, CH-8´); 7.42 (t, 1H, $J_{2',1'}$= $J_{2',3'}$= 7.7 Hz, CH-2´); 7.52 (ddd, 1H, $J_{7',6'}$= 8.3 Hz, $J_{7',8'}$= 7.3 Hz, $J_{7',9'}$= 1.4 Hz, CH-7´); 7.59 (s, 1H, CH-6); 7.67 (dt, 1H, $J_{6',7'}$= 8.3 Hz, $J_{6',8'}$= $J_{6',9'}$= 0.8 Hz, CH-6´); 7.80 (dd, 1H, $J_{3',2'}$= 7.7 Hz, $J_{3',1'}$= 1.3 Hz, CH-3´); 8.01 (dd, 1H, $J_{1',2'}$= 7.7 Hz, $J_{1',3'}$= 1.3 Hz, CH-1´); 8.16 (ddd, 1H, $J_{9',8'}$= 7.7 Hz, $J_{9',7'}$ = 1.3 Hz, $J_{9',6'}$ = 0.8 Hz, CH-9´). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): -1.12 ($(CH_3)_3Si$); 17.46 (CH_2-3´´); 53.20 (CH_3O-4); 65.59 (CH_2-2´´); 72.53 (CH_2-1´´); 95.81 (C-4a); 110.02 (C-5); 111.75 (CH-6´); 118.92 (CH-1´); 119.54 (C-4´); 121.36 (CH-9´); 123.11 (CH-2´/8´); 123.24 (CH-2´/8´); 123.44 (CH-6); 123.72 (C-9a´/9b´); 124.07 (C-9a´/9b´); 127.66 (CH-7´); 128.55 (CH-3´); 153.12 (C-4a´); 155.46 (C-5a´/7a); 155.56 (C-5a´/7a); 159.97 (C-2); 163.63 (C-4). HRMS (ESI) calculated for $C_{25}H_{28}N_4O_3NaSi$ [M+Na]: 483.1822; found 483.1821.

4-Methoxy-5-phenyl-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine
(2-amino-6-methoxy-7-phenyl-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (55g)



Compound **55g** was prepared from **49** (420 mg, 1.0 mmol) and phenylboronic acid (183 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (40-50 % EtOAc in hexanes) provided a yellowish oil (252 mg, 68 %). ^{1}H NMR (500 MHz, DMSO-d$_6$): -0.07 (s, 9H, CH_3Si); 0.84 (m, 2H, OCH_2CH_2Si); 3.53 (m, 2H, OCH_2CH_2Si); 3.90 (s, 3H, CH_3O-4); 5.39 (s, 2H, NCH_2O); 6.31 (s, 2H, NH_2); 7.22 (s, 1H, H-6); 7.23 (m, 1H, H-*p*-Ph); 7.36 (m, 2H, H-*m*-Ph); 7.60 (m, 2H, H-*o*-Ph). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): -1.16 (CH_3Si); 17.37 (OCH_2CH_2Si); 53.12 (CH_3O-4); 65.45 (OCH_2CH_2Si); 72.35 (NCH_2O); 95.12 (C-4a); 116.68 (C-5); 121.20 (CH-6); 126.12 (CH-*p*-Ph); 128.11 and 128.25 (CH-*m*,*o*-Ph); 134.72 (C-*i*-Ph); 155.69 (C-7a); 159.77 (C-2); 163.55 (C-4). HRMS (ESI) calculated for $C_{19}H_{27}N_4O_2Si$ [M+H]: 371.1897; found 371.1899.

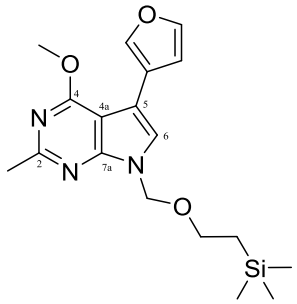
5-(Furan-2-yl)-4-methoxy-2-methyl-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine
(2-methyl-6-methoxy-7-(furan-2-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine)
(56a)



Compound **56a** was prepared from **50** (419 mg, 1.0 mmol) and furan-2-boronic acid (168 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (0-5 % EtOAc in hexanes) provided a colorless oil (246 mg, 68 %). ^{1}H NMR (500 MHz, DMSO-d$_6$): -0.10 (s, 9H, CH_3Si); 0.83 (m, 2H, OCH_2CH_2Si); 2.56 (s, 3H, CH_3-2); 3.53 (m, 2H, OCH_2CH_2Si); 4.07 (s, 3H, CH_3O-4); 5.56 (s, 2H, NCH_2O); 6.54 (dd, 1H, $J_{4,3}$ = 3.3 Hz, $J_{4,5}$ = 1.9 Hz, H-4-furyl); 6.90 (dd, 1H, $J_{3,4}$ = 3.3 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.64 (dd, 1H, $J_{5,4}$ = 1.9 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 7.71 (s, 1H, H-6). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): -1.26 (CH_3Si); 17.27 (OCH_2CH_2Si); 25.69 (CH_3-2); 53.70 (CH_3O-4); 65.76 (OCH_2CH_2Si); 72.67 (NCH_2O); 98.78 (C-4a); 106.71 (C-5); 107.12 (CH-3-furyl); 111.81 (CH-4-furyl); 123.00 (CH-6); 141.60 (CH-5-furyl); 148.46 (C-2-furyl); 153.31 (C-7a); 160.76 (C-2); 162.49 (C-4). IR(KBr): 3119, 2954, 1743, 1590, 1424, 1249, 1084, 920, 837, 697 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{26}N_3O_3Si$ [M+H]: 360.1738; found 360.1738.

5-(Furan-3-yl)-4-methoxy-2-methyl-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine

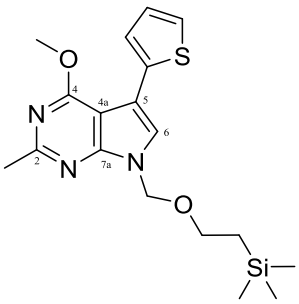
(2-methyl-6-methoxy-7-(furan-3-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (56b)



Compound **56b** was prepared from **50** (419 mg, 1.0 mmol) and furan-3-boronic acid (168 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (0-5 % EtOAc in hexanes) provided a yellowish oil (274 mg, 76 %). ^{1}H NMR (500 MHz, DMSO-d$_6$): -0.10 (s, 9H, CH_3Si); 0.84 (m, 2H, OCH_2CH_2Si); 2.56 (s, 3H, CH_3-2); 3.52 (m, 2H, OCH_2CH_2Si); 4.06 (s, 3H, CH_3O-4); 5.53 (s, 2H, NCH_2O); 6.91 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.68 (t, 1H, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, H-5-furyl); 7.73 (s, 1H, H-6); 8.09 (m, 1H, H-2-furyl). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): -1.23 (CH_3Si); 17.27 (OCH_2CH_2Si); 25.72 (CH_3-2); 53.65 (CH_3O-4); 65.70 (OCH_2CH_2Si); 72.51 (NCH_2O); 99.92 (C-4a); 106.90 (C-5); 110.10 (CH-4-furyl); 118.63 (C-3-furyl); 123.90 (CH-6); 139.93 (CH-2-furyl); 143.48 (CH-5-furyl); 153.54 (C-7a); 160.42 (C-2); 162.52 (C-4). IR(KBr): 3115, 2951, 1756, 1591, 1462, 1253, 1097, 932, 851, 700 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{26}N_3O_3Si$ [M+H]: 360.1738; found 360.1739.

4-Methoxy-2-methyl-5-(thiophen-2-yl)-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine

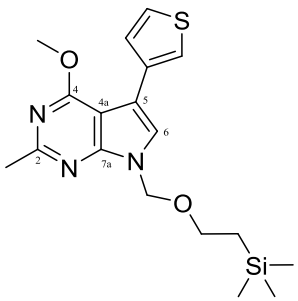
(2-methyl-6-methoxy-7-(thiophen-2-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (56c)



Compound **56c** was prepared from **50** (419 mg, 1.0 mmol) and thiophen-2-boronic acid (192 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (0-5 % EtOAc in hexanes) provided a pinkish oil (301 mg, 80 %). ^{1}H NMR (500 MHz, DMSO-d$_6$): -0.09 (s, 9H, CH_3Si); 0.84 (m, 2H, OCH_2CH_2Si); 2.57 (s, 3H, CH_3-2); 3.54 (m, 2H, OCH_2CH_2Si); 4.01 (s, 3H, CH_3O-4); 5.55 (s, 2H, NCH_2O); 7.08 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.6 Hz, H-4-thienyl); 7.41 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.46 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 7.70 (s, 1H, H-6). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): -1.27 (CH_3Si); 17.25 (OCH_2CH_2Si); 25.68 (CH_3-2); 53.54 (CH_3O-4); 65.77 (OCH_2CH_2Si); 72.54 (NCH_2O); 99.80 (C-4a); 109.52 (C-5);

124.30 (CH-6, CH-5-thienyl); 125.65 (CH-3-thienyl); 127.86 (CH-4-thienyl); 135.90 (C-2-thienyl); 153.34 (C-7a); 160.55 (C-2); 162.53 (C-4). IR(KBr): 3107, 2950, 1747, 1556, 1414, 1277, 1086, 978, 838, 697 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{26}N_3O_2SSi$ [M+H]: 376.1509; found 376.1510.

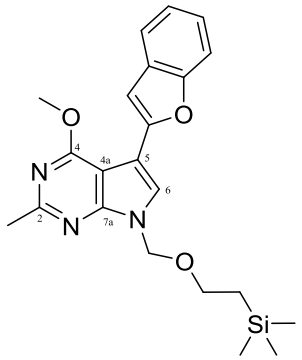
4-Methoxy-2-methyl-5-(thiophen-3-yl)-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine
(2-methyl-6-methoxy-7-(thiophen-3-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (56d)



Compound **56d** was prepared from **50** (419 mg, 1.0 mmol) and thiophen-3-boronic acid (192 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (0-5 % EtOAc in hexanes) provided a greenish oil (331 mg, 88 %). ^{1}H NMR (500 MHz, DMSO-d_6): -0.10 (s, 9H, CH_3Si); 0.84 (m, 2H, OCH_2CH_2Si); 2.56 (s, 3H, CH_3-2); 3.53 (m, 2H, OCH_2CH_2Si); 4.05 (s, 3H, CH_3O-4); 5.54 (s, 2H, NCH_2O); 7.51 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 7.54 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.77 (s, 1H, H-6); 7.84 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.27 (CH_3Si); 17.25 (OCH_2CH_2Si); 25.68 (CH_3-2); 53.54 (CH_3O-4); 65.77 (OCH_2CH_2Si); 72.54 (NCH_2O); 99.80 (C-4a); 109.52 (C-5); 124.30 (CH-6, CH-5-thienyl); 125.65 (CH-3-thienyl); 127.86 (CH-4-thienyl); 135.90 (C-2-thienyl); 153.34 (C-7a); 160.55 (C-2); 162.53 (C-4). IR(KBr): 3130, 2951, 1599, 1556, 1344, 1209, 1089, 926, 776, 697 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{26}N_3O_2SSi$ [M+H]: 376.1509; found 376.1510.

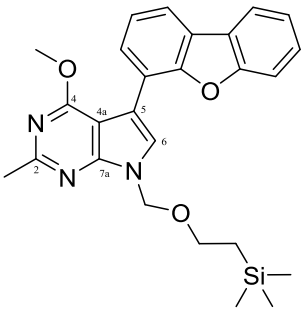
5-(Benzofuran-2-yl)-4-methoxy-2-methyl-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine
(2-methyl-6-methoxy-7-(benzofuran-2-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (56e)

Compound **56e** was prepared from **50** (419 mg, 1.0 mmol) and benzofuran-2-boronic acid (243 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (5-10 % EtOAc in hexanes) provided a colorless oil (312 mg, 76 %). ^{1}H NMR (500 MHz, DMSO-d_6): -0.09 (s, 9H, CH_3Si); 0.85 (m, 2H, OCH_2CH_2Si); 2.59 (s, 3H, CH_3-2); 3.57 (m, 2H, OCH_2CH_2Si); 4.15 (s,



3H, CH_3O-4); 5.61 (s, 2H, NCH_2O); 7.23 (btd, 1H, $J_{5,6} = J_{5,4} = 7.4$ Hz, $J_{5,7} = 1.3$ Hz, H-5-benzofuryl); 7.27 (ddd, 1H, $J_{6,7} = 7.9$ Hz, $J_{6,5} = 7.3$ Hz, $J_{6,4} = 1.5$ Hz, H-6-benzofuryl); 7.39 (d, 1H, $J_{3,7} = 1.0$ Hz, H-3-benzofuryl); 7.54 (dq, 1H, $J_{7,6} = 7.9$ Hz, $J_{7,54} = J_{7,4} = J_{7,3} = 1.0$ Hz, H-7-benzofuryl); 7.64 (dm, 1H, $J_{4,5} = 7.4$ Hz, H-4-benzofuryl); 8.00 (s, 1H, H-6). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.23 (CH_3Si); 17.30 (OCH_2CH_2Si); 25.74 (CH_3-2); 53.96 (CH_3O-4); 65.92 (OCH_2CH_2Si); 72.90 (NCH_2O); 99.15 (C-4a); 103.08 (CH-3-benzofuryl); 105.95 (C-5); 110.68 (CH-7-benzofuryl); 121.00 (CH-4-benzofuryl); 123.18 (CH-5-benzofuryl); 124.19 (CH-6-benzofuryl); 125.32 (CH-6); 129.44 (C-3a-benzofuryl); 150.87 (C-2-benzofuryl); 153.73 and 153.75 (C-7a, C-7a-benzofuryl); 161.21 (C-2); 162.55 (C-4). IR(KBr): 3059, 2950, 1593, 1463, 1347, 1249, 1093, 862, 750, 696 cm^{-1}. HRMS (ESI) calculated for $C_{22}H_{28}N_3O_3Si$ [M+H]: 410.1894; found 410.1898.

5-(Dibenzo[*b,d*]furan-4-yl)-4-methoxy-2-methyl-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine
(2-methyl-6-methoxy-7-(dibenzofuran-4-yl)-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (56f)

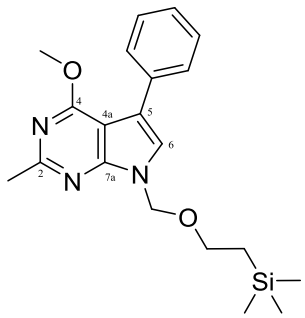


Compound **56f** was prepared from **50** (419 mg, 1.0 mmol) and dibenzo[*b,d*]furan-4-boronic acid (318 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (5-10 % EtOAc in hexanes) provided a colorless oil (327 mg, 71 %). ^1H NMR (500 MHz, DMSO-d_6): -0.06 (s, 9H, CH_3Si); 0.89 (m, 2H, OCH_2CH_2Si); 2.61 (s, 3H, CH_3-2); 3.63 (m, 2H, OCH_2CH_2Si); 3.91 (s, 3H, CH_3O-4); 5.67 (s, 2H, NCH_2O); 7.41 (td, 1H, $J_{8,9} = J_{8,7} = 7.5$ Hz, $J_{8,6} = 1.0$ Hz, H-8-$C_{12}H_7O$); 7.46 (t, 1H, $J_{2,1} = J_{2,3} = 7.7$ Hz, H-2-$C_{12}H_7O$); 7.52 (ddd, 1H, $J_{7,6} = 8.2$ Hz, $J_{7,8} = 7.3$ Hz, $J_{7,9} = 1.4$ Hz, H-7-$C_{12}H_7O$); 7.67 (dt, 1H, $J_{6,7} = 8.2$ Hz, $J_{6,8} = J_{6,9} = 0.9$ Hz, H-6-$C_{12}H_7O$); 7.81 (dd, 1H, $J_{3,2} = 7.6$ Hz, $J_{3,1} = 1.3$ Hz, H-3-$C_{12}H_7O$); 7.97 (s, 1H, H-6); 8.07 (dd, 1H, $J_{1,2} = 7.7$ Hz, $J_{1,3} = 1.3$ Hz, H-1-$C_{12}H_7O$); 8.18 (ddd, 1H, $J_{9,8} = 7.7$ Hz, $J_{9,7} = 1.4$ Hz, $J_{9,6} = 0.7$ Hz, H-9-$C_{12}H_7O$). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.22 (CH_3Si); 17.36 (OCH_2CH_2Si); 25.74 (CH_3-2); 53.55 (CH_3O-4); 65.92 (OCH_2CH_2Si); 72.79 (NCH_2O); 101.03 (C-4a); 109.51 (C-5); 111.75 (CH-6-$C_{12}H_7O$); 118.80 (C-4-$C_{12}H_7O$); 119.40 (CH-1-$C_{12}H_7O$); 121.38 (CH-9-$C_{12}H_7O$); 123.13 (CH-2-$C_{12}H_7O$); 123.26 (CH-8-$C_{12}H_7O$); 123.79 (C-9b-$C_{12}H_7O$); 123.97 (C-9a-$C_{12}H_7O$);

126.79 (CH-6); 127.70 (CH-7-$C_{12}H_7O$); 128.79 (CH-3-$C_{12}H_7O$); 153.18 (C-4a-$C_{12}H_7O$); 153.37 (C-7a); 155.56 (C-5a-$C_{12}H_7O$); 160.40 (C-2); 162.70 (C-4). IR(KBr): 3055, 2951, 1591, 1450, 1347, 1207, 1090, 923, 757, 697 cm^{-1}. IR(KBr): 3055, 2951, 1591, 1450, 1347, 1207, 1090, 923, 757, 697 cm^{-1}. HRMS (ESI) calculated for $C_{26}H_{30}N_3O_3Si$ [M+H]: 460.2051; found 460.2052.

4-Methoxy-2-methyl-5-phenyl-7-{[2-(trimethylsilyl)ethoxy]methyl}-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine

(2-methyl-6-methoxy-7-phenyl-9-[2-(trimethylsilyl)ethoxy]methyl]-7-deazapurine) (56g)



Compound **56g** was prepared from **50** (419 mg, 1.0 mmol) and phenylboronic acid (183 mg, 1.5 mmol) according to the general procedure for aqeous Suzuki-Miyaura cross-coupling reaction. Purification by flash column chromatography (0-5 % EtOAc in hexanes) provided a yellowish oil (237 mg, 64 %). ^{1}H NMR (500 MHz, DMSO-d_6): -0.10 (s, 9H, CH_3Si); 0.84 (m, 2H, OCH_2CH_2Si); 2.58 (s, 3H, CH_3-2); 3.56 (m, 2H, OCH_2CH_2Si); 3.98 (s, 3H, CH_3O-4); 5.57 (s, 2H, NCH_2O); 7.26 (m, 1H, H-*p*-Ph); 7.39 (m, 2H, H-*m*-Ph); 7.63 (s, 1H, H-6); 7.64 (m, 2H, H-*o*-Ph). ^{13}C NMR (125.7 MHz, DMSO-d_6): -1.29 (CH_3Si); 17.28 (OCH_2CH_2Si); 25.66 (CH_3-2); 53.47 (CH_3O-4); 65.77 (OCH_2CH_2Si); 72.59 (NCH_2O); 100.23 (C-4a); 116.20 (C-5); 124.73 (CH-6); 126.44 (CH-*p*-Ph); 128.31 (CH-*m*-Ph); 128.43 (CH-*o*-Ph); 134.04 (C-*i*-Ph); 153.63 (C-7a); 160.12 (C-2); 162.61 (C-4). IR(KBr): 2951, 2895, 1590, 1347, 1201, 1090, 919, 838, 763, 697 cm^{-1}. HRMS (ESI) calculated for $C_{20}H_{28}N_3O_2Si$ [M+H]: 370.1945; found 370.1947.

Synthesis of free 7-(het)aryl-7-deazapurines.

2-(Trimethylsilyl)ethoxy)methyl (SEM) protecting group cleavage.

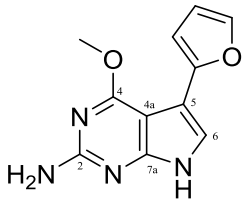
General procedure A (TBAF SEM cleavage)**:**

A mixture of a SEM-protected deazapurine derivative (compounds **55a-g, 56b, 56d, 56g** 1 mmol), tetrabutylammonium fluoride (3 equiv) and ethylenediamine (6 equiv) in *N*,*N*-dimethylformamide (0.5 mL) was stirred at 50 °C for 96 h. After cooling the volatiles were removed by evaporation in vacuo and co-evaporation with toluene (3x). The residue was purified by flash column chromatography.

General procedure B (acidic SEM cleavage)**:**

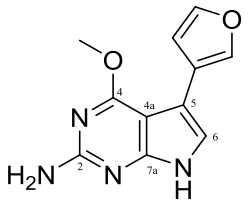
A SEM-protected deazapurine derivative (compounds **56a, 56c, 56e, 56f** 1 mmol) was dissolved in dichloromethane (2 mL) and trifluoroacetic acid (4 mL). After 4 h at ambient temperature (TLC usually revealed full conversion of starting material) the volatiles were removed by evaporation and co-evaporation with methanol (3x). The residue was stirred with methanol (2 mL) and aqueous ammonia (25% w/w, 4 mL) for additional 12 h. The mixture then was evaporated to dryness and the crude product was crystallized as given for individual compounds or purified by flash column chromatography on silica gel prior final crystallization.

5-(Furan-2-yl)-4-methoxy-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (2-amino-6-methoxy-7-(furan-2-yl)-9-NH-7-deazapurine) (57a)



Compound **57a** was prepared from **55a** (270 mg, 0.75 mmol) according to general procedure A. Purification by flash column chromatography (70-80 % EtOAc in hexanes), followed by crystalization from methanol, provided a yellowish solid (120 mg, 69 %). M. p. 208-209 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 3.97 (s, 3H, CH_3O-4); 6.15 (bs, 2H, NH_2); 6.48 (dd, 1H, $J_{4,3}$ = 3.3 Hz, $J_{4,5}$ = 1.9 Hz, H-4-furyl); 6.77 (dd, 1H, $J_{3,4}$ = 3.3 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.12 (d, 1H, $J_{6,NH}$ = 2.4 Hz, H-6); 7.54 (dd, 1H, $J_{5,4}$ = 1.9 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 11.30 (bd, 1H, $J_{NH,6}$ = 2.3 Hz, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 53.07 (CH_3O-4); 93.51 (C-4a); 105.64 (CH-3-furyl); 106.72 (C-5); 111.60 (CH-4-furyl); 116.47 (CH-6); 140.69 (CH-5-furyl); 149.85 (C-2-furyl); 155.79 (C-7a); 159.88 (C-2); 163.26 (C-4). IR(KBr): 3342, 3138, 1617, 1576, 1392, 1093, 968, 794, 700, 551 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{11}N_4O_2$ [M+H]: 231.0876; found 231.0876.

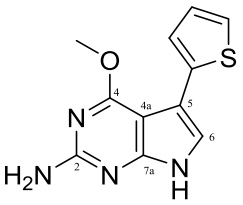
5-(Furan-3-yl)-4-methoxy-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (2-amino-6-methoxy-7-(furan-3-yl)-9-NH-7-deazapurine) (57b)



Compound **57b** was prepared from **55b** (340 mg, 0.94 mmol) according to general procedure A. Purification by flash column chromatography (70-80 % EtOAc in hexanes), followed by crystalization from methanol, provided an orange solid (169 mg, 78 %). M. p. 223-224 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 3.96 (s, 3H, CH_3O); 6.08 (bs, 2H, NH_2); 6.84 (dd, 1H, $J_{4,5}$ = 1.8 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.14 (d, 1H, $J_{6,NH}$ = 2.3 Hz, H-6); 7.61 (t, 1H, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, H-5-furyl); 7.98 (dd, 1H, $J_{2,5}$ = 1.6 Hz, $J_{2,4}$ = 0.9 Hz, H-2-furyl); 11.14 (d, 1H, $J_{NH,6}$ = 2.3

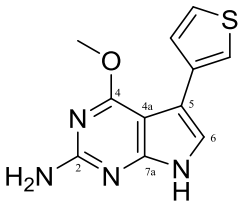
Hz, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 52.99 (CH_3O-4); 94.72 (C-4a); 106.53 (C-5); 110.11 (CH-4-furyl); 117.25 (CH-6); 119.74 (C-3-furyl); 139.03 (CH-2-furyl); 142.99 (CH-5-furyl); 155.89 (C-7a); 159.64 (C-2); 163.26 (C-4). IR(KBr): 3316, 3102, 1629, 1575, 1391, 1316, 1098, 1013, 776, 595 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{11}N_4O_2$ [M+H]: 231.0876; found 231.0876.

4-Methoxy-5-(thiophen-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (2-amino-6-methoxy-7-(thiophen-2-yl)-9-NH-7-deazapurine) (57c)



Compound **57c** was prepared from **55c** (508 mg, 1.35 mmol) according to general procedure A. Purification by flash column chromatography (70-80 % EtOAc in hexanes), followed by crystalization from methanol, provided a white solid (239 mg, 72 %). M. p. 266-267 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 3.94 (s, 3H, CH_3O-4); 6.14 (bs, 2H, NH_2); 7.02 (dd, 1H, $J_{4,5}$ = 5.2 Hz, $J_{4,3}$ = 3.6 Hz, H-4-thienyl); 7.09 (s, 1H, H-6); 7.30 (dd, 1H, $J_{5,4}$ = 5.2 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.36 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{5,3}$ = 1.2 Hz, H-3-thienyl); 11.30 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 52.93 (CH_3O-4); 94.64 (C-4a); 109.47 (C-5); 117.69 (CH-6); 123.04 (CH-5-thienyl); 124.41 (CH-3-thienyl); 127.63 (CH-4-thienyl); 137.63 (C-2-thienyl); 155.83 (C-7a); 159.72 (C-2); 163.31 (C-4). IR(KBr): 3337, 3103, 1624, 1575, 1393, 1316, 1093, 826, 697, 568 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{11}N_4OS$ [M+H]: 247.0648; found 247.0647.

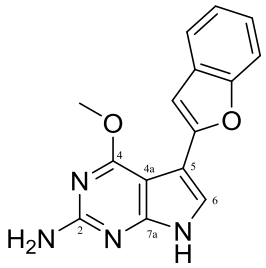
4-Methoxy-5-(thiophen-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (2-amino-6-methoxy-7-(thiophen-3-yl)-9-NH-7-deazapurine) (57d)



Compound **57d** was prepared from **55d** (480 mg, 1.27 mmol) according to general procedure A. Purification by flash column chromatography (70-80 % EtOAc in hexanes), followed by crystalization from methanol, provided a brownish solid (190 mg, 61 %). M. p. 260-261 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 3.96 (s, 3H, CH_3O); 6.10 (bs, 2H, NH_2); 7.20 (d, 1H, $J_{6,NH}$ = 2.3 Hz, H-6); 7.46 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.6 Hz, H-4-thienyl); 7.47 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 2.7 Hz, H-5-thienyl); 7.72 (dd, 1H, $J_{2,5}$ = 2.7 Hz, $J_{2,4}$ = 1.6 Hz, H-2-thienyl); 11.21 (d, 1H, $J_{NH,6}$ = 2.2 Hz, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 53.07 (CH_3O-4); 94.85 (C-4a); 111.32 (C-5); 118.01 (CH-6); 1119. 57 (CH-2-thienyl); 125.35 and 127.90 (CH-4,5-thienyl); 135.68 (C-3-thienyl); 155.75 (C-7a); 159.49 (C-2); 163.40 (C-4). IR(KBr): 3336, 3099, 1624,

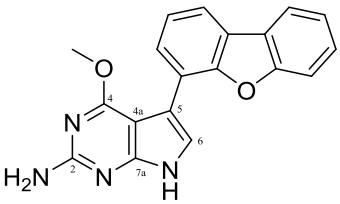
1570, 1389, 1307, 1095, 854, 772, 571 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_{11}N_4OS$ [M+H]: 247.0648; found 247.0648.

5-(Benzofuran-2-yl)-4-methoxy-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (2-amino-6-methoxy-7-(benzofuran-2-yl)-9-NH-7-deazapurine) (57e)



Compound **57e** was prepared from **55e** (400 mg, 0.97 mmol) according to general procedure A. Purification by flash column chromatography (80-90 % EtOAc in hexanes), followed by crystalization from methanol, provided a yellowish solid (145 mg, 56 %). M. p. 238-239 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 4.06 (s, 3H, CH_3O-4); 6.25 (bs, 2H, NH_2); 7.19 (btd, 1H, $J_{5,6} = J_{5,4}$ = 7.3 Hz, $J_{5,7}$ = 1.4 Hz, H-5-benzofuryl); 7.22 (btd, 1H, $J_{6,7} = J_{6,5}$ = 7.2 Hz, $J_{6,4}$ = 1.7 Hz, H-6-benzofuryl); 7.26 (d, 1H, $J_{3,7}$ = 1.1 Hz, H-3-benzofuryl); 7.42 (d, 1H, $J_{6,NH}$ = 2.5 Hz, H-6); 7.49 (m, 1H, H-7-benzofuryl); 7.59 (m, 1H, H-4-benzofuryl); 11.55 (d, 1H, $J_{NH,6}$ = 2.5 Hz, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 53.29 (CH_3O-4); 93.71 (C-4a); 101.52 (CH-3-benzofuryl); 106.01 (C-5); 110.51 (CH-7-benzofuryl); 118.97 (CH-6); 120.60 (CH-4-benzofuryl); 122.96 (CH-5-benzofuryl); 123.60 (CH-6-benzofuryl); 129.77 (C-3a-benzofuryl); 152.35 (C-2-benzofuryl); 153.59 (C-7a-benzofuryl); 156.31 (C-7a); 160.15 (C-2); 163.30 (C-4). IR(KBr): 3344, 3117, 1612, 1579, 1452, 1321, 1092, 791, 739, 557 cm^{-1}. HRMS (ESI) calculated for $C_{15}H_{13}N_4O_2$ [M+H]: 281.1033; found 281.1033.

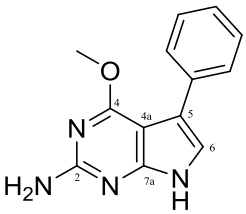
5-(Dibenzo[*b,d*]furan-4-yl)-4-methoxy-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (2-amino-6-methoxy-7-(dibenzofuran-4-yl)-9-NH-7-deazapurine) (57f)



Compound **57f** was prepared from **55f** (540 mg, 1.17 mmol) according to general procedure A. Purification by flash column chromatography (80-90 % EtOAc in hexanes), followed by crystalization from methanol, provided a brownish solid (190 mg, 51 %). M. p. 257-258 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 3.84 (s, 3H, CH_3O); 6.15 (bs, 2H, NH_2); 7.40 (btd, 1H, $J_{8,9} = J_{8,7}$ = 7.5 Hz, $J_{8,6}$ = 1.0 Hz, H-8-$C_{12}H_7O$); 7.41 (t, 1H, $J_{2,1} = J_{2,3}$ = 7.7 Hz, H-2-$C_{12}H_7O$); 7.43 (d, 1H, $J_{6,NH}$ = 2.4 Hz, H-6); 7.51 (ddd, 1H, $J_{7,6}$ = 8.2 Hz, $J_{7,8}$ = 7.3 Hz, $J_{7,9}$ = 1.4 Hz, H-7-$C_{12}H_7O$); 7.72 (dt, 1H, $J_{6,7}$ = 8.2 Hz, $J_{6,8} = J_{6,9}$ = 0.9 Hz, H-6-$C_{12}H_7O$); 7.81 (dd, 1H, $J_{3,2}$ = 7.6 Hz, $J_{3,1}$ = 1.3 Hz, H-3-$C_{12}H_7O$); 7.99 (dd, 1H, $J_{1,2}$ = 7.7 Hz, $J_{1,3}$ = 1.3 Hz, H-1-$C_{12}H_7O$); 8.15 (ddd, 1H, $J_{9,8}$ = 7.7 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.7 Hz, H-9-$C_{12}H_7O$); 11.47 (d, 1H, $J_{NH,6}$ = 2.4 Hz, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 52.96 (CH_3O-4); 95.64 (C-4a); 109.42 (C-5); 111.86 (CH-6-$C_{12}H_7O$); 118.43 (CH-1-$C_{12}H_7O$); 120.23 (C-4-$C_{12}H_7O$);

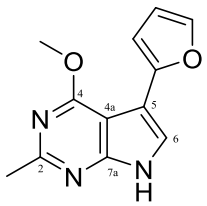
120.35 (CH-6); 121.24 (CH-9-$C_{12}H_7O$); 123.02 and 123.14 (CH-2,8-$C_{12}H_7O$); 123.61 (C-9b-$C_{12}H_7O$); 124.08 (C-9a-$C_{12}H_7O$); 127.51 (CH-7-$C_{12}H_7O$); 128.41 (CH-3-$C_{12}H_7O$); 153.12 (C-4a-$C_{12}H_7O$); 155.52 (C-5a-$C_{12}H_7O$); 155.88 (C-7a); 159.70 (C-2); 163.46 (C-4). IR(KBr): 3362, 3122, 1634, 1576, 1450, 1302, 1197, 1096, 734, 631 cm^{-1}. HRMS (ESI) calculated for $C_{19}H_{15}N_4O_2$ [M+H]: 331.1189; found 331.1191.

4-Methoxy-5-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (2-amino-6-methoxy-7-phenyl-9-NH-7-deazapurine) (57g)



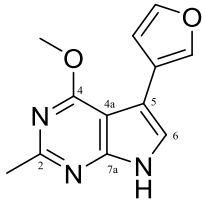
Compound **57g** was prepared from **55g** (185 mg, 0.50 mmol) according to general procedure A. Purification by flash column chromatography (70-80 % EtOAc in hexanes), followed by crystalization from methanol, provided a white solid (65 mg, 54 %). M. p. 226-227 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 3.89 (s, 3H, CH_3O-4); 6.08 (bs, 2H, NH_2); 7.05 (d, 1H, $J_{6,NH}$ = 2.4 Hz, H-6); 7.19 (m, 1H, H-*p*-Ph); 7.33 (m, 2H, H-*m*-Ph); 7.61 (m, 2H, H-*o*-Ph); 11.26 (bd, 1H, $J_{NH,6}$ = 2.3 Hz, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 52.92 (CH_3O-4); 94.99 (C-4a); 116.16 (C-5); 118.01 (CH-6); 125.66 (CH-*p*-Ph); 128.04 and 128.14 (CH-*o*,*m*-Ph); 135.40 (C-*i*-Ph); 156.12 (C-7a); 159.51 (C-2); 163.41 (C-4). IR(KBr): 3312, 3118, 1630, 1574, 1379, 1314, 1091, 971, 785, 608 cm^{-1}. HRMS (ESI) calculated for $C_{13}H_{13}N_4O$ [M+H]: 241.1083; found 241.1084.

5-(Furan-2-yl)-4-methoxy-2-methyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-methoxy-7-(furan-2-yl)-9-NH-7-deazapurine) (58a)



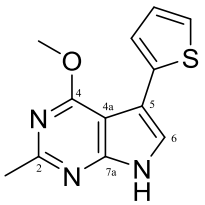
Compound **58a** was prepared from **56a** (240 mg, 0.67 mmol) according to general procedure B. Purification by flash column chromatography (0-5 % MeOH in DCM), followed by crystalization from methanol, provided a white solid (140 mg, 91 %). M. p. 246-247 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 2.53 (s, 3H, CH_3-2); 4.06 (s, 3H, CH_3O-4); 6.52 (dd, 1H, $J_{4,3}$ = 3.3 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.85 (dd, 1H, $J_{3,4}$ = 3.3 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.52 (d, 1H, $J_{6,NH}$ = 2.5 Hz, H-6); 7.60 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 12.06 (bs, 1H, NH). ^{13}C NMR (150.9 MHz, DMSO-d_6): 25.58 (CH_3-2); 53.41 (CH_3O-4); 98.41 (C-4a); 106.34 (CH-3-furyl); 106.41 (C-5); 111.75 (CH-4-furyl); 119.99 (CH-6); 141.19 (CH-5-furyl); 149.19 (C-2-furyl); 153.93 (C-7a); 160.22 (C-2); 162.43 (C-4). IR(KBr): 3115, 2949, 1569, 1347, 1288, 1207, 1102, 820, 772, 604 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{12}N_3O_2$ [M+H]: 230.0924; found 230.0924.

5-(Furan-3-yl)-4-methoxy-2-methyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-methoxy-7-(furan-3-yl)-9-NH-7-deazapurine) (58b)



Compound **58b** was prepared from **56b** (310 mg, 0.86 mmol) according to general procedure A. Purification by flash column chromatography (0-5 % MeOH in DCM), followed by crystalization from methanol, provided a yellowish solid (125 mg, 61 %). M. p. 242-243 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 2.53 (s, 3H, CH$_3$-2); 4.05 (s, 3H, CH$_3$O-4); 6.92 (dd, 1H, $J_{4,5}$ = 1.8 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.55 (d, 1H, $J_{6,NH}$ = 2.4 Hz, H-6); 7.66 (t, 1H, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, H-5-furyl); 8.06 (dd, 1H, $J_{2,5}$ = 1.6 Hz, $J_{2,4}$ = 0.9 Hz, H-2-furyl); 11.90 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 25.58 (CH$_3$-2); 53.36 (CH$_3$O-4); 99.49 (C-4a); 106.28 (C-5); 110.23 (CH-4-furyl); 119.25 (C-3-furyl); 120.76 (CH-6); 139.43 (CH-2-furyl); 143.22 (CH-5-furyl); 154.08 (C-7a); 159.76 (C-2); 162.38 (C-4). IR(KBr): 3101, 2947, 1570, 1348, 1296, 1105, 1035, 817, 777, 592 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{12}N_3O_2$ [M+H]: 230.0924; found 230.0924.

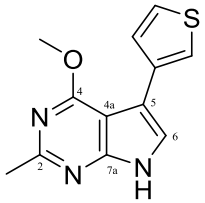
4-Methoxy-2-methyl-5-(thiophen-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-methoxy-7-(thiophen-2-yl)-9-NH-7-deazapurine) (58c)



Compound **58c** was prepared from **56c** (350 mg, 0.93 mmol) according to general procedure B. Purification by flash column chromatography (0-5 % MeOH in DCM), followed by crystalization from methanol, provided a white solid (208 mg, 87 %). M. p. 219-220 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 2.54 (s, 3H, CH$_3$-2); 4.03 (s, 3H, CH$_3$O-4); 7.06 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.5 Hz, H-4-thienyl); 7.37 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.42 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 7.51 (s, 1H, H-6); 12.06 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 25.56 (CH$_3$-2); 53.30 (CH$_3$O-4); 99.40 (C-4a); 109.07 (C-5); 121.31 (CH-6); 123.84 (CH-5-thienyl); 125.09 (CH-3-thienyl); 127.72 (CH-4-thienyl); 136.76 (C-2-thienyl); 153.93 (C-7a); 159.96 (C-2); 162.43 (C-4). IR(KBr): 3101, 2945, 1568, 1351, 1289, 1100, 1021, 792, 710, 615 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{12}N_3OS$ [M+H]: 246.0696; found 246.0696.

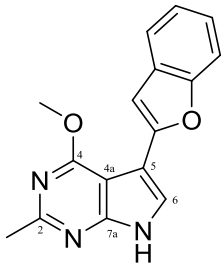
4-Methoxy-2-methyl-5-(thiophen-3-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-methoxy-7-(thiophen-3-yl)-9-NH-7-deazapurine) (56d)

Compound **58d** was prepared from **56d** (450 mg, 1.20 mmol) according to general procedure A. Purification by flash column chromatography (0-5 % MeOH in DCM), followed by



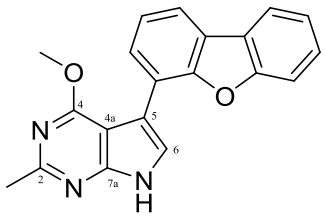
crystalization from methanol, provided a white solid (171 mg, 58 %). M. p. 312-313 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 2.54 (s, 3H, CH$_3$-2); 4.04 (s, 3H, CH$_3$O-4); 7.52 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 2.7 Hz, H-5-thienyl); 7.54 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.6 Hz, H-4-thienyl); 7.61 (s, 1H, H-6); 7.81 (dd, 1H, $J_{2,5}$ = 2.7 Hz, $J_{2,4}$ = 1.6 Hz, H-2-thienyl); 11.96 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 25.35 (CH$_3$-2); 53.35 (CH$_3$O-4); 99.53 (C-4a); 110.86 (C-5); 120.34 (CH-2-thienyl); 121.44 (CH-6); 125.58 (CH-4-thienyl); 128.00 (CH-5-thienyl); 135.03 (C-3-thienyl); 154.04 (C-7a); 159.59 (C-2); 162.41 (C-4). IR(KBr): 3099, 2950, 2828, 1570, 1347, 1288, 1102, 1006, 777, 605 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{12}N_3OS$ [M+H]: 246.0696; found 246.0696.

5-(Benzofuran-2-yl)-4-methoxy-2-methyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-methoxy-7-(benzofuran-2-yl)-9-NH-7-deazapurine) (58e)



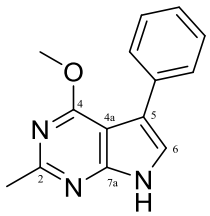
Compound **58e** was prepared from **56e** (300 mg, 0.81 mmol) according to general procedure B. Purification by flash column chromatography (0-5 % MeOH in DCM), followed by crystalization from methanol, provided a yellowish solid (174 mg, 77 %). M. p. 111-112 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 2.56 (s, 3H, CH$_3$-2); 4.14 (s, 3H, CH$_3$O-4); 7.21 (btd, 1H, $J_{5,6}$ = $J_{5,4}$ = 7.2 Hz, $J_{5,7}$ = 1.3 Hz, H-5-benzofuryl); 7.25 (btd, 1H, $J_{6,7}$ = $J_{6,5}$ = 7.6 Hz, $J_{6,4}$ = 1.5 Hz, H-6-benzofuryl); 7.35 (d, 1H, $J_{3,7}$ = 1.1 Hz, H-3-benzofuryl); 7.53 (bdq, 1H, $J_{7,6}$ = 7.6 Hz, $J_{7,5}$ = $J_{7,4}$ = $J_{7,3}$ = 1.1 Hz, H-7-benzofuryl); 7.62 (bd, 1H, $J_{4,5}$ = 7.4 Hz, H-4-benzofuryl); 7.81 (s, 1H, H-6); 12.31 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 25.60 (CH$_3$-2); 53.70 (CH$_3$O-4); 98.76 (C-4a); 102.24 (CH-3-benzofuryl); 105.67 (C-5); 110.63 (CH-7-benzofuryl); 120.80 (CH-4-benzofuryl); 122.30 (CH-6); 123.07 (CH-5-benzofuryl); 123.88 (CH-6-benzofuryl); 129.61 (C-3a-benzofuryl); 151.66 (C-2-benzofuryl); 153.69 (C-7a-benzofuryl); 154.41 (C-7a); 160.66 (C-2); 162.44 (C-4). IR(KBr): 3099, 2940, 1571, 1344, 1272, 1099, 1017, 798, 707, 614 cm^{-1}. HRMS (ESI) calculated for $C_{16}H_{14}N_3O_2$ [M+H]: 280.1081; found 280.1082.

5-(Dibenzo[*b*,*d*]furan-4-yl)-4-methoxy-2-methyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-methoxy-7-(dibenzofuran-4-yl)-9-NH-7-deazapurine) (58f)



Compound **58f** was prepared from **56f** (496 mg, 1.08 mmol) according to general procedure B. Purification by flash column chromatography (0-5 % MeOH in DCM), followed by crystalization from methanol, provided a white solid (295 mg, 83 %). M.p. 290-291 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 2.58 (s, 3H, CH_3-2); 3.90 (s, 3H, CH_3O-4); 7.41 (td, 1H, $J_{8,9} = J_{8,7}$ = 7.5 Hz, $J_{8,6}$ = 1.0 Hz, H-8-$C_{12}H_7O$); 7.44 (t, 1H, $J_{2,1} = J_{2,3}$ = 7.6 Hz, H-2-$C_{12}H_7O$); 7.52 (ddd, 1H, $J_{7,6}$ = 8.2 Hz, $J_{7,8}$ = 7.3 Hz, $J_{7,9}$ = 1.4 Hz, H-7-$C_{12}H_7O$); 7.72 (dt, 1H, $J_{6,7}$ = 8.2 Hz, $J_{6,8} = J_{6,9}$ = 0.9 Hz, H-6-$C_{12}H_7O$); 7.79 (s, 1H, H-6); 7.81 (dd, 1H, $J_{3,2}$ = 7.6 Hz, $J_{3,1}$ = 1.3 Hz, H-3-$C_{12}H_7O$); 8.04 (dd, 1H, $J_{1,2}$ = 7.7 Hz, $J_{1,3}$ = 1.3 Hz, H-1-$C_{12}H_7O$); 8.17 (ddd, 1H, $J_{9,8}$ = 7.7 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.7 Hz, H-9-$C_{12}H_7O$); 12.21 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 25.63 (CH_3-2); 53.35 (CH_3O-4); 100.59 (C-4a); 109.09 (C-5); 111.91 (CH-6-$C_{12}H_7O$); 119.03 (C-4-$C_{12}H_7O$); 121.33 (CH-9-$C_{12}H_7O$); 123.12 and 123.23 (CH-2,8-$C_{12}H_7O$); 123.72 (CH-6); 123.73 (C-9b-$C_{12}H_7O$); 124.03 (C-9a-$C_{12}H_7O$); 127.64 (C-7-$C_{12}H_7O$); 128.75 (CH-3-$C_{12}H_7O$); 153.25 (C-4a-$C_{12}H_7O$); 154.00 (C-7a); 155.59 (C-5a-$C_{12}H_7O$); 159.85 (C-2); 162.63 (C-4). HRMS (ESI) calculated for $C_{20}H_{16}N_3O_2$ [M+H]: 330.1237; found 330.1238.

4-Methoxy-2-methyl-5-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (2-methyl-6-methoxy-7-phenyl-9-NH-7-deazapurine) (58g)



Compound **58g** was prepared from **56g** (368 mg, 0.90 mmol) according to general procedure A. Purification by flash column chromatography (0-5 % MeOH in DCM), followed by crystalization from methanol, provided a white solid (134 mg, 62 %). M.p. 227-228 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 2.55 (s, 3H, CH_3-2); 3.98 (s, 3H, CH_3O-4); 7.24 (m, 1H, H-*p*-Ph); 7.37 (m, 2H, H-*m*-Ph); 7.47 (s, 1H, H-6); 7.66 (m, 2H, H-*o*-Ph); 12.02 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 25.23 (CH_3-2); 53.27 (CH_3O-4); 99.75 (C-4a); 115.75 (C-5); 121.62 (CH-6); 126.04 (CH-*p*-Ph); 128.24 (CH-*m*-Ph); 128.40 (CH-*o*-Ph); 134.75 (C-*i*-Ph); 154.24 (C-7a); 159.51 (C-2); 162.49 (C-4). IR(KBr): 3111, 2948, 2840, 1560, 1335, 1188, 1007, 835, 728, 616 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_{14}N_3O$ [M+H]: 240.1131; found 240.1132.

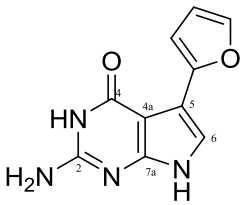
Synthesis of 7-(het)aryl 7-deazaguanines and 7-deazahypoxanthines.

General procedure for *O*-demethylation:

To a stirred mixture of 6-methoxy deazapurine **57-58a-g** and NaI (5 equiv) in anhydrous MeCN, TMSCl (5 equiv) was added slowly and the mixture was stirred at 80 °C

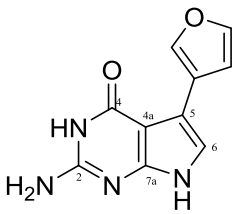
for 4 hours. The precipitate was filtered off, washed carefully with MeCN, dissolved in water and pH was adjusted to 7 by using solid K_2CO_3. The precipitated product was filtered off and repurified by flash column chromatography if needed.

2-Amino-5-(furan-2-yl)-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (7-(furan-2-yl)-7-deazaguanine) (59a)



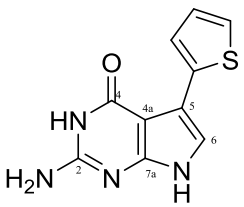
Compound **59a** (56 mg, 64 %) was obtained as a brownish solid from **57a** (86 mg, 0.40 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d$_6$): 6.19 (bs, 2H, NH_2); 6.44 (dd, 1H, $J_{4,3}$ = 3.3 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.91 (bs, 1H, H-6); 7.25 (dd, 1H, $J_{3,4}$ = 3.3 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.49 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 10.39 (bs, 1H, NH-3); 11.20 (bs, 1H, NH-7). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 96.08 (C-4a); 106.87 (CH-3-furyl); 110.52 (C-5); 111.51 (CH-4-furyl); 113.17 (CH-6); 140.46 (CH-5-furyl); 150.04 (C-2-furyl); 152.40 (C-7a); 152.98 (C-2); 159.12 (C-4). IR(KBr): 3198, 3006, 2887, 1686, 1570, 1405, 1139, 774, 516 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_9N_4O_2$ [M+H]: 217.0720; found 217.0719.

2-Amino-5-(furan-3-yl)-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (7-(furan-3-yl)-7-deazaguanine) (59b)



Compound **59b** (50 mg, 58 %) was obtained as a brownish solid from **57b** (93 mg, 0.40 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d$_6$): 6.11 (bs, 2H, NH_2); 6.86 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.8 Hz, H-4-furyl); 6.97 (d, 1H, $J_{6,NH}$ = 2.4 Hz, H-6); 7.56 (t, 1H, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, H-5-furyl); 8.44 (bd, 1H, $J_{2,5}$ = 1.6 Hz, H-2-furyl); 10.23 (bs, 1H, NH-3); 11.05 (bd, 1H, $J_{NH,6}$ = 1.8 Hz, NH-7). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 97.29 (C-4a); 109.50 (CH-4-furyl); 110.44 (C-5); 114.26 (CH-6); 119.73 (C-3-furyl); 140.36 (CH-2-furyl); 142.83 (CH-5-furyl); 152.44 (C-7a); 152.71 (C-2); 159.45 (C-4). IR(KBr): 3202, 2879, 2758, 1667, 1570, 1388, 1152, 1020, 777, 486 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_9N_4O_2$ [M+H]: 217.0720; found 217.0720.

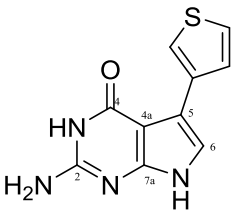
2-Amino-5-(thiophen-2-yl)-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (7-(thiophen-2-yl)-7-deazaguanine) (59c)



Compound **59c** (54 mg, 65 %) was obtained as a yellowish solid from **57c** (90 mg, 0.36 mmol) according to the general procedure for *O*-

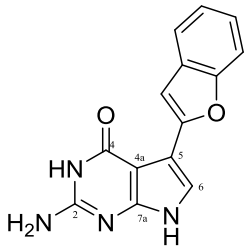
demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d$_6$): 6.17 (bs, 2H, NH$_2$); 6.93 (s, 1H, H-6); 6.97 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.5 Hz, H-4-thienyl); 7.22 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.88 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 10.38 (bs, 1H, NH-3); 11.19 (bs, 1H, NH-7). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 97.02 (C-4a); 113.63 (C-5); 114.43 (CH-6); 122.40 (CH-5-thienyl); 125.50 (CH-3-thienyl); 127.56 (CH-4-thienyl); 137.63 (C-2-thienyl); 152.53 (C-7a); 152.81 (C-2); 159.19 (C-4). IR(KBr): 3187, 3021, 2869, 1690, 1573, 1400, 1137, 770, 686, 506 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_9N_4OS$ [M+H]: 233.0491; found 233.0491.

2-Amino-5-(thiophen-3-yl)-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (7-(thiophen-3-yl)-7-deazaguanine) (59d)



Compound **59d (**63 mg, 68 %) was obtained as a white solid from **57d** (98 mg, 0.40 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d$_6$): 6.12 (bs, 2H, NH$_2$); 7.08 (d, 1H, $J_{6,NH}$ = 2.4 Hz, H-6); 7.41 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.2 Hz, H-4-thienyl); 7.55 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 3.0 Hz, H-5-thienyl); 8.37 (dd, 1H, $J_{2,5}$ = 3.0 Hz, $J_{2,4}$ = 1.2 Hz, H-2-thienyl); 10.33 (bs, 1H, NH-3); 11.10 (bd, 1H, $J_{NH,6}$ = 2.3 Hz, NH-7). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 97.36 (C-4a); 115.22 (CH-6); 115.35 (C-5); 120.46 (CH-2-thienyl); 125.30 (CH-5-thienyl); 127.30 (CH-4-thienyl); 135.81 (C-3-thienyl); 152.68 and 152.74 (C-7a, 2); 159.73 (C-4). IR(KBr): 3181, 3020, 2858, 1691, 1574, 1402, 1130, 777, 684, 507 cm^{-1}. HRMS (ESI) calculated for $C_{10}H_9N_4OS$ [M+H]: 233.0491; found 233.0491.

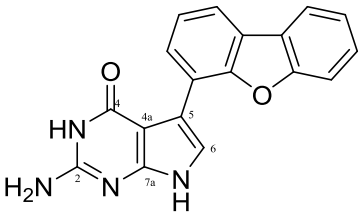
2-Amino-5-(benzofuran-2-yl)-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (7-(benzofuran-2-yl)-7-deazaguanine) (59e)



Compound **59e** (82 mg, 77 %) was obtained as a greenish solid from **57e** (101 mg, 0.36 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d$_6$): 6.25 (bs, 2H, NH$_2$); 7.17 (m, 1H, H-5-benzofuryl); 7.17 – 7.22 (m, 2H, H-6-benzofuryl, H-6); 7.47 (dm, 1H, $J_{7,6}$ = 7.4 Hz, H-7-benzofuryl); 7.56 (dm, 1H, $J_{4,5}$ = 7.0 Hz, H-4-benzofuryl); 7.78 (d, 1H, $J_{3,7}$ = 1.1 Hz, H-3-benzofuryl); 10.52 (bs, 1H, NH-3); 11.45 (d, 1H, $J_{NH,6}$ = 2.0 Hz, NH-7). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 96.55 (C-4a); 102.86 (CH-3-benzofuryl); 109.79 (C-5); 110.57 (CH-7-benzofuryl); 115.86 (CH-6); 120.69 (CH-4-benzofuryl); 123.00 (CH-5-benzofuryl); 123.62 (CH-6-

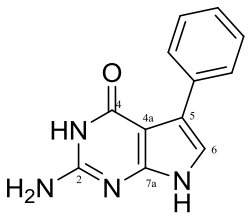
benzofuryl); 129.85 (C-3a-benzofuryl); 152.55 (C-2-benzofuryl); 153.12 and 153.32 (C-7a, 2); 153.73 (C-7a-benzofuryl); 159.26 (C-4). IR(KBr): 3349, 3123, 1624, 1577, 1345, 1257, 1175, 783, 684, 547 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_{11}N_4O_2$ [M+H]: 267.0876; found 267.0877.

2-amino-5-(dibenzo[*b,d*]furan-4-yl)-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (7-(dibenzofuran-4-yl)-7-deazaguanine) (59f)



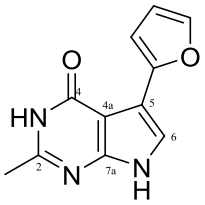
Compound **59f** (62 mg, 73 %) was obtained as a brownish solid from **57f** (90 mg, 0.27 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6): 6.21 (bs, 2H, NH_2); 7.37 (t, 1H, $J_{2,1}$ = $J_{2,3}$ = 7.6 Hz, H-2-$C_{12}H_7O$); 7.40 (btd, 1H, $J_{8,9}$ = $J_{8,7}$ = 7.5 Hz, $J_{8,6}$ = 1.0 Hz, H-8-$C_{12}H_7O$); 7.51 (ddd, 1H, $J_{7,6}$ = 8.2 Hz, $J_{7,8}$ = 7.3 Hz, $J_{7,9}$ = 1.4 Hz, H-7-$C_{12}H_7O$); 7.58 (d, 1H, $J_{6,NH}$ = 2.2 Hz, H-6); 7.76 (dt, 1H, $J_{6,7}$ = 8.2 Hz, $J_{6,8}$ = $J_{6,9}$ = 0.8 Hz, H-6-$C_{12}H_7O$); 7.92 (dd, 1H, $J_{1,2}$ = 7.6 Hz, $J_{1,3}$ = 1.3 Hz, H-1-$C_{12}H_7O$); 8.13 (ddd, 1H, $J_{9,8}$ = 7.7 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.7 Hz, H-9-$C_{12}H_7O$); 8.67 (dd, 1H, $J_{3,2}$ = 7.7 Hz, $J_{3,1}$ = 1.3 Hz, H-3-$C_{12}H_7O$); 10.45 (bs, 1H, NH-3); 11.45 (bd, 1H, $J_{NH,6}$ = 2.1 Hz, NH-7). ^{13}C NMR (125.7 MHz, DMSO-d_6): 97.86 (C-4a); 112.20 (CH-6-$C_{12}H_7O$); 113.95 (C-5); 118.24 (CH-1-$C_{12}H_7O$); 118.90 (CH-6); 120.18 (C-4-$C_{12}H_7O$); 121.39 (CH-9-$C_{12}H_7O$); 123.30 and 123.48 (CH-2,8-$C_{12}H_7O$); 123.70 (C-9b-$C_{12}H_7O$); 124.35 (C-9a-$C_{12}H_7O$); 127.65 (CH-7-$C_{12}H_7O$); 129.19 (CH-3-$C_{12}H_7O$); 152.79 (C-4a-$C_{12}H_7O$); 153.03 and 153.07 (C-2,7a); 155.60 (C-5a-$C_{12}H_7O$); 159.63 (C-4). IR(KBr): 3324, 3257, 1643, 1451, 1195, 842, 783, 750, 631 cm^{-1}. HRMS (ESI) calculated for $C_{18}H_{13}N_4O_2$ [M+H]: 317.1033; found 317.1034.

2-Amino-5-phenyl-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (7-phenyl-7-deazaguanine) (59g)



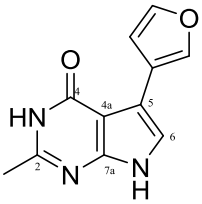
Compound **59g** (68 mg, 62 %) was obtained as a white solid from **57g** (116 mg, 0.48 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6): 6.13 (bs, 2H, NH_2); 7.02 (m, 1H, H-*p*-Ph); 7.18 (m, 2H, H-*m*-Ph); 7.29 (s, 1H, H-6); 7.94 (m, 2H, H-*o*-Ph); 10.36 (bs, 1H, NH-3); 11.19 (bs, 1H, NH-7). ^{13}C NMR (125.7 MHz, DMSO-d_6): 97.29 (C-4a); 115.33 (CH-6); 119.81 (C-5); 125.50 (CH-*p*-Ph); 127.60 (CH-*o*-Ph); 128.03 (CH-*m*-Ph); 135.12 (C-*i*-Ph); 151.66 (C-7a); 152.60 (C-2); 159.36 (C-4). IR(KBr): 3180, 3017, 2859, 1688, 1573, 1401, 1130, 779, 683, 506 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{11}N_4O$ [M+H]: 227.0927; found 227.0927.

5-(Furan-2-yl)-2-methyl-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (2-methyl-7-(furan-2-yl)-7-deazahypoxanthine) (60a)



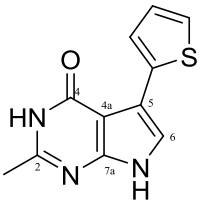
Compound **60a** (78 mg, 91 %) was obtained as a yellowish solid from **58a** (98 mg, 0.40 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d$_6$): 2.30 (s, 3H, CH$_3$-2); 6.47 (dd, 1H, $J_{4,3}$ = 3.3 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 7.22 (d, 1H, $J_{6,NH}$ = 2.6 Hz, H-6); 7.32 (dd, 1H, $J_{3,4}$ = 3.3 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.54 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 11.78 (bs, 1H, NH-3); 11.87 (bs, 1H, NH-7). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 20.96 (CH$_3$-2); 101.19 (C-4a); 107.46 (CH-3-furyl); 110.64 (C-5); 111.60 (CH-4-furyl); 115.82 (CH-6); 140.87 (CH-5-furyl); 149.48 (C-2-furyl); 149.83 (C-7a); 153.66 (C-2); 159.37 (C-4). IR(KBr): 3099, 2912, 1664, 1600, 1452, 1301, 911, 816, 775, 673 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_8N_3O_2$ [M-H]: 214.0622; found 214.0618.

5-(Furan-3-yl)-2-methyl-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (2-methyl-7-(furan-3-yl)-7-deazahypoxanthine) (60b)



Compound **60b** (53 mg, 61 %) was obtained as a yellowish solid from **58b** (100 mg, 0.40 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d$_6$): 2.30 (s, 3H, CH$_3$-2); 6.94 (dd, 1H, $J_{4,5}$ = 1.8 Hz, $J_{4,2}$ = 0.8 Hz, H-4-furyl); 7.29 (s, 1H, H-6); 7.60 (t, 1H, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, H-5-furyl); 8.49 (bd, 1H, $J_{2,5}$ = 1.7 Hz, H-2-furyl); 11.27 – 12.11 (m, 2H, NH-1,7). ^{13}C NMR (125.7 MHz, DMSO-d$_6$): 20.92 (CH$_3$-2); 102.29 (C-4a); 109.60 (CH-4-furyl); 110.60 (C-5); 116.92 (CH-6); 119.31 (C-3-furyl); 140.59 (CH-2-furyl); 142.98 (CH-5-furyl); 149.87 (C-7a); 153.13 (C-2); 159.73 (C-4). IR(KBr): 3100, 2922, 1662, 1604, 1448, 1307, 1035, 814, 787, 673 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_8N_3O_2$ [M-H]: 214.0622; found 214.0619.

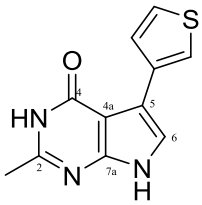
2-Methyl-5-(thiophen-2-yl)-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (2-methyl-7-(thiophen-2-yl)-7-deazahypoxanthine) (60c)



Compound **60c** (56 mg, 87 %) was obtained as a yellowish solid from **58c** (69 mg, 0.30 mmol) according to the general procedure for *O*-demethylation. M. p. 409-410 °C. ^{1}H NMR (500 MHz, DMSO-d$_6$): 2.30 (s, 3H, CH$_3$-2); 7.01 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.5 Hz, H-4-thienyl); 7.25 (d, 1H, $J_{6,NH}$ = 2.5 Hz, H-6); 7.29 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.91 (dd,

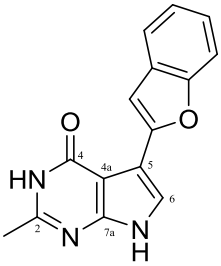
1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 11.78 (bs, 1H, NH-1); 11.86 (bs, 1H, NH-7). ^{13}C NMR (125.7 MHz, DMSO-d_6): 20.89 (CH_3-2); 101.98 (C-4a); 113.68 (C-5); 117.15 (CH-6); 123.09 (CH-5-thienyl); 125.97 (CH-3-thienyl); 127.64 (CH-4-thienyl); 136.92 (C-2-thienyl); 149.93 (C-7a); 153.40 (C-2); 159.41 (C-4). IR(KBr): 3093, 2923, 1651, 1600, 1551, 1297, 1099, 808, 787, 681 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_9N_3ONaS$ [M+Na]: 254.0359; found 254.0359.

2-Methyl-5-(thiophen-3-yl)-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (2-methyl-7-(thiophen-3-yl)-7-deazahypoxanthine) (60d)



Compound **60d** (54 mg, 58 %) was obtained as a white solid from **58d** (100 mg, 0.40 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6): 2.31 (s, 3H, CH_3-2); 7.41 (s, 1H, H-6); 7.47 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 3.0 Hz, H-5-thienyl); 7.64 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.2 Hz, H-4-thienyl); 8.43 (dd, 1H, $J_{2,5}$ = 3.0 Hz, $J_{2,4}$ = 1.2 Hz, H-2-thienyl); 11.43 – 12.00 (m, 2H, NH-1,7). ^{13}C NMR (125.7 MHz, DMSO-d_6): 20.86 (CH_3-2); 102.25 (C-4a); 115.30 (C-5); 117.66 (CH-6); 120.93 (CH-2-thienyl); 125.35 (CH-5-thienyl); 127.36 (CH-4-thienyl); 135.22 (C-3-thienyl); 149.99 (C-7a); 153.08 (C-2); 159.82 (C-4). IR(KBr): 3091, 2920, 1647, 1601, 1548, 1288, 1082, 809, 787, 672 cm^{-1}. HRMS (ESI) calculated for $C_{11}H_9N_3ONaS$ [M+Na]: 254.0394; found 254.0390.

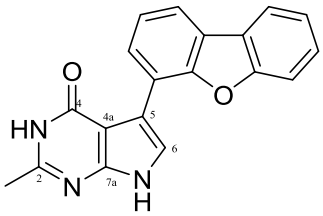
5-(Benzofuran-2-yl)-2-methyl-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (2-methyl-7-(benzofuran-2-yl)-7-deazahypoxanthine) (60e)



Compound **60e** (70 mg, 77 %) was obtained as a yellowish solid from **58e** (96 mg, 0.40 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6): 2.33 (s, 3H, CH_3-2); 7.19 (td, 1H, $J_{5,6}$ = $J_{5,4}$ = 7.3 Hz, $J_{5,7}$ = 1.2 Hz, H-5-benzofuryl); 7.23 (m, 1H, H-6-benzofuryl); 7.50 (m, 1H, H-7-benzofuryl); 7.51 (d, 1H, $J_{6,NH}$ = 2.5 Hz, H-6); 7.61 (m, 1H, H-4-benzofuryl); 7.86 (d, 1H, $J_{3,7}$ = 1.1 Hz, H-3-benzofuryl); 11.94 (bs, 1H, NH-1); 12.11 (bs, 1H, NH-7). ^{13}C NMR (125.7 MHz, DMSO-d_6): 20.97 (CH_3-2); 101.76 (C-4a); 103.34 (CH-3-benzofuryl); 109.82 (C-5); 110.56 (CH-7-benzofuryl); 118.18 (CH-6); 120.79 (CH-4-benzofuryl); 122.97 (CH-5-benzofuryl); 123.73 (CH-6-benzofuryl); 129.62 (C-3a-benzofuryl); 150.46 (C-7a); 151.93 (C-2-benzofuryl); 153.71 (C-7a-benzofuryl); 154.17 (C-2); 159.40 (C-4). IR(KBr): 3094, 2928, 1643, 1599,

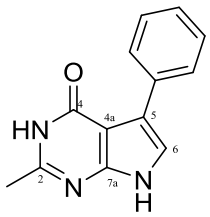
1452, 1255, 1115, 818, 792, 742 cm^{-1}. HRMS (ESI) calculated for $C_{15}H_{10}N_3O_2$ [M-H]: 264.0779; found 264.0773.

5-(Dibenzo[*b,d*]furan-4-yl)-2-methyl-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (2-methyl-7-(dibenzofuran-4-yl)-7-deazahypoxanthine) (60f)



Compound **60f** (79 mg, 83 %) was obtained as a yellowish solid from **58f** (99 mg, 0.30 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6): 2.63 (s, 3H, CH_3-2); 7.38 - 7.44 (m, 2H, H-2,8-$C_{12}H_7O$); 7.52 (bt, 1H, $J_{7,6}$ = $J_{7,8}$ = 7.8 Hz, H-7-$C_{12}H_7O$); 7.77 (bd, 1H, $J_{6,7}$ = 8.2 Hz, H-6-$C_{12}H_7O$); 7.81 (s, 1H, H-6); 7.98 (bd, 1H, $J_{1,2}$ = 7.5 Hz, H-1-$C_{12}H_7O$); 8.16 (bd, 1H, $J_{9,8}$ = 7.7 Hz, H-9-$C_{12}H_7O$); 8.58 (bd, 1H, $J_{3,2}$ = 7.6 Hz, H-3-$C_{12}H_7O$); 11.10 - 12.68 (m, 2H, NH-1,7). ^{13}C NMR (125.7 MHz, DMSO-d_6): 20.91 (CH_3-2); 102.83 (C-4a); 111.98 (CH-6-$C_{12}H_7O$); 113.76 (C-5); 118.51 (CH-1-$C_{12}H_7O$); 119.44 (C-4-$C_{12}H_7O$); 120.93 (CH-6); 121.19 (CH-9-$C_{12}H_7O$); 123.08 and 123.24 (CH-2,8-$C_{12}H_7O$); 123.56 (C-9b-$C_{12}H_7O$); 124.05 (C-9a-$C_{12}H_7O$); 127.46 (C-7-$C_{12}H_7O$); 129.20 (CH-3-$C_{12}H_7O$); 150.16 (C-7a); 152.69 (C-4a-$C_{12}H_7O$); 153.45 (C-2); 155.41 (C-5a-$C_{12}H_7O$); 159.58 (C-4). IR(KBr): 3055, 2911, 2826, 1650, 1613, 1452, 1196, 933, 819, 743 cm^{-1}. HRMS (ESI) calculated for $C_{19}H_{14}N_3O_2$ [M+H]: 316.1081; found 316.1081.

2-Methyl-5-phenyl-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one (2-methyl-7-phenyl-7-deazahypoxanthine) (60g)



Compound **60g** (55 mg, 52 %) was obtained as a white solid from **58g** (102 mg, 0.40 mmol) according to the general procedure for *O*-demethylation. M. p. > 300 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6): 2.32 (s, 3H, CH_3-2); 7.17 (m, 1H, H-*p*-Ph); 7.32 (s, 1H, H-6); 7.32 (m, 2H, H-*m*-Ph); 7.96 (m, 2H, H-*o*-Ph); 11.50 – 12.10 (m, 2H, NH-1,7). ^{13}C NMR (125.7 MHz, DMSO-d_6): 20.84 (CH_3-2); 102.31 (C-4a); 118.03 (CH-6); 119.93 (C-5); 125.79 (CH-*p*-Ph); 127.92 (CH-*o*-Ph); 128.10 (CH-*m*-Ph); 134.60 (C-*i*-Ph); 150.29 (C-7a); 153.00 (C-2); 159.59 (C-4). IR(KBr): 3090 2919, 1648, 1600, 1548, 1288, 1086, 802, 785, 677 cm^{-1}. HRMS (ESI) calculated for $C_{13}H_{10}N_3O$ [M-H]: 224.0829; found 224.0827.

5.9 X-ray crystallography

The X-ray crystallographic analysis was performed by Dr. Blanka Klepetářová. Crystallographic data for compounds **5a, 7a, 7b, 8a, 12a, 28g, 39c** were obtained from Xcalibur X-ray diffractometer by monochromatized CuK_{α} radiation (λ=1.54180 Å) at 180 K (**7a, 8a, 12a, 28g, 39c**), 200 K **5a** and **7b** 290 K. Data for **28k** were collected on a Bruker D8 VENTURE system employing Mo(*Kα*) radiation (λ=0.71073 Å) at 293 K. Data collection and unit cell refinemet were done with CrysAlisProCCD[159] or APEX3[160] and data reduction with SAINT.[161]The structures were solved by direct methods (SIR92)[161] (**7a, 7b, 8a, 12a, 28g, 28k 39c**) and by charge flipping (SUPERFLIP)[162] for compound **5a**. All structures were refined by full-matrix least-squares based on F with (CRYSTALS).[163] Hydrogen atoms were located in a Fourier difference map, recalculated into idealized positions (those attached to carbon atoms) and then refined with riding constraints. All other atoms were refined anisotropically.

Crystal data for compound 5a (colourless, 0.09 x 0.18 x 0.37 mm)**:**
$C_{27}H_{24}N_4O_2S_1$, monoclinic, space group *C*2/*c*, *a* = 20.7725(4) Å, *b* = 10.3703(3) Å, *c* = 22.3779(5) Å, *β* = 104.039(2)°, *V* = 4676.61(18) Å^3, *Z* = 8, *M* = 468.58, 24824 reflections measured, 4828 independent reflections. Final *R* = 0.043, *wR* = 0.045, *GoF* = 1.109 for 3729 reflections with $I > 2\sigma(I)$ and 307 parameters. CCDC 1014819.

Crystal data for compound 7a (orange, 0.45 x 0.68 x 0.72 mm)**:**
$C_{26}H_{21}N_5O_4S_1$, triclinic, space group *P*-1, *a* = 12.8359(2) Å, *b* = 14.6425(2) Å, *c* = 16.3039(3) Å, α = 81.5862(13)°, *β* = 70.0238(15)°, γ = 67.3666(15)°, *V* = 2657.75(8) Å^3, *Z* = 4, *M* = 499.54, 10790 reflections measured, 10790 independent reflections. Final *R* = 0.042, *wR* = 0.040, *GoF* = 0.968 for 9618 reflections with $I > 2\sigma(I)$ and 650 parameters. CCDC 1014820. The asymmetric unit consists of two molecules of **7a.** Furthermore, it contains solvent molecules – disordered ethyl acetate and partially occupied water molecules. These were not included in the refinement and the disordered density was taken into account using the SQUEEZE procedure (from PLATON[164]).

Crystal data for compound 7b (colourless, 0.21 x 0.30 x 0.83 mm)**:**
$C_{21}H_{19}N_5O_5S_1$, triclinic, space group *P*-1, *a* = 8.0254(2) Å, *b* = 8.5175(2) Å, *c* = 16.5553(4) Å, α = 76.069(2)°, *β* = 76.692(2)°, γ = 76.024(2)°, *V* = 1047.92(5) Å^3, *Z* = 2, *M* = 453.48, 18491 reflections measured, 4263 independent reflections. Final *R* = 0.036, *wR* = 0.042, *GoF* = 0.820 for 3984 reflections with $I > 2\sigma(I)$ and 290 parameters. CCDC 1014818.

Crystal data for comound 8a (colourless, 0.48 x 0.53 x 0.79 mm)**:**
$C_{26}H_{20}Cl_1N_5O_4S_1$, monoclinic, space group $P2_1/n$, a = 10.3204(3) Å, b = 10.7781(2) Å, c = 22.4546(7) Å, β = 103.112(3)°, V = 2432.59(12) Å^3, Z = 4, M = 533.99, 17639 reflections measured, 4993 independent reflections. Final R = 0.035, wR = 0.039, GoF = 1.033 for 4759 reflections with $I > 2\sigma(I)$ and 335 parameters. CCDC 1014817.

Crystal data for compound 12a (0.09 x 0.23 x 0.66 mm)**:**
$C_{23}H_{18}N_4O_2$, monoclinic, space group $P2_1/n$, a = 6.07198(18) Å, b = 26.2431(7) Å, c = 11.6359(3) Å, β = 96.071(2)°, V = 1843.75(9) Å^3, Z = 4, M = 382.42, 24402 reflections measured, 3854 independent reflections. Final R = 0.041, wR = 0.048, GoF = 1.110 for 3408 reflections with $I > 2\sigma(I)$ and 263 parameters.

Crystal data for compound 28g (0.16 x 0.24 x 0.28 mm)**:**
$C_{10}H_{13}Cl_1N_3O_3P_1$, triclinic, space group P-1, a = 7.8996(4) Å, b = 8.2513(4) Å, c = 10.2912(4) Å, α = 93.736(3)°, β = 97.778(4)°, γ = 91.382(4)°, V = 662.85(5) Å^3, Z = 2, M = 289.66, 16239 reflections measured, 2697 independent reflections. Final R = 0.045, wR = 0.055, GoF = 1.063 for 2403 reflections with $I > 2\sigma(I)$ and 164 parameters. CCDC 1495148.

Crystal data for compound 28k (0.09 x 0.11 x 0.57 mm)**:**
$C_{10}H_{14}Cl_1N_4O_3P_1$, triclinic, space group P-1, a = 8.221(3) Å, b = 10.018(3) Å, c = 10.186(4) Å, α = 113.60(2)°, β = 94.47(3)°, γ = 109.16(2)°, V = 704.5(5) Å^3, Z = 2, M = 304.67, 21458 reflections measured, 3089 independent reflections. Final R = 0.062, wR = 0.055, GoF = 1.130 for 2061 reflections with $I > 2\sigma(I)$ and 200 parameters. One of the ethoxy groups was found to be disordered over two positions with with site occupancy factors of 0.594 and 0.406. Several restraints were used to regularize its thermal motion. CCDC 1495150.

Crystal data for compound 39c (0.11 x 0.18 x 0.59 mm)**:**
$C_{10}H_{13}Cl_1N_3O_3P_1$, triclinic, space group P-1, a = 8.5724(16) Å, b = 9.5217(11) Å, c = 10.0248(18) Å, α = 64.703(14)°, β = 65.550(17)°, γ = 85.194(12)°, V = 669.1(2) Å^3, Z = 2, M = 289.66, 6115 reflections measured, 2658 independent reflections. Final R = 0.076, wR = 0.065, GoF = 1.319 for 1917 reflections with $I > 2\sigma(I)$ and 190 parameters. One of the ethoxy groups was found to be disordered over two positions with with site occupancy factors of 0.5293 and 0.4707. Several restraints were used to regularize its thermal motion. CCDC 1495149.

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