**Univerzita Karlova v Praze**
**Přírodovědecká fakulta**

Studijní program: Organická chemie
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# C-H aktivace deazapurinových heterocyklů

# C-H activations of deazapurine heterocycles

Disertační práce

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

Praha, 2015

**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, 29.10.2015

Podpis

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# Abstract

Direct C-H borylations of 7-deazapurines (*7H*-pyrrolo[2,3-*d*]pyrimidine) were developed at position 8 using $B_2pin_2$ and Ir catalysis. The obtained boronates were efficiently applied in the Suzuki cross-couplings with aryl halides and other functional group transformations to give diverse 6-substituted 8-aryl-7-deazapurine derivatives. Furthermore, I was also interested in the synthesis of biologically relevant 8-aryl-7-deazaadenines and -7-deazahypoxanthines. As the direct C-H borylation of 7-deazaadenines was unsuccessful and the borylation/Suzuki reaction of 6-chloro-7-deazapurine gave only low yield (20%) of the desired 8-aryl derivative, I focused on the one-pot borylation/arylation of SEM-protected 6-methylsulfanyl- or 6-methoxy-7-deazapurines. The one-pot borylation/Suzuki coupling reactions were followed either by demethylation and deprotection to yield deazahypoxanthine base, or by oxidation of sulfide to sulfone, amination and deprotection to give deazaadenines. In addition, the boronate intermediates were successfully converted to 8-halo- or 8-trifluoromethyl-7-deazapurine derivatives. While the 7-deazahypoxantine analogues were almost entirely inactive, most of the 8-subtituted 6-methoxy-7-deazapurine and 7-deazaadenines bases showed significant cytostatic activities.

Also a general method for Cu-catalysed C–H sulfenylation of purines, 7-deaza- and 9-deazapurines (*5H*-pyrrolo[3,2-*d*]pyrimidine) with aryl or alkyldisulfides was developed. In purines, the reaction occurs at position 8, in 7-deazapurines at position 7 and in 9-deazapurines at position 9, leading to new interesting arylsulfanyl derivatives of purine or deazapurine bases. The resulting 8-arylsulfanylpurines undergo the Liebesking–Srogl coupling with arylstannanes or boronic acids, whereas the (arylsulfanyl)deazapurines are not reactive under these conditions.

Later on, a series of 7-phenylsulfanyl- or 7-(2-thienyl)sulfanyl-7-deazapurine bases bearing diverse substituents at the position 6 was prepared through C-H sulfenylation of 6-chloro-7-deazapurine followed by cross-couplings or nucleophilic substitutions. The corresponding ribonucleosides (as thia-analogues of known nucleoside cytostatics) were prepared by glycosylation of 6-chloro-7-arylsulfanyl-7-deazapurines followed by the same transformations at position 6. The 7-thienylsulfanyl-7-deazapurine bases exerted micromolar cytostatic activities, whereas the nucleosides showed no significant biological effects.

# Abstrakt

Nejprve byla vyvinuta přímá C-H borylace 7-deazapurinů (*7H*-pyrrolo[2,3-*d*]pyrimidin) v poloze 8 za použití $B_2pin_2$ a Ir katalýzy. Takto získané boronáty byly efektivně využity v Suzukiho cross-coupling reakci s arylhalogenidy a jiné další transformace vedly ke vzniku různě 6-substituovaným 8-aryl-7-deazapurinům. Následným cílem práce byla syntéza potencionálně biologicky aktivních 8-aryl-7-deazaadeninů a -7-deazahypoxantinů. Vzhledem k tomu, že přímá C-H borylace 7-deazaadeninů nebyla úspěšná a "one-pot" borylace/Suzukiho reakce 6-chlor-7-deazapurinu poskytovala pouze nízký výtěžek (20%) tíženého 8-arylovaného derivátu, zaměřil jsem se na borylaci/arylaci SEM-chráněného 6-methylsulfanyl nebo 6-methoxy-7-deazapurinu. Borylace/Suzukiho reakce byla následována buď demethylací a deprotekcí za vzniku deazahypoxantinové báze, nebo oxidací sulfidu na sulfon, aminací a odstranění chránící skupiny za vzniku deazaadeninů. Kromě toho byly boronáty úspěšně převedeny na 8-halogen- nebo 8-trifluormethyl-7-deazapurinové deriváty. Zatímco 7-deazahypoxantinové analogy byly téměř úplně neaktivní, většina z 8-subtituovaných 6-methoxy-7-deazapurinů a 7- deazaadeninů měla cytostatický účinek v mikromolární koncentraci.

Dále byla vyvinuta mědí katalyzovaná C-H sulfenylace purinů, 7-deaza- a 9-deazapurinů (*5H*-pyrrolo[3,2-*d*]pyrimidin) s aryl nebo alkyldisulfidy. U purinů reakce probíhá v poloze 8, u 7-deazapurinů v poloze 7 a u 9-deazapurinů v poloze 9, což vede k novým zajímavým arylsulfanyl derivátům purinových nebo deazapurinových bází. Výsledné 8-arylsulfanylpuriny reagují v Liebesking-Šrogl coupligu s arylstanany nebo boronovými kyselinami, zatímco arylsulfanyldeazapuriny za těchto podmínek nereagují.

Později byla pomocí C-H sulfenylace 6-chlor-7-deazapurinu připravena série 7-phenylsulfanyl- nebo 7-(2-thienyl)sulfanyl-7-deazapurinových bází nesoucích různé substituenty v poloze 6, které byly zavedeny pomocí cross-couplingů nebo nukleofilní substitucí. Odpovídající ribonukleosidy (jako sirné-analogy známých nukleosidových cytostatik) byly připraveny nejprve glykosylací 6-chlor-7-arylsulfanyl-7-deazapurinů, po které následovaly stejné transformace v poloze 6. 7-Thienylsulfanyl-7-deazapurinové báze mají cytostatický účinek v mikromolární koncentraci, zatímco nukleosidy neprokázaly žádnou významnou biologickou aktivitu.

# List of abbreviations

| | |
|---|---|
| Ac | acetyl |
| acac | acetylacetone |
| Ar | aryl |
| Bn | benzyl |
| $B_2pin_2$ | bis(pinacolato)diboron |
| bpy | 2,2'-Bipyridine |
| BSA | *N*,*O*-bis(trimethylsilyl)acetamide |
| Bu | butyl |
| Bz | benzoyl |
| COE | cyclooctene |
| COD | 1,5-cyclooctadiene |
| Cp | cyclopentadienyl |
| CuTc | copper(I) thiophene-2-carboxylate |
| DCM | dichloromethane |
| dba | dibenzylideneacetone |
| DMF | *N*,*N*-dimethylformamide |
| DMSO | dimethylsulfoxid |
| dppe | 1,2-bis(diphenylphosphino)ethane |
| dppf | 1,1'-bis(diphenylphosphino)ferrocene |
| dppp | 1,3-bis(diphenylphosphino)propane |
| dtbpy | 4,4′-di-tert-butyl-2,2′bipyridyl |
| EtOAc | ethyl-acetate |
| EtOH | ethanol |
| equiv. | equivalent |
| Et | ethyl |
| EtOH | ethanol |
| HPFC | high performance flash chromatography |
| *i*Pr | isopropyl |

| | |
|---|---|
| LDA | lithium diisopropylamide |
| M | metal |
| m.p. | melting point |
| *m*CPBA | *meta*-Chloroperoxybenzoic acid |
| Me | methyl |
| MeCN | acetonitrile |
| MeOH | methanol |
| MW | microwave reactor |
| Ph | phenyl |
| r.t. | room temperature |
| Sal | salicylate |
| SEM | 2-(Trimethylsilyl)ethoxymethyl |
| *t*Bu | *tert*-butyl |
| TFA | trifluoroacetic acid |
| Togni reagent | 3,3-Dimethyl-1-(trifluoromethyl)-1,2-benziodoxole |
| THF | tetrahydrofuran |
| TM | transition metal |
| TMSCl | trimethylsilyl chloride |
| TMSOTf | trimethylsilyl trifluoromethanesulfonate |

# List of publications of the author related to the thesis

1. Klečka, M.; Pohl, R.; Klepetářová, B.; Hocek, M.: "Direct C–H borylation and C–H arylation of pyrrolo[2,3-d]pyrimidines: synthesis of 6,8-disubstituted 7-deazapurines" *Org. Biomol. Chem.* **2009**, *7*, 866–868.

2. Klečka, M.; Pohl, R.; Čejka, J.; Hocek, M.: "Direct C–H sulfenylation of purines and deazapurines" *Org. Biomol. Chem.* **2013**, *11*, 5189-5193.

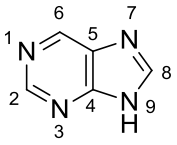
3. Klečka, M.; Slavětínská, L.; Tloušťová, E.; Džubák, P.; Hajdúch, M.; Hocek, M.: "Synthesis and cytostatic activity of 7-arylsulfanyl-7-deazapurine bases and ribonucleosides" *Med. Chem. Commun.* **2015**, *6*, 576–580.

4. Klečka, M.; Slavětínská, L.; Hocek, M.: " Modification of pyrrolo[2,3-*d*]pyrimidines by C-H borylation followed by cross-coupling or other transformations. Synthesis of 6,8-disubstituted 7-deazapurine bases " *Eur.J. Org. Chem.* in press

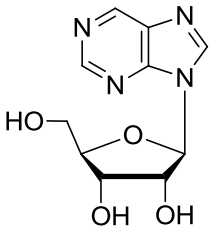
# Contents

# 1 Introduction

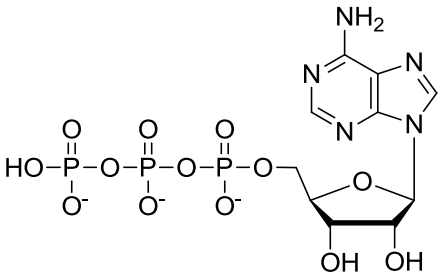
Purine is the most widely distributed N heterocycle in nature. The name "purine" (purum uricum) was given by Emil Fischer, who synthesized this colorless crystalline weak base for the first time from uric acid. Although the unsubstituted purine base does not exist in nature, its derivatives are found in various organisms and plants, one of the simplest form is the ribonucleoside nebularine (Figure 1), a nucleoside antibiotic isolated from the mushroom Agaricus nebularis. Of course, two others derivatives are probably the most famous, adenine and guanine, which form bases found in nucleic acids (DNA, RNA). In addition, many purine derivatives, especially adenine derivatives, are involved in numerous metabolic processes as co-factors or co-substrates associated with a great number of enzymes and receptors, notably ATP, GTP, GDP, cAMP, cGMP, Acetyl-CoA, NAD, NADP, FAD (Figure 1). Adenosine 5'-triphosphate (ATP) is used for the storage of energy in all living cells and has a crucial role in energetic metabolism. Adenosine 3',5'-cyclophosphate (cyclic-AMP; cAMP) acts as a so-called second messenger controlling the activation of protein kinases and the $K^+$ levels in the cell, as well as in transcription and other metabolic processes. Nicotinamide adenine dinucleotide (NAD) and flavin adenine dinucleotide (FAD) are coenzymes involved in cellular reduction/oxidation processes. Another purine-containing molecule of particular biological relevance is acetyl-coenzyme A, which possesses high C2-group-transfer potential. It should be noted that all of these associated proteins contain a purine recognition site and, therefore, purine derivatives have been long in development to act as selective inhibitors of these enzymes and agonists/antagonists of these receptors. In addition to that, it is a co-substrate for kinases, enzymes that regulate cellular metabolism, gene expression, cell proliferation and signaling pathways.



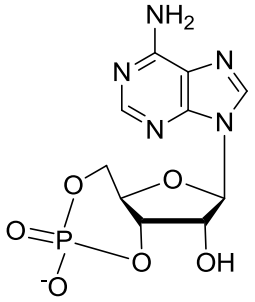
**9*H*-purine**



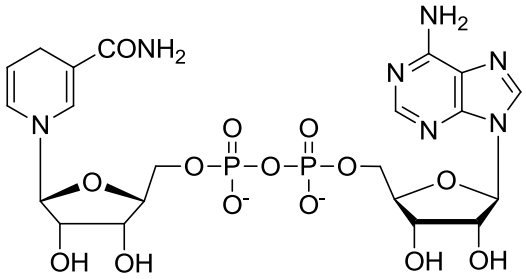
**Nebularine**



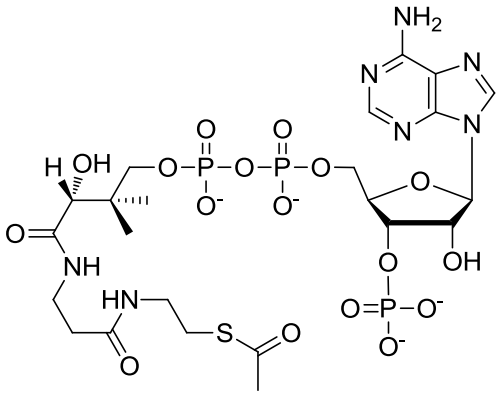
**ATP**
(Storage of energy)



**cAMP**
(Secondary messenger)



**NADH**
(Coenzyme)



**Acetyl-CoA**
(transfer of $C_2$ group)

**Figure 1** Purine and his derivatives

## 1.1 Biologically active purine bases and their analogues

Purine (bases, nucleosides and nucleotides) derivatives and analogues possess a high variety of biological activities.[1] Apart from direct inhibition of diverse enzymes of nucleic acids metabolism resulting in antineoplastic or antiviral effects, many purines and analogues interact with kinases and other ATP or GTP dependent enzymes and proteins (i.e., tubuline). Large libraries of diverse 2,6,8,9-tetrasubstituted purines were prepared[2] and tested in a variety of biological (enzyme, cell-based, phenotype, etc.) assays. Several derivatives were selected to display novel modes of biological effects (Figure 2). One of the oldest known and simplest biologically active derivatives is 6-methyl-*9H*-purine that shows a wide range of antineoplastic activity,[3] but unfortunately it is also heavily systematically toxic. Roscovitine[4] is a potent inhibitor of cyclin-dependent kinases. Myoseverine[5] induces a reversible fission of myotubes and inhibits microtubule assembly. Purmorphamine[6] induces osteogenesis in pluripotent mesenchymal progenitor cells. Stemregenin1 (SR1)[7] promotes the expansion of human hematopoietic stem cells. Reversine[8] causes de-differentiation of myoblasts into multipotent progenitor cells and specifically inhibits Aurora kinases. Stem-cell targeting of small molecules (in particular purine derivatives) is considered[9] to be one of the emerging future approaches to personalized medicinal chemistry and regeneration medicine.

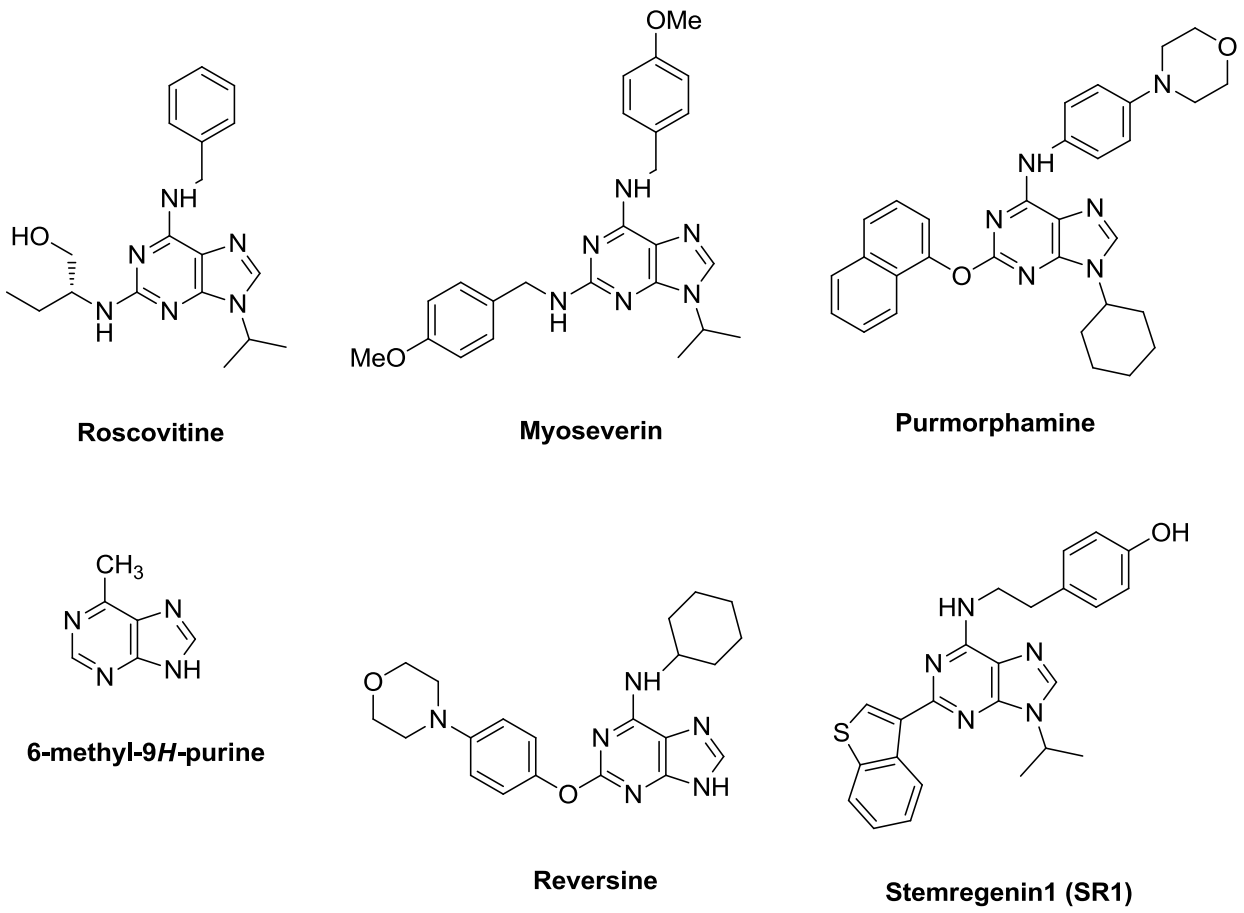



**Figure 2** Examples of purines with diverse modes of biological activity

## 1.2 Deazapurine bases and nucleosides

One of the possible strategies for modification of the natural purine motive is replacement of nitrogen atoms of the purine base by carbon atoms to get deazapurine analogues. The deazapurine provides extra valence that allow the introduction of diverse functional groups and substituents. All deazapurines have not been studied as much as purines due to the more difficult syntheses of the libraries.

According to the IUPAC nomenclature recommendation, for example, 7-deazapurine should be called 7*H*-pyrrolo[2,3-*d*]pyrimidine, but the semi trivial name for the 7-deazapurine and also purine ring numbering I will use in my thesis (except for experimental part where both – IUPAC and semitrivial – are used) as I have found the semi trivial name to be more illustrative (Figure 3).

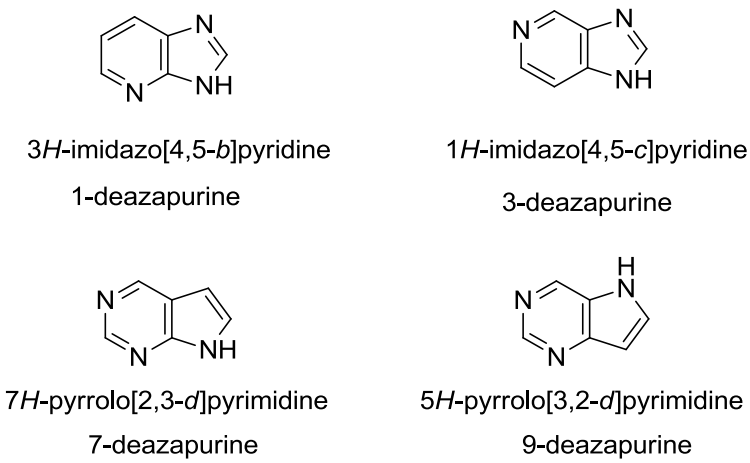



**Figure 3** Deazapurines

Wide and versatile spectrum of biological activities has been identified by synthesis of diverse biologically active deazapurine derivatives and some examples are listed below.

In 1-deazapurine series, the well-known Sulmazole (Figure 4) has shown phosphodiesterase (PDE) inhibitory activity[10] and later on has also been identified as antiarrhythmic agent.[11] Besides, compounds contain the *3H*-imidazo-[4,5-*b*]pyridin-2-one class (Figure 4) has been shown by Merck to be nonsteroidal anti-inflammatory and analgesic agents.[12] On the other hand, the 1,6,8-trisubstituted derivative CCT137690 and its analogues has been shown as an inhibition of Aurora kinases enzymes.[13] Also, another 2,6,8-trisubstituted derivative LUF5981 and its analogues has been identified by IJzerman and coworkers as the antagonists of the human adenosine A1 receptor.[14]

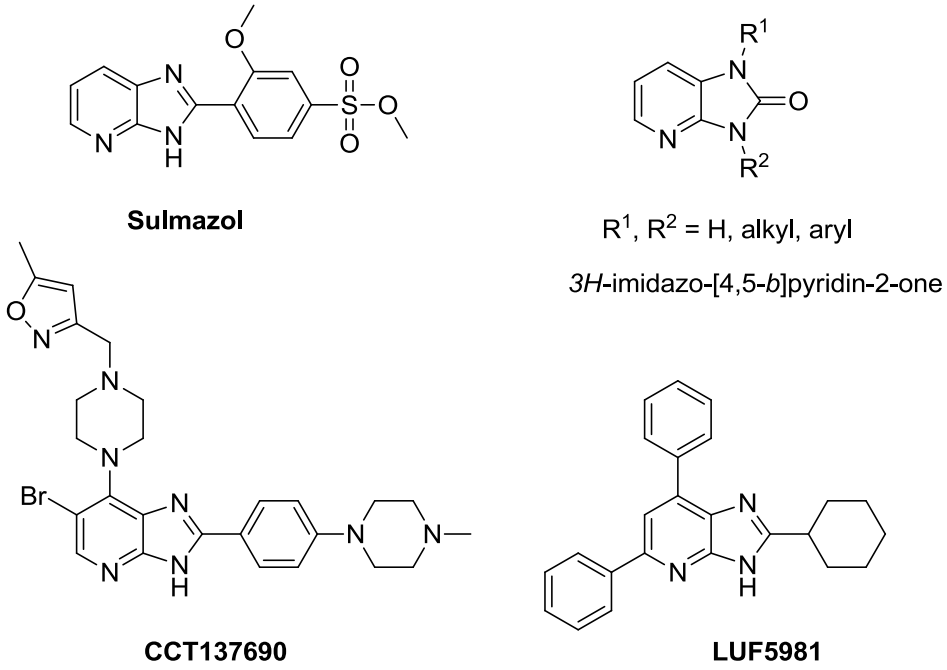



**Figure 4** Examples of biologically active 1-deazapurines

In 3-deazapurine series, Montgomery and coworkers showed that 3-deazaadenosine (c3A, 4-amino-*1H*-imidazo[4,5-*c*]pyridine, Figure 5) and its analogues are substrates and potent inhibitors of S-adenosyl-L-homocysteine hydrolase and possesses antiviral activity against HSV-1, Vaccinia Virus, and HL-23 C-type virus.[15] An anticancer natural product Ageladine A was recently isolated from the marine sponge Agelas nakamurai by Fusetani and co-workers[16] as the first example of an imidazolopyridine natural product. Ageladine A has

shown inhibition against various matrix metalloproteinases (MMPs) and strong antiangiogenic activity that is believed to be associated with its MMP inhibition.[17]

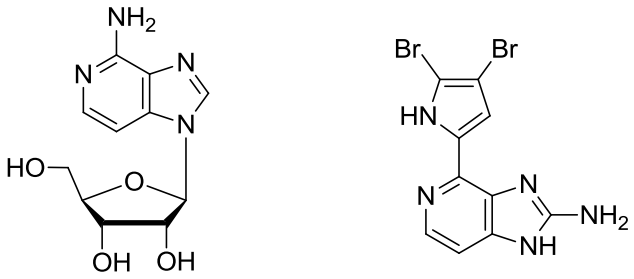



**Figure 5** Examples of biologically active 3-deazapurines

In 7-deazapurine series, the derivative TWS119[18] (Figure 6) was identified to direct the differentiation of neuronal cells in mice by GSK-3b inhibition. The compounds PKI-166[19] (Figure 6) was found to be EGFR-tyrosine kinases inhibitors. Another example is molecule LX7101 as the drug candidate in clinical trials for the treatment of glaucoma.[20]

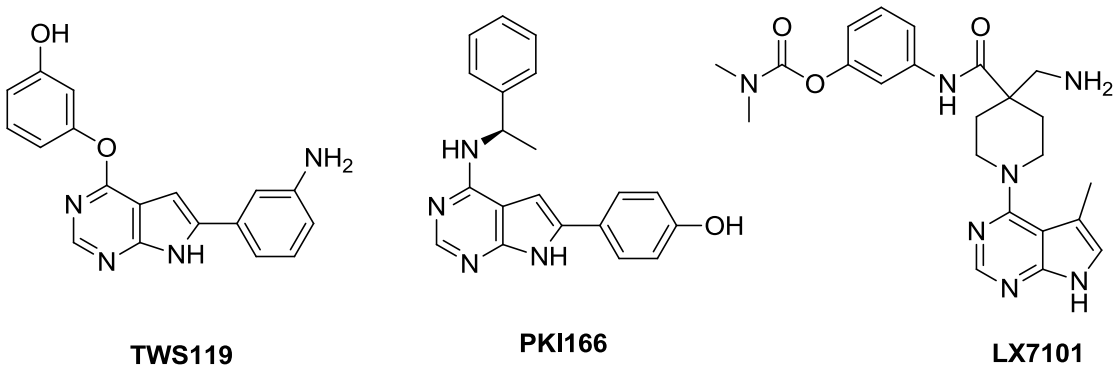
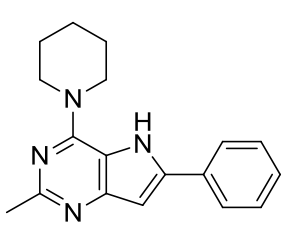
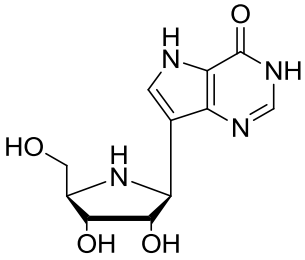



**Figure 6** Examples of biologically active 7-deazapurines

In 9-deazapurine series, the derivative 2-methyl-6-phenyl-4-piperidyl-*5H*-pyrrolo[3,2-*d*]pyrimidine was identified by Amgen company as neuropeptide Y5 receptor antagonists. Neuropeptide Y has been shown to play an important role in the regulation of food intake and energy balance and therefore it might be a useful therapeutic agent for the treatment of obesity.[21] Finally, Forodesine (also known as Immucillin H, Figure 7) has been found as a transition-state analogue inhibitor of purine nucleoside phosphorylase and the clinical trials are under development for the treatment of relapsed B-cell chronic lymphocytic leukemia.[22]




2-methyl-6-phenyl-4-piperidyl-*5H*-pyrrolo[3,2-*d*]pyrimidine




**Forodesine**

**Figure 7** Examples of biologically active 9-deazapurines

Since a high specificity in inhibition of kinases is required for medicinal applications, the development of synthetic methodologies for the preparation of a large series and libraries of deazapurines is a very important and attractive goal. However, there is limited knowledge on the bioactivity of structurally related deazapurines and it could modify the toxicity profile by a structural alteration. As a first step, the new active compounds must be identified. In this thesis I will focus primarily on 7-deazapurines as the most explored area in our group.

### 1.2.1 Natural 7-deazapurine nucleosides

There are several 7-deazapurine nucleosides among natural products. Three structurally related 7-deazapurine ribonucleosides, tubercidin, toyocamycin and sangivamycin, have shown interesting antitumor activity (Figure 8). All three compounds were found and isolated from bacteria *Streptomyces.*

Specifically, Tubercidin (7-deazaadenosine) is a natural antibiotic found in culture filtrates of *Streptomyces tubercidicus*. Tubercidin has shown significant activity against *Mycobacterium tuberculosis*, vaccinia virus, mengovirus and reovirus, including cytostatic activity in various cancer cell lines.[23, 24] Several cellular processes are damaged by tubercidin, for example mitochondrial respiration, purine synthesis, rRNA processing, methylation of tRNA.[25] Tubercidin play a role as a potent inhibitor of the *S*-adenosylhomocysteine hydrolase.[26] The main cytostatic effect of tubercidin is caused by its incorporation into both RNA and DNA which damage the nucleic acid functions.[23]

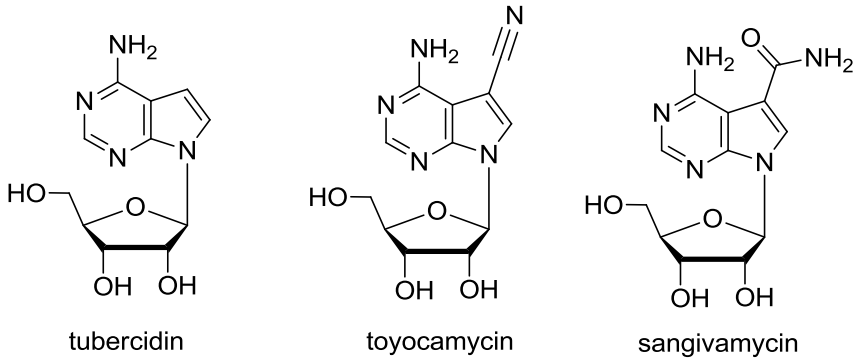



**Figure 8** Natural 7-deazapurine nucleosides

Toyocamycin (7-cyano-7-deazaadenosine) is also a product of *Streptomyces* metabolism that has shown tough cytostatic effect in several cancer cell lines.[27] Tubercidin, toyocamycin is incorporated in the same way into RNA and DNA.[28] In addition to that, toyocamycin inhibits rRNA synthesis and maturation.[29,30] Toyocamycin has been studied as a device for exogenous gene regulation technology as it inhibits RNA self-cleavage in mammalian cells.[31]

Sangivamycin (7-carbamoyl-7-deazaadenosine) is a natural antibiotic also isolated from *Streptomyces* cultures. Despite its structure, sangivamycin is very similar to the structure of toyocamycin and the antitumor effect of sangivamycin is caused by potent and selective inhibition of protein kinase C.[32] Also incorporation of sangivamycin into RNA and DNA *in vivo* has been studied and described.[33] Unfortunately, none of previously described natural 7-deazapurine nucleoside analogues are clinically used in case of their toxicity.

## 1.2.2 Hetaryl purine and deazapurine nucleosides from our group

Our research group has studied the biological activity of 6-aryl- and 6-hetarylpurine ribonucleosides for a long time. It has been found that 6-(het)arylpurine ribonucleosides possess a strong cytostatic effect against cancer cell lines in (sub)micromolar concentrations.[34] Replacing purine-ring N-atoms by carbon to form deazapurine analogues has also been explored. While some 6-(het)aryl-1-deazapurine nucleosides possessed moderate cytostatic activities,[35] the corresponding 6-(het)aryl-3-deazapurine nucleosides were devoid of cytostatic and antiviral activities.[36] This shows that the N-3 nitrogen is crucial for the interaction of these compounds with the target biological system (probably a kinase or RNA polymerase), while the N-1 nitrogen is not (Figure 9).

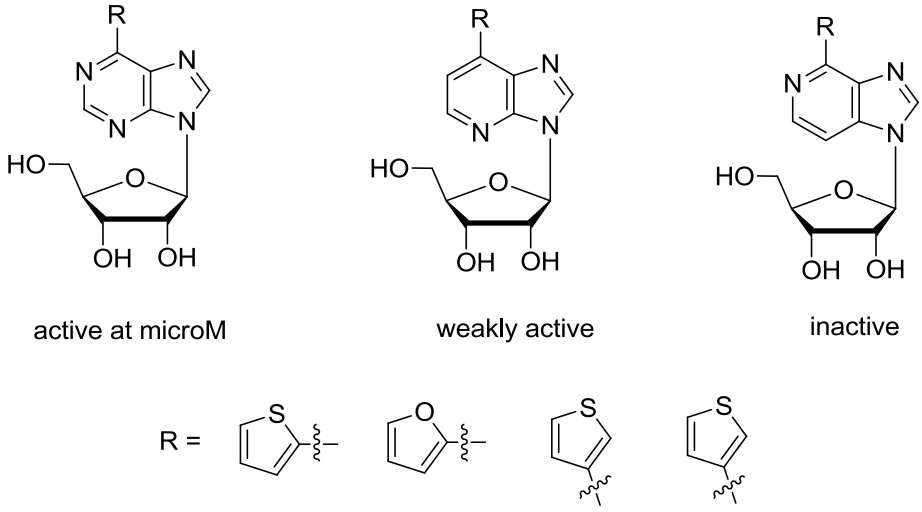



**Figure 9** 6-Hetarylpurine and deazapurine ribonucleosides

Therefore, the next logical step was to assess the role of N-7 nitrogen, which is engaged neither in H-bonds with the complementary pyrimidine nucleobase during the biosynthesis of RNA nor in minor groove interactions in the active site of the RNA polymerase. It was studied whether the replacement of the N-7 nitrogen by C-H, C-F, or C-Cl would result in improved selectivity toward viral RNA polymerase or enhanced cytostatic effect. It was discovered a potent cytostatic activity of 6-hetaryl- 7-deazapurine ribonucleosides **I** against several leukemic and tumor cell lines.[37] The most active were derivatives bearing furyl or thienyl groups at the position 6 and either hydrogen **I** or fluorine **II** at position 7 of the 7-deazapurine., whereas 7-chloro-substituted analogues **III** displayed lower activity.[37]

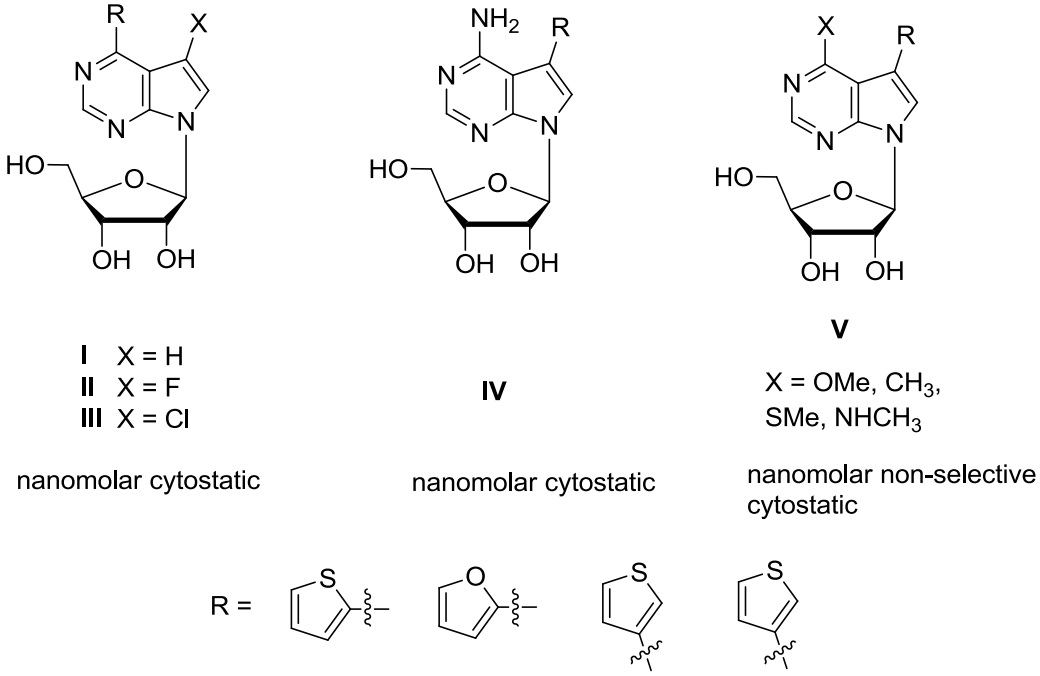



**Figure 10** Our recently reported biologically active 7-deazapurine nucleosides

As 6-hetaryl-7-deazapurine ribonucleosides show a strong cytostatic effect, the hetaryl group was also introduced into the natural antibiotic tubercidin to the position 7. 7-hetaryl-7-deazaadenosines (7-hetaryltubercidins) **IV** were prepared by our group and tested for the cytostatic activity against cancer cell lines.[24] Again the most active compounds were thienyl and furyl derivatives exhibited a cytostatic effect in nanomolar concentrations. The

mechanism of action has not yet been fully explored. These nucleosides interfere with RNA synthesis, although their triphosphates are only weak inhibitors of RNA polymerases.[24]

Later on, some others derivatives of 7-deaza-7-hetaryl nucleosides **V** were prepared. Several nucleosides, in particular 6-methoxy-, 6-methylsulfanyl-, 6-methylamino-, and 6-methyl-7-(2-furyl)-deazapurine nucleosides have been found to possess cytostatic effects at low nanomolar concentrations. On the other hand, all 7-deazahypoxanthine derivatives were completely inactive. The 6-methoxy-7-deaza(2-thienyl)purine nucleoside and 6-methyl-7-deaza(2-thienyl)purine nucleoside displayed significant activity and no toxicity to fibroblast, which indicates a promising therapeutic index. This study showed that H-bond donating $NH_2$ group at position 6 can be replaced by an isosteric nonpolar methyl group or H-bond acceptor group retaining cytotoxic activity.[38]

Generally, 6-hetaryl-7-deazapurine,[37] 7-hetaryl-7-deazaadenine[24] and 6-substituted 7-hetaryl-7-deazapurine ribonucleosides[38] (Figure 10) showed cytostatic effects at nanomolar concentrations, however, their mechanism of action is not yet fully understood. They are inhibitors of adenosine kinases,[39, 40] but they are substrates at the same time and are phosphorylated to nucleoside triphosphates which then interfere with the RNA synthesis or are incorporated to DNA and RNA. In all three series, the most active were derivatives bearing thiophene or furan.

## 1.2.3 Methods of preparation of 7-deazapurine bases

Compounds possessing a functionalized 7-deazapurines (*7H*-pyrrolo[2,3-*d*]pyrimidine) scaffold can be prepared in principle by:

- heterocyclization
- cross-coupling reactions
- nucleophilic aromatic substitution

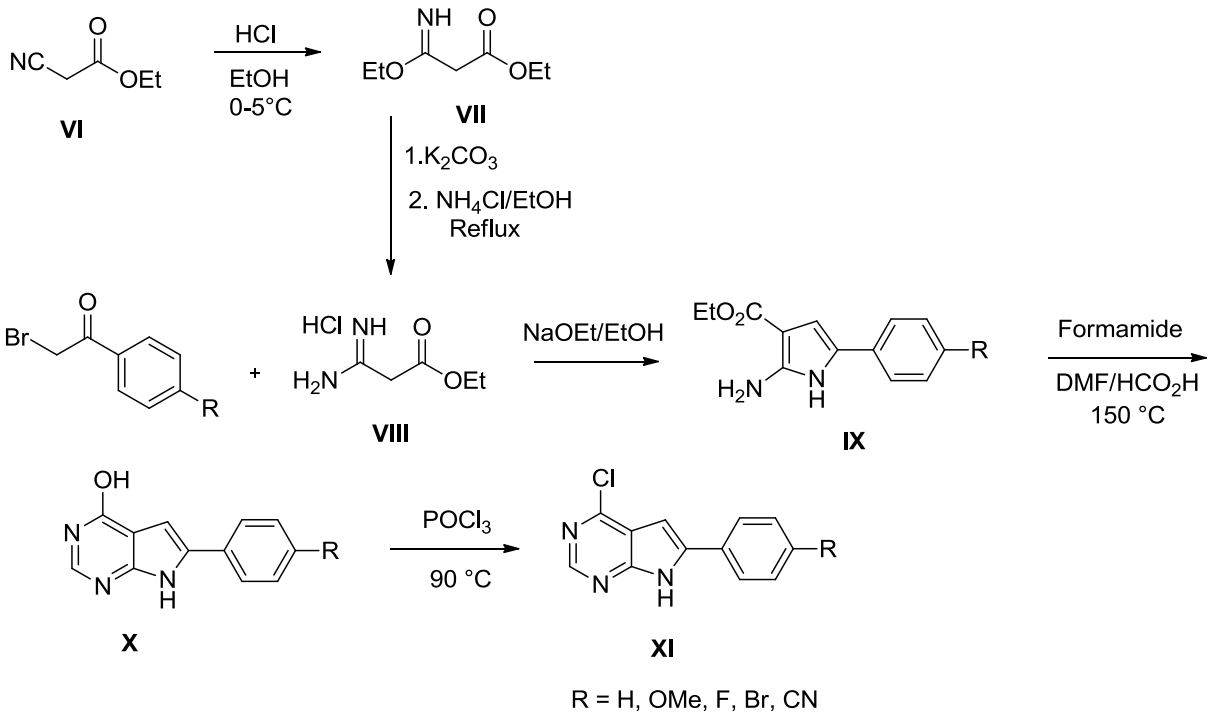
### 1.2.3.1 Heterocyclization

The heterocyclization reaction starts either from the appropriately substituted pyrrole[41] or pyrimidine[42, 43] derivatives as common intermediates. However, these strategies often

require multistep syntheses, and thus the synthesis of polysubstituted pyrrolopyrimidines using such methods tends to be lengthy.

### 1.2.3.1.1 Heterocyclization from pyrrole precursors

In 2011 Sundby and co-coworkers[41] published a synthesis of 8-arylated 7-deazapurines based on the heterocyclization of pyrimidine ring as a key step. Ethyl cyanoacetate **VI** was reacted with HCl saturated ethanol to yield compound **VII** which was subsequently transformed to ethyl 3-amino-3-iminopropanoate hydrochloride **VIII**. Then the five-member pyrrole ring was formed to obtain 2-amino-3-ethoxycarbonylpyrroles **IX.** Conversion of **IX** to **X** was performed by a condensation where formamide reacts with the 1,3-aminoester function in a formic acid/DMF mixture. Finally, the chlorination of **X** to **XI** was performed at 90°C using neat $POCl_3$ (Scheme 1).



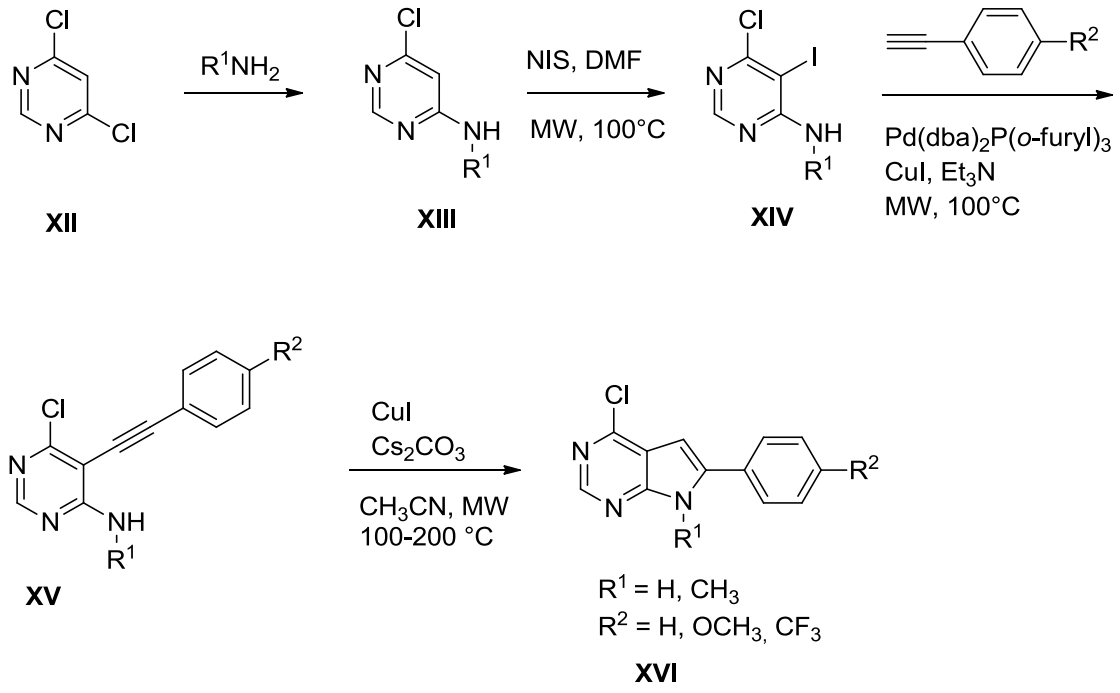

VI VII VIII IX X XI

**Scheme 1** Heterocyclization of 8-aryl-7-deazapurine from pyrrole precursors[41]

### 1.2.3.1.2 Heterocyclization from pyrimidine precursors

A complementary work was performed by Fujii and co-coworkers[42] who published synthesis of 8-arylated 7-deazapurines based on heterocyclyzation of pyrrole ring as a key step. Later on the same synthetic strategy was used for the synthesis of series N- protected polysubstituted 7-deazapurines.[43]

The synthesis starts from 4,6-dichloropyrimidine **XII** by nucleophilic substitution with appropriate amine to form **XIII** that was subsequently transformed by iodination under classical conditions to get **XIV**. The next step is the conventional Sonogashira coupling under microwave assistance of 6-amino-4-chloro-5-iodopyrimidine **XIV** affording alkyne **XV**. The reaction was chemoselective to the 5-iodo and no bisalkynylated products were formed. In the presence of base ($Cs_2CO_3$) and a catalytic amount of CuI (1 mol-%) under microwave irradiation, the intramolecular cyclization finally afforded 8-aryl-7-deazapurine **XVI** in an excellent yield with a good tolerance of different substituent groups (Scheme 2).




**Scheme 2** Heterocyclization of 8-aryl-7-deazapurine from pyrimidine precursors[42, 43]

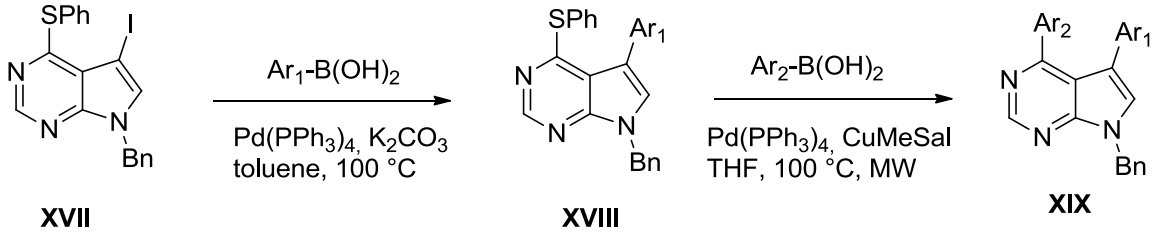
### 1.2.3.2 Cross-coupling reaction of 6-chloro-7-deazapurines

As the most powerful and straightforward methodology for the introduction of C-substituents to the 7-deazapurine base were found cross-coupling reactions catalyzed by transition-metals. The reaction conditions of 7-deazapurine for cross-coupling reactions were derived from previously reported procedures for the modification of purine derivatives that have been studied intensively.[34,44] Palladium-catalyzed cross-couplings of 6-chloro-7-deazapurine derivatives with $Me_3Al$ are used for the methylation of position 6.[37,45] Organozinc reagents are used to introduce either functionalized alkyl substituents or benzyl- and hetaryl groups by Negishi cross-coupling.[37,46] However the most widely used methods for synthesis of 6-(het)aryl-7-deazapurine derivatives are the Stille cross-coupling reaction with tributylstannes and Suzuki cross-coupling reaction with boronic acids, trifluoroborates or boronic esters. Stille cross-couplings of 6-chloro-7-deazapurine derivatives with organotin reagents are usually made under catalysis with $Pd(PPh_3)_2Cl_2$ in DMF at 100 °C.[37] Suzuki cross-coupling is a palladium-catalyzed reaction between chloro- or iodo-7-deazapurine derivatives with boronic acids, trifluoroborates or boronic esters. The main advantage of the Suzuki cross-coupling reaction is non-toxicity and majority stability of boronic acids. In addition, there is a great structural variety of commercially available boronic acids which can lead to great diversity of (het)aryl-7-deazapurine products. Suzuki cross-coupling with protected 6-chloro-7-deazapurine derivatives can be performed under anhydrous conditions, usually are made in toluene in the presence of $Pd(PPh_3)_4$ as a catalyst and potassium carbonate as a base.[34,37] However, reactions with some labile boronic acids, such as 2-thienyl- and 2-furyl boronic acid, proceed with very low conversions and therefore Stille coupling is more favorable in some cases.

### 1.2.3.3 Cross-coupling reaction of 6-phenylsulfanyl-7-deazapurines

Although a plethora of highly selective and reliable methods for the construction of carbon-carbon bonds are known to organic chemists, there is growing interest in the development of new protocols that offer different or orthogonal reactivity to that of existing methods. In 2000, Liebeskind and Srogl described[47] a mechanistically unprecedented transition-metal-catalyzed cross-coupling of thioesters with boronic acids. This desulfitative

cross-coupling process is catalytic in palladium(0), stoichiometric in copper(I), and applicable to a range of organosulfur derivatives and nucleophilic organometallic reagents. Since 2000, the scope of this intriguing carbon-carbon bond-forming process has been extended considerably to enable successful cross-coupling reactions between a variety of organosulfur and organometallic reagents.[48]




**Scheme 3** Cross-coupling reaction of 6-phenylsulfanyl-7-deazapurines[49]

A new chemoselective synthesis of 7-deazapurines bearing two different aryl groups at positions 6 and 7 was developed based on two orthogonal cross-couplings. Starting from 9-benzyl-6-(phenylsulfanyl)-7-iodo-7-deazapurine (**XVII)**, the palladium-catalyzed Suzuki coupling with arylboronic acids proceeded selectively at position 7 (**XVIII**), followed by the palladium-catalyzed copper-mediated Liebeskind–Srogl coupling at position 6 (**XIX**). These two orthogonal cross-couplings are a fully chemoselective and a small library of 6,7-diaryl derivatives was prepared.[49]

### 1.2.3.4 Nucleophilic aromatic substitution

6,8-Disubstituted deazapurines bearing a heteroatom (nitrogen, or oxygen) substituent at positions 6 are potent inhibitors of GSK-3b (e.g., TWS119, Figure 6) or EGFR-tyrosine kinases inhibitors (e.g., PKI 166, Figure 6). These compounds are accessible via nucleophilic aromatic substitution of various 6-halo-7-deazapurines (the most common is chlorine). In the reaction with amines the reagent is basic itself, otherwise it must be the base added to the reaction (Figure 11).

The substrates bearing 6-sulfanyl group are potentially interesting either themselves or can be after oxidation to an appropriate 6-sulfon used for other nucleophilic aromatic substitutions with different amines[50] (Figure 11).

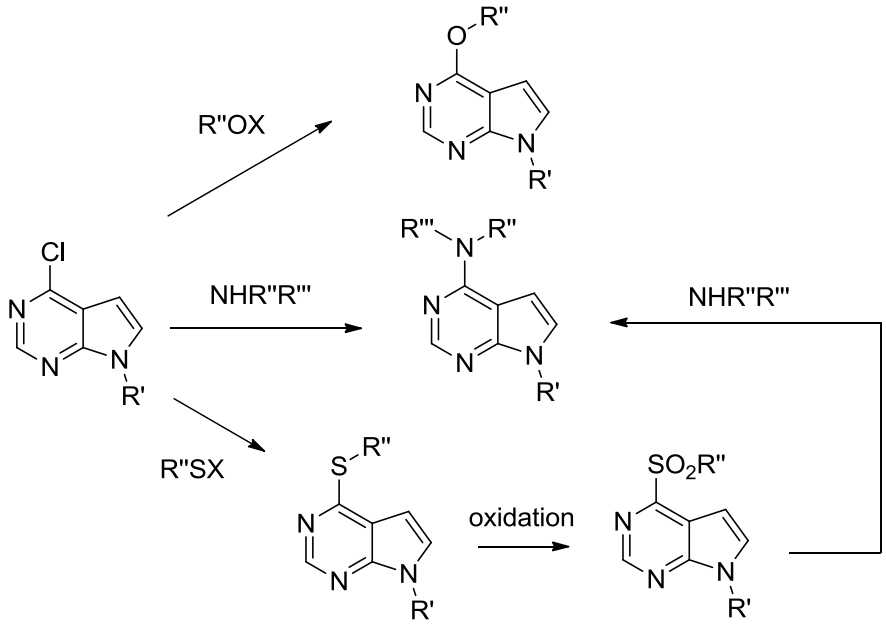


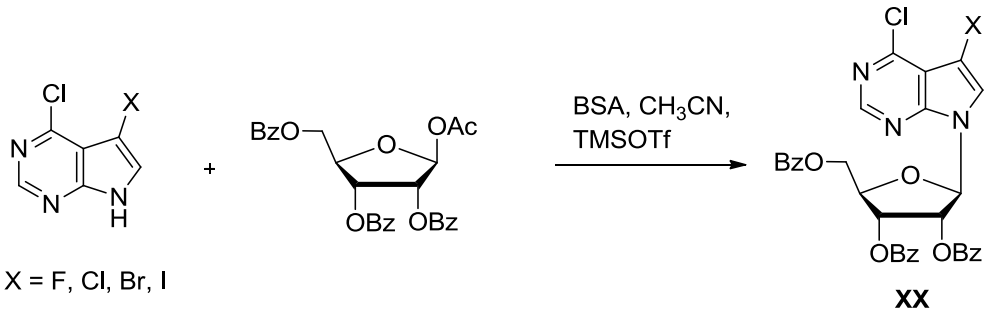

**Figure 11** $S_{NAr}$ of 6-chloro-7-deazapurines

## 1.2.4 Glycosylation of 7-deazapurine bases

The Vorbrüggen reaction is the most widely used method for the synthesis of ribonucleosides.[51] In this reaction a silylated heterocyclic base to react with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose in the presence of Lewis acid and trimethylsilyl trifluoromethanesulfonate (TMSOTf). Only β-nucleoside is selectively formed as the result of neighboring group participation. Oxonium ion formed during the reaction effectively directs an attack of the silylated base only to the β-face of the ribose moiety.

So, for the stereoselectivity of the reaction the acyl protecting group in position 2 of the ribose is crucial. The one-pot Vorbrüggen reaction was successfully performed in the synthesis of 7-substituted 7-deazapurine ribonucleosides (**XX**).[52] With the one-pot protocol,

firstly 7-deazapurine base was silylated by *N*,*O*-bis(trimethylsilyl)acetamide (BSA) in acetonitrile ($CH_3CN$) at room temperature and then secondly ribose reagent and TMSOTf are added and the reaction mixture heated to 80 °C (Scheme 4).




**Scheme 4** Synthesis of 7-deazapurine ribonucleosides by Vobrüggen reaction

# 1.3 C-H activation

Organic synthesis relies on transformations of functional groups or structural features exhibiting relatively high chemical reactivity. C–H bonds are not generally viewed as functional groups in this context. Direct and selective replacement of carbon-hydrogen bonds with new bonds is an important and long-standing goal in chemistry. These transformations have broad potential in synthesis because C–H bonds are ubiquitous in organic substances. At the same time, achieving selectivity among many different C–H bonds remains a challenge. Therefore, development of transition metal catalyzed C-H bonds activation is one of the major challenges of modern chemistry.[53] Direct C-H activation reactions catalysed by transition metals (TM) (Rh, Ru, Co, Ir etc.) have received prominent attention[54] during the last two decades as an attractive alternative to classical cross-couplings.

## 1.3.1 C-H activation of arenes and heteroarenes

One of the biggest disadvantages of C-H bond activations of arenes is that C–H bond proceed under rather harsh reaction conditions (high temperature, strongly acidic or basic conditions, strong oxidant, etc.) that significantly limits their utility. However, mild methods have been developed that significantly expand the scope of these transformations.[54]

### 1.3.1.1 Direct C-H arylation

The traditional coupling reactions (Kumada, Stille, Negishi, Suzuki-Miyaura, Hiyama) catalysed by TM require two activated substrates, one is the organometallic (Sn, B, Zn, Mg, and Si) component and the second one contain a halide or pseudohalide. (Figure 12, Pathway A). Owing to the high impact of these reactions in organic synthesis, natural product synthesis and pharmaceutical applications, the 2010 Nobel Prize in Chemistry was awarded jointly to Richard F. Heck, Ei-ichi Negishi and Akira Suzuki. Cross-coupling reactions are generally carried out under mild conditions and can be performed in the presence of most functional groups. The main disadvantage is necessity to pre-activate starting compounds that involves the installation and subsequent disposal of stoichiometric activating agents.

As an alternative to this approach is to consider the aryl C-H bond as a functional group, analogous to a carbon-halogen or carbon-metal bond. The simplest approach involves cross-couplings between two inactivated substrates [cross-dehydrogenative coupling (CDC), (Figure 12, Pathway B), but this process is unfavourable from a thermodynamic perspective due to the high bond strength of aryl C-H bond. The solution can be use of C-H activated bond as one coupling partner and halides as a pre-activated substrate which, in turn, require selective C-H activation (Figure 12, Pathway C).

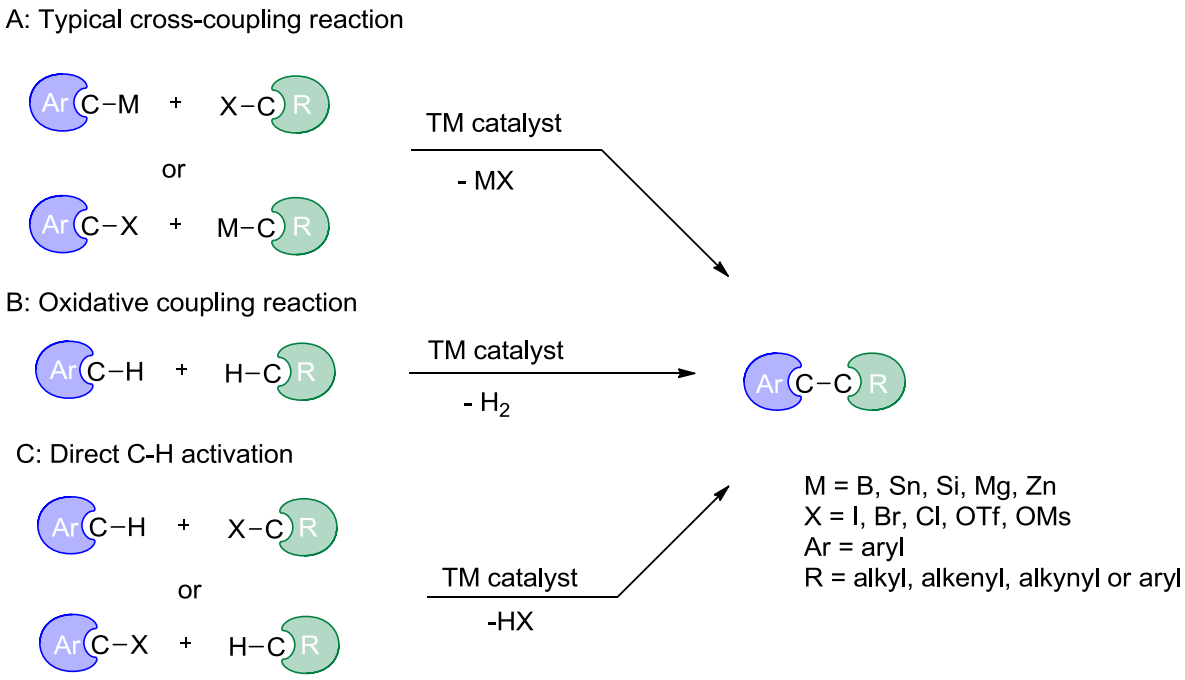



**Figure 12** Possible pathways in new carbon-carbon bond formation

Direct C-H arylations[55] currently attracts much attention and are being developed into complementary techniques for efficient and straightforward functionalization of arenes and heterocycles for medicinal chemistry applications.[56]

### 1.3.1.2 Direct C-H Borylation

In the past decade, iridium-catalyzed C−H borylation of arenes has become a widely used method for the functionalization of arenes because of its ability to produce highly versatile aryl organoboronate ester intermediates from arenes without the need for reactive groups, such as halides or sulfonates.[57]

Traditionally there are two commonly used methods for the synthesis of arylboronic acids (Figure 15). One involves the conversion of an aryl halide to a Grignard or lithium reagent, followed by the reaction of the main group organometallic reagent with a trialkylborate. The addition of either a diol or an acid converts the initial organoboron product to the final ester or the acid, respectively. Alternatively, a widely employed route to boronate esters is the palladium-catalyzed Miyaura borylation of an aryl halide with a mono- or diboron reagent.[58] In addition, analogous copper catalyzed borylation of aryl halides with diboron reagents has recently been reported.[59]

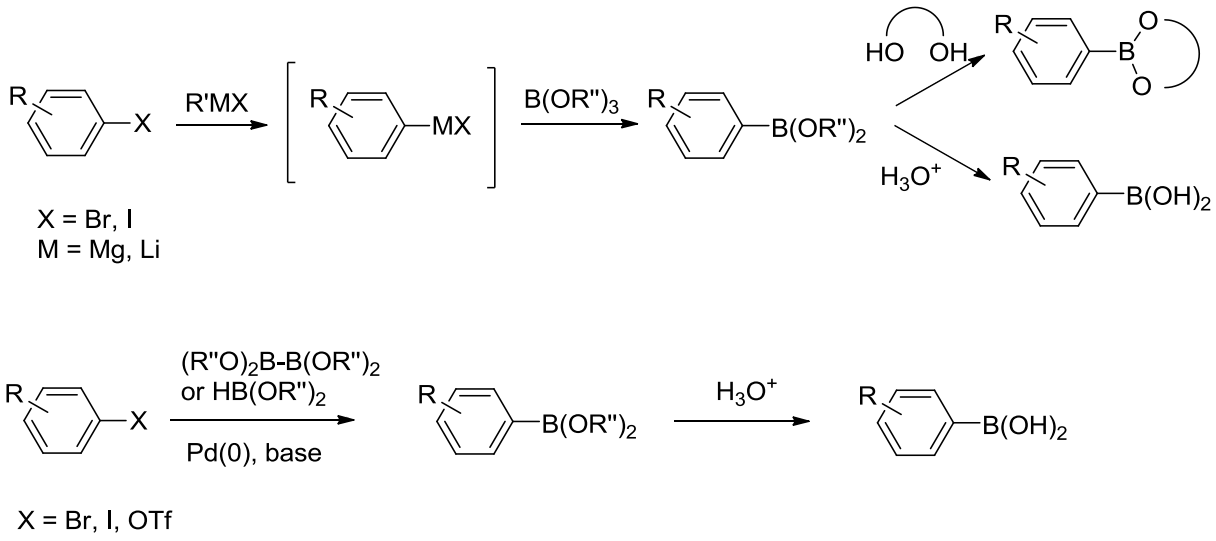


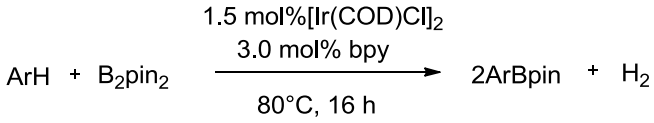

**Figure 15** Common Syntheses of Arylboronate Esters and Acids

In contrast, the direct borylation of arenes and alkanes provides access to synthetically useful compounds without relying on the accessibility of aryl or alkyl halides. This direct borylation, therefore, reduces synthetic steps.

#### 1.3.1.2.1 Reactivity of arenes

Although Cp*Ir complexes were the first catalysts reported for the direct borylation of arenes,[60] other combinations of iridium precursors and ligands generate more active catalysts for this process. In 2002, Ishiyama, Miyaura, Hartwig, and their co-workers reported the borylation of arenes catalyzed by iridium complexes of bipyridine and di-*tert*-butylbipyridine.[61] The initial paper on this system was published concurrently with that of Smith, Maleczka, and co-workers on the borylation of arenes catalyzed by iridium complexes of phosphines.[62] The catalysts containing bipyridine derivatives were found more reactive for most borylation of arenes and heteroarenes than those containing phosphine ligands. The reactions catalyzed by the iridium catalyst containing the bipyridine derivative occur at room temperature to 80 °C in many cases with turnover numbers between 500 and 1,000, and with turnover numbers exceeding 24,000 in favorable cases.[63] In contrast, the reactions catalyzed by the phosphine-ligated iridium complexes occur at 100-150 °C.[62]

A variety of arylboronate esters[62] was synthesized in moderate to excellent yields from the reaction of arenes with $B_2pin_2$ catalyzed by 1.5 mol % $[Ir(COD)Cl]_2$ and 3 mol % bpy (Scheme 5). For example, PhBpin was produced in 95% yield from benzene. The reaction of monosubstituted arenes, such as anisole, toluene, and trifluoromethylbenzene, yielded an approximately statistical mixture of products arising from *meta*- and *para*borylation, with the product from *ortho*-borylation being observed (1%) only from the reaction of anisole. However, the borylation of 1,2- disubstituted arenes formed 3,4- disubstituted arylboronate esters exclusively. Similarly, 1,3-disubstituted arenes formed 3,5- disubstituted arylboronate esters exclusively, and the reaction of the symmetric 1,4-disubstituted arene, *p*-xylene, with $B_2pin_2$ catalyzed by 1.5 mol % $[Ir(COD)Cl]_2$ and 3 mol % bpy yielded the 2,5-dimethylphenylboronic ester, but in a somewhat lower yield. From this observation it can be concluded that the regioselectivity of the C-H borylation of substituted arenes is controlled by steric effects.

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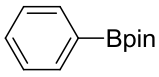
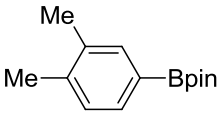
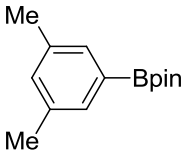
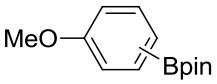
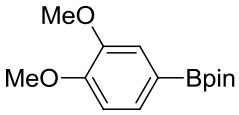
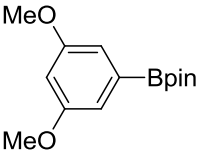
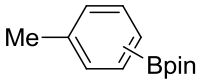
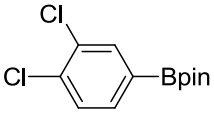
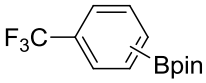
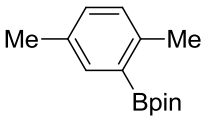
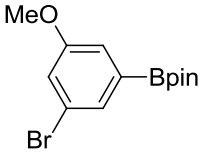
|  | 95 |  | 83 |  | 86 |
|  | 95 (1:74:25) (*o*: *m*: *p*) |  | 86 |  | 72 |
|  | 82 (0:69:31) (*o*: *m*: *p*) |  | 83 | | |
|  | 80 (0:70:30) (*o*: *m*: *p*) |  | 58 |  | 73 |

**Scheme 5** Borylation of Arenes[61]

### 1.3.1.2.2 Mechanistic Studies of (bpy)Ir-Catalysed Arene Borylation

Ishiyama, Miyaura, Hartwig and co-workers reported extensive studies that provided insight into the mechanism of arene borylation catalyzed by the combination of iridium precursors and dtbpy.[61] Later on Hartwig, Ishiyama, and Miyaura reported an improved synthesis of [Ir(dtbpy)($\eta^2$-COE)(Bpin)$_3$] (Figure 16) that was isolated after many experiments in 80-95% yield.[63]

Hartwig and co-workers then conducted studies on the reactivity of [(dtbpy)($\eta^2$-COE)Ir(Bpin)$_3$]. The reaction of [Ir(dtbpy)($\eta^2$-COE)(Bpin)$_3$] with arenes yielded 3 equivalent of ArBpin. The yields and regioselectivities of the borylated products observed from the reaction of [Ir(dtbpy)($\eta^2$-COE)-(Bpin)$_3$] and arenes were similar to those of the borylated

products observed from the reaction of arenes and $B_2pin_2$ catalyzed by the combination of $[Ir(COD)(OMe)]_2$ and dtbpy. Two different types of iridium complexes were considered to be possible intermediates that cleave the C-H bond of the arene.[63]

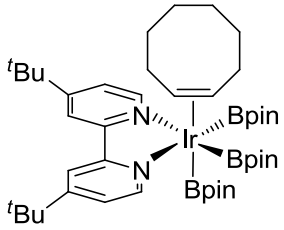



**Figure 16** Active catalyst generated from $[Ir(COD)(OMe)]_2$, dtbpy, and $B_2pin_2$

On the basis of these data obtained from NMR spectroscopy of catalytic systems, the isolation of kinetically competent intermediates, and kinetic data, Hartwig and co-workers proposed the mechanism shown in Figure 17 for the borylation of arenes catalyzed by dtbpy-ligated complexes of iridium.[63] First, COE dissociates reversibly from the stable iridium trisboryl complex. The resulting 16-electron complex then reacts with the arene in a turnover-limiting step to form the arylboronate ester. This latter process likely occurs by coordination of arene and subsequent oxidative addition of the aryl C-H bond to form an iridium(V) intermediate. Reductive elimination of Ph-Bpin from the iridium(V) intermediate then forms the free functionalized product and an iridium(III) species. A combination of oxidative addition of $B_2pin_2$ and reductive elimination of HBpin would then regenerate the active iridium trisboryl complex.

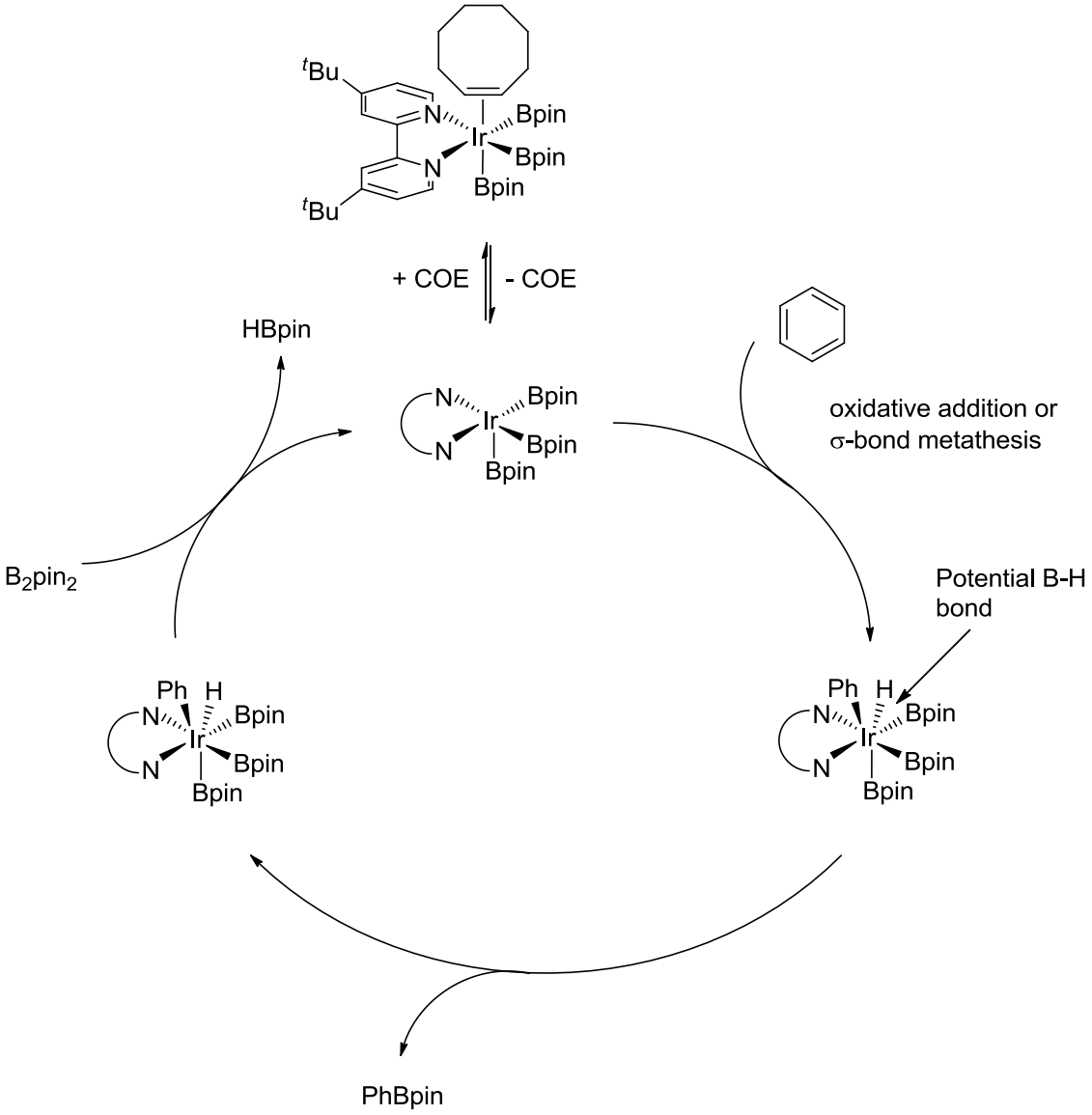



**Figure 17** Proposed Mechanisms for the Iridium-Catalyzed Borylation of Arenes[63]

Alternatively, $\sigma$-bond metathesis between [Ir(dtbpy)(Bpin)$_3$] and Ph-H could produce an intermediate phenyliridium complex containing a coordinated borane [Ir(dtbpy)(Bpin)$_2$(HBpin)-(Ph)]. This phenyliridium complex would eliminate PhBpin to generate the same bisboryliridium hydride complex as would be formed by the sequence of C-H oxidative addition and B-C reductive elimination.

#### 1.3.1.2.3 Subsequent functionalization of aryl boronate esters

The synthetic importance of aromatic C–H borylation is shown in Figure 18, where a 1,2,3-trisubstited aromatic compound can be directly converted to a 1,2,3,5-organoborane compound and subsequently functionalized. Clearly, the products from the borylation of aromatic C-H bonds can be used as reagents for the Suzuki-Miyaura cross coupling[64] or by the oxidation has been shown to generate phenols from arenes.[65]

In one case, it was shown that iridium-catalyzed arene borylations, followed by halogenation of the initial organoboronate product with cupric bromide formed aryl bromides.[66] This sequence constitutes a sterically controlled halogenation of an arene that complements the electronically controlled halogenation of arenes by electrophilic aromatic substitution. Related chlorinations were achieved with cupric chloride.[66]

Most recently, Hartwig and co-workers developed a protocol to convert pinacolboronate esters to aromatic nitriles.[67] Again, the regioselectivity of the overall process is controlled by steric effects that dictate the regioselectivity of the C-H borylation step. Hartwig and co-workers extended the Lam-Chan functionalization[68] of arylboronate esters to the functionalization of the pinacol boronate esters resulting from C-H borylation. This sequence constitutes a sterically controlled amination of an aromatic C-H bond.[69] Related sequences to form aryl ethers via the C-H borylation were also developed, but required the generation of the boronic acids as an intermediate.[69]

Although the pinacolboronate esters are convenient to use because they are stabile toward air and chromatography, a similar process that generates more reactive boronic acids or trifluoroborates would be desirable. A one-pot protocol for the generation of a boronic acid via the C-H bond functionalization chemistry was achieved[70] by iridium catalyzed borylation, followed by an oxidative hydrolysis of the pinacol boronate ester with added periodate. A simple process for generating the trifluoroborates was achieved by the sequence of C-H borylation, followed by the addition of excess $KHF_2$ to the pinacolboronate ester.[70]

Finally, Ritter and Furuya reported the formation of aryl fluorides by converting the aryl pinacolboronate to the arylboronic acid by the method described above, and then converting the arylboronic acid to the aryl fluoride by a silver-mediated process.[71]

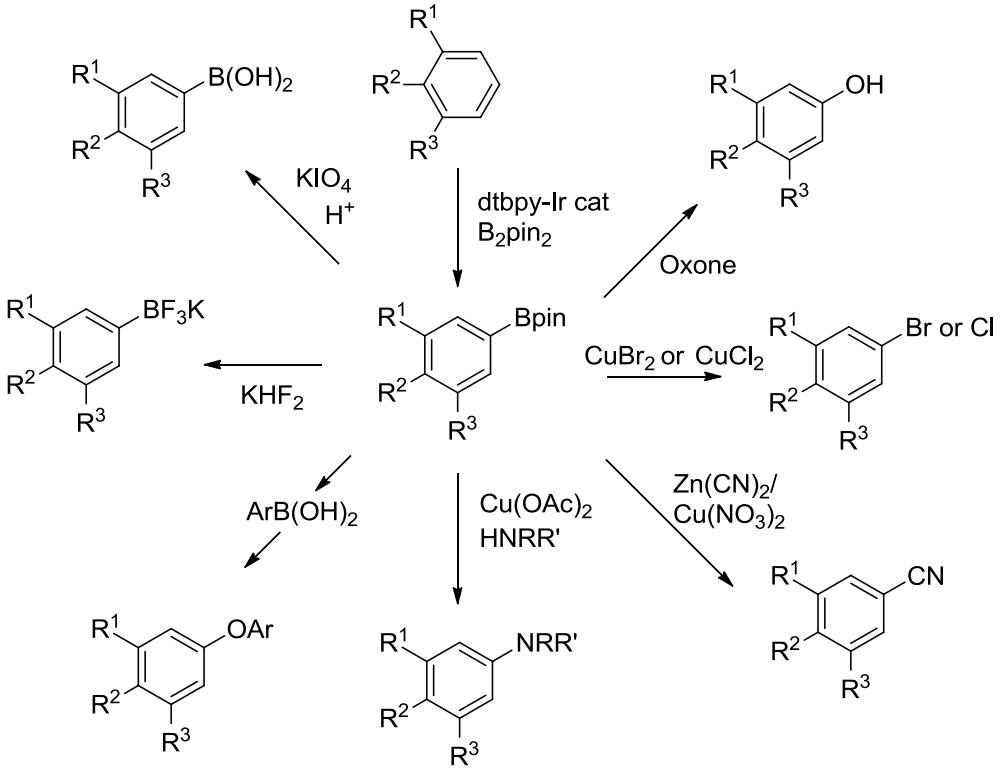
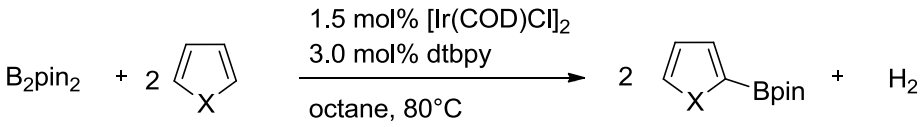


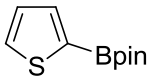
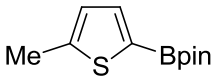
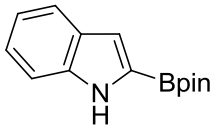
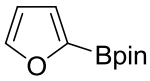
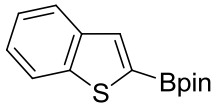
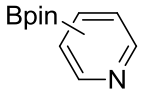
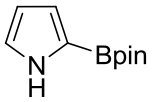
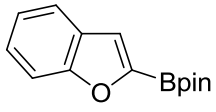
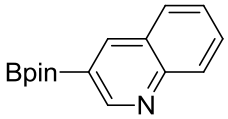

**Figure 18** Subsequent functionalization of aryl boronate esters

### 1.3.1.2.4 Reactivity of heteroarenes

Several research groups have investigated the scope of iridium-catalyzed borylation of heteroarenes.[72] Early studies of the borylation of heteroarenes were focused on the selectivity of borylation of 5-membered heteroarenes. In 2002, Hartwig, Ishiyama, Miyaura, and co-workers reported the borylation of thiophene, pyrrole, and furan with $B_2pin_2$ catalyzed by the combination $[Ir(COD)Cl]_2$ and dtbpy in octane at 80 or 100 °C (Scheme 6).[73] Several heteroarenes were shown to react with $B_2pin_2$ in the presence of the iridium-dtbpy catalyst to provide heteroarylboronate esters. The C-H borylation of thiophene, furan, or pyrrole yielded to heteroarylboronate esters in high yields, and the borylation occurred selectively at the 2-position of these heteroarenes. Related reactions of thiophene, furan or pyrrole with an excess of the diboron reagent produced 2,5-diborylated products. Thiophene, pyrrole and furan 2,5-bisboronate esters were obtained in 80%, 80%, and 71% yields, respectively, when the Ir-catalyzed borylation of these heteroarenes was performed in the presence of 1.1 equivalent of

$B_2pin_2$. Indole and benzofuran also underwent selective borylation at the 2-position in the presence of an iridium catalyst to form 2-boryl indole and 2-boryl benzofuran in excellent yields. The reaction of pyridine was conducted at a higher reaction temperature (100 °C), and a mixture of 3- and 4-borylated pyridine products was observed. Quinoline, however, underwent borylation exclusively at the 3-position in a high yield. The origin of the regioselectivity of pyridine has not been established.




| product | yield % | product | yield % | product | yield % |
|---|---|---|---|---|---|
|  | 83[a] |  | 91 |  | 92 |
|  | 83[a] |  | 89 |  | 42[a, b, c] |
|  | 67[a] |  | 91 |  | 84[b] |

[a] Diborylated products were produced in 12 - 17% yield. [b] Reaction conducted at 100°C.
[c] Ratio of 3- and 3- boryl pyridine was 67:33.

**Scheme 6** Iridium-catalyzed borylation of heteroaromatic substrates[73]

In contrast to the site-selectivity for the borylation of arenes, the site-selectivity for the borylation of heteroarenes is largely controlled by electronic effects.[72a,73] Furans, pyrroles, and thiophenes undergo reaction at the C-H bond alpha to the heteroatom. Reactions of benzo-fused heterocycles occur at the C-H bond alpha to the heteroatoms, without competing

reaction at the aromatic ring. Later on it was found that the most active catalytic system for C-H borylation of arenes and heteroarenes was generated from $[Ir(COD)(OMe)]_2$ a dtbpy in ratio (1:2).[63]

### 1.3.1.3 Direct C-H sulfenylation

Aryl sulfides are a common functionality found in numerous pharmaceutically active compounds and also some examples of biologically active hetarylthioethers were previously described.[74] The traditional transition metal-catalyzed cross coupling of ArX (X=Cl, Br, I, OTf, and $B(OH)_2$) and ArSH is a powerful method for the construction of a C-S bond (Figure 19, eq 1).[75] However, thiols are prone to undergo oxidative S-S coupling reactions, resulting in the undesired formation of disulfides. Moreover, organic sulfur compounds may bind to metal, causing the deactivation of metal catalyst.[76] Employing disulfides may solve these drawbacks (Figure 19, eq 2).[77] Nevertheless, in general, 1 equiv. of reductant such as Zn or Mg was added in the reaction of ArX and RSSR, and prefunctionalization is still required for such transformation, which significantly restricts potential applications of these methods.

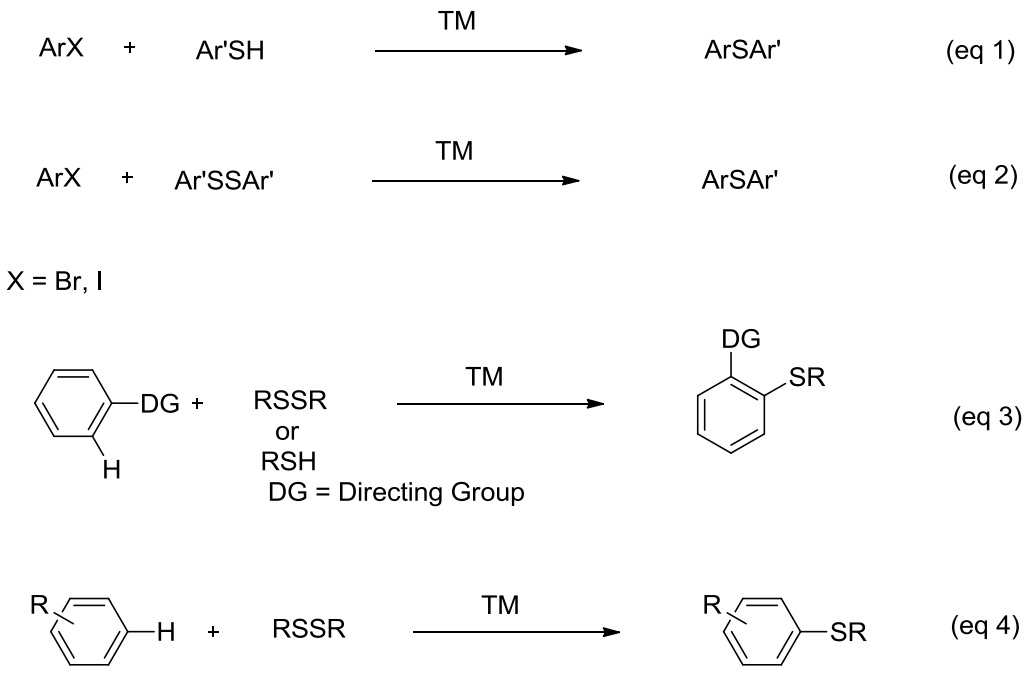



**Figure 19** Formation of a C-S Bond Catalyzed by Transition Metal

The direct functionalization of a C-H bond is a straightforward transformation[78] and few examples of the formation of a C-S bond through C-H bond cleavage have been reported.
In 2006, Yu and co-workers reported a $Cu(OAc)_2$-catalyzed thiolation of the 2-phenylpyridine with PhSH and MeSSMe under oxygen atmosphere (Figure 19, eq 3).[79] Subsequently, Dong and co-workers described the Pd-catalyzed direct sulfonylation of a 2-phenylpyridine C-H bond with $ArSO_2Cl$.[80] Recently, a nonchelation-assisted Cu-catalyzed thiolation of the di- or trimethoxybenzene arene C-H bond with ArSSAr was reported. (Figure 19, eq 4).[81]

#### 1.3.1.3.1 Reactivity of heteroarenes

Since the discovery of the potential utility of 3-sulfenylindoles as pharmaceuticals[82] significant efforts have devoted to the development of new sulfenyl-substituted indoles. Several efficient strategies for synthesis of 3-sulfenylindoles have been developed, including electrophilic substitution of indoles with sulfur-containing electrophiles, such as sulfenyl chloride,[83] N-thiophthalimides,[84] and quinone mono-O,S-acetals,[85] sulfoamination of 2-alkynylanilines with disulfides[86] or arylsulfenyl chlorides,[87] sulfanyl radical addition to alkynyl azides,[88] nucleophilic substitution of indole halides with metal mercaptides,[89] coupling reactions of indoles with disulfides and thiols in the presence of stoichiometric strong base.[90] Despite the synthetic utility of these transformations, most of these processes require the use of the strong bases, unavailable thiolating reagents or per-activated promoters, which are limited by undesired byproducts and are not suitable for sensitive substrates.

On the other hand, several examples of direct C-H sulfenylation were also reported. In 1989 an example of alkylsulfenylation of indole with dimethyl disulfide using copper (I) iodine catalyst at 132-160°C was described.[91] Subsequently, Uemura and co-workers have developed an efficient protocol for the sulfenylation of indoles with thiols in the presence of $VO(acac)_3$, 2,6-di-*tert*-butyl-*p*-cresol, potassium iodone and oxygen, but an excess amount of the thiol is required and undesired disulfide byproducts are formed.[92] Afterwards, Yadav and co-workers reported an iron (III) chloride catalyzed sulfenylation reaction using indoles and thiols as the reaction partners.[93] However, the reaction is limited to aryl thiols and benzyl thiols, which have a foul smell and a pungent flavor. Later on, Li and co-workers disclosed

iron-catalyzed sulfenylation of an indole C-H bond with diaryl disulfides, whereas a catalytic amount of iodine was supplied to promote the reaction (Figure 20, eq 1).[94] Recently, Li and co-coworkers published very useful example of sulfenylation of indole with various disulfide using catalyst copper (I) iodine under air atmosphere utilizes $O_2$ as a clean and cheap oxidant (Figure 20, eq 2).[95] Finally, Bolm and co-workers published convenient transition metal-free procedure for the direct sulfenylation of indole C–H bonds using diaryl disulfides and cesium carbonate (Figure 20, eq 3).[96a]

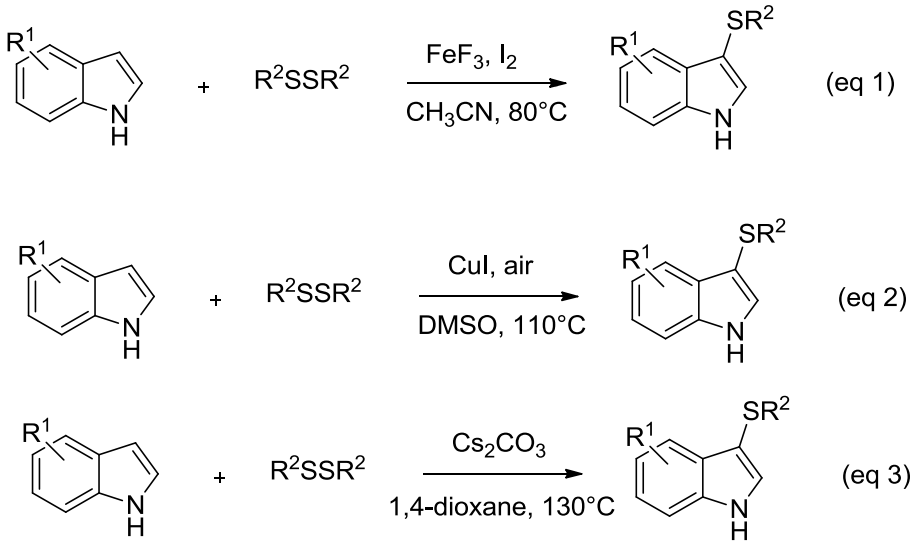



**Figure 20** Formation of 3-sulfenylindoles by different C-H sulfenylation

## 1.3.2 C-H activation of purines and deazapurines

Traditional cross-coupling of the nucleobases as well as DNA or RNA fragments have been well-established in nucleic acid chemistry. For the direct C-H activation of heteroarenes applies generally the same patterns as in activation of arenes. However, the higher control of regioselectivity can be observed due to the different nature of each C-H bond in heteroarenes. Purines are generally functionalized via direct activation of the C8-H bond and the most widely TM catalysts used for activation are palladium and copper.[97] On the other hand, other transition metals used in catalysis of C-H activations (Rh, Ru, Co etc.) could strongly

coordinate purine at N7. Therefore, there is certainly a great potential of the development of C-H activations in 7- or 9-deazapurines that are supposed not to coordinate the metals as strongly as purines.

### 1.3.2.1 Direct C-H arylation

Previously our group developed Pd-catalyzed C-H arylations of purines[98] at position 8 by diverse aryl iodides in the presence of CuI and $Cs_2CO_3$ (Figure 13). The methodology is general and efficient and was applied in the consecutive regioselective synthesis of 2,6,8-trisubstituted purines bearing three different C-substituents in combination with two cross-coupling reactions. The C-H arylation was subsequently applied for the synthesis of diverse trisubstituted and tetrasubstituted purines[99] and also fused purine heterocycles.[100]

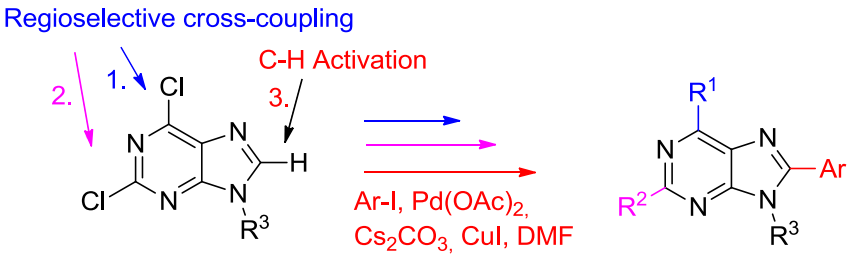



**Figure 13** Synthesis of diverse trisubstituted and tetrasubstituted purines

Our former colleague, Igor Cerna,[101] and others[102] successfully performed C-H arylations of unprotected purine nucleosides with aryl iodides at position 8 to allow a straightforward single-step introduction of diverse aryl groups (Figure 14).

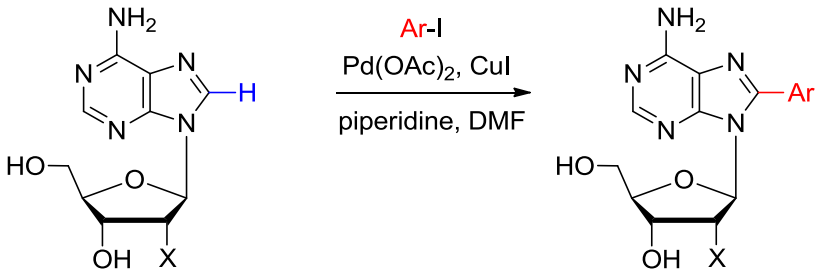



**Figure 14** Direct C–H arylation of unprotected purine nucleosides

To the best of my knowledge, there was no reported example of a direct C-H arylation of deazapurine moiety prior to starting of my project.

### 1.3.2.2 Others C-H activation

To the best of my knowledge, there were no reported examples of a direct C-H borylation or C-H sulfenylation of purines and deazapurine moiety prior to starting of my project.

# 2 Specific aims of the thesis

1. Development of the direct C-H borylation of deazapurines
2. Development of the direct C-H sulfenylation of deazapurines
3. Combinations of C-H activations with cross-coupling reactions, nucleophilic substitutions and construction of libraries di- and trisubstituted deazapurines

## Rationale of the Specific Aims

In recent years, direct C-H borylation and C-H sulfenylation of arenes has become a widely used method for the functionalization of arenes because of its ability to produce aryl organoboronate ester or arylsulfanyl derivatives without needing reactive groups (such as halides) or strong bases (like LDA). Since no literature exists for evidence of this type of borylation or sulfenylation on deazapurines, my major goal in this PhD thesis is the development of these direct C-H activations.

The newly developed methods can then be combined with the previously known methodologies of cross-couplings and nucleophilic substitutions of these heterocycles in order to attach two, three, four or even five different substituents onto the heterocyclic moiety. One-pot tandem reactions will be used for straight-forward substitutions of single derivatives.

All the newly synthesized functionalized and substituted heterocycles were intended to be tested for cytostatic activity in a panel of cancer and leukaemia cell lines (in collaboration with Dr. H. Mertlíková-Kaiserová at IOCB ASCR and Prof. M. Hajdúch at Palacky University, Olomouc). Selected derivatives were intended to be also submitted for antiviral screening in Gilead Sciences, Inc.

# 3 Results and discussion

## 3.1 C-H Borylation of purines and deazapurines

Ir-catalyzed C–H borylation of aromatic compounds is a one step method to generate aryl boronates and the reactions should lead to hetarylboronates suitable for further functional group transformations by the Suzuki cross-coupling or by other substitutions (Chapter 1.3.1.2.3, Figure 18). The most active catalyst for this transformation is generated from dtbpy and $[Ir(COD)(OMe)]_2$ in ratio (1:2).[63] So far, not only have such reactions not been reported on these two heterocyclic systems, but also the corresponding hetarylboronates or -boronic acids are unknown. The direct C-H borylation presents an important task as it will remarkably simplify the synthesis of hetarylboronates suitable for further functional group transformations.

### 3.1.1 Direct C-H borylation of purines

9-Benzyl-6-phenylpurine (**1**) was chosen as the first model substrate for studying the C–H borylation. It was employed the above mentioned catalytic system for C-H borylation of purine (Chart 1) under diverse conditions (from r.t. to 80 °C and MW irradiation). Unfortunately, no formation of 8-borylated purine was observed (mostly just the starting compound was recovered accompanied by minor byproducts). The most plausible explanation of this lack of reactivity is the formation of stable complex of purine with Ir catalyst at N7. Another problem might be the limited stability of the purine-8-boronate that may undergo protodeborylation back to the starting compound.

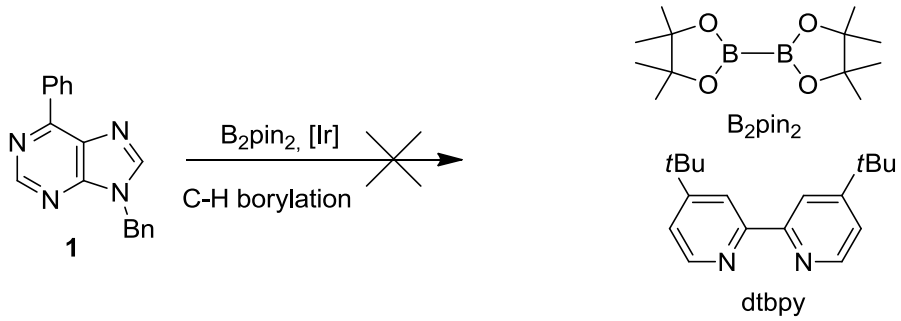
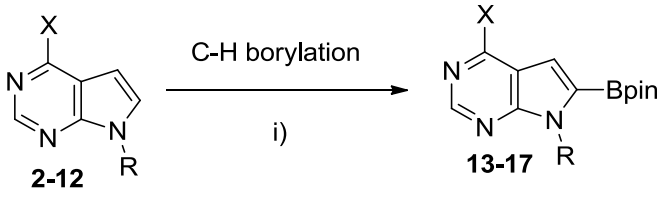



**Chart 1.** Direct C–H borylation of purines

### 3.1.2 Direct C-H borylation of 7-deazapurines

Therefore, my further effort was focused on 7-deazapurines (lacking the N7 coordination site). The next model starting compound was 9-benzyl-6-phenyl-7-deazapurine (**2**, 7-benzyl-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine). THF was solvent of choice due to solubility of starting compounds. The reaction of **2** with bispinacolatodiboron in presence of dtbpy and $[Ir(COD)(OMe)]_2$ proceeded well to give selectively 8-borylated product **13** in in high yield (85%, Table 1, entry 1). The regioselectivity was in accord with the literature examples of borylation of indoles[72a,73] to position 2 and was unequivocally proved by X-ray diffraction analysis of **13** (Figure 1).




**Scheme 1.** Reagents and conditions: i) $B_2pin_2$ (1.2 equiv.), $[Ir(COD)OMe]_2$ (5%), dtbpy (10%), THF, 80°C, 20 h

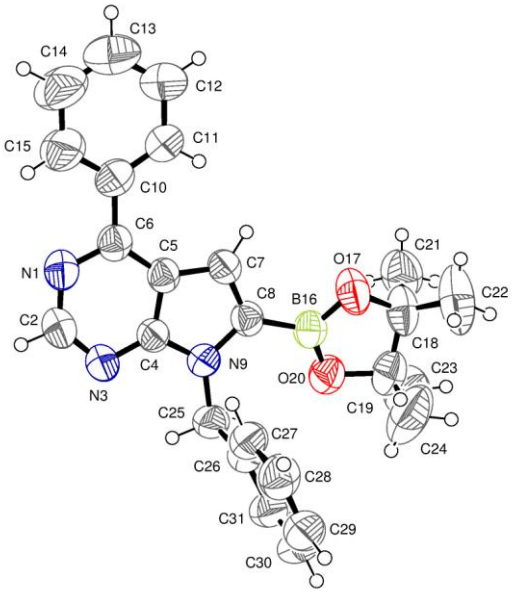



**Figure 1.** ORTEP drawings of crystal structures of compounds **13** (CCDC 703631)

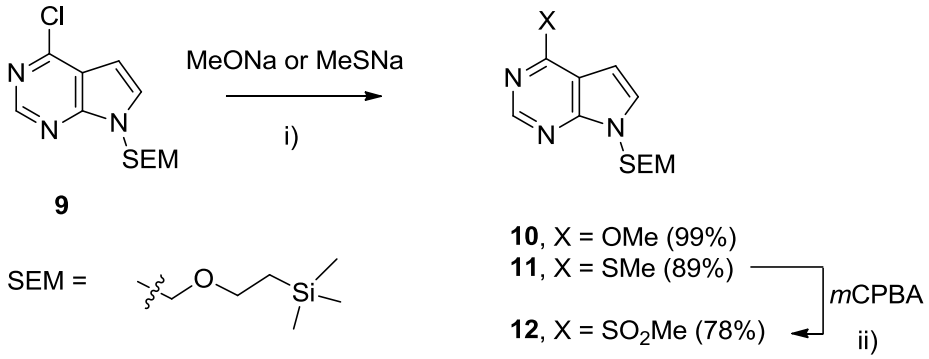
**Table 1.** Scope and limitations of direct C-H borylation of 7-deazapurines **2-12**

| Entry | Starting compound | X | R | Yield (%) |
|---|---|---|---|---|
| 1 | **2** | Ph- | Bn | **13** (85%) |
| 2 | **3** | Ph- | H | no reaction |
| 3 | **4** | Me- | 2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl | no reaction |
| 4 | **5** | $NH_2$ | Bn | no reaction |
| 5 | **6** | $(CH_3)_2NCH=N$- | Bn | no reaction |
| 6 | **7** | Cl | Bn | **14** (53%) |
| 7 | **8** | Cl | H | no reaction |
| 8 | **9** | Cl | SEM | **15** (78%) |
| 9 | **10** | OMe | SEM | **16** (81%) |
| 10 | **11** | SMe | SEM | **17** (83%) |
| 11 | **12** | $SO_2Me$ | SEM | no reaction |

Later on, I found that neither 9-unsubstituted 6-phenyl-7-deazapurine **3** nor nucleoside **4** formed the desired boronates. 6-Amino-9-benzyl-7-deazapurine (deazaadenine) **5** as well as its N-(dimethylamino)methylidene-protected derivative **6** also did not give any C-H borylation products. 9-Benzyl-6-chloro-7-deazapurine **7** gave the desired 8-borylated product **14** in moderate 53% yield, whereas the 9-unprotected 6-chloro-7-deazapurine **8** did not undergo the borylation. Apparently, the Ir-catalyzed C-H borylation only works on 9-substituted 7-deazapurines bearing functional groups lacking any acidic protons and/or coordinating nitrogens. On the other hand, I have no plausible explanation for the lack of reactivity of nucleoside **4**.

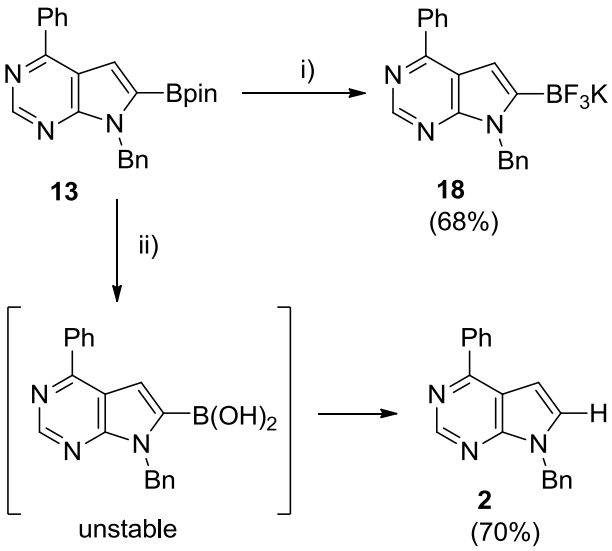
In order to access the biologically relevant substituted deazaadenine or deazahypoxanthine bases, I need to introduce a protecting group at position 9 and a suitable functional group at position 6. The protecting group need to be sufficiently stable and non-interfering with the borylation but easily removable at the end. Based on my previous experience with difficult removal of *N*-benzyl group from 7-deazapurines, I choose (trimethylsilyl)ethoxymethyl (SEM) group which is easily removable by TFA followed by ammonia. As possible transformable or leaving groups at position 6, it was considered Cl, $OCH_3$, $SCH_3$ and $SO_2CH_3$ which should be prone to either nucleophilic substitutions or demethylations. The SEM-protected 6-chloro-7-deazapurine **9** was prepared according to literature[103] and was converted to 6-methoxy- and

6-methylsulfanyl derivatives **10** and **11** by nucleophilic substitution with MeONa or MeSNa, respectively (Scheme 2). The sulphide **11** was oxidized to sulfone **12** by *m*CPBA. The corresponding 9-SEM-6-substituted deazapurines **9-12** were then tested in the Ir-catalyzed C-H borylation under the same conditions as above (Table 1, entries 8-11). The 6-chloro-, 6-methoxy- and 6-methylsulfanyl- SEM-protected 7-deazapurines reacted well to give the corresponding boronates **15-17** in good yields (78-83%), whereas the sulfone **12** did not give any reaction under these conditions.




**Scheme 2.** Reagents and conditions: i) 2M MeONa/MeOH, acetone, rt, overnight or MeSNa (1.5 equiv.), MeOH, rt, 1h; ii) *m*CPBA (2 equiv.), DCM, rt, overnight.

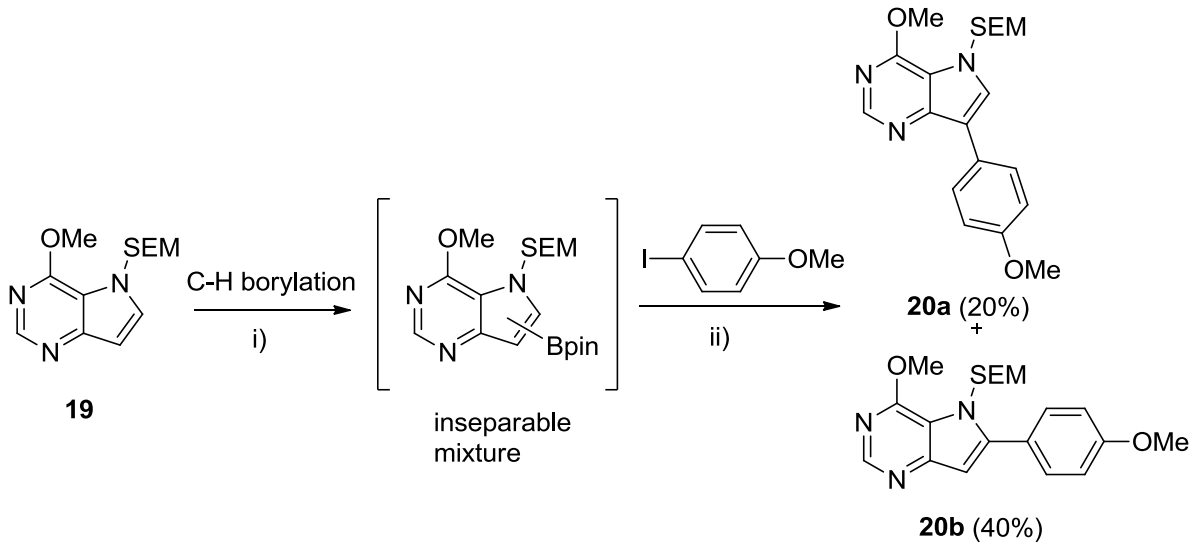
I also explored the possible conversions of the boronate **13** to either free boronic acids or trifluoroborates[104] (Scheme 3). The reaction of **13** with $KHF_2$ under standard conditions[70] gave the desired trifluoroborate **18** in acceptable 68% yield. However, the oxidation followed by hydrolysis under literature conditions,[70] which should give the boronic acid, gave only 8-unsubstituted deazapurine **2** as a product of protodeborylation. This is an indicator, that the corresponding deazapurine-8-boronic acid is too unstable to be isolated under these reaction conditions.




**Scheme 3.** Reagents and conditions: i) $KHF_2$ (6 equiv.), THF/$H_2O$ (5:3), rt, 5 h; ii) $NaIO_4$ (4 equiv.), THF/$H_2O$ (4:1), 1M HCl, rt, 1 h.

### 3.1.3 Direct C-H borylation of 9-deazapurines

Later on, my effort was also focused on C-H borylation of 9-deazapurines and I applied the same conditions used for C-H borylation of 7-deazapurine on model compound 6-methoxy-7-SEM-9-deazapurine (**19**, 4-methoxy-5-SEM-*5H*-pyrrolo[3,2-*d*]pyrimidine). The C-H borylation of 9-deazapurine **19** did not proceed regioselectively and two borylated (according LC-MS) unseparable products were formed. Therefore the mixture was then used in Suzuki coupling under conditions previously optimized[105] with 4-iodoanisole and the formation of two regioisomers were confirmed. The two 9-deazapurines **20a** (7-arylated) and **20b** (8-arylated) were isolated in 20%, respectively 40 % (Scheme 4).



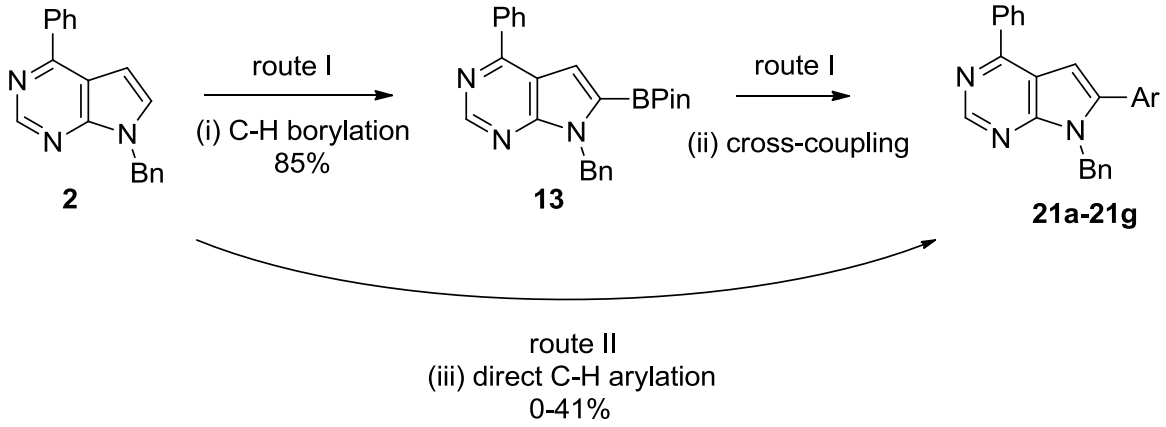

**Scheme 4.** Reagents and conditions: i) $B_2pin_2$ (1.2 equiv.), $[Ir(COD)OMe]_2$ (5%), dtbpy (10%), THF, 80°C, 20 h; ii) Ar-I (1.1 equiv.), $Pd(dppf)Cl_2$ (5%), $K_2CO_3$ (4 equiv.), DMF, 90°C, 1 h.

## 3.1.4 Application of C-H borylation in synthesis of 6,8-disubstituted 7-deazapurines

Having a regioselective access to the 8-subtituted 7-deazapurines, I have further explored synthetic applications of boronates. The most obvious use is in the Suzuki cross-coupling reaction or in transformation to other functional groups (halogen, cyano, hydroxyl, CF3) generally by the copper catalysed substitution (Chapter 1.3.1.2.3).

### 3.1.4.1 Synthesis of 8-aryl-7-deazapurines

The Suzuki cross-coupling reactions were performed on model benzylated boronate **13** with diverse aryl halides under conditions previously optimized[105] for other hetarylboronates ($Pd(dppf)Cl_2$ and $K_2CO_3$ in DMF). Generally, all the aryl halides (diverse aryl iodides and 2-bromopyrene) reacted well to give the desired 8-aryl products **21a-21g** in very high yields (Scheme 5, Table 2). One example (**21b**) was also characterized by X-ray diffraction (Figure 2).




**Scheme 5.** Reagents and conditions: $B_2pin_2$ (1.2 equiv.), $[Ir(COD)OMe]_2$ (5%), dtbpy (10%), THF, 80°C, 20 h; ii) Ar-I (1.1 equiv.), $Pd(dppf)Cl_2$ (5%), $K_2CO_3$ (4 equiv.), DMF, 90°C, 1 h.; iii) Ar-X (2 equiv.), $Pd(OAc)_2$ (5%), $Cs_2CO_3$ (2.5 equiv.), CuI (3 equiv.), DMF, 160 °C, 60 h.

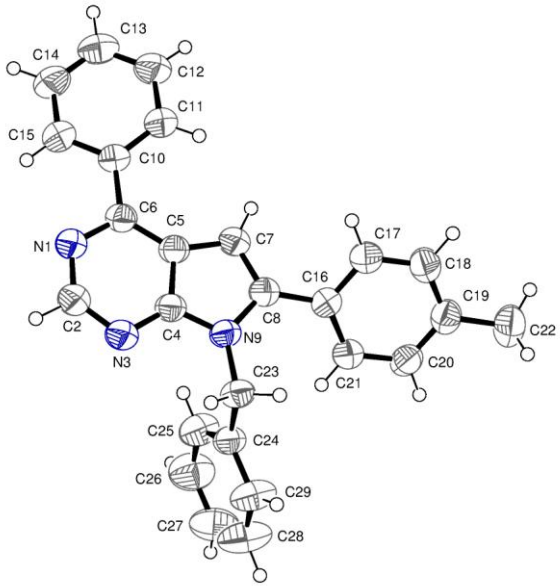
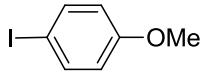
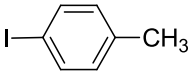
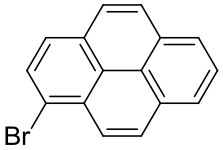
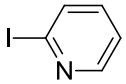
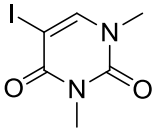
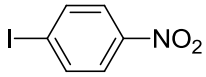
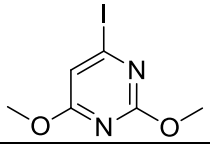



**Figure 2.** ORTEP drawings of crystal structures of compounds **21b** (CCDC 703632)

Interesting products **21e** and **21g** arrised from the coupling with methylated 5- or 6-iodouracils (entries 5 and 7) as novel types of Janus-nucleobases[106] or fleximers.[107] In the case of compound **21g**, the acid hydrolysis gave the free 9-benzyl-6-phenyl-8-(uracil-6-yl)-7-deazapurine **21h**. The overall yields of the 6,8-diaryl-7-deazapurines over the two steps (C-H borylation and cross-coupling, Table 2 - Route I) were very good (67-81%).

**Table 2.** Synthesis of 8-arylated deazapurines by C-H activation

| Entry | Ar-X | Product | Route I - coupling[a] (overall yield)[b] | Route II (yield) |
|---|---|---|---|---|
| 1 |  | **21a** | 87%[a] (74%)[b] | 39% |
| 2 |  | **21b** | 90%[a] (76%)[b] | 41% |
| 3 |  | **21c** | 79%[a] (67%)[b] | 35% |
| 4 |  | **21d** | 95%[a] (81%)[b] | traces |
| 5 |  | **21e** | 92%[a] (78 %)[b] | 0% |
| 6 |  | **21f** | 91%[a] (77%)[b] | 0% |
| 7 |  | **21g** | 92%[a,c] (78%)[b,c] | 0% |

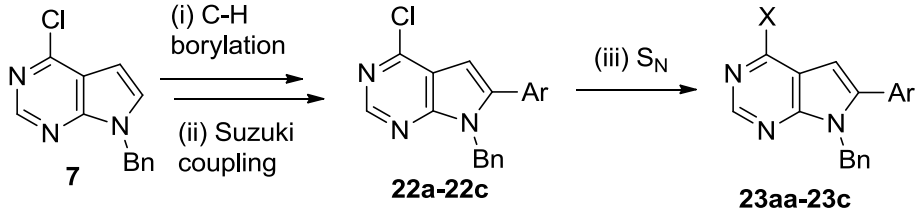
[a] cross coupling; [b] overall yield after two steps (C-H borylation and cross coupling); [c] overall yield after acidic deprotection to free uracil **21h**[109]

### 3.1.4.1.1 Synthesis of 8-aryl-7-deazapurines by direct C-H arylation

As a complementary alternative method, I have also tried direct C-H arylation of **2** with the same aryl halides under the conditions optimized[98] for arylation of purines (Table 2, Route II). However, these reactions did not proceed well giving very low yields (entries 1-3) or no reaction what so ever (entries 4-7). Comparison of the two routes to diaryl-7-deazapurines **21** revealed that the two step sequence (Route I) is much more efficient (Table 2). The coordination of Cu(I) to *N7* of purine ring is probably essential and proposed to assist the deprotonation at C-8 of purines. [102b]

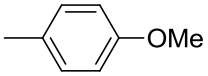
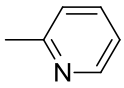
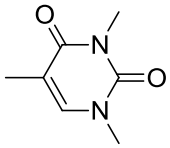
### 3.1.4.2 Two-step synthesis of 6,8-disubstituted 7-deazapurines – scope and limitations

I was also interested in synthesis of 8-aryl-7-deazaadenines. As the direct C-H activations of 7-deazaadenine **5** were unsuccessful, I have envisaged the use of 6-chloro derivative that can be readily transformed to 6-amino compounds (Table 3). The two-step arylation (C-H borylation followed by the Suzuki coupling) of 9-benzyl-6-chloro-7-deazapurine **7** with three different aryl iodides proceeded with acceptable 31-42% overall yields (the yield of the first step was the moderate 54% as mentioned above). The follow-up aminations of the 6-chloro-7-deazapurines **22a-22c** with methanolic ammonia gave the 8-aryl-7-deazaadenines **23aa**, **23b** and **23c** in very good yields (Table 3). Other nucleophilic substitutions were also pursued with 6-chloro-7-deazapurine **22a**. Its reactions with aniline, benzylamine, as well as with sodium phenolate gave the corresponding 6-N- or 6-O-substituted products **23ab**, **23ac** and **23ad**, respectively (Scheme 6).

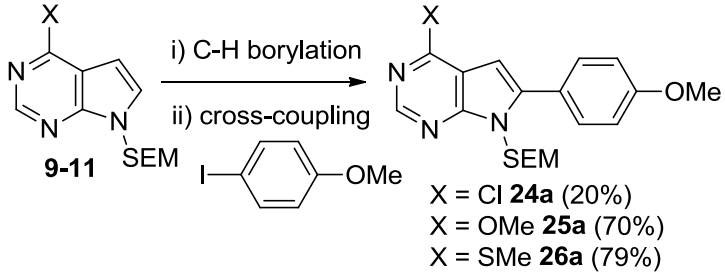



**Scheme 6.** Reagents and conditions: $B_2pin_2$ (1.2 equiv.), $[Ir(COD)OMe]_2$ (5%), dtbpy (10%), THF, 80°C, 20 h; ii) Ar-I (1.1 equiv.), $Pd(dppf)Cl_2$ (5%), $K_2CO_3$ (4 equiv.), DMF, 90°C, 1 h.; (iii) a) $NH_3$/MeOH, 120 °C, overnight b,c) R-$NH_2$ (3 equiv.), butanol, reflux, overnight d) phenol (1.2 equiv.), KO*t*-Bu (1.2 equiv.), $K_2CO_3$ (0.75 equiv.), DMF, 110 °C, 16 h.

**Table 3.** Two-step synthesis of 6,8-disubstituted 7-deazapurines

| Entry | Ar | Product (yield) | X | Product (yield) |
|---|---|---|---|---|
| 1 |  | **22a** (42%) | $NH_2$ | **23aa** (83%) |
| 2 | | | NH-Ph | **23ab** (65%) |
| 3 | | | NH-Bn | **23ac** (77%) |
| 4 | | | O-Ph | **23ad** (93%) |
| 5 |  | **22b** (31%) | $NH_2$ | **23b** (85%) |
| 6 |  | **22c** (36%) | $NH_2$ | **23c** (79%) |

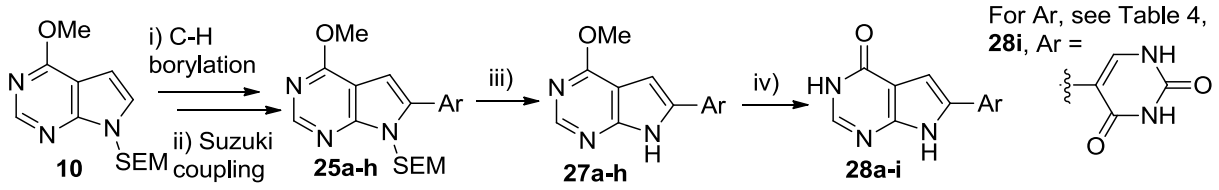
Having confirmed the reactivity of the SEM-protected deazapurines **9-11** in C-H borylations (Table 1, entries 8-10), I have further explored synthetic applicability of one-pot reaction sequence: C-H borylation/Suzuki cross-coupling with 4-iodoanisole. Whereas the borylation/Suzuki reaction of 9-benzyl-6-chloro-7-deazapurine **7** procedeed in moderate (but still acceptable) 42 % yield, the borylation/Suzuki reaction of 6-chlorodeazapurine **9** gave only low yield (20%) of the desired 8-aryl derivative **24a** because the Suzuki cross-coupling step was accompanied by competitive deborylation back to starting compound **9**. Therefore, I focused on the one-pot borylation/arylation of 6-methoxy and 6-MeS derivatives **10** and **11**. These reactions proceeded smoothly and efficiently to give the desired SEM-protected 8-arylated 7-deazapurines **25a** (70%) and **26a** (79%, Scheme 7).




**Scheme 7.** Reagents and conditions: i) $B_2pin_2$ (1.2 equiv.), $[Ir(COD)OMe]_2$ (5%), dtbpy (10%), THF, 80°C, 20 h; ii) Ar-I (1.1 equiv.), $Pd(dppf)Cl_2$ (5%; 10% in case of **26a**), $K_2CO_3$ (4 equiv.), DMF, 90°C, 1 h.

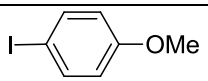
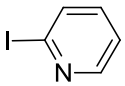
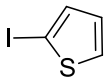
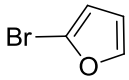
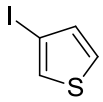
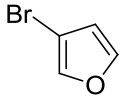
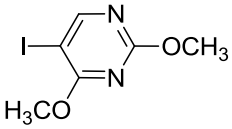
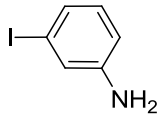
### 3.1.4.3 Synthesis of 8-aryl 7-deazahypoxantines

Encouraged by these successful reactions, I envisaged the use of the one-pot borylation/arylation of 6-methoxy-7-deazapurine **10** in combination with *O*-demethylation and SEM-deprotection for the synthesis of 8-aryl-7-deazahypoxanthine bases. It was performed a series of one-pot borylation/Suzuki coupling of methoxydeazapurine **10** with several aryl iodides (Scheme 8, Table 4). Generally, the reactions proceeded very well to give the desired SEM-protected 8-(het)aryl-6-methoxy-7-deazapurines **25a–h** in high yields (Scheme 8, Table 4). In case of several couplings of hetaryl halides, the reaction time for the Suzuki reaction was increased to 18 h to reach complete conversion. Deprotection[108] of the SEM group using trifluoroacetic acid (TFA) followed by aqueous ammonia furnished free 8-aryl-6-methoxy-7-deazapurine bases **27a-f** in good yields of 65–90 % (Scheme 8, Table 4). In deprotection of aminophenyl-derivative **25h**, the isolated yield of deazapurine base **27h** was low (22%) due to difficult separation of the highly polar derivative on column chromatography. In the case of compound **25g**, the deprotection of SEM group was directly followed by the acid hydrolysis[109] to the free 8-(uracil-5-yl)-7-deazahypoxantine **28i**. The final cleavage of methyl ethers **27a-h** was performed with in situ generated iodotrimethylsilane (from TMSCl and NaI)[110] in acetonitrile to give 8-(het)aryl-7-deazahypoxantine **28a-h** in high yields.




**Scheme 8.** Reagents and conditions: i) $B_2pin_2$ (1.2 equiv.), $[Ir(COD)OMe]_2$ (5%), dtbpy (10%), THF, 80°C, 20 h; ii) Ar-X (1.1 equiv.), $Pd(dppf)Cl_2$ (5%), $K_2CO_3$ (4 equiv.), DMF, 90°C, 1 h (or 18 h); iii) TFA (2 mL), rt, 1 h, followed by aq. ammonia (25% [w/w], rt, 18 h; iv) TMSCl (5 equiv.), NaI (5 equiv.), MeCN, 80°C, 18 h.

**Table 4.** Synthesis of 8-aryl-7-deazahypoxantines

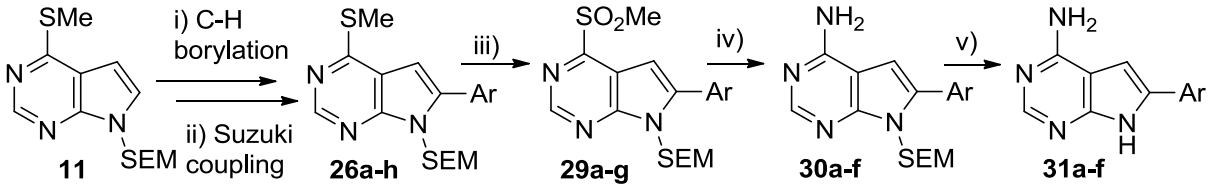
| Entry | Ar-X | Product **25** (yield) | Product **27** (yield) | Product **28** (yield) |
|---|---|---|---|---|
| 1 |  | **25a** (70%) | **27a** (90%) | **28a** (85%) |
| 2 |  | **25b** (50%)[b] | **27b** (85%) | **28b** (71%) |
| 3 |  | **25c** (65%) | **27c** (90%) | **28c** (90%) |
| 4 |  | **25d** (45%)[b] | **27d** (80%) | **28d** (92%) |
| 5 |  | **25e** (77%) | **27e** (90%) | **28e** (70%) |
| 6 |  | **25f** (58%) | **27f** (65%) | **28f** (80%) |
| 7 |  | **25g** (66%)[b] | ------ | **28i** (97%)[a] |
| 8 |  | **25h** (74%) | **27h** (22%) | **28h** (75%) |

[a] Overall yield after acidic deprotection to **28i**; [b] reaction time 18 hours

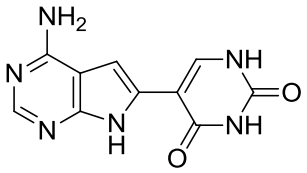
### 3.1.4.4 Synthesis of 8-aryl-7-deazaadenines

In order to synthesize the corresponding 8-aryl-7-deazaadenine bases, I started by an analogous one-pot two-step borylation/arylation of SEM-protected 6-MeS-7-deazapurine **11**. Due to the presence of sulphur, 10 mol% of Pd catalyst was needed for the Suzuki coupling, but otherwise the reaction with $B_2pin_2$ followed by cross-coupling with a series of aryl halides proceeded similarly well as to give the desired 8-(het)aryl products **26a-h** in high yields (Scheme 9, Table 5). Also here, for several hetaryl halides, the reaction time for the Suzuki reaction was increased to 18 h to reach complete conversion. The second step was the oxidation[111] of methylsulfanyl derivatives **26a-h** methylsulfones **29a-g** (which are more reactive electrophiles for nucleophilic substitution). The reactions proceeded well with exception of derivative **26h** (entry 8) which gave inseparable complex mixture only. The

original procedure ($NH_3$/MeOH) for amination of sulfones[111] was modified to $NH_3$/dioxane (to avoid formation of methyl ethers observed in methanol) which gave the desired SEM-protected 8-aryl-7-deazaadenines **30a-f** in good yields. Deprotection of SEM group using trifluoroacetic acid (TFA) followed by aqueous ammonia furnished free 8-substituted 7-deazaadenines **31a-f** in 65–80 % yields. In the case of compound **30g**, the deprotection of SEM group was directly followed by the acid hydrolysis to the free 8-(uracil-5-yl)-7-deazaaadenine **31i** (Figure 3).



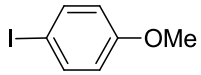
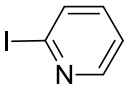
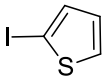
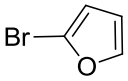
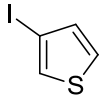
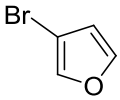
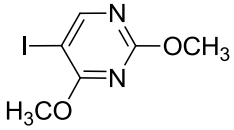
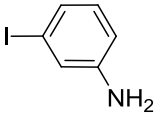

**Scheme 9.** Reagents and conditions: i) $B_2pin_2$ (1.2 equiv.), $[Ir(COD)OMe]_2$ (5%), dtbpy (10%), THF, 80°C, 20 h; ii) Ar-X (1.1 equiv.), $Pd(dppf)Cl_2$ (10%), $K_2CO_3$ (4 equiv.), DMF, 90°C, 1 h (or 18 h); iii) *m*CPBA (2 equiv.), $CH_2Cl_2$, r.t., 1 h; iv) aq. ammonia (25% [w/w]), dioxane, 50 °C, 18 h; v) TFA (2 mL), rt, 1 h, followed by aq. ammonia (25% [w/w], rt, 18 h.




**31i**

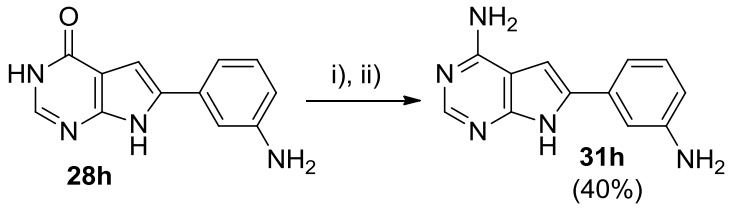
**Figure 3.** Structure of compound **31i**

**Table 5.** Synthesis of 8-aryl-7-deazaadenines

| Entry | Ar-X | Product **26** (yield) | Product **29** (yield) | Product **30** (yield) | Product **31** (yield) |
|---|---|---|---|---|---|
| 1 |  | **26a** (79%) | **29a** (77%) | **30a** (83%) | **31a** (80%) |
| 2 |  | **26b** (64%)[b] | **29b** (65%) | **30b** (94%) | **31b** (74%) |
| 3 |  | **26c** (69%) | **29c** (89%) | **30c** (91%) | **31c** (74%) |
| 4 |  | **26d** (62%) | **29d** (76%) | **30d** (85%) | **31d** (79%) |
| 5 |  | **26e** (70%)[b] | **29e** (62%) | **30e** (84%) | **31e** (72%) |
| 6 |  | **26f** (50%)[b] | **29f** (62%) | **30f** (71%) | **31f** (65%) |
| 7 |  | **26g** (39%)[b] | **29g** (86%) | **30g** (93%) | **31i** (77%)[a] |
| 8 |  | **26h** (78%) | complex mixture | ------- | -------- |

[a] Overall yield after acidic deprotection to **31i** (for structure see Figure 3.); [b] 18 hours

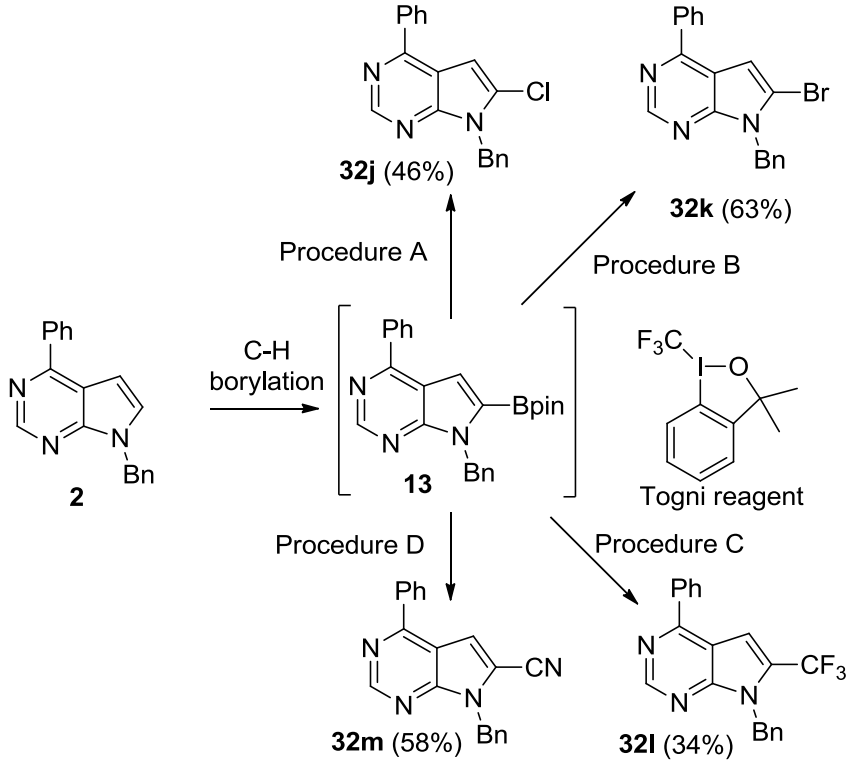
As the above reaction sequence did not work for preparation the 8-(3-aminophenyl)-7-deazaadenine **31h**, I used an alternative synthetic protocol. The corresponding 7-deazahypoxantine derivative **28h** was first chlorinated with $POCl_3$ followed by amination ($NH_3$ in dioxane) to give the desired deazaadenine **31h** in 40% overal yield (Scheme 10).




**Scheme 10.** Reagents and conditions: i) $POCl_3$ (5 equiv.), $BnEt_3N^+Cl$ (2 equiv.), $PhNMe_2$ (1.1 equiv.), MeCN, reflux, 4 h; ii) aq. ammonia (25% [w/w]), dioxane, 120 °C, 18 h.

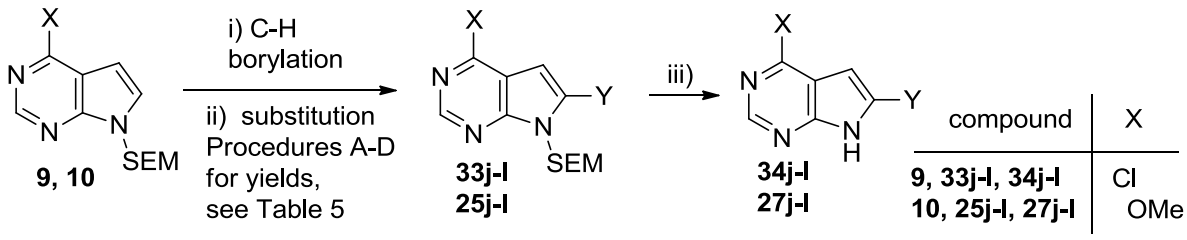
### 3.1.4.5 One-pot C–H borylation/Cu-catalyzed substitution

Having an easy access to 8-borylated 7-deazapurines, I also explored the possibility of their conversion to other functional groups. I tested the reactions of model 8-borylated 9-benzyl-deazapurine **13** generated in situ from **2** and directly functionalized by copper catalyzed substitutions (Scheme 11). Halogenation[66] of the boronate **13** with cupric chloride formed 8-chlorodeazapurine **32j** (46%), whereas analogous bromination with cupric bromide gave 8-bromo-derivative **32k** (63%). This two-step halogenation at position 8 is complementary to electrophilic halogenation which proceeds at position 7.[112] The boronate **13** was also converted to 8-trifluoromethyl derivative **32l** by treatment with the Togni reagent, CuTC and phenanthroline[113] but the yield was only 34% due to competitive protodeborylation. Treatment of **13** with $Zn(CN)_2$ in presence of $Cu(NO_3)_2$ and CsF[67] gave the 8-cyano-derivative **32m** in 58%.




**Scheme 11.** Reagents and conditions: A: $CuCl_2$ (3 equiv.), acetone/$H_2O$ (1:1), 80°C, 3h; B: $CuBr_2$ (3 equiv.), acetone/$H_2O$ (1:1), 80°C, 3h; C: Togni reagent (1.1 equiv.), CuTc (10%), 1,10-phenantroline (20%), $LiOH.H_2O$ (2 equiv.), $CH_2Cl_2$, 45°C, 18 h; D: $Cu(NO_3)_2$ (2 equiv.), $Zn(CN)_2$ (3 equiv.), CsF (1 equiv.), acetone/$H_2O$ (2,5:1), 100°C, 2 h.

This one-pot two-step reaction sequence C-H borylation/Cu-catalyzed substitution was then applied on SEM-protected 6-chloro- and 6-methoxy-7-deazapurines **9** and **10**. The halogenations and trifluoromethylations proceeded, though with moderate conversions (probably due to partial protodeborylation), to give the desired 8-substituted products **25j-l** and **33j-l** in modest yields 32-56% (Scheme 12, Table 6). On the other hand, the cyanation did not proceed at all and only the recovery of strating materials was observed. Cleavage of SEM groups using trifluoroacetic acid (TFA) followed by aqueous ammonia furnished the corresponding free 8-substituted 7-deazapurine bases **27j-l** and **34j-l** (Scheme 12, Table 6).

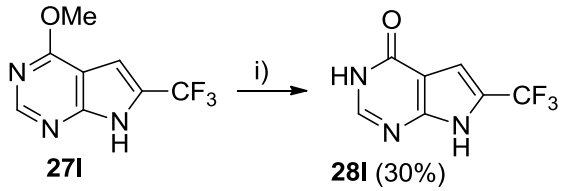



**Scheme 12.** Reagents and conditions: i) $B_2pin_2$ (1.2 equiv.), $[Ir(COD)OMe]_2$ (5%), dtbpy (10%), THF, 80°C, 20 h; ii) A: $CuCl_2$ (3 equiv.), acetone/$H_2O$ (1:1), 80°C, 3h; B: $CuBr_2$ (3 equiv.), acetone/$H_2O$ (1:1), 80°C, 3h; C: Togni reagent (1.1 equiv.), CuTc (10%), 1,10-phenantroline (20%), $LiOH.H_2O$ (2 equiv.), $CH_2Cl_2$, 45°C, 18 h; D: $Cu(NO_3)_2$ (2 equiv.), $Zn(CN)_2$ (3 equiv.), CsF (1 equiv.), acetone/$H_2O$ (2,5:1), 100°C, 2 h; iii) TFA (2 mL), rt, 1 h, followed by aq. ammonia (25% [w/w], rt, 18 h; iv) TMSCl (5 equiv.), NaI (5 equiv.), MeCN, 80°C, 18 h.

**Table 6.** One-pot C–H borylation/Cu-catalyzed substitution of SEM-protected deazapurines followed by deprotection

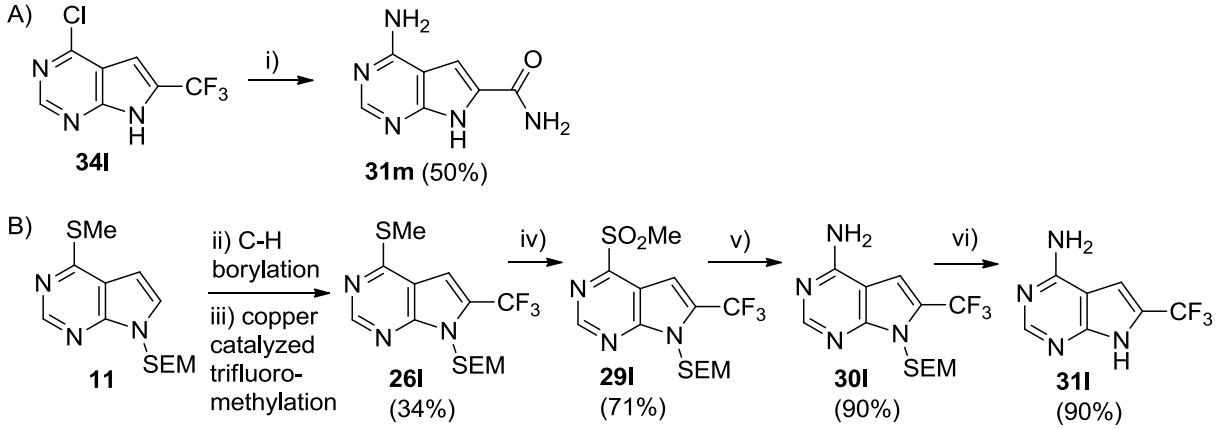
| Entry | Starting compound | Procedure | X | Y | Product **33** or **25** (yield) | Product **34** or **27** (yield) |
|---|---|---|---|---|---|---|
| 1 | **9** | A | Cl | -Cl | **33j** (55%) | **34j** (66%) |
| 2 | **9** | B | Cl | -Br | **33k** (56%) | **34k** (75%) |
| 3 | **9** | C | Cl | $-CF_3$ | **33l** (38%) | **34l** (73%) |
| 4 | **9** | D | Cl | -CN | no reaction | ---------- |
| 5 | **10** | A | OMe | -Cl | **25j** (47%) | **27j** (55%) |
| 6 | **10** | B | OMe | -Br | **25k** (34%) | **27k** (50%) |
| 7 | **10** | C | OMe | $-CF_3$ | **25l** (32%) | **27l** (75%) |
| 8 | **10** | D | OMe | -CN | no reaction | ---------- |

The last goal was the preparation of 8-trifluoromethyl-7-deazahypoxanthine **28l** and 8-trifluoromethyl-7-deazaadenine **31l**. The former was easily prepared by cleavage of methyl ether **27l** with in situ generated iodotrimethylsilane (from TMSCl and NaI) in acetonitrile. The desired 8-trifluoromethyl-7-deazahypoxantine **28l** was isolated in low 30% yield (Scheme 13).




**Scheme 13.** Reagents and conditions: i) TMSCl (5 equiv.), NaI (5 equiv.), MeCN, 80°C, 18 h.

More difficult was the preparation of the corresponding 8-trifluoromethyl-7-deazaadenine **31l** (Scheme 14). An obvious way was an amination of 6-chloro derivative **34l**. However, under mild conditions, the reaction did not proceed, whereas at 120°C, the formation of unexpected amide **31m** was observed due to hydrolysis/ammonolysis of $CF_3$ group. Therefore, I used a longer sequence starting by borylation/trifluoromethylation of **11**, followed by oxidation and amination of sulfone **29l** under mild conditions to give SEM-protected deazaadenine **30l** in good yield. The final deprotection gave 8-trifluoromethyl-7-deazaadenine **31l** in 90% yield.




**Scheme 14.** Reagents and conditions: i) aq. ammonia (25% [w/w]), dioxane, 120 °C, 18 h; ii) $B_2pin_2$ (1.2 equiv.), $[Ir(COD)OMe]_2$ (5%), dtbpy (10%), THF, 80°C, 20 h; iii) Togni reagent (1.1 equiv.), CuTc (10%), 1,10-phenantroline (20%), $LiOH.H_2O$ (2 equiv.), $CH_2Cl_2$, 45°C, 18 h; iv) *m*CPBA (2 equiv.), $CH_2Cl_2$, r.t., 1h; v) aq. ammonia (25% [w/w]), dioxane, 50 °C, 18 h; vi) TFA (2 mL), r.t., 1 h, followed by aq. ammonia (25% [w/w], r.t., 18 h.

### 3.1.5 Biological activity screening 6,8-disubstituted 7-deazapurines

*In vitro* cytotoxic/cytostatic activity all final nucleobases **27a-27l, 28a-28l, 31a-31h, 34j-34l** was initially evaluated against seven 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. Concentrations inhibiting the cell growth by 50% ($IC_{50}$) were determined using a quantitative metabolic staining with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) following a 3-day treatment. All cytostatic/cytotoxic activity screening were performed by our collaborators from the group of Dr. Hana Mertlikova-Kaiserova and from the group of prof. Hajdúch.

**Table 7.** Cytostatic activities of selected compounds

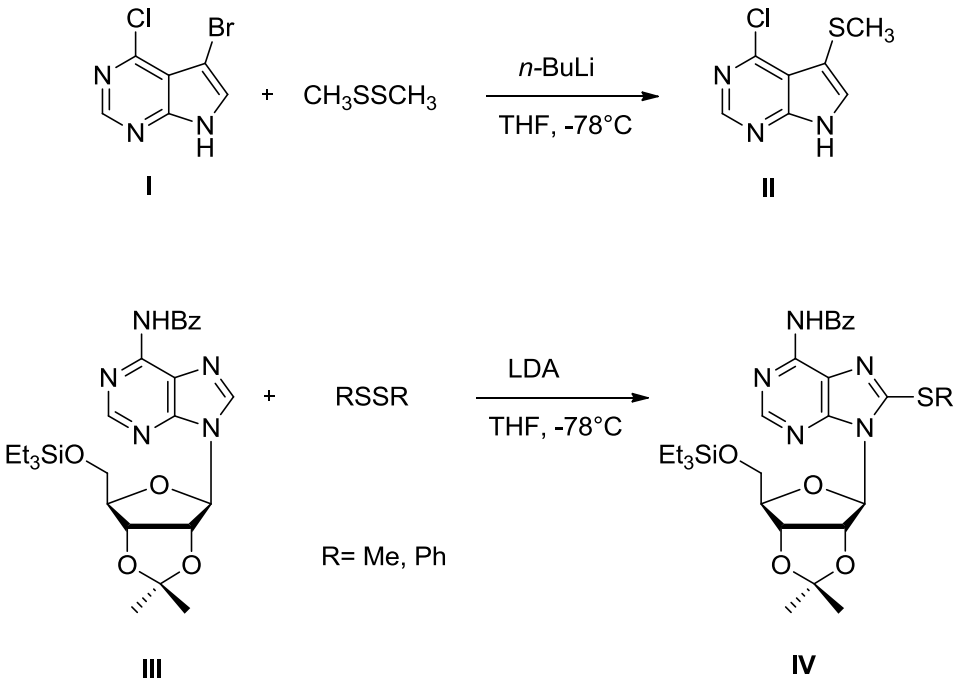
| | $IC_{50}$ (μM) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | A549 | CCRF-CEM | CEM-DNR | HCT116 | HCT116p53-- | K562 | K562-TAX | HepG2 | HL60 | HeLa S3 | BJ | MRC-5 |
| **27c** | 44.62 | >50 | 45.73 | 25.2 | 37.38 | 9.1 | 27.56 | >10 | >10 | >10 | >50 | 46.07 |
| **27d** | 42.13 | >50 | 49.28 | 32.66 | 48.5 | 8.07 | 37 | >10 | >10 | >10 | >50 | 45.02 |
| **27e** | 11.97 | 24.62 | 19.68 | 13.29 | 12.73 | 6.33 | 11.33 | >10 | >10 | >10 | 46.55 | 20.97 |
| **27f** | 36.84 | 44.1 | 29.71 | 18.66 | 35.53 | 25.48 | 19.39 | >10 | >10 | >10 | >50 | 36.05 |
| **27h** | 33.12 | 30 | 9.05 | 21.61 | 22.26 | 7.15 | 18.56 | >10 | >10 | >10 | >50 | >50 |
| **28e** | >50 | >50 | >50 | >50 | >50 | 21.64 | >50 | >10 | >10 | >10 | >50 | >50 |
| **31a** | >50 | >50 | 17.47 | >50 | >50 | 12.6 | 13.5 | >10 | >10 | >10 | >50 | 27.8 |
| **31b** | >50 | >50 | 32.93 | >50 | >50 | 25.47 | 8.86 | >10 | >10 | >10 | >50 | >50 |
| **31c** | >50 | 18.91 | 10.9 | 25.28 | 32.83 | 0.26 | 7.36 | >10 | >10 | >10 | >50 | 29.87 |
| **31d** | >50 | >50 | 25.16 | >50 | >50 | 28.92 | 17.11 | >10 | >10 | >10 | >50 | >50 |
| **31e** | >50 | 44.02 | 9.29 | >50 | >50 | 8.74 | 5.56 | >10 | >10 | >10 | >50 | >50 |
| **31f** | >50 | 27.04 | >50 | >50 | >50 | 36.97 | 17.92 | >10 | >10 | >10 | >50 | >50 |
| **31h** | >50 | >50 | 31.11 | >50 | >50 | 39.28 | 15.25 | >10 | >10 | >10 | >50 | >50 |
| **34l** | >50 | 18.81 | >50 | >50 | >50 | >50 | >50 | >10 | >10 | >10 | >50 | >50 |

Selected results are summarized in Table 7. Surprisingly, most of the 8-substituted-7-deazahypoxantines **28a-28l** were entirely inactive in these assays with the exception of 8-(3-thienyl)-7-deazahypoxantine **28e** showing moderate cytotoxic activities at > 20 μM concentrations. On the other hand, the 6-methoxy-7-deazapurine and 7-deazaadenine bases bearing diverse het(aryl) substituents at the position 8 showed significant cytostatic effects

at micromolar concentrations. The most active were 2-furyl-, 3-thienyl-, 3-aminophenyl-6-methoxy-7-deazapurines (**27d,e,h**) and 2-pyridyl-, 2-thienyl-, 3-thienyl-7-deazaadenine (**31b,c,e**) derivatives having $IC_{50}$ values in low micromolar range. In addition to that these compounds (**27h, 31b, 31e**) were non-toxic to BJ and MRC-5 fibroblasts showing promising therapeutic index.

## 3.2 C-H sulfenylation of purines and deazapurines

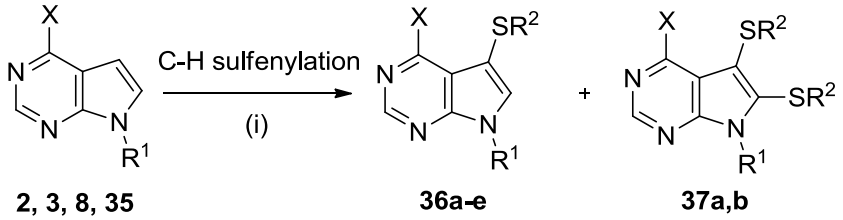
To the best of my knowledge, there was no reported example of a direct C-H sulfenylation of purines and deazapurine moiety. I have found only one reported example of 7-sulfanyl-7-deazapurine that was published by Ugarkar and co-workers.[74b] Lithium halogen exchange of 7-bromo-6-chloro-7-deazapurine (**I**) was performed under previously reported protocol. [114] Freshly formed lithium intermediate was added to dimethyl disulfide to give 7-methylsulfanyl-7-deazapurine base (**II**) in 52% yield. Also a preparation of 8-sulfanylated purine (**IV**) is based on preparation of lithium intermediate by LDA followed by addition of appropriate disulfide (Scheme 15). [115]




**Scheme 15.** Preparation of sulfanyl purine and deazapurine derivatives

### 3.2.1 Direct C-H sulfenylation of 7-deazapurines

The project started with the study of C–H sulfenylations of 7-deazapurines which are closely related to indoles. The model starting compound of choice was 6-phenyl-7-deazapurine (**3**). I have started by testing several literature catalytic systems and conditions for direct C–H sulfenylation.[92-96] The most efficient was the reaction of **3** with disulphides in the presence of copper(I) catalyst (by analogy to the literature[95] but replacing DMSO with DMF) giving the desired 7-substituted product **36a** in excellent yield (96%, Table 8, entry 1). On a larger scale, a 7,8-bis(phenylsulfanyl) derivative **37a** was also isolated as a minor by-product (3%, entry 1). The reaction work-up by EDTA was very important to break up stable complexes of the product with copper (without such a work-up, the isolated yield of **36a** was only moderate, ~50%). These optimised conditions were then used for the synthesis of three other examples, 7-alkyl- or -arylsulfanyl derivatives **36b-d**. While the reactions with methyl and methoxyphenyl disulfide gave products **36b, c** in good yields (entries 2, 3), the yield of nitrophenylsulfanyl derivative **36d** was moderate. Also the reaction of 7-deazaadenine (**35**) proceeded under the same conditions to give 7-(phenylsulfanyl)-7-deazaadenine (**36e**) in good yield (entry 5). Another interesting substrate was 6-chloro-7-deazapurine **8** that is suitable for further functional group transformations at position 6. In this case, the C–H sulfenylation proceeded well to give the desired product **44a** in high (90%) yield (entry 6) without any trace of nucleophilic substitution at position 6. The reaction with 9-benzylated 6-phenyl-7-deazapurine **2** gives the 7-substituted product **53a** in poor yield (20%, entry 7) due to low conversion. The structure of **53a** was confirmed by X-ray (Fig. 4). Apparently, the free NH at position 7 is crucial for the efficiency of this reaction. (Scheme 16).




**44a** (X = Cl, $R^1$ = H, $R^2$ = Ph)
**53a** (X = Ph, $R^1$ = Bn, $R^2$ = Ph)

**Scheme 16.** Reagents and conditions: i) $R^2S$-$SR^2$ (0.75 equiv.), CuI (10%), air, DMF, 110 °C, 18-60 h.

**Table 8.** Direct C-H Sulfenylation of 7-Deazapurines

| Entry | starting compound | $R^1$ | X | $R^2$ | Product (yield) |
|---|---|---|---|---|---|
| 1 | **3** | H | Ph- | Ph- | **36a** (96%) + **37a** (3%) |
| 2[a] | **3** | H | Ph- | Me- | **36b** (71%) + **37b** (15%) |
| 3 | **3** | H | Ph- | 4-MeO-Ph- | **36c** (91%) |
| 4 | **3** | H | Ph- | 4-$NO_2$-Ph- | **36d** (47%) |
| 5 | **35** | H | $NH_2$- | Ph- | **36e** (79%) |
| 6[a] | **8** | H | Cl- | Ph- | **44a** (90%) |
| 7[b] | **2** | Bn | Ph- | Ph- | **53a** (20%)[b] |

[a]5 equiv of $R^2S$-$SR^2$; [b]2.5 equiv of $R^2S$-$SR^2$ and recovery of starting compound (71%).

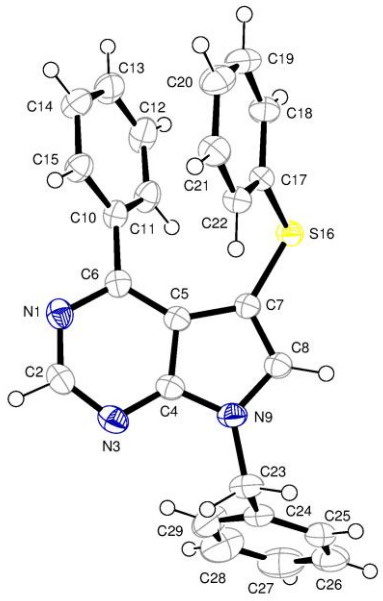
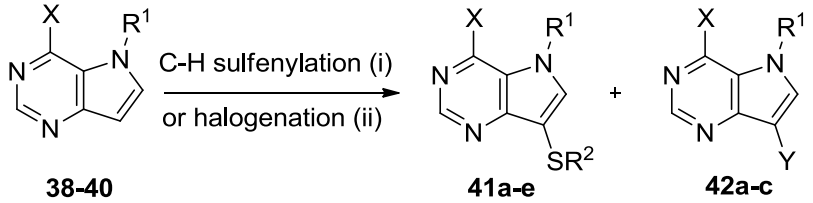



**Figure 4.** ORTEP drawings of crystal structure of compound **53a** (CCDC 926544)

## 3.2.2 Direct C-H sulfenylation of 9-deazapurines




**Scheme 17.** Reagents and conditions: i) $R^2S$-$SR^2$ (1.5 equiv.), CuI (10%), air, bpy or dtbpy (0.2 equiv.), DMF, 110 °C, 48-90 h; ii) CuI or $CuBr_2$ (1.1 equiv.), air, DMF, 110 °C, 18 h.

The same C–H sulfenylation protocol was then tested on 9-deazapurines (*5H*-pyrrolo[3,2 *d*]pyrimidines, Scheme 17). However, in this case a competitive iodination of the heterocycle by CuI occurred (Table 9, entry 1). The halogenation was suppressed by complexation of the copper catalyst by a 2,2′-dipyridine (bpy) ligand. The reaction of 6-phenyl-9-deazapurine (**38**) with diphenyl disulfide in the presence of CuI + bpy (entry 2) gave quantitatively the desired 9-phenylsulfanyl derivative **41a** (for confirmation of its structure by X-ray, see Fig. 5). The reaction with other disulfides allowed me to synthesize the target 9-alkyl- or -arylsulfanyl derivatives in moderate (**41b** and **41d**, 30% and 50%, respectively, entries 3, 5) or high yields (**41c**, 85%, entry 4). The reaction with 9-benzyl-6-phenyl-9-deazapurine (**39**) did not proceed at all (entry 6). The C–H sulfenylation of 6-chloro-9-deazapurine (**40**) under standard conditions gave a complex mixture of products (TLC, entry 7). Therefore, I tried the reaction in the presence of a more bulky and electron-rich ligand dtbpy to give the desired product **41e** in good 90% yield (entry 8). The dtbpy ligand was then also tested in the reactions of **38** with diverse disulfides. The phenylsulfenylation proceeded with quantitative conversion (as with bpy) but in the case of other disulfides, the yields of products were lower than with bpy (entries 10–12). Therefore, the dtbpy ligand was only practical for the reaction of 6-chloro derivative **40**. On the other hand, using a stoichiometric amount of CuI or $CuBr_2$ in the absence of bpy led to the formation of 9-halogenated products **42a-c** in high yields (entries 13-15). The same reaction with CuCl or $CuCl_2$ proceeded as well but only in poor yield.

**Table 9.** Direct C-H Sulfenylation of 9-Deazapurines

| Entry | Starting compound | Ligand | $R^1$ | X | $R^2$ (or Y) | Product (yield) |
|---|---|---|---|---|---|---|
| 1 | **38** | - | H | Ph | Ph | **41a** (14%) + **42a** (9%) |
| 2 | **38** | Bpy | H | Ph | Ph | **41a** (98%) |
| 3 | **38** | Bpy | H | Ph | Me | **41b** (30%)[a] |
| 4 | **38** | Bpy | H | Ph | 4-MeO-Ph | **41c** (85%) |
| 5 | **38** | Bpy | H | Ph | 4-$NO_2$-Ph | **41d** (50%) |
| 6 | **39** | Bpy | Bn | Ph | Ph | No reaction |
| 7 | **40** | Bpy | H | Cl | Ph | Complex mixture |
| 8[b] | **40** | dtbpy | H | Cl | Ph | **41e** (90%) |
| 9 | **38** | dtbpy | H | Ph | Ph | **41a** (98%) |
| 10 | **38** | dtbpy | H | Ph | Me | **41b** (25%) |
| 11 | **38** | dtbpy | H | Ph | 4-MeO-Ph | **41c** (41%) |
| 12 | **38** | dtbpy | H | Ph | 4-$NO_2$-Ph | No reaction |
| 13[c] | **38** | - | H | Ph | Y = I | **42a** (81%) |
| 14[c] | **38** | - | H | Ph | Y = Br | **42b** (75%) |
| 15[c] | **40** | - | H | Cl | Y = I | **42c** (65%) |

[a] Recovery of starting compound (40%). [b] 7 equiv. of $R^2S$-$SR^2$. [c] Conditions ii) applied.

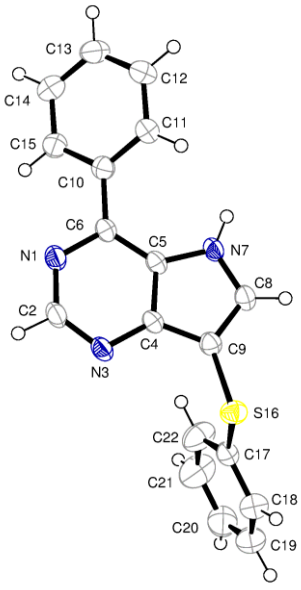
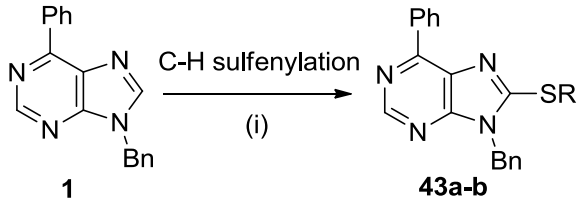



**Figure 5.** ORTEP drawings of crystal structure of compound **41a** (CCDC 926543)

### 3.2.3 Direct C-H sulfenylation of purines

Later on, my further efforts focused on the direct C–H sulfenylation of purines. Unfortunately, employing the same catalytic systems as above, no sulfenylation was observed. Using an alternative protocol based on a Lewis acid activation,[96b] the reaction proceeded to give 8-(phenylsulfanyl)purine **43a** in moderate ~40% yield. Finally, the sulfenylation in the presence of *t*BuOLi[96a] in dioxane at 130 °C for 120 h gave the desired product **43a** in acceptable 60% yield (Scheme 18, Table 10, entry 1). An analogous reaction with electron-rich bis-(methoxyphenyl)disulphide proceeded well to give **43b** in 56% (entry 2), whereas the reaction with electron-poor bis(nitrophenyl)disulfide did not work.




**1** **43a-b**

**Scheme 18.** Reagents and conditions: RS-SR (2.5 equiv), *t*BuOLi (3 equiv), 1,4-dioxane, 130 °C, 120 h.

**Table 10.** Direct C-H Sulfenylation of Purine **1**

| Entry | X | R | Product (yield) |
|---|---|---|---|
| 1 | Ph- | Ph- | **43a** (60 %) |
| 2 | Ph- | 4-MeO-Ph- | **43b** (56 %) |
| 3 | Ph- | 4-$NO_2$-Ph- | no reaction |

### 3.2.4 Application of C-H sulfenylation in synthesis of substituted 7-deazapurine bases and ribonucleosides

Recently, in our group has been discovered new types nucleoside cytostatics: 6-hetaryl-7-deazapurine,[37] 7-hetaryl-7-deazaadenine[24] and 6-substituted 7-hetaryl-7-deazapurine[38] ribonucleosides and they all showed cytostatic effect at nanomolar concentrations (Chapter 1.2.2). In all three series, the most active were derivatives bearing thiophene or furan (Chart 2). Recentely reported C-H sulfenylation of 7-deazapurines gave me access to 7-arylsulfanyl-7-deazapurine bases,[116] which can be considered extended thia-analogues of 7-aryl-7-deazapurines that are components of the above mentioned nucleoside cytostatics.[24,38] Therefore, I decided to prepare a series of 7-phenylsulfanyl- and 7-(2-thienyl)sulfanyl-7-deazapurine 7-deazapurine bases and ribonucleosides for screening of their anticancer activity.

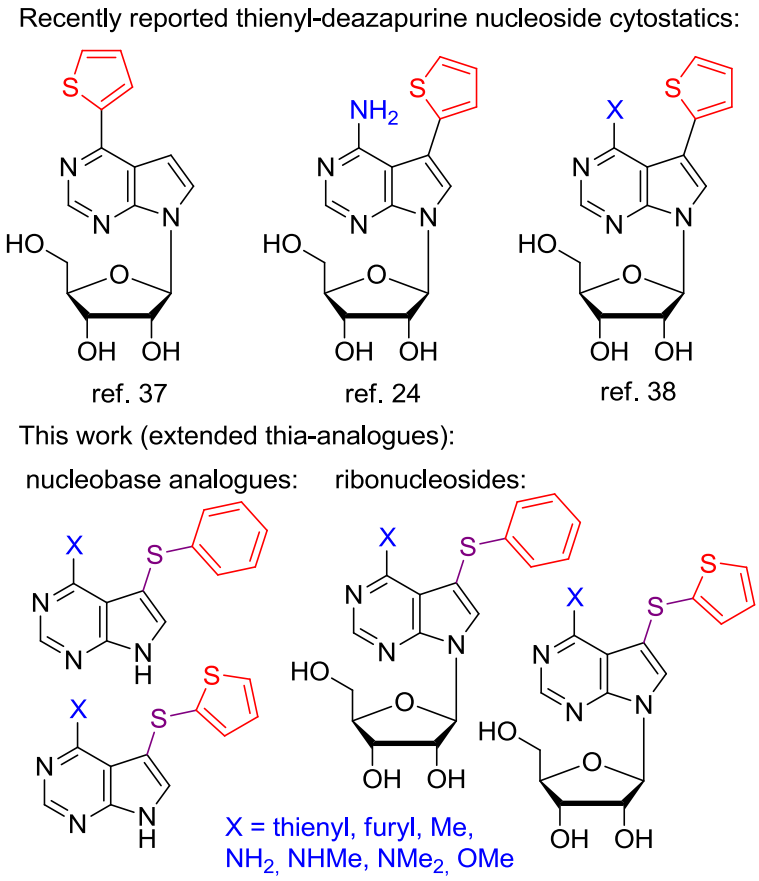
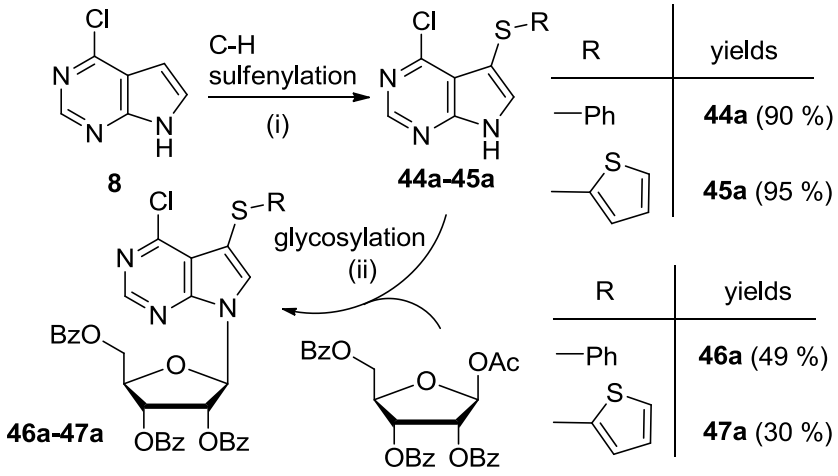



**Chart 2.** Previously reported nucleoside cytostatics and the design of their thia-analogues

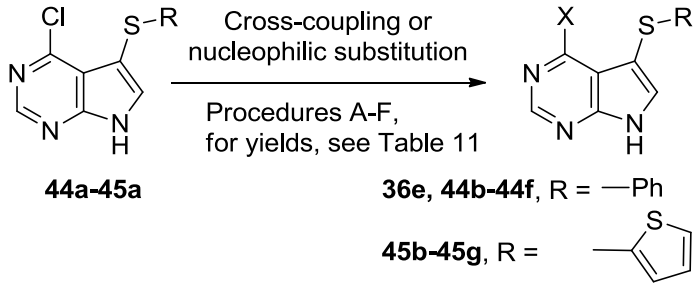
### 3.2.4.1 Synthesis of 7-arylsulfanyl-7-deazapurine bases

The synthetic approach to target 7-arylsulfanyl-7-deazapurines was based on recently developed direct C-H sulfenylation[116] of 6-chloro-7-deazapurine (**8**) catalysed by CuI and dtbpy under oxygen atmosphere. This modified procedure (oxygen atmosphere and dtbpy) gave better results than previously published methods developed for related heterocycles.[116] By the reaction with diphenyldisulfide and bis(2-thienyl)disulfide, two modified 7-(het)arylsulfanyl-7-deazapurines **44a** and **45a** were synthesized in excellent yield 90 % or 95% (Scheme 19). After one-pot silylation by N,O-bis(trimethylsilyl)acetamide (BSA) of **44a** followed by glycosylation using commercially available 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose, in analogy to the modified Vorbrüggen procedure,[117] the desired protected 7-phenylsulfanyl-7-deazapurine ribonucleoside intermediate **46a** was obtained in good yield of 49% (Scheme 19). In case of 7-thienylsulfanyl-7-deazapurine **45a**, the silylation was not completed under standard conditions and therefore 2 equiv. of BSA were used to fully dissolve the starting material, even though the yield of the following glycosylation to **47a** was only 30%, which was still sufficient to make multigram amounts of this key intermediate.




**Scheme 19**. Reagents and conditions: i) RS-SR (1 equiv.), CuI (10%), dtbpy (20%), $O_2$, DMF, 110°C, 18h. ii) 1. BSA (1 or 2 equiv.), MeCN, 15 min, rt, 2. TMSOTf (2 equiv.), sugar (1 equiv.), 80 °C, 6 h.

In order to synthesize a series of target 6-substituted 7-deazapurine nucleobase analogues, 6-chlorodeazapurine intermediates **44a** and **45a** were modified at the position 6. The first goal was to introduce thiophene and furan substituents (previously reported[37] in cytostatic nucleosides). Since attempted Suzuki-Miyaura cross-coupling reactions with the corresponding thienyl- or furylboronic acids gave very low conversions (<10%), I further focused on the Stille coupling. Thus the Stille reactions of **44a** or **45a** with thienyl- or furyl(tributyl)stannanes under standard conditions in presence of $PdCl_2(PPh_3)_2$ in DMF proceeded smoothly to give desired 6-hetaryl derivatives **44b-44c** and **45b-45c** in good yields (57–87%) (Scheme 20, Table 11, entries 1,2,7,8). Methyl group was introduced through Pd-catalysed cross-coupling of **44a** or **45a** with $Me_3Al$ to give **44d**, **45d** in good yields (entries 3,9). Finally, dimetylamino, methylamino and amino groups were introduced through aromatic nucleophilic substitution of 6-chloro-derivatives **44a** or **45a** with amines or ammonia to give **36e**, **44e-44f** and **45e-45g** in good yields (58-85%, entries 4-6,10-12).

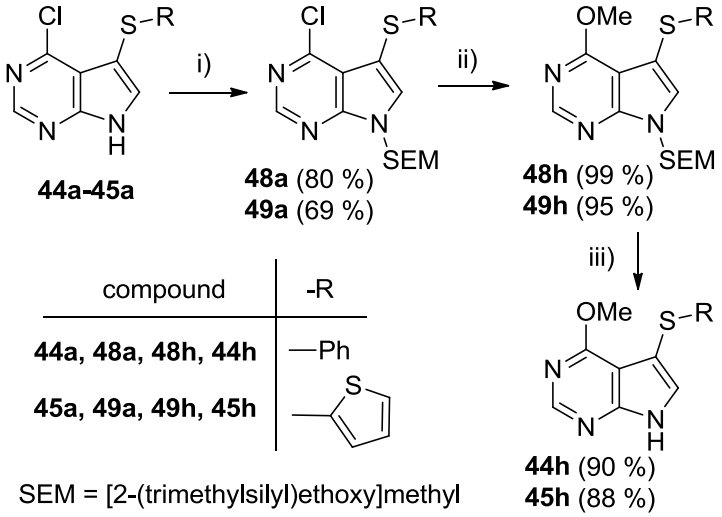



**Scheme 20.** Reagents and conditions, A: 2-thienyl$SnBu_3$ (1.2 equiv.), $PdCl_2(PPh_3)_2$ (5%), DMF, 100°C, 18 h; B: 2-furyl$SnBu_3$ (1.2 equiv.), $PdCl_2(PPh_3)_2$ (5%), DMF, 100°C, 18 h; C: $Me_3Al$ (3 equiv.), $Pd(PPh_3)_4$ (5%), THF, 70°C, 12 h; D: $Me_2NH$ in THF (3 equiv.), propan-2-ol, 70°C, 24 h; E: aq. methylamine (40% [w/w]), dioxane, 120 °C, 18 h; F: aq. ammonia (25% [w/w]), dioxane, 120 °C, 18 h.

**Table 11.** Yields of the transformations of 7-deazapurine bases

| Entry | Proced. | Reagent | X- | R- | Product (yield %) |
|---|---|---|---|---|---|
| 1 | A | 2-thienylSnBu$_3$ | 2-thienyl- | Ph- | **44b** (80%) |
| 2 | B | 2-furylSnBu$_3$ | 2-furyl- | Ph- | **44c** (87%) |
| 3 | C | Me$_3$Al | Me- | Ph- | **44d** (73%) |
| 4 | D | Me$_2$NH | Me$_2$N- | Ph- | **44e** (84%) |
| 5 | E | MeNH$_2$ | MeNH- | Ph- | **44f** (83%) |
| 6 | F | NH$_3$ | NH$_2$- | Ph- | **36e** (85%) |
| 7 | A | 2-thienylSnBu$_3$ | 2-thienyl- | 2-thienyl- | **45b** (57%) |
| 8 | B | 2-furylSnBu$_3$ | 2-furyl- | 2-thienyl- | **45c** (72%) |
| 9 | C | Me$_3$Al | Me- | 2-thienyl- | **45d** (66%) |
| 10 | D | Me$_2$NH | Me$_2$N- | 2-thienyl- | **45e** (63%) |
| 11 | E | MeNH$_2$ | MeNH- | 2-thienyl- | **45f** (58%) |
| 12 | F | NH$_3$ | NH$_2$- | 2-thienyl- | **45g** (85%) |

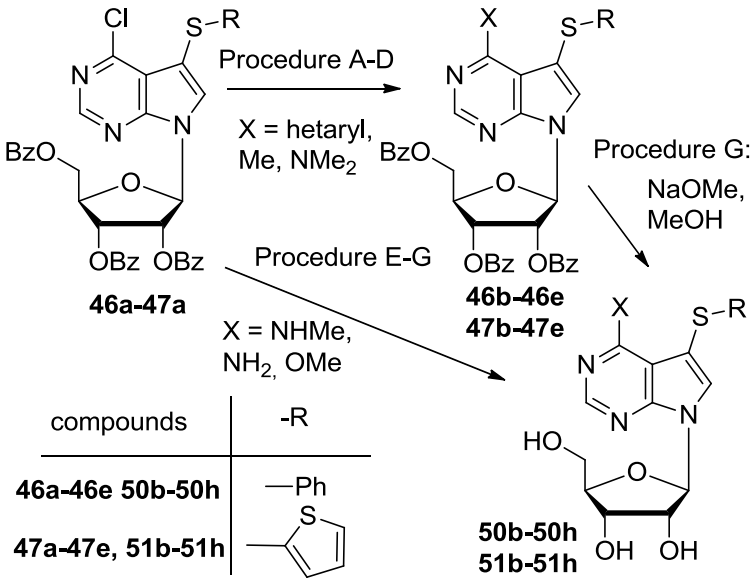
On the other hand, direct methoxylation of **44a-45a** by reaction with NaOMe in MeOH was not successful. Therefore, I firstly protected the NH at position 9 by SEM group and then the methoxylation of **48a** or **49a** by MeONa proceeded quantitatively to give intermediates **48h** and **49h**. Final cleavage of the SEM groups by TFA afforded the desired 6-methoxy-7-deazapurines **44h** and **45h** in high yields (Scheme 21).




**Scheme 21.** Reagents and conditions: i) NaH (60 wt%, 1.1 equiv.), SEM-Cl (1.1 equiv.), DMF, 0°C to rt, 30 min.; ii) 1 M MeONa in MeOH (2 equiv.), acetone, rt., 18 h; iii) 1.$CF_3COOH$, rt, 18h, 2. aq. ammonia (25% [w/w]), rt, 18 h.

### 3.2.4.2 Synthesis of 7-arylsulfanyl-7-deazapurine ribonucleosides

The target nucleoside analogues were prepared by analogous modifications of 6-chloro-7-(het)aryl-7-deazapurine nucleoside intermediates **46a** and **47a** (Scheme 22, Table 12). The Stille coupling reactions with thienyl- or furylstannanes gave the corresponding benzoylated 6-hetaryl-7-deazapurine nucleosides **46b,c** and **47b,c**, whereas the couplings with trimethylaluminum afforded 6-methyl derivatives **46d** and **47d**. The reactions with trimethylamine furnished 6-(dimethylamino)-7-deazapurine nucleosides **46e** and **47e**. Final Zemplén deprotection using sodium methoxide in methanol furnished free 6,7-disubstituted nucleosides **50b-50e** and **51b-51e** in 59–87 % yields (Scheme 22, Table 12). Nucleophilic substitutions of protected nucleoside intermediates **46a** or **47a** with methylamine, ammonia or NaOMe proceeded with concomitant de-benzoylation to give directly unprotected 6-methylamino-, 6-amino or 6-methoxy-7-(het)arylsulfanyl-7-deazapurine ribonucleosides **50f-50h** and **51f-51h** in good yields.




**Scheme 22.** Reagents and conditions, A: 2-thienylSnBu$_3$ (1.2 equiv.), PdCl$_2$(PPh$_3$)$_2$ (5%), DMF, 100°C, 18 h; B: 2-furylSnBu$_3$ (1.2 equiv.), PdCl$_2$(PPh$_3$)$_2$ (5%), DMF, 100°C, 18 h; C: Me$_3$Al (3 equiv.), Pd(PPh$_3$)$_4$ (5%), THF, 70°C, 12h; D: Me$_2$NH in THF (3 equiv.), propan-2-ol, 70°C, 24 h; E: aq. methylamine (40% [w/w]), dioxane, 120 °C, 18 h; F: aq. ammonia (25% [w/w]), dioxane, 120 °C, 18 h; G: 1 M MeONa in MeOH (1.5 equiv.), MeOH, rt., 18 h.

**Table 12.** Yields of the transformations of 7-deazapurine nucleosides

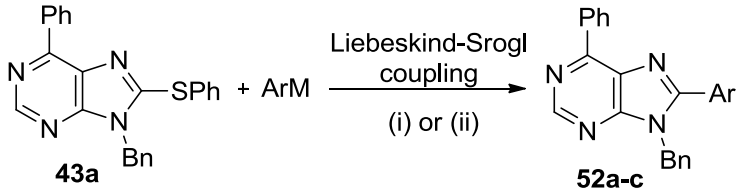
| Proced | Reagent | X- | R- | Product (yield %) | Deprotect product (yield %) |
|---|---|---|---|---|---|
| A | thienylSnBu$_3$ | 2-thienyl- | Ph- | **46b** (72%) | **50b** (75%) |
| B | furylSnBu$_3$ | 2-furyl- | Ph- | **46c** (92%) | **50c** (78%) |
| C | Me$_3$Al | Me- | Ph- | **46d** (55%) | **50d** (87%) |
| D | Me$_2$NH | Me$_2$N- | Ph- | **46e** (88%) | **50e** (87%) |
| E | MeNH$_2$ | MeNH- | Ph- | - | **50f** (90%) |
| F | NH$_3$ | NH$_2$- | Ph- | - | **50g** (86%) |
| G | NaOMe | MeO- | Ph- | - | **50h** (75%) |
| A | thienylSnBu$_3$ | 2-thienyl- | 2-thienyl- | **47b** (78%) | **51b** (59%) |
| B | furylSnBu$_3$ | 2-furyl- | 2-thienyl- | **47c** (41%) | **51c** (57%) |
| C | Me$_3$Al | Me- | 2-thienyl- | **47d** (67%) | **51d** (64%) |
| D | Me$_2$NH | Me$_2$N- | 2-thienyl- | **47e** (88%) | **51e** (65%) |
| E | MeNH$_2$ | MeNH- | 2-thienyl- | - | **51f** (75%) |
| F | NH$_3$ | NH$_2$- | 2-thienyl- | - | **51g** (70%) |
| G | NaOMe | MeO- | 2-thienyl- | - | **51h** (77%) |

## 3.2.5 Reactivity of sulfanyl deazapurine and purine bases

Having access to the arylsulfanyl derivatives of purines and deazapurines, I further explored their synthetic applications.

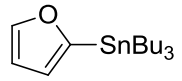
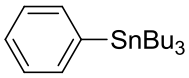
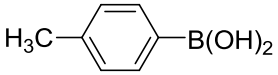
### 3.2.5.1 Liebeskind–Srogl cross-coupling of sulfanyl deazapurine and purine bases

The most obvious option was the Liebeskind–Srogl cross-coupling reaction.[47] The reactions of the 8-(phenylsulfanyl)purine **43a** with *p*-tolylboronic acid and diverse stannanes were performed under standard conditions proceeded generally well to give the desired 8-aryl products **52a-52c** in high yields (57-83%, Scheme 23, Table 13).




**Scheme 23.** Reagents and conditions: i) ArSnBu$_3$(1.2 equiv), Pd(PPh$_3$)$_4$ (5 mol %), CuMeSal (2.2 equiv), 50 °C, THF, 17 h; ii) ArB(OH)$_2$, Pd$_2$(dba)$_3$ (4 mol %), (2-furyl)$_3$P (16 mol %), CuTc (1.3 equiv), 50 °C, THF, 18 h.

**Table 13**. The Liebeskind-Srogl reactions of 8-(phenylsulfanyl)purine **43a**

| entry | Ar-M | Product (yield) |
|---|---|---|
| 1 |  | **52a** (70%) |
| 2 |  | **52b** (83%) |
| 3 |  | **52c** (54%)[a] |

[a]recovery of starting compound (15%)

Surprisingly, analogous Liebeskind–Srogl reactions of 7-phenylsulfanyl-7-deazapurines **36a, 53a** or 9-phenylsulfanyl-9-deazapurine **41a** did not proceed at all. Neither stannanes nor boronic acids gave any reaction under a number of different catalytic systems (Cu, Pd, In) and conditions tried (including MW irradiation). This lack of reactivity of arylsulfanyl-deazapurines is probably due to the electron-rich nature of the deazapurine moiety which prevents efficient oxidative addition (Chart 3).

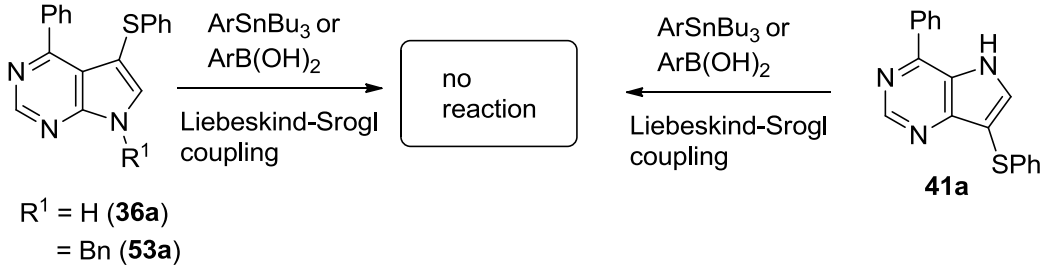


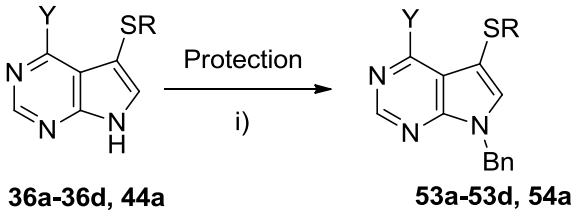

**Chart 3.** Unsuccessful Liebeskind–Srogl coupling of sulfanyldeazapurines

Using electron withdrawing protecting group (tosyl) gave also no reaction. Since no literature example of the Liebeskind–Srogl reaction of the related 3-(arylsulfanyl)indole was reported, I have tried this reaction under the standard conditions and have confirmed that it does not proceed either. Apparently, this reaction is not applicable for electron-rich indole-type heterocycles.

### 3.2.5.2 Kumada cross-coupling of 7- sulfanyl deazapurine bases

As the Liebeskind–Srogl reactions of 7-phenylsulfanyl-7-deazapurines did not proceed at all the other possibility was Kumada cross coupling of sulfanyl deazapurines with Grignard

reagents, but not used often.[118] I performed the reaction under previously optimized conditions for Kumada coupling of 6-(methylthio)purine with PhMgCl. [119] With unprotected deazapurine **36b**, the reaction proceed non-selectively to various mixtures of products, therefore I decided to protect acidic NH group with the benzyl group (Scheme 24, Table 14).



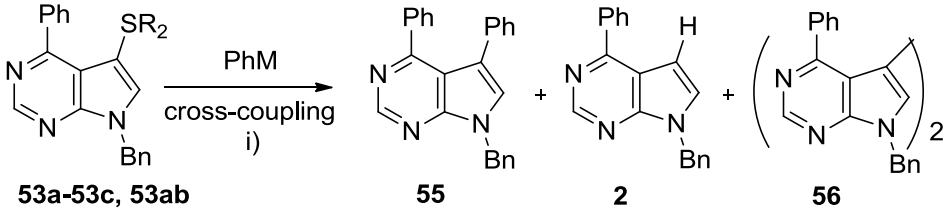

**36a-36d, 44a** **53a-53d, 54a**

**Scheme 24.** Reagents and conditions: i) $K_2CO_3$ (1.05 equiv.), Bn-Cl (1.1 equiv.), DMF, rt.,18h

**Table 14.** Benzylation of 7-sulfenyl-7-deazapurines

| Entry | Starting compound | Y | R | Product (yield) |
|---|---|---|---|---|
| 1 | **36a** | Ph | Ph | **53a** (90%) |
| 2 | **36b** | Ph | Me | **53b** (85%) |
| 3 | **36c** | Ph | 4-MeO-Ph | **53c** (90%) |
| 4 | **36d** | Ph | 4-$NO_2$-Ph | **53d** (80%) |
| 5 | **44a** | Cl | Ph | **54a** (90%) |

With the benzyl protecting group the model starting compound of choice was 6-phenyl-7-phenylsulfanyl-7-deazapurine (**53a**). The product of Kumada coupling 6,7-diphenyl-7-deazapurine **55** was isolated just in 40% due to the formation by-products of competitive desulfenylation **2** (32%) and dimerization **56** (5%) (Scheme 25, Table 15, entry 1). All compounds were fully characterized and the structure of compound **56** was unequivocally proved by X-ray diffraction analysis (Fig. 6).




**53a-53c, 53ab** **55** **2** **56**

**Scheme 25.** Reagents and conditions: i) PhM (2.5 equiv.), catalyst (5 mol%), 70°C, THF, 15 min.

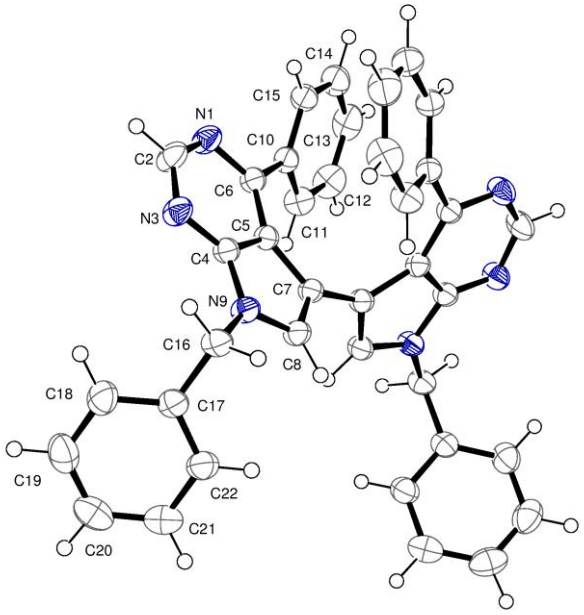
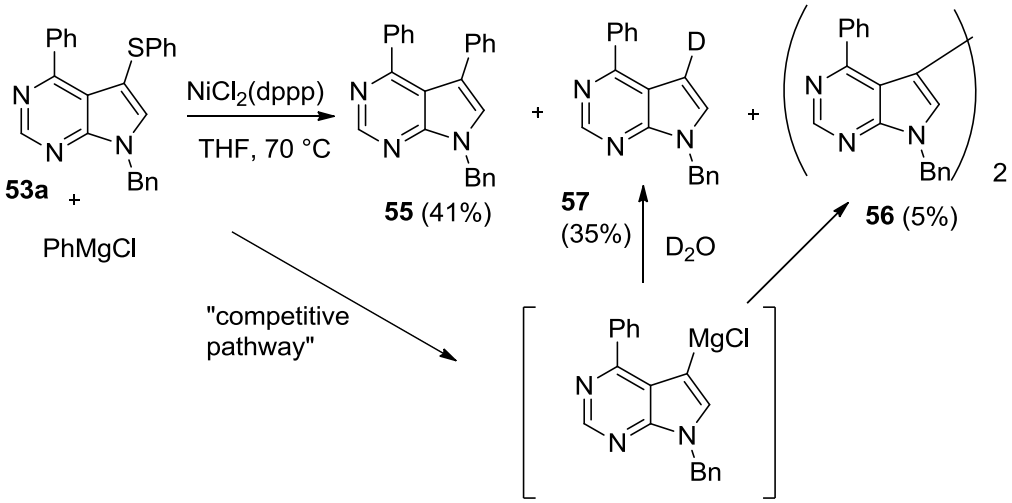



**Figure 6.** ORTEP drawings of crystal structures of compounds **56**

The most obvious option to form byproducts **2** and **56** was the formation of new Grignard reagent *in suitu* by transmetalation of 7-sulfanyl-7-deazapurine with phenyl magnesium chloride catalyzed by $NiCl_2$(dppp). This idea was confirmed in an experiment where $D_2O$ was used during the workup of a reaction mixture and an appropriate 9-benzyl-7-deutherium-6-phenyl-7-deazapurine **57** (Scheme 26) was formed in a similar yield as was compound **2** (Table 15, entry 1, where $H_2O$ was used).




**Scheme 26.** Proposed formation of **56** and **57.** Reagents and conditions: i) PhMgCl (2.5 equiv.), $NiCl_2$(dppp) (5 mol%), 70°C, THF, 15 min; $D_2O$ was used during work-up.

**Table 15.** Optimization of coupling sulfanyldeazapurines with phenyl Grignard reagents[i)]

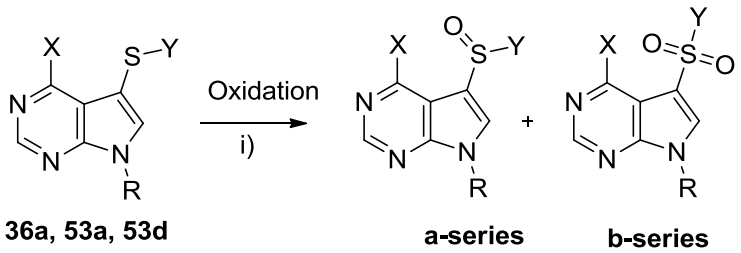
| Entry | starting compound | M | cat. | Unreacted starting compound | **55** | **2** | **56** |
|---|---|---|---|---|---|---|---|
| 1 | **53a** | MgCl | $NiCl_2$(dppp) | 6 | 48 [40] | 38 [32] | 8 [5] |
| 2[a] | **53a** | MgCl | $NiCl_2$(dppp) | 67 | 3 | 26 | 4 |
| 3[b] | **53a** | MgCl | $NiCl_2$(dppp) | 0 | 46 [41] | 38 [30] | 8 [4] |
| 4[c] | **53a** | MgCl | $NiCl_2$(dppp) | 0 | 45 [39] | 35 [29] | 7 [4] |
| 5 | **53ab** | MgCl | $NiCl_2$(dppp) | 0 | 48 | 40 | 12 |
| 6 | **53b** | MgCl | $NiCl_2$(dppp) | 28 | 19 | 25 | 18 |
| 7 | **53c** | MgCl | $NiCl_2$(dppp) | 9 | 29 [18] | 55 [37] | 7 |
| 8[d] | **53a** | MgCl | $NiCl_2$(dppp) | 7 | 46 | 36 | 11 |
| 9[e] | **53a** | MgCl | $NiCl_2$(dppp) | 0 | 63 [47] | 17 [11] | 20 [15] |
| 10 | **53a** | MgCl.LiCl | $NiCl_2$(dppp) | 100 | | No reaction | |
| 11 | **53a** | ZnCl | $NiCl_2$(dppp) | 100 | | No reaction | |
| 12 | **53a** | MgCl | Pd(dppf)$Cl_2$ | 100 | | No reaction | |
| 13 | **53a** | MgCl | Nickelocene | 0 | 63 [50] | 19 [11] | 18 [13] |
| 14 | **53a** | MgCl | $CoCl_2$ | 53 | 7 | 34 | 6 |
| 15 | **53a** | MgCl | Fe(acac)$_3$ | 100 | | No reaction | |
| 16 | **53a** | MgCl | $MgCl_2$ | 100 | | No reaction | |
| 17 | **53a** | MgCl | none | 100 | | No reaction | |
| 18 | **53a** | MgCl | $NiCl_2$(dppe) | 23 | 33 | 24 | 20 |
| 19 | **53a** | MgCl | Ni(COD)$_2$ | 6 | 30 | 51 | 13 |

[i)]NMR conversion (%) [Isolated yields (%)]

[a]room temperature, 15min; [b]room temperature, 19 h; [c] slow addition of PhMgCl (1drop/30 s)
[d]MW, 5 min, 100°C; [e]$NiCl_2$(dppp) (10mol%) + LiCl (3equiv.)

The reaction was performed later at room temperature and after 15 minutes was found mainly the product of desulfenylation **2** (26%, Entry 2) and product of coupling **53** just in 4% (Entry 2). After 18 hours at room temperature the reaction produced similar results as that at 70°C during 15 min (compare Entry 1 and Entry 3). Transmetallation is probably a much faster process than coupling, so I tried several ways to suppress the formation of a new Grignard reagent in this competitive pathway. Unfortunately, no significant improvement was found in such conditions using: slow addition of Grignard reagent (Entry 4), modification of sulfanyl group (Entry 5-7), MW heating (Entry 7), additive (Entry 8), Turbo Grignard or zinc reagent (Entry 10-11) or different catalytic systems (Entry 12-19). The best result was just a moderate 50% yield of 6,7-diphenyl-7-deazapurine **55** with nickelocene (Entry 13, Table 15). The reactivity of other aryl Grignard reagents procced in a similar way and the reaction isn't too synthetically useful.

### 3.2.5.3 Oxidation of sulfanyl deazapurine bases




**Scheme 27.** Reagents and conditions: i) *m*CPBA (10 equiv.), NaOH (10 equiv.), 1,4-dioxane/$H_2O$ (9:1), 0°C up to rt, 18 h.

As the reactivity sulfanyl derivatives were not sufficient, the next step was the oxidation to achieve more reactive sulfoxides or sulfones to study their reactivity (Kumada coupling etc.). The oxidation of sulfanyl derivatives was performed with *meta*-Chloroperoxybenzoic acid. Under these conditions the oxidation of N-benzylated 7-sulfanyl-7-deazapurines proceeded mostly to sulfones **53ab** and **53db** (Entries 2 and 3) whereas NH unprotected 7-sulfanyl-7-deazapurine produces dominantly sulfoxide **36aa** (Scheme 27, Table 16, Entry 1).

**Table 16.** Oxidation of 7-sulfenyl-7-deazapurines

| entry | starting compound | X | Y | R | Yield (%) sulfoxide | Yield (%) sulfone |
|---|---|---|---|---|---|---|
| 1 | **36a** | Ph | Ph | **H** | **36aa** (78%) | **36ab** (15%) |
| 2 | **53a** | Ph | Ph | **Bn** | **53aa** (13%) | **53ab** (73%) |
| 3 | **53d** | Ph | 4-$NO_2$Ph | **Bn** | **53da** (20%) | **53db** (68%) |

### 3.2.5.4 Nucleophilic addition to sulfonyl deazapurine base

In 1982 Ueda and co-workers[120] presented the reaction of 7-methylsulfonyl-7-deazaadenine ribonucleoside (**V**) with sodium cyanide in dimethylformamide to give a product in high yield containing a cyano group. The physical properties, however, were different from those of toyocamycin (7-cyano-7-deazaadenine ribonucleoside, see Chapter 1.2.1, Figure 8). They proposed the mechanism as the substitution that go through the addition of a cyanide ion to the position 8 and subsequent elimination of methylsulfonyl group to furnish 8-cyano-7-deazaadenine ribonucleoside (**VI**) (Chart 4).

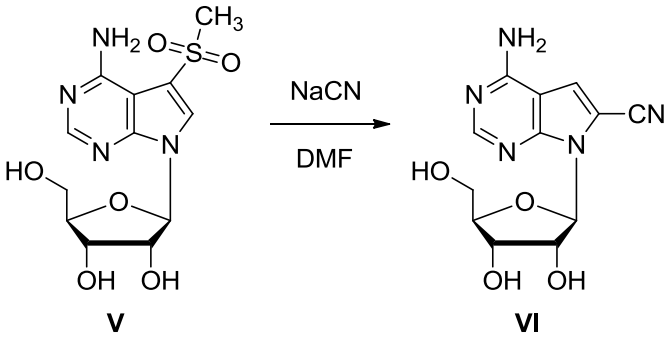
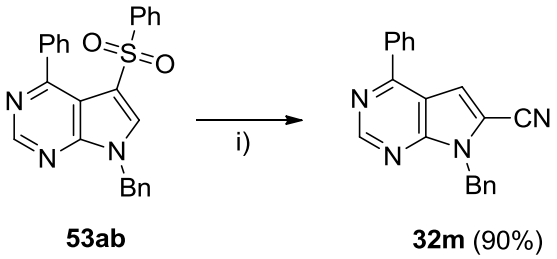



**Chart 4.** Formation of 8-cyano-7-deazaadenine

Firstly, I performed a confirmative experiment of above described reaction. Without doubt, 7-methylsulfonyl-7-deazapurine (**53ab**) with NaCN in DMF gave the product **32m** in high yield (Scheme 28) and the cyano group at position 8 was unequivocally proved by X-ray diffraction analysis (Fig. 7).




**Scheme 28.** Reagents and conditions: i) NaCN (3 equiv.), DMF, 130°C, 3 hours

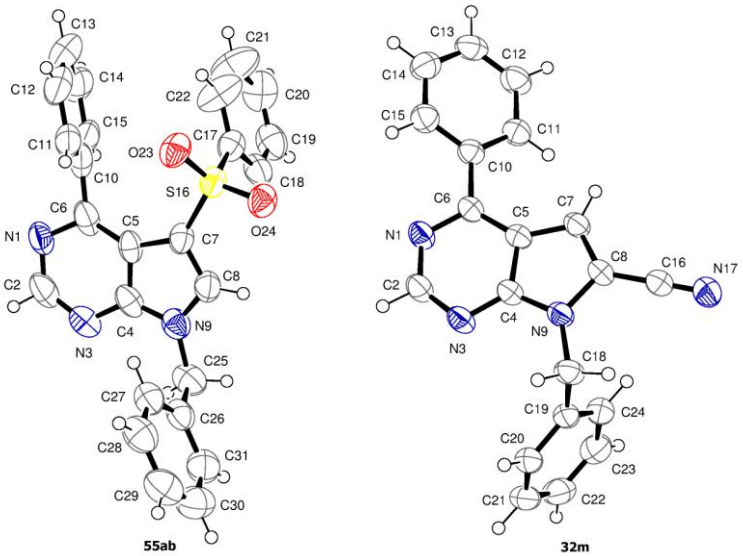



**Figure 7.** ORTEP drawings of crystal structures of compounds **53ab** and **32m**

Later on, I have tried different types of nucleophiles, but unfortunately in no case the above described reaction proceeded. Only a recovery of starting material or mixture of numerous products was found (Entries 2-10). Surprisingly, this was also the case with the recovery of starting material of other nucleophiles contains cyano group - $Zn(CN)_2$ and CuCN (Entry 11-12, Table 17).

**Table 17.** Reactivity of **53ab** with other nucleophiles

| entry | Nucleophile | Product (Yield) |
|---|---|---|
| 1 | NaCN | **32m** (90%) |
| 2 | $CH_3ONa$ | mixture of compounds |
| 3 | PhONa | No reaction |
| 4 | PhSNa | No reaction |
| 5 | $Me_2NH$ | No reaction |
| 6 | $NaN_3$ | No reaction |
| 7 | Lithium hexamethyldisilazide | mixture of compounds |
| 8 | NaOCN | No reaction |
| 9 | NaOH | No reaction |
| 10 | $CF_3SO_2Na$ | No reaction |
| 11 | $Zn(CN)_2$ | No reaction |
| 12 | CuCN | No reaction |

Aryl(alkyl)sulfanyl deazapurine derivatives were prepared by direct C-H sulfenylation in high yield, nevertheless their synthetic usability is very limited.

### 3.2.6 Biological activity screening

*In vitro* cytotoxic/cytostatic activity all final nucleobases **44b-44h** and **45b-45h**, as well as nucleosides **50b-50h** and **51b-51h**, was initially evaluated against seven 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. Concentrations inhibiting the cell growth by 50% ($IC_{50}$) were determined using a quantitative metabolic staining with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) following a 3-day treatment. In addition, the anti-proliferative effect was tested against a human hepatocarcinoma Hep G2, human T-lymphoblastic promyelocytic leukemia HL-60 and cervical carcinoma HeLa S3 growing in liquid suspension. Cell viability was determined following a 3-day incubation using 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2*H*-tetrazolium-5-carboxanilide (XTT) assay.

All cytostatic/cytotoxic activity screening and antiviral screening were performed by our collaborators from Gilead Sciences, from the group of Dr. Hana Mertlikova-Kaiserova and from the group of prof. Hajdúch.

**Table 18.** Cytostatic activities of selected compounds

| | $IC_{50}$ (μM) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | A549 | CCRF-CEM | CEM-DNR | HCT116 | HCT116p53-- | K562 | K562-TAX | HepG2 | HL60 | HeLa S3 | BJ | MRC-5 |
| **45b** | 16.19 | 10.55 | 17.67 | 13.03 | 5.06 | 5.14 | 21.664 | >25 | 21.1 | >25 | 23.38 | 54.48 |
| **45c** | 11.43 | 7.73 | 20.83 | 6.75 | 19.53 | 4.26 | 18.90 | >25 | 7.63 | 8.49 | 22.06 | 32.87 |
| **45d** | > 50 | > 50 | > 50 | 38.12 | 29.10 | 13.99 | > 50 | >25 | >25 | >25 | > 150 | 135.50 |
| **45e** | 19.80 | 14.63 | 35.25 | 11.01 | 27.54 | 3.83 | 22.14 | >25 | >25 | >25 | 144.56 | > 150 |
| **45f** | 28.58 | 14.72 | 26.15 | 18.98 | 45.30 | 4.95 | 21.00 | >25 | 13.5 | 17.6 | 132.24 | 148.21 |
| **45g** | 22.82 | 16.68 | 20.34 | 22.79 | > 50 | 17.88 | 17.92 | >25 | 13.9 | 17.9 | > 150 | 135.71 |
| **45h** | 21.47 | 18.23 | > 50 | 17.15 | > 50 | > 50 | 43.95 | >25 | >25 | 23.9 | 122.60 | 148.13 |
| **50g** | 22.91 | 33.96 | > 50 | 20.80 | 22.41 | 23.09 | 29.62 | >25 | >25 | >25 | 67.88 | 67.70 |
| **51g** | 43.76 | 64.66 | > 100 | 36.72 | 23.18 | 23.43 | 55.77 | >25 | >25 | >25 | 93.59 | 138.24 |

Selected results are summarized in Table 18. Surprisingly, most of the nucleosides **50** and **51** were entirely inactive in these assays with the exception of 6-amino-7-deazapurine nucleosides **50g** and **51g** showing moderate cytotoxic activities at > 20 μM concentrations.

Also none of the 7-(phenylsulfanyl)-7-deazapurine bases **44b**-**44h** exerted any significant cytostatic activity. On the other hand, all the 7-(2-thienylsulfanyl)-7-deazapurine bases bearing diverse substituents at the position 6 showed significant cytostatic effects at micromolar concentrations. The most active were 6-hetaryl- (**45b,c**) and 6-methylamino and –dimethylamino (**45e,f**) derivatives having $IC_{50}$ values in low micromolar range. Compounds **45e,f** were non-toxic to BJ and MRC-5 fibroblasts showing promising therapeutic index.

Since the nucleosides **50** and **51** were inactive with the exception of moderately active adenosine analogues **50g** and **51g** (thia-analogues of cytostatic 7-aryl-7-deazaadenosines[24]), it can be concluded that replacement of the (het)aryl group at position 7 by extended (het)arylsulfanyl group is not tolerated by the biological target(s) of the previously developed nucleoside cytostatics.[24,37,38] Further studies will be necessary to explain the significant cytostatic effect of the 7-(thienylsulfanyl)-7-deazapurine bases which is apparently caused by a different mechanism (presumably by kinase inhibition).

In addition, all compounds were also tested on antiviral activity (HCV 1B and 2A replicon and RSV) by and antimicrobial activity (panel of gram-positive and gram-negative bacteria) and antifungal activity (several strains of *Candida* species) but did not show any significant activity in these assays.

# 4 Conclusion

The Ir-catalyzed C-H borylation of 7-deazapurines proceeded selectively in position 8. The follow-up Suzuki cross-coupling reactions can be efficiently used for introduction of aryl groups to position 8. This is the first efficent methodology for 8-arylation of important 7-deazapurines (so far the 8-substituted 7-deazapurines were prepared only by multistep heterocyclizations).[41-43] In contrast, the borylation of 9-deazapurines did not proceed regioselectively and two borylated products were formed. The C-H borylation of purines failed completely (probably due to the formation of a stable complex of purine with Ir catalyst at N7 or limited stability of the purine-8-boronate).

I used a general approach for the synthesis of biologically relevant 6,8-disubstituted 7-deazapurines (4,6-disubstituted *7H*-pyrrolo[2,3-*d*]pyrimidines) based on a one-pot, two-step Ir-catalyzed C-H borylation of 9-substituted or SEM-protected followed by Pd-catalyzed Suzuki coupling with aryl halides. Manipulation of substituents at position 6, gave the desired 8-aryl-7-deazahypoxanthines, or -7-deazaadenines, respectively, after cleavage of the SEM protection group. The 8-pinacolboronate intermediates were also converted to 8-chloro-, 8-bromo and 8-trifluoromethyl-7-deazapurines by the Cu-catalyzed displacements. The approach gives easy access to an underexplored group of biologically relevant modified deazapurine bases which could be further N-alkylated or glycosylated to a variety of nucleoside and nucleotide analogues. While the 7-deazahypoxantine analogues were almost entirely inactive, most of the 8-subtituted 6-methoxy-7-deazapurine and 7-deazaadenines bases showed significant cytostatic activities.

The Cu-catalyzed C–H sulfenylation of 7- and 9-deazapurines proceeded very well and selectively at position 7 or 9, respectively, to give novel and interesting (arylsulfanyl)-deazapurine derivatives. On the other hand, the C–H sulfenylation of purines was less efficient, and the conditions had to be changed. All these C–H sulfenylations can be performed with 6-chloro(deaza)purines, so I used this potential in combination with classical cross-couplings in the synthesis of libraries of new di- and trisubstituted 7-deazapurine derivatives combining aryl(alkyl)sulfanyl and aryl or amino substituents for biological activity screening. While the ribonucleoside analogues were almost entirely inactive, most of the 7-(thienylsulfanyl)-7-deazapurine bases showed significant cytostatic activities.

However, the 8-(arylsulfanyl)purines smoothly undergo the Liebeskind–Srogl cross-coupling reactions leading to 8-arylpurines, whereas the 7- and 9-arylsulfanyldeazapurines were unreactive in these reactions. Also the Kumada cross-coupling of 7-phenylsulfanyl-7-deazapurine with PhMgCl gave only a moderate yield (50%) of desired 7-phenyl-7-deazapurine due to competitive transmetalation to 7-deazapurine-7-yl magnesium chloride. The synthetic usability of prepared aryl(alkyl)sulfanyl deazapurine derivatives is very limited.

# 5 Experimental section

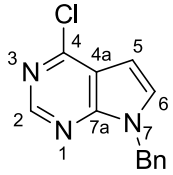
## 5.1 General remarks

All reactions with organometalic reagents as well as all iridium, palladium and nickel catalyzed reactions were done in flame-dried glassware under argon atmosphere. 6-Chloro-7-deazapurine (**8**), 6-chloro-9-deazapurine (**40**), disulfides, boronic acid and stannanes were purchased from commercial supplier and used without any further purification. 9-Benzyl-6-phenylpurine (**1**)[121] and 6-methyl-9-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)-7-deazapurine (**4**)[45] were prepared according to literature. Dry DMF and THF 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 $CDCl_3$ or DMSO and chemical shifts (in ppm, δ-scale) were referenced to solvent signal ($\delta(^1H)$ = 7.26 ppm, $\delta(^1H)$ = 77.0 ppm) or in or DMSO ($\delta(^1H)$ = 2.50 ppm, $\delta(^1H)$ = 39.43 ppm) Coupling constants (*J*) are given in Hz. High performance flash chromatography (HPFC) were performed with Biotage SP1 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. Optical rotations were measured at 25 °C, $[\alpha]_D$ values are given in $10^{-1}$degcm$^2$g$^{-1}$. IR spectra (wavenumbers in cm$^{-1}$) were recorded on Bruker Alpha FT-IR spectrometer using ATR technique. High resolution mass spectra were measured on a LTQ Orbitrap XL (Thermo Fisher Scientific) spectrometer using EI ionization technique. Melting points were determined on a Buchi Melting Point B-545 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 X-ray diffractometer using CuKα radiation (λ=1.54180 Å).

## 5.2 Preparation of starting compounds

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

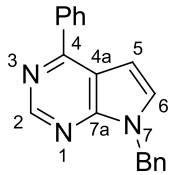
**(9-Benzyl-6-chloro-7-deazapurine) (7)**




Dry DMF (300 mL) was added to a stirred solution of potassium carbonate (22.8 g, 165 mmol) and 6-choro-7-deazapurine **8** (23 g, 150 mmol) under Ar. After 20 min, benzyl chloride (18.4 mL, 157.5 mmol) was added and the resulting mixture was stirred overnight at rt. After that brine was added and mixture were extracted with EtOAc 3x 250 mL and dried over $Na_2SO_4$. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 8:2) to give product **7** (32.9 g, 90 %) as yellowish crystals. $^1$H NMR was checked by published data.[122]

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

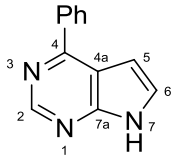
**(9-Benzyl-6-phenyl-7-deazapurine) (2)**




Dry toluene (250 ml) was added to a stirred solution of potassium carbonate (27.64 g, 200 mmol), 9-benzyl-6-chloro-7-deazapurine **7** (23.4 g, 100 mmol), phenylboronic acid (18.29 g, 150 mmol) and $Pd(PPh_3)_4$ (4.62 g, 4 mmol) under Ar. The mixture was stirred for 18 h at temperature 100°C. After cooling to rt brine was added and mixture were extracted with EtOAc 3x 250 mL and dried over $Na_2SO_4$. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 8:2) to give product **2** (25.9 g, 91 %) as white crystals. M.p. 75-78 °C. $^1$H NMR (500 MHz, $CDCl_3$): 5.51 (s, 2H, $CH_2$); 6.83 (d, 1H, $J_{5,6}$ = 3.7, H-5); 7.23 (d, 1H, $J_{6,5}$ = 3.7, H-6); 7.25 (m, 2H, H-*o*-Bn); 7.29 (m, 1H, H-*p*-Bn); 7.33 (m, 2H, H-*m*-Bn); 7.51 (m, 1H, H-*p*-Ph); 7.55 (m, 2H, H-*m*-Ph); 8.13 (m, 2H, H-*o*-Ph); 9.01 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 47.98 ($CH_2$Ph); 100.83 (CH-5); 115.64 (C-4a); 127.60 (CH-*o*-Bn); 127.96 (CH-*p*-Bn); 128.72 and 128.74 (CH-6 and CH-*m*-Ph); 128.84 and 128.85 (CH-*m*-Bn and CH-*o*-Ph); 129.96 (CH-*p*-Ph); 136.81 (C-*i*-Bn); 138.23 (C-*i*-Ph); 151.72 (CH-2); 151.83 (C-7a); 157.57 (C-4). IR ($CHCl_3$): 3067, 2983, 1585, 1564, 1515, 1497, 1466, 1455, 1442, 1423, 1390, 1345, 1302, 1250, 1157. HRMS (ESI) calculated for $C_{19}H_{15}N_3$: 286.1339; found: 286.1339.

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

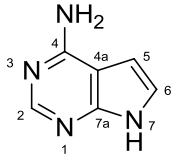
**(6-Phenyl-7-deazapurine) (3)**



Dry toluene (250 ml) was added to a stirred solution of potassium carbonate (27.64 g, 200 mmol), 6-chloro-7-deazapurine **8** (15.36 g, 100 mmol), phenylboronic acid (18.29 g, 150 mmol) and $Pd(PPh_3)_4$ (4.62 g, 4 mmol) under Ar. The mixture was stirred for 18 h at temperature 100°C. After cooling to rt brine was added and mixture were extracted with EtOAc 5x 250 mL and dried over $Na_2SO_4$. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 6:4) to give product **3** (17.57 g, 90 %) as white crystals. M.p. 220-221 °C. $^1$H NMR (500.0 MHz, $CDCl_3$): 6.89 (d, 1H, $J_{5,6}$ = 3.6, H-5); 7.55 (m, 1H, H-*p*-Ph); 7.59 (m, 2H, H-*m*-Ph); 7.66 (d, 1H, $J_{6,5}$ = 3.5, H-6); 8.18 (m, 2H, H-*o*-Ph); 8.84 (s, 1H, H-2); 12.27 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 100.17 (CH-5); 114.71 (C-4a); 127.93 (CH-6); 128.76 (CH-*o*-Ph); 129.05 (CH-*m*-Ph); 130.23 (CH-*p*-Ph); 138.14 (C-*i*-Ph); 151.14 (CH-2); 152.80 (C-7a); 155.73 (C-4). IR (KBr): 3205, 3133, 3006, 2865, 1598, 1581, 1563, 1503, 1412, 1349. HRMS (ESI) calculated for $C_{12}H_{10}N_3$: 196.0869; found: 196.0869. Anal. calculated for $C_{12}H_9N_3$ (195.08): C 73.83%, H 4.65%, N 21.52%; found: C 73.59%, H 4.63%, N 21.19%.

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

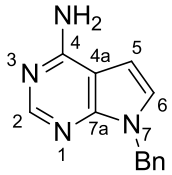
**(7-Deazaadenine) (35)**



6-chloro-7-deazapurine **8** (5 g; 31.73 mmol) was dissolved in 70 mL of mixture 1,4-dioxane/ aqueous ammonia (1:1) in a steel bomb and was heated at 130 °C for 19 h. After cooling, the mixture was evaporated. The crude mixture was separated by flash chromatography (gradient elution chloroform → chloroform/methanol 95:5) to give product **35** (4.25 g, 91 %) as white crystals. $^1$H NMR was checked by published data.[123]

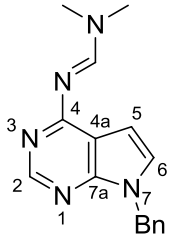
**7-Benzyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine**

**(9-Benzyl-7-deazaadenine) (5)**



Dry DMF (6 ml) was added to a stirred solution of potassium carbonate (0.974 g. 7.05 mmol) and 6-amino-7-deazapurine **35** (0.315 g, 2.35 mmol) under Ar. After 20 min, benzyl chloride (0.41 ml, 3.53 mmol) was added and the resulting mixture was stirred for 2 h at temperature 110°C, filtered and evaporated. The crude mixture was separated by flash chromatography on silica gel using $CHCl_3/CH_3OH$ 10:1 for elution to give product **5** (275 mg, 53%) as brown solid. Crystallization in hexan/EtOAc gave brownish crystals. M.p. 174-178 °C. $^1$H NMR (600 MHz, $CDCl_3$): 5.39 (s, 2H, $CH_2$); 5.41 (bs, 2H, $NH_2$); 6.38 (d, 1H, $J_{5,6}$ = 3.6, H-5); 6.93 (d, 1H, $J_{6,5}$ = 3.6, H-6); 7.19 (m, 2H, H-*o*-Bn); 7.28 (m, 1H, H-*p*-Bn); 7.31 (m, 2H, H-*m*-Bn); 8.36 (s, 1H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): 47.92 ($CH_2$Ph); 97.98 (CH-5); 102.97 (C-4a); 124.67 (CH-6); 127.40 (CH-*o*-Bn); 127.73 (CH-*p*-Bn); 128.72 (CH-*m*-Bn); 137.15 (C-*i*-Bn); 150.49 (C-7a); 151.92 (CH-2); 156.75 (C-4). IR($CHCl_3$): 3416, 2977, 1619, 1588, 1564, 1511, 1471, 1455, 1398, 1356, 1337, 1265, 991, 897, 705, 665. HRMS (ESI) calculated for $C_{13}H_{12}N_4$: 225.1135; found: 225.1135

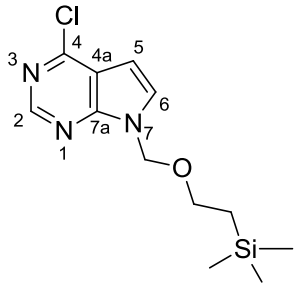
**7-Benzyl-4-[(*N,N*-dimethylaminomethylidene)amino]-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**9-Benzyl-6-[(*N,N*-dimethylaminomethylidene)amino]-7-deazapurine) (6)**



1,1-dimethoxy-*N,N*-dimethylmethanamine (1.7 ml, 12.7 mmol) was added to a flask containing 6-amino-9-benzyl-7-deazapurine **5** (275 mg, 1.27 mmol). The reaction mixture was stirred for 2 h (complete consumption of starting material according to TLC), evaporated and purified by silica gel flash chromatography ($CHCl_3/CH_3OH$ 10:1) to give **6** (315 mg, 89%) as white solid. Crystallization in hexan/EtOAc gave white crystals. M.p. 184-187 °C. $^1$H NMR (600 MHz, $CDCl_3$): 3.17 (s, 3H, $CH_3N$); 3.21 (d, 3H, $^4J$ = 0.7, $CH_3N$); 5.43 (s, 2H, $CH_2$); 6.67 (d, 1H, $J_{5,6}$ = 3.5, H-5); 6.99 (d, 1H, $J_{6,5}$ = 3.5, H-6); 7.17 (m, 2H, H-*o*-Bn); 7.26 (m, 1H, H-*p*-Bn); 7.30 (m, 2H, H-*m*-Bn); 8.53 (s, 1H, H-2); 8.79 (bs, 1H, HC=N). $^{13}$C NMR (151 MHz, $CDCl_3$): 34.82, 41.00 ($CH_3N$); 47.82 ($CH_2$Ph); 100.07 (CH-5); 111.43 (C-4a); 125.57 (CH-6); 127.29 (CH-*o*-Bn); 127.61 (CH-*p*-Bn); 128.68 (CH-*m*-Bn); 137.40 (C-*i*-Bn); 151.58 (CH-2); 151.88 (C-7a); 156.55 (HC=N); 160.72 (C-4). IR($CHCl_3$): 2971, 1672, 1629, 1576, 1447, 1425, 1382, 1344, 1254, 1112. HRMS (ESI) calculated for $C_{16}H_{17}N_5$: 280.1557; found: 280.1558

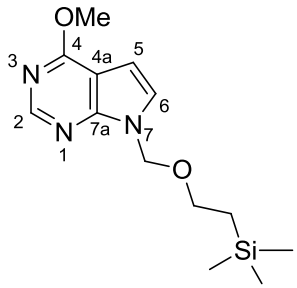
**4-Chloro-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**(6-Chloro-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (10)**



To a flask equipped with an addition funnel was added 6-choro-7-deazapurine **8** (15.35 g, 100 mmol) and DMF (250 mL). The mixture was cooled to – 5 °C in an ice/brine bath. Sodium hydride (NaH, 60 wt%, 4.45 g, 110 mmol, 1.1 equiv.) was added in portions as a solid. The solution darkened over 15 minutes. 2-(Trimethylsilyl)ethoxymethyl chloride (SEM-Cl, 19.5 mL, 110 mmol, 1.1 equiv.) was added slowly *via* an addition funnel at a rate such that the temperature did not exceed 5 °C. The reaction was stirred for 30 minutes, determined to be complete by TLC. Water (250 mL) was slowly added to quench the reaction. The mixture was then diluted with EtOAc (250 mL). The layers were separated and the aqueous layer was extracted with EtOAc (250 mL). The combined organic layers and dried over $Na_2SO_4$. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 8:2) to give 6-chloro-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (26.8 g, 94 %) as a pale yellow oil which solidified upon standing at room temperature. $^1$H NMR was checked by published data. [104]

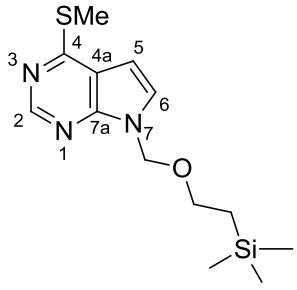
**4-Methoxy-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Methoxy-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (10)**



Protected deazapurine **9** (25.54 g, 90 mmol, 1 equiv.) was dissolved in acetone (50 mL) and 1 M solution of MeONa in MeOH (180 mL, 180 mmol, 2 equiv.) was added and the reaction mixture was stirred at r.t. overnight. Solvents were evaporated under reduced pressure and the mixture was then diluted with water (150 mL) and EtOAc (150 mL). The layers were separated and the aqueous layer was extracted two times with EtOAc (150 mL). The combined organic layers were dried over sodium sulphate ($Na_2SO_4$), filtrate and concentrated under the reduced pressure to give product **10** (24.94 g, 99%) as a yellow oil. $^1$H NMR (499.8 MHz, DMSO-$d_6$): -0.11 (s, 9H, $CH_3Si$); 0.79-0.83 (m, 2H, SiC**H$_2$**$CH_2O$); 3.48-3.51 (m, 2H, OC**H$_2$**$CH_2Si$); 4.05 (s, 3H, $CH_3O$); 5.58 (s, 2H, $NCH_2O$); 6.57 (d, 1H, $J_{5,6}$ = 3.6 Hz, H-5); 7.54 (dd, 1H, $J_{6,5}$ = 3.6 Hz, $J_{6,2}$ = 0.2 Hz, H-6); 8.45 (d, 1H, $J_{2,6}$ = 0.2 Hz, H-2). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): -1.2

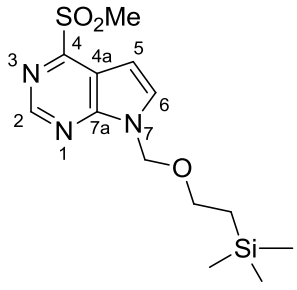
($CH_3Si$); 17.3 (Si**C**$H_2CH_2O$); 53.7 ($CH_3O$); 65.7 (O**C**$H_2CH_2Si$); 72.8 ($NCH_2O$); 98.6 (CH-5); 104.8 (C-4a); 127.7 (CH-6); 151.0 (CH-2); 152.2 (C-7a); 162.5 (C-4). IR (KBr): 2950, 2923, 2896, 1592, 1559, 1512, 1476, 1416, 1314, 1236, 1096, 1078, 1060, 863, 842, 764, 731, 647. HRMS (ESI) calculated for $C_{13}H_{21}O_2N_3NaSi$: 302.1295; found: 302.1295.

**4-(Methylsulfanyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (6-(Methylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (11)**




Protected deazapurine **9** (27 g, 95 mmol, 1 equiv.) was dissolved in methanol (150 mL) and MeSNa (10 g, 142.5 mmol, 1.5 equiv.) was added. Reaction mixture was stirred at r.t. for 1 h. Solvents were evaporated under reduced pressure and the mixture was then diluted with water (150 mL) and EtOAc (150 mL). The layers were separated and the aqueous layer was extracted two times with EtOAc (150 mL). The combined organic layers were dried over sodium sulphate ($Na_2SO_4$), solvents were evaporated and the residue was purified by flash chromatography in DCM/EtOAc (20:1) to give product **11** (25 g, 89%) as yellowish solid. M.p. 55°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.07 (s, 9H, $CH_3Si$); 0.88-0.91 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 2.71 (s, 3H, $CH_3S$); 3.49-3.52 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.61 (s, 2H, $NCH_2O$); 6.56 (d, 1H, $J_{5,6}$ = 3.7 Hz, H-5); 7.23 (d, 1H, $J_{6,5}$ = 3.7 Hz, H-6); 8.69 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 11.8 ($CH_3S$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 66.4 (O**C**$H_2CH_2Si$); 72.8 ($NCH_2O$); 100.0 (CH-5); 116.1 (C-4a); 129.7 (CH-6); 148.8 (C-7a); 151.2 (CH-2); 161.7 (C-4). IR (KBr): 3105, 3087, 3052, 2956, 2935, 2899, 2875, 1550, 1506, 1464, 1446, 1413, 1344, 1251, 1213, 1162, 1096, 1084, 394, 922, 860, 842, 758, 743. HRMS (ESI) calculated for $C_{13}H_{22}ON_3SSi$: 296.1247; found: 296.1248.

**4-(Methylsulfonyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (6-(Methylsulfonyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (12)**

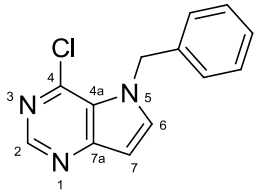



6-Methylsulfanyl-7-deazapurine **11** (1.48 g, 5 mmol, 1 equiv.) was dissolved in DCM (20 mL) and *m*-CPBA (1.72 g, 10 mmol, 2 equiv.) was slowly added (cooling by water/ice during addition) and the reaction mixture was stirred at r.t. overnight. Then, 1M NaOH (10 mL) was added to the mixture to remove residual *m*-CPBA. The layers were separated and the aqueous layer was extracted two times

with DCM (15 mL). The combined organic layers were dried over sodium sulphate, solvents were evaporated and the residue was purified by flash chromatography (HPFC) in $CHCl_3$/MeOH (20:1) to give product **12** (1.28 g, 78%) as white solid. M.p. 91°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.05 (s, 9H, $CH_3Si$); 0.90-0.93 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.36 (s, 3H, $CH_3SO_2$); 3.51-3.54 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.71 (s, 2H, $NCH_2O$); 7.16 (d, 1H, $J_{5,6}$ = 3.7 Hz, H-5); 7.59 (d, 1H, $J_{6,5}$ = 3.7 Hz, H-6); 8.98 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 39.9 ($CH_3SO_2$); 67.0 ($O\mathbf{C}H_2CH_2Si$); 73.2 ($NCH_2O$); 101.3 (CH-5); 114.2 (C-4a); 132.1 (CH-6); 150.6 (CH-2); 154.0 (C-7a); 155.7 (C-4). IR (KBr): 3111, 3078, 3010, 2953, 2917, 1577, 1550, 1518, 1455, 1443, 1425, 1341, 1323, 1308, 1266, 1248, 1236, 1213, 1123, 1096, 1081, 976, 970, 911, 863, 851, 842, 755, 656, 525. HRMS (ESI) calculated for $C_{13}H_{22}O_3N_3SSi$: 328.1146; found: 328.1147.

**5-Benzyl-4-chloro-*5H*-pyrrolo[3,2-*d*]pyrimidine**

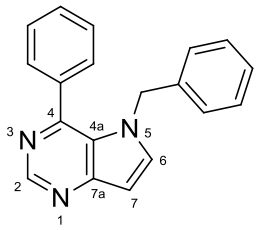
**(7-Benzyl-6-chloro-9-deazapurine)**




Dry DMF (150 ml) was added to a stirred solution of potassium carbonate (11.4 g, 82.5 mmol) and 6-choro-9-deazapurine **40** (11.5 g, 75 mmol) under Ar. After 20 min, benzyl chloride (9.2 ml, 78.75 mmol) was added and the resulting mixture was stirred overnight at rt. After that brine was added and mixture were extracted with EtOAc 3x 250 mL and dried over $Na_2SO_4$. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 8:2) to give product 7-benzyl-6-chloro-9-deazapurine (16.63 g, 91 %) as yellowish crystals. M.p. 122-126 °C. $^1$H NMR (600.1 MHz, DMSO-$d_6$): 5.51 (s, 2H, $CH_2Ph$); 6.69 (d, 1H, $J_{7,6}$ = 3.6, H-7); 7.27 (m, 3H, H-*o*,*p*-Ph); 7.32 (m, 2H, H-*m*-Ph); 7.85 (d, 1H, $J_{6,7}$ = 3.6, H-6); 8.66 (s, 1H, H-2). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 47.99 ($CH_2Ph$); 99.01 (CH-7); 116.91 (C-4a); 127.54 (CH-*o*-Ph); 127.87 (CH-*p*-Ph); 128.84 (CH-*m*-Ph); 131.66 (CH-6); 137.33 (C-*i*-Ph); 150.65 (CH-2); 150.72, 150.90 (C-4,7a). IR(KBr): 3113, 3070, 3032, 1593, 1522, 1496, 1460, 1452, 1444, 1409, 1399, 1350. HRMS (ESI) calculated for $C_{18}H_{14}N_3S$: 243.0563; found: 243.0569.

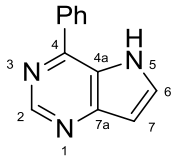
**5-Benzyl-4-phenyl-*5H*-pyrrolo[3,2-*d*]pyrimidine**

**(7-Benzyl-6-phenyl-9-deazapurine) (39)**



Dry toluene (100 ml) was added to a stirred solution of potassium carbonate (11.06 g, 80 mmol), 7-benzyl-6-chloro-9-deazapurine (9.72 g, 40 mmol), phenylboronic acid (7.32 g, 60 mmol) and $Pd(PPh_3)_4$ (1.85 g, 1.6 mmol) under Ar. The mixture was stirred for 18 h at temperature 110°C. After cooling to rt brine was added and mixture were extracted with EtOAc 5x 250 mL and dried over $Na_2SO_4$. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 7:3) to give product **39** (11.07 g, 97 %) as white crystals. M.p. 110-111 °C. $^1$H NMR (499.8 MHz, DMSO-$d_6$): 5.21 (s, 2H, $CH_2$Ph); 6.37 (m, 2H, H-*o*-Bn); 6.81 (d, 1H, $J_{7,6}$ = 3.2, H-7); 7.07 (m, 2H, H-*m*-Bn); 7.10 (m, 1H, H-*p*-Bn); 7.41 (m, 2H, H-*o*-Ph); 7.45 (m, 2H, H-*m*-Ph); 7.53 (m, 1H, H-*p*-Ph); 8.10 (d, 1H, $J_{6,7}$ = 3.2, H-6); 8.85 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 51.85 ($CH_2$Ph); 101.83 (CH-7); 124.45 (C-4a); 125.97 (CH-*o*-Bn); 127.45 (CH-*p*-Bn); 128.21 (CH-*m*-Ph); 128.47 (CH-*m*-Bn); 129.32 (CH-*o*-Ph); 129.38 (CH-*p*-Ph); 137.35 (C-*i*-Ph); 137.44 (C-*i*-Bn); 138.99 (CH-6); 150.02 (CH-2); 150.37 (C-4); 152.14 (C-7a). IR(KBr): 3436, 3062, 3030, 1583, 1575, 1537, 1510, 1490, 1454, 1443, 1394, 1360. HRMS (ESI) calculated for $C_{19}H_{16}N_3$: 286.1339; found: 286.1339.

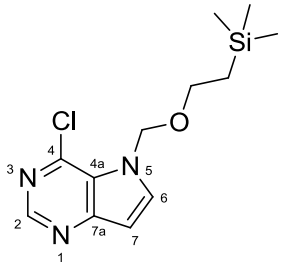
**4-Phenyl-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(6-Phenyl-9-deazapurine) (38)**



Dry toluene (250 ml) was added to a stirred solution of potassium carbonate (27.64 g, 200 mmol), 6-chloro-9-deazapurine **40** (15.36 g, 100 mmol), phenylboronic acid (18.29 g, 150 mmol) and $Pd(PPh_3)_4$ (4.62 g, 4 mmol) under Ar. The mixture was stirred for 18 h at temperature 100°C. After cooling to rt brine was added and mixture were extracted with EtOAc 5x 250 mL and dried over $Na_2SO_4$. The crude mixture was separated by flash chromatography (gradient elution hexanes →
hexanes/ethyl acetate 6:4) to give product **38** (16.59 g, 85 %) as yellowish crystals. M.p. 136-142 °C. $^1$H NMR (499.8 MHz, DMSO-$d_6$): 6.71 (dd, 1H, $J_{7,6}$ = 3.1, $J_{7,NH}$ = 1.5, H-7); 7.58 (m, 1H, H-*p*-Ph); 7.62 (m, 2H, H-*m*-Ph); 7.91 (dd, 1H, $J_{6,7}$ = $J_{6,NH}$ = 3.1, H-6); 8.09 (m, 2H, H-*o*-Ph); 8.90 (s, 1H, H-2); 11.99 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 101.82 (CH-7); 123.70 (C-4a); 128.79 (CH-*o*-Ph); 129.11 (CH-*m*-Ph); 130.32 (CH-*p*-Ph); 134.20 (CH-6); 136.34 (C-*i*-Ph); 147.64 (C-4); 150.38 (CH-2); 151.45 (C-7a). IR (KBr): 3205, 3135, 3081,

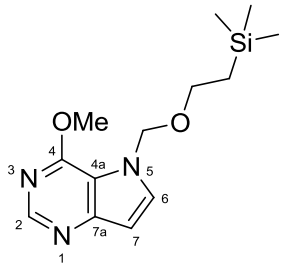
3007, 2867, 1599, 1582, 1563,1503, 1438, 1412, 1350. HRMS (ESI) calculated for $C_{12}$ $H_{11}$ $N_3$: 196.0796; found: 196.0869. Anal. calculated for $C_{12}H_9N_3$ (195.08): C 73.83%, H 4.65%, N 21.52%; found: C 73.68%, H 4.54%, N 21.12%.

**4-Chloro-5-((2-(trimethylsilyl)ethoxy)methyl)-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(6-Chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-9-deazapurine)**




To a flask equipped with an addition funnel was added 6-chloro-9-deazapurine **40** (3.84 g, 25 mmol) and DMF (60 mL). The mixture was cooled to – 5 °C in an ice/brine bath. Sodium hydride (NaH, 60 wt%, 1.11 g, 27.5 mmol, 1.1 equiv.) was added in portions as a solid. The solution darkened over 15 minutes. 2-(Trimethylsilyl)ethoxymethyl chloride (SEM-Cl, 5 mL, 27.5 mmol, 1.1 equiv.) was added slowly *via* an addition funnel at a rate such that the temperature did not exceed 5 °C. The reaction was stirred for 30 minutes, determined to be complete by TLC. Water (60 mL) was slowly added to quench the reaction. The mixture was then diluted with EtOAc (50 mL). The layers were separated and the aqueous layer was extracted with EtOAc (50 mL). The combined organic layers and dried over $Na_2SO_4$. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 6:4) to give 6-chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-9-deazapurine (5.9 g, 84 %) as a pale yellow oil. $^1$H NMR (499.8 MHz, DMSO-$d_6$): -0.12 (s, 9H, $CH_3Si$); 0.80 (m, 2H, SiC**H$_2$**$CH_2O$); 3.49 (m, 2H, OC**H$_2$**$CH_2Si$); 5.79 (s, 2H, $NCH_2O$); 6.79 (d, 1H, $J_{7,6}$ = 3.2, H-7); 8.20 (d, 1H, $J_{6,7}$ = 3.2, H-6); 8.68 (s, 1H, H-2).$^{13}$C NMR (125.7 MHz, DMSO-$d_6$): -1.28 ($CH_3Si$); 17.23 (Si**C**$H_2CH_2O$); 65.34 (O**C**$H_2CH_2Si$); 76.85 ($NCH_2O$); 102.36 (CH-7); 123.15 (C-4a); 139.57 (CH-6); 141.97 (C-4); 150.06 (CH-2); 151.13 (C-7a). HRMS (ESI) calculated for $C_{12}H_{19}ON_3ClSi$: 284.0980; found: 284.0980.

**4-Methoxy-5-((2-(trimethylsilyl)ethoxy)methyl)-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(6-Methoxy-7-((2-(trimethylsilyl)ethoxy)methyl)-9-deazapurine) (19)**



6-Chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-9-deazapurine (5.68 g, 20 mmol, 1 equiv.) was dissolved in acetone (50 mL) and 1 M solution of MeONa in MeOH (40 mL, 40 mmol, 2 equiv.) was added and the reaction mixture was stirred at r.t. overnight. Solvents were evaporated under reduced pressure and the mixture was then diluted with water (100 mL) and EtOAc (100 mL). The layers were separated and the aqueous layer was extracted two times with EtOAc (100 mL). The combined organic layers were dried over sodium sulphate ($Na_2SO_4$), filtrate and concentrated under the reduced pressure to give product **19** (5.4 g, 97%) as a yellow oil. $^1$H NMR (499.8 MHz, $CDCl_3$): -0.07 (s, 9H, $CH_3Si$); 0.87 (m, 2H, SiC**H$_2$**$CH_2O$); 3.50 (m, 2H, OC**H$_2$**$CH_2Si$); 4.17 (s, 3H, $CH_3O$); 5.67 (s, 2H, $NCH_2O$); 6.70 (d, 1H, $J_{7,6}$ = 3.2, H-7); 7.42 (d, 1H, $J_{6,7}$ = 3.2, H-6); 8.56 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.52 ($CH_3Si$); 17.68 (Si**C**$H_2CH_2O$); 53.67 ($CH_3O$); 65.97 (O**C**$H_2CH_2Si$); 77.55 ($NCH_2O$); 103.46 (CH-7); 115.50 (C-4a); 133.02 (CH-6); 149.91 (CH-2); 150.73 (C-7a); 156.43 (C-4). HRMS (ESI) calculated for $C_{13}H_{22}O_2N_3Si$: 280.1476; found: 280.1476.

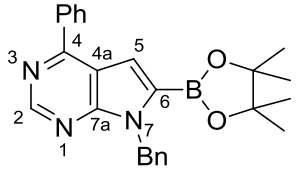
## 5.3 C-H Borylation of purines and deazapurines

### Borylation of deazapurines. General Procedure:

7-Deazapurines **2-12** (2 mmol, 1 equiv.), bispinacolatodiboron (0.609 g, 2.4 mmol, 1.2 equiv.), $[Ir(COD)OMe]_2$ (66 mg, 0.1 mmol, 5 mol %) and 4,4'-di-tert-butyl-2,2'-bipyridine (54 mg, 0.2 mmol, 10 mol %) were dissolved in dry THF (15 ml) under Ar. The solution was heated at 80 °C in a septum-sealed flask for 20 hours. The solvent was evaporated and the residue was purified by silica gel flash chromatography.

**7-Benzyl-4-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**(9-Benzyl-6-phenyl-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7-deazapurine) (13)**

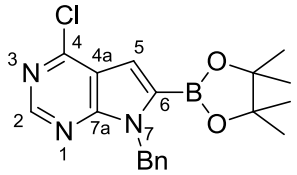


9-Benzyl-6-phenyl-7-deazapurine **2** (570 mg, 2 mmol) was used as starting compound to give product **13** (698 mg, 85%) as white foam after chromatography hexane/EtOAc 5:1. Crystallization in hexan/EtOAc gave white crystals. M.p. 128-134 °C. $^1$H NMR (600

MHz, $CDCl_3$): 1.28 (s, 12H, $CH_3$); 5.81(s, 2H, $CH_2$); 7.17-7.26 (m, 5H, H-*o,m,p*-Bn); 7.46 (s, 1H, H-5); 7.50 (m, 1H, H-*p*-Ph); 7.54 (m, 2H, H-*m*-Ph); 8.16 (m, 2H, H-*o*-Ph); 9.02 (s, 1H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): 24.65 ($(CH_3)_2C$); 47.17 ($CH_2Ph$); 84.39 ($C(CH_3)_2$); 113.54 (CH-5); 115.44 (C-4a); 127.14 (CH-*p*-Bn); 127.28 (CH-*o*-Bn); 128.25 (CH-*m*-Bn); 128.71 (CH-*m*-Ph); 129.06 (CH-*o*-Ph); 130.10 (CH-*p*-Ph); 132.15 (C-6); 138.16 (C-*i*-Ph); 138.79 (C-*i*-Bn); 152.94 (CH-2); 154.25 (C-7a); 158.73 (C-4). IR($CHCl_3$):2983, 1562, 1525, 1468, 1449, 1428, 1382, 1374, 1335, 1139. HRMS (ESI) calculated for $C_{25}H_{26}BN_3O_2$: 412.2191; found: 412.2192.

**7-Benzyl-4-chloro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**

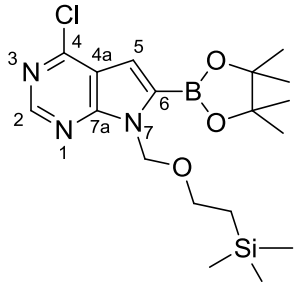
**(9-Benzyl-6-chloro-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7-deazapurine) (14)**




9-Benzyl-6-chloro-7-deazapurine **7** (486 mg, 2 mmol) and bispinacolatodiboron (0.762 g, 3.0 mmol, 1.5 equiv.), $[Ir(COD)OMe]_2$ (106 mg, 0.1 mmol, 8 mol %) and 4,4'-di-tert-butyl-2,2'-bipyridine (86 mg, 0.2 mmol, 16 mol %) were used. The residue after C-H activation was purified by silica gel flash chromatography (hexane/EtOAc 5:1→ ethyl acetate/hexanes 1:1) to give product **14** (390 mg, 53%) as white solid. Crystallization in hexan/EtOAc gave white crystals. M.p. 172-175 °C. $^1$H NMR (500 MHz, $CDCl_3$): 1.28 (s, 12H, $CH_3$); 5.75 (s, 2H, $CH_2$); 7.16-7.25 (m, 6H, H-5 and H-*o,m,p*-Bn); 8.68 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 24.62 ($(\mathbf{C}H_3)_2C$); 47.60 ($CH_2Ph$); 84.56 ($\mathbf{C}(CH_3)_2$); 112.23 (CH-5); 117.21 (C-4a); 127.22 (CH-*o*-Bn); 127.34 (CH-*p*-Bn); 128.30 (CH-*m*-Bn); 132.79 (C-6); 138.12 (C-*i*-Bn); 151.91 (CH-2); 153.28 and 153.42 (C-4 and C-7a). IR($CHCl_3$): 2984, 1579, 1541, 1525, 1469, 1430, 1374, 1355, 1330, 1259, 1177, 1137. HRMS (ESI) calculated for $C_{19}H_{21}BClN_3O_2$: 370.1499; found: 370.1488.

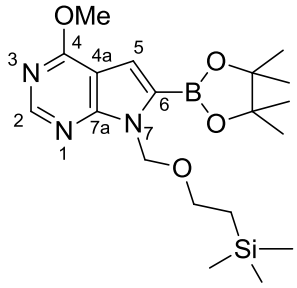
**4-chloro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**(6-chloro-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (15)**



Starting from **9** (284 mg, 1 mmol), the product **15** (322 mg, 78%) was obtained as brownish solid after chromatography performed in pure dichloromethane. Finally, the crude product was rinsed with hexanes and heated at 60 °C under vacuum (6 mtorr) to remove residual pinacol. M.p. 99°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.08 (s, 9H, $CH_3Si$); 0.85-0.89 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 1.38 (s, 12H, $(CH_3)_2C$); 3.50-3.53 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.89 (s, 2H, $NCH_2O$); 7.23 (s, 1H, H-5); 8.68 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.8 ($OCH_2\mathbf{C}H_2Si$); 24.8 (($\mathbf{C}H_3)_2C$); 66.3 ($O\mathbf{C}H_2CH_2Si$); 72.6 ($NCH_2O$); 84.7 (($CH_3)_2\mathbf{C}$); 112.6 (CH-5); 117.5 (C-4a), 133.0 (C-6); 152.2 (CH-2); 153.3 (C-4); 154.0 (C-7a). IR (KBr): 2989, 2956, 2914, 2893, 1580, 1538, 1428, 1365, 1326, 1254, 1180, 1141, 1087, 866, 827, 746. HRMS (ESI) calculated for $C_{18}H_{30}O_3N_3BClSi$: 410.1833; found: 410.1831.

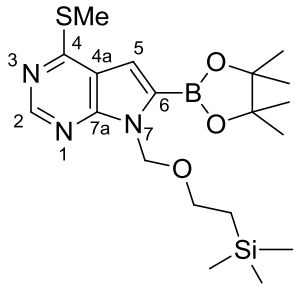
**4-Methoxy-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Methoxy-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (16)**



Starting from **10** (279 mg, 1 mmol) the product **16** (328 mg, 81%) was obtained as brownish oil after chromatography performed in pure dichloromethane. Finally, the crude product was rinsed with hexanes and heated at 60 °C under vacuum (6 mtorr) to remove residual pinacol. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.09 (s, 9H, $CH_3Si$); 0.85-0.88 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 1.36 (s, 12H, $(CH_3)_2C$); 3.50-3.54 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.11 ($CH_3O$); 5.86 (s, 2H, $NCH_2O$); 7.17 (s, 1H, H-5); 8.52 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 17.8 ($OCH_2\mathbf{C}H_2Si$); 24.8 (($\mathbf{C}H_3)_2C$); 53.7 ($CH_3O$); 65.9 ($O\mathbf{C}H_2CH_2Si$); 72.4 ($NCH_2O$); 84.1 (($CH_3)_2\mathbf{C}$); 105.7 (C-4a); 112.3 (CH-5); 129.3 (C-6); 152.6 (CH-2); 155.1 (C-7a); 163.7 (C-7a). IR (KBr): 2977, 2950, 2893, 1682, 1595, 1553, 1524, 1479, 1425, 1374, 1331, 1320, 1260, 1222, 1147, 1090, 970, 860, 836, 797, 761. HRMS (ESI) calculated for $C_{19}H_{33}O_4N_3BSi$: 406.2328; found: 406.2331.

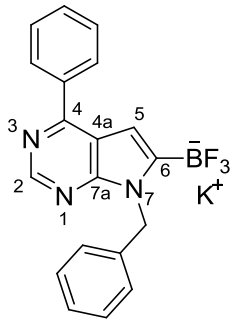
**4-(Methylthio)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**(6-(Methylthio)-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (17)**




Starting from **11** (295 mg, 1 mmol), the product **17** (350 mg, 83%) was obtained as brownish oil after chromatography performed in pure dichloromethane. Finally, the crude product was rinsed with hexanes and heated at 60 °C under vacuum (6 mtorr) to remove residual pinacol. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.08 (s, 9H, $CH_3Si$); 0.85-0.88 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 1.37 (s, 12H, $(CH_3)_2C$); 2.69 ($CH_3S$); 3.50-3.53 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.86 (s, 2H, $NCH_2O$); 7.17 (s, 1H, H-5); 8.70 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 11.8 ($CH_3S$); 17.8 ($OCH_2\mathbf{C}H_2Si$); 24.8 (($\mathbf{C}H_3)_2C$); 66.0 ($O\mathbf{C}H_2CH_2Si$); 72.3 ($NCH_2O$); 84.3 ($(CH_3)_2\mathbf{C}$); 112.4 (CH-5); 116.0 (C-4a); 130.1 (C-6); 151.4 (C-7a); 152.2 (CH-2); 163.2 (C-4). IR (KBr): 2974, 2950, 2929, 2893, 1553, 1527, 1458, 1425, 1371, 1314, 1263, 1222, 1180, 1141, 1084, 857, 839. HRMS (ESI) calculated for $C_{19}H_{33}O_3N_3BSSi$: 422.2099; found: 422.2099.

**(7-Benzyl-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)trifluoroborate (potassium salt) ((9-benzyl-6-phenyl-7-deazapurine-8-yl)trifluoroborate (potassium salt)) (18)**



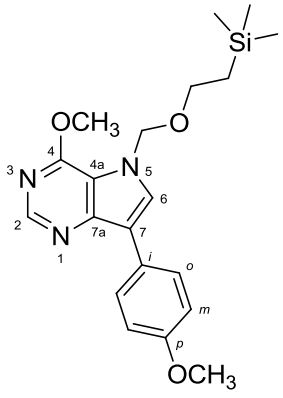

To a flask containing **13** (412 mg, 1 mmol, 1 equiv.) and $KHF_2$ (469 mg, 6 mmol), THF (5 mL) and $H_2O$ (3 mL) were added. The reaction mixture was stirred for 5 h at room temperature. The solvents were evaporated and the residue was purified by flash chromatography (HPFC) in EtOAc/MeOH (9:1) to give product **18** (266 mg, 68%) as white solid. M.p. > 300°C. $^{1}$H NMR (500 MHz, $CD_3OD$): 5.67 (s, 2H, $CH_2$); 6.86 (H-5); 7.14-7.15 (m, 1H, H-*p*-Bn); 7.18-7.25 (m, 4H, H-*o*,*m*-Bn); 7.52-7.53 (m, 1H, H-*p*-Ph); 7.56-7.58 (m, 2H, H-*m*-Ph); 8.06-8.07 (m, 2H, H-*o*-Ph); 8.63 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CD_3OD$): 48.7 ($CH_2Ph$); 104.2 (CH-5); 118.1 (C-4a); 127.7 (CH-*p*-Bn); 128.2 (CH-*o*-Bn); 129.0 (CH-*m*-Bn); 129.8 (CH-*m*-Ph); 130.0 (CH-*o*-Ph); 131.0 (CH-*p*-Ph); 138.9 (C-*i*-Ph); 140.3 (C-*i*-Bn); 149.5 (CH-2); 154.3 (C-7a); 155.8 (C-4); C-6 not detected. $^{19}$F NMR (470.3 MHz, $CD_3OD$): -137.91. $^{11}$B NMR (160.4 MHz, $CD_3OD$): 1.96. IR (KBr): 3428, 3254, 3062, 3031, 2949, 1617, 1584, 1562, 1550, 1497, 1474, 1455, 1432, 1148, 1028, 1007, 937, 761, 697. HRMS (ESI) calculated for $C_{19}H_{15}N_3BF_3Na$: 376.1203; found: 376.1205.

## C-H borylation of 9-deazapurine:

A 9-deazapurine **19** (558 mg, 2 mmol, 1 equiv.), bispinacolatodiboron (610 mg, 2.4 mmol, 1.2 equiv.), $[Ir(COD)OMe]_2$ (66 mg, 0.1 mmol, 5 mol %) and 4,4'-di-tert-butyl-2,2'-bipyridine (54 mg, 0.2 mmol, 10 mol %) was dissolved in dry THF (15 ml) under Ar. The solution was heated at 80 °C in a septum sealed vial and stirred under argon for 20 h. According TLC, LC-MS, NMR (reaction mixture) inseparable mixture of two borylated was obtained. The solvent was removed under reduced pressure. The residue was then combined with 4-iodoanisole (515 mg, 2.2 mmol, 1.1 equiv.), $Pd(dppf)Cl_2$ (73 mg, 0.1 mmol, 5 mol %) and $K_2CO_3$ (1.1 g, 8 mmol, 4 equiv.) in DMF (15 mL) and stirred under Ar at 90 °C for 1 h. The solution was then cooled to room temperature, diluted with EtOAc (50 mL) and water (50 mL). Aqueous solution was then extracted three times with EtOAc and combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. Purification was performed by HPFC (hexane/EtOAc, 0–60% EtOAc) to give products **20a** (154 mg, 20%) and **20 b** (308 mg, 40%) as yellowish oils.

**4-Methoxy-7-(4-methoxyphenyl)-5-((2-(trimethylsilyl)ethoxy)methyl)-*5H*-pyrrolo[3,2-*d*]pyrimidine**

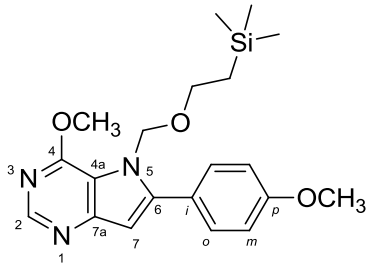
**(6-Methoxy-9-(4-methoxyphenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-9-deazapurine) (20a)**




$^1$H NMR (499.8 MHz, $CDCl_3$): -0.06 (s, 9H, $CH_3Si$); 0.90 (m, 2H, SiC**H$_2$**$CH_2O$); 3.54 (m, 2H, OC**H$_2$**$CH_2Si$); 3.84 (s, 3H, $CH_3O$-*p*); 4.17 (s, 3H, $CH_3O$-4); 5.69 (s, 2H, $NCH_2O$); 7.00 (m, 2H, H-*m*-$C_6H_4OMe$); 7.58 (s, 1H, H-6); 7.95 (m, 2H, H-*o*-$C_6H_4OMe$); 8.64 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.52 ($CH_3Si$); 17.70 (Si**C**$H_2CH_2O$); 53.51 ($CH_3O$-4); 55.31 ($CH_3O$-*p*); 65.98 (O**C**$H_2CH_2Si$); 77.49 ($NCH_2O$); 114.19 (CH-*m*-$C_6H_4OMe$); 116.22 (C-4a); 117.51 (C-7); 125.44 (C-*i*-$C_6H_4OMe$); 128.03 (CH-*o*-$C_6H_4OMe$); 128.76 (CH-6); 148.57 (C-7a); 150.11 (CH-2); 156.36 (C-4); 158.40 (C-*p*-$C_6H_4OMe$). HRMS (ESI) calculated for $C_{20}H_{28}O_3N_3Si$: 386.1894; found: 386.1894.

**4-Methoxy-6-(4-methoxyphenyl)-5-((2-(trimethylsilyl)ethoxy)methyl)-*5H*-pyrrolo[3,2-*d*]pyrimidine**

**(6-Methoxy-8-(4-methoxyphenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-9-deazapurine) (20b)**



$^{1}$H NMR (499.8 MHz, $CDCl_3$): -0.07 (s, 9H, $CH_3Si$); 0.84 (m, 2H, SiC**H$_2$**$CH_2O$); 3.50 (m, 2H, OC**H$_2$**$CH_2Si$); 3.87 (s, 3H, $CH_3O$-*p*); 4.18 (s, 3H, $CH_3O$-4); 5.62 (s, 2H, $NCH_2O$); 6.69 (s, 1H, H-7); 7.02 (m, 2H, H-*m*-$C_6H_4OMe$); 7.59 (m, 2H, H-*o*-$C_6H_4OMe$); 8.56 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.52 ($CH_3Si$); 17.93 (Si**C**$H_2CH_2O$); 53.66 ($CH_3O$-4); 55.38 ($CH_3O$-*p*); 65.66 (O**C**$H_2CH_2Si$); 74.33 ($NCH_2O$); 103.30 (CH-7); 114.18 (CH-*m*-$C_6H_4OMe$); 116.64 (C-4a); 123.22 (C-*i*-$C_6H_4OMe$); 131.16 (CH-*o*-$C_6H_4OMe$); 147.31 (C-6); 149.99 (CH-2, C-7a); 156.04 (C-4); 160.41 (C-*p*-$C_6H_4OMe$). HRMS (ESI) calculated for $C_{20}H_{28}O_3N_3Si$: 386.1894; found: 386.1894.

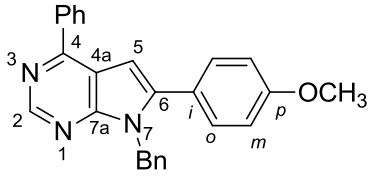
# 5.4 Application of C-H borylation in synthesis of 6,8-disubstituted 7-deazapurines

## 5.4.1 Synthesis of 8-aryl-7-deazapurines

### Suzuki coupling arylboronic ester with aryl halogens. General procedure:

Aryl halide (0.269 mmol, 1.1 equiv.), **13** (100 mg, 0.244 mmol, 1 equiv.), Pd(dppf)$Cl_2$ (9 mg, 0.0112 mmol, 5 mol %), $K_2CO_3$ (135 mg, 0.976 mmol, 4 equiv.) were combined in DMF (4 mL) and stirred under argon at 90 °C for 1 h. The solvent was removed under reduced pressure, the residue was purified by silica gel flash chromatography (hexane/EtOAc 5/1) to give products **21a-21g.**

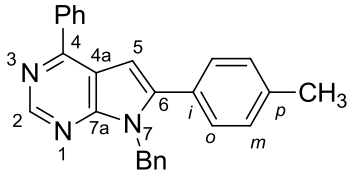
**7-Benzyl-6-(4-methoxyphenyl)-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-6-phenyl-8-(4-methoxyphenyl)-7-deazapurine) (21a)**



Product **21a** (83 mg, 87%) was obtained as yellow solid. Crystallization in hexan/EtOAc gave yellowish crystals. M.p. 116-121 °C. $^{1}$H NMR (500 MHz, $CDCl_3$): 3.85 (s, 3H, $CH_3O$); 5.56 (s, 2H, $CH_2$); 6.85 (s, 1H, H-5); 6.93 (m, 2H, H-*m*-$C_6H_4OMe$); 7.00 (m, 2H, H-*o*-Bn); 7.19-7.26 (m, 3H, H-*m*,*p*-Bn); 7.32 (m, 2H, H-*o*-

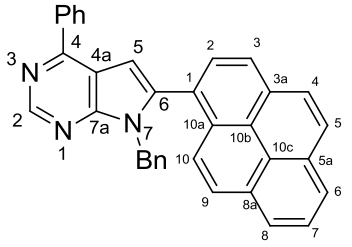
$C_6H_4OMe$); 7.51 (m, 1H, H-*p*-Ph); 7.55 (m, 2H, H-*m*-Ph); 8.17 (m, 2H, H-*o*-Ph); 8.98 (s, 1H, H-2). $^{13}C$ NMR (125.7 MHz, $CDCl_3$): 46.10 ($CH_2Ph$); 55.35 ($CH_3O$); 99.96 (CH-5); 114.12 (CH-*m*-$C_6H_4OMe$); 115.90 (C-4a); 123.65 (C-*i*-$C_6H_4OMe$); 126.58 (CH-*o*-Bn); 127.35 (CH-*p*-Bn); 128.61 (CH-*m*-Bn); 128.74 (CH-*m*-Ph); 128.80 (CH-*o*-Ph); 129.89 (CH-*p*-Ph); 130.63 (CH-*o*-$C_6H_4OMe$); 137.60 (C-*i*-Bn); 138.30 (C-*i*-Ph); 142.92 (C-6); 151.49 (CH-2); 153.38 (C-7a); 156.51 (C-4); 160.18 (C-*p*-$C_6H_4OMe$). IR($CHCl_3$): 3010, 1612, 1567, 1498, 1464, 1455, 1441, 1419, 1344, 1293, 1251, 1177, 1032, 838. HRMS (ESI) calculated for $C_{26}H_{21}N_3O$: 392.1757; found: 392.1764.

**7-Benzyl-4-phenyl-6-p-tolyl-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-6-phenyl-8-p-tolyl-7-deazapurine) (21b)**




Product **21b** (83 mg, 90%) was obtained as yellow solid. Crystallization in hexan/EtOAc gave yellowish crystals. M.p. 125-130 °C. $^1H$ NMR (500 MHz, $CDCl_3$): 2.40 (s, 3H, $CH_3$); 5.56 (s, 2H, $CH_2$); 6.87 (s, 1H, H-5); 7.00 (m, 2H, H-*o*-Bn); 7.19-7.26 (m, 5H, H-*m*,*p*-Bn and H-*m*-$C_6H_4Me$); 7.30 (m, 2H, H-*o*-$C_6H_4Me$); 7.50 (m, 1H, H-*p*-Ph); 7.55 (m, 2H, H-*m*-Ph); 8.17 (m, 2H, H-*o*-Ph); 8.99 (s, 1H, H-2). $^{13}C$ NMR (125.7 MHz, $CDCl_3$): 21.29 ($CH_3$); 46.13 ($CH_2Ph$); 100.21 (CH-5); 115.87 (C-4a); 126.60 (CH-*o*-Bn); 127.32 (CH-*p*-Bn); 128.43 (C-*i*-$C_6H_4Me$); 128.57 (CH-*m*-Bn); 128.73 (CH-*m*-Ph); 128.80 (CH-*o*-Ph); 129.18 (CH-*o*-$C_6H_4Me$); 129.37 (CH-*m*-$C_6H_4Me$); 129.89 (CH-*p*-Ph); 137.59 (C-*i*-Bn); 138.32 (C-*i*-Ph); 139.02 (C-*p*-$C_6H_4Me$); 143.11 (C-6); 151.58 (CH-2); 153.45 (C-7a); 156.65 (C-4). IR($CHCl_3$): 3066, 2983, 1567, 1497, 1463, 1454, 1441, 1420, 1344, 1267, 699. HRMS (ESI) calculated for $C_{26}H_{21}N_3$: 376.1819; found: 376.1808.

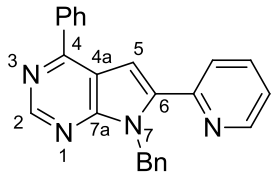
**7-Benzyl-4-phenyl-6-(pyren-1-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-6-phenyl-8-(pyren-1-yl)-7-deazapurine) (21c)**




Product **21c** (93 mg, 79%) was obtained as yellow oil which solidified on standing. M.p. 57-76 °C. $^1H$ NMR (500 MHz, $CDCl_3$): 5.13 and 5.67 (2 × bd, 2H, $J_{gem}$ = 15.6, $CH_2$); 6.65 (m, 2H, H-*o*-Bn); 6.95 (m, 2H, H-*m*-Bn); 7.01 (m, 1H, H-*p*-Bn); 7.08 (s, 1H, H-5); 7.48 (m, 1H, H-*p*-Ph); 7.53 (m, 2H, H-*m*-Ph); 7.81

(d, 1H, $J_{2,3}$ = 7.8, H-2-pyr); 7.84 (d, 1H, $J_{10,9}$ = 9.2, H-10-pyr); 7.98 (d, 1H, $J_{9,10}$ = 9.2, H-9-pyr); 8.03 (t, 1H, $J_{7,6} = J_{7,8}$ = 7.6, H-7-pyr); 8.09 (d, 1H, $J_{4,5}$ = 9.0, H-4-pyr); 8.12 (d, 1H, $J_{3,2}$ = 7.8, H-3-pyr); 8.14 (d, 1H, $J_{5,4}$ = 9.0, H-5-pyr); 8.18 (dd, 1H, $J_{6,7}$ = 7.6, $J_{6,8}$ = 1.1, H-6-pyr); 8.18 (m, 3H, H-8-pyr and H-*o*-Ph); 9.12 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.31 ($CH_2$Ph); 102.70 (CH-5); 115.93 (C-4a); 124.23 (CH-3-pyr); 124.35 (CH-10-pyr); 124.39 (C-10c-pyr); 124.52 (C-10b-pyr); 125.61 (CH-6-pyr); 125.76 (C-1-pyr); 125.80 (CH-8-pyr); 126.34 (CH-7-pyr); 127.19 (CH-*o*-Bn); 127.22, 127.23 (CH-*p*-Bn and CH-4-pyr); 128.17 (CH-*m*-Bn); 128.43 (CH-5-pyr); 128.57 (CH-2,9-pyr); 128.77 (CH-*m*-Ph); 128.88 (CH-*o*-Ph); 129.97 (CH-*p*-Ph); 130.31 (C-10a-pyr); 130.71 (C-8a-pyr); 131.20 (C-5a-pyr); 131.93 (C-3a-pyr); 137.06 (C-*i*-Bn); 138.28 (C-*i*-Ph); 141.02 (C-6); 151.80 (CH-2); 153.07 (C-7a); 156.94 (C-4). IR($CHCl_3$): 3407, 3047, 3000, 1604, 1585, 1559, 1497, 1463, 1455, 1435, 1421, 1342, 1263, 1244, 1054, 851. HRMS (ESI) calculated for $C_{35}H_{23}N_3$: 486.1965; found: 486.1958.

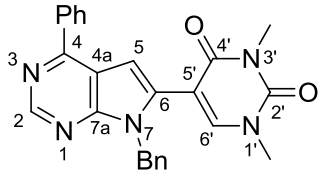
**7-Benzyl-4-phenyl-6-(pyridin-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-6-phenyl-8-(pyridin-2-yl)-7-deazapurine) (21d)**




Product **21d** (84 mg, 95%) was obtained as yellowish solid. Crystallization in hexan/EtOAc gave white crystals. M.p. 105-110 °C. $^1$H NMR (500 MHz, $CDCl_3$): 6.17 (s, 2H, $CH_2$); 7.02 (m, 2H, H-*o*-Bn); 7.10-7.16 (m, 3H, H-*m,p*-Bn); 7.17 (s, 1H, H-5); 7.25 (ddd, 1H, $J_{5,4}$ = 7.5, $J_{5,6}$ = 4.8, $J_{5,3}$ = 1.3, H-5-py); 7.52 (m, 1H, H-*p*-Ph); 7.56 (m, 2H, H-*m*-Ph); 7.63 (ddd, 1H, $J_{3,4}$ = 7.9, $J_{3,5}$ = 1.3, $J_{3,6}$ = 1.0, H-3-py); 7.70 (ddd, 1H, $J_{4,3}$ = 7.9, $J_{4,5}$ = 7.5, $J_{4,6}$ = 1.9, H-4-py); 8.16 (m, 2H, H-*o*-Ph); 8.70 (ddd, 1H, $J_{6,5}$ = 4.8, $J_{6,4}$ = 1.9, $J_{6,3}$ = 1.0, H-6-py); 9.03 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.28 ($CH_2$Ph); 102.08 (CH-5); 115.50 (C-4a); 122.86 (CH-5-py); 123.39 (CH-3-py); 127.04 (CH-*p*-Bn); 127.07 (CH-*o*-Bn); 128.26 (CH-*m*-Bn); 128.79 (CH-*m*-Ph); 128.83 (CH-*o*-Ph); 130.05 (CH-*p*-Ph); 136.76 (CH-4-py); 138.14 (C-*i*-Ph); 138.17 (C-*i*-Bn); 139.79 (C-6); 149.22 (CH-6-py); 151.12 (C-2-py); 152.31 (CH-2); 153.89 (C-7a); 157.68 (C-4). IR($CHCl_3$): 3066, 2985, 1587, 1566, 1497, 1462, 1442, 1348, 1323, 1272, 1248. HRMS (ESI) calculated for $C_{24}H_{18}N_4$: 363.1604; found: 363.1603. Anal. calculated for $C_{24}H_{18}N_4$ (362.43): C 79.54%, H 5.01%, N 15.46%, found: C 79.02%, H 4.92%, N 15.05%.

**5-(7-Benzyl-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)-1,3-dimethylpyrimidine 2,4(1*H*,3*H*)-dione**

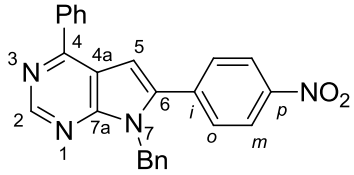
**(9-Benzyl-6-phenyl-8-(1,3-dimethyluracil-5-yl)-7-deazapurine) (21e)**




Product **21e** (95 mg, 92%) was obtained as white solid. Crystallization in hexan/EtOAc gave white crystals. M.p. 169-176 °C. $^{1}$H NMR (600 MHz, $CDCl_3$): 3.24 (s, 3H, $CH_3$-1′); 3.44 (s, 3H, $CH_3$-3′); 5.60 (s, 2H, $CH_2$); 6.83 (s, 1H, H-5); 6.92 (s, 1H, H-6′); 6.96 (m, 2H, H-*o*-Bn); 7.19-7.25 (m, 3H, H-*m*,*p*-Bn); 7.51 (m, 1H, H-*p*-Ph); 7.54 (m, 2H, H-*m*-Ph); 8.13 (m, 2H, H-*o*-Ph); 9.02 (s, 1H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): 28.36 ($CH_3$-3′); 37.10 ($CH_3$-1′); 46.42 ($CH_2$Ph); 102.69 (CH-5); 105.86 (C-5′); 115.22 (C-4a); 126.92 (CH-*o*-Bn); 127.44 (CH-*p*-Bn); 128.59 (CH-*m*-Bn); 128.76 and 128.80 (CH-*o*,*m*-Ph); 130.04 (CH-*p*-Ph); 134.11 (C-6); 137.91 (C-*i*-Bn); 138.06 (C-*i*-Ph); 143.58 (CH-6′); 151.09 (C-2′); 152.10 (CH-2); 153.22 (C-7a); 157.31 (C-4); 161.71 (C-4′). IR($CHCl_3$): 3029, 3013, 1710, 1661, 1585, 1565, 1497, 1464, 1456, 1442, 1433, 1342, 1249, 1232. HRMS (ESI) calculated for $C_{25}H_{21}N_5O_2$: 424.1768; found: 424.1764. Anal. calculated for $C_{25}H_{21}N_5O_2$ (423.47): C 70.91%, H 5.00%, N 16.54%, found: C 70.51%, H 4.87%, N 16.31%.

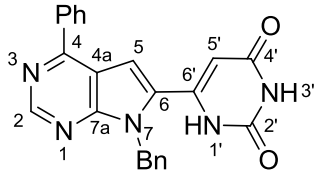
**7-Benzyl-6-(4-nitrophenyl)-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**(9-Benzyl-6-phenyl-8-(4-nitrophenyl)-7-deazapurine) (21f)**




Product **21f** (90 mg, 91%) was obtained as yellow solid. Crystallization in hexan/EtOAc gave yellow crystals. M.p. 212-219 °C $^{1}$H NMR (500 MHz, $CDCl_3$): 5.62 (s, 2H, $CH_2$); 6.96 (m, 2H, H-*o*-Bn); 7.03 (s, 1H, H-5); 7.22-7.26 (m, 3H, H-*m*,*p*-Bn); 7.53-7.60 (m, 5H, H-*m*,*p*-Ph, H-*o*-$C_6H_4NO_2$); 8.17 (m, 2H, H-*o*-Ph); 8.26 (m, 2H, H-*m*-$C_6H_4NO_2$); 9.06 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.45 ($CH_2$Ph); 102.67 (CH-5); 115.56 (C-4a); 123.93 (CH-*m*-$C_6H_4NO_2$); 126.43 (CH-*o*-Bn); 127.79 (CH-*p*-Bn); 128.86, 128.88 and 128.92 (CH-*m*-Bn and CH-*o*,*m*-Ph); 129.88 (CH-*o*-$C_6H_4NO_2$); 130.35 (CH-*p*-Ph); 136.93 (C-*i*-Bn); 137.87 (C-*i*-Ph and C-*i*-$C_6H_4NO_2$); 140.11 (C-6); 147.82 (C-*p*-$C_6H_4NO_2$); 152.58 (CH-2); 154.00 (C-7a); 158.01 (C-4). IR($CHCl_3$): 3032, 2987, 1602, 1585, 1566, 1522, 1497, 1485, 1463, 1454, 1442, 1421, 1348. HRMS (ESI) calculated for $C_{25}H_{18}N_4O_2$: 407.1503; found: 407.1499.

**6-(7-Benzyl-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)pyrimidine-2,4(1*H*,3*H*)-dione (9-Benzyl-6-phenyl-8-(uracil-6-yl)-7-deazapurine) (21g)**




The crude product after cross-coupling was directly deprotected by refluxing in 2 ml solution of THF: dioxane: HCl (1:1:1) for 2 hours. The reaction mixture was evaporated and ethanol (2 ml) was added. The mixture was then kept in a fridge overnight to furnish **21g** (79 mg, 83 %) as white crystals. M.p. >300 °C. $^{1}$H NMR (500 MHz, DMSO-$d_6$): 5.69 (t, 1H, 4J = 1.7, H-5´); 5.71 (s, 2H, $CH_2$); 6.99 (m, 2H, H-*o*-Bn); 7.24 (m, 1H, H-*p*-Bn); 7.29 (m, 2H, H-*m*-Bn); 7.54 (s, 1H, H-5); 7.59-7.65 (m, 3H, H-*m*,*p*-Ph); 8.26 (m, 2H, H-*o*-Ph); 9.01 (s, 1H, H-2); 11.25 (bs, 1H, NH-3´); 11.31 (bs, 1H, NH-1´). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 46.29 ($CH_2$Ph); 101.35 (CH-5´); 105.01 (CH-5); 114.02 (C-4a); 126.63 (CH-*o*-Bn); 127.81 (CH-*p*-Bn); 128.98 (CH-*m*-Bn); 129.07 (CH-*o*-Ph); 129.25 129.07 (CH-*m*-Ph); 131.04 (CH-*p*-Ph); 133.00 (C-6); 137.19 (C-*i*-Bn and C-*i*-Ph); 143.59 (C-6´); 151.53 (C-2´); 153.08 (CH-2); 153.57 (C-7a); 157.76 (C-4); 163.71 (C-4´). IR($CHCl_3$): 3417, 3146, 3031, 2805, 1711, 1687, 1637, 1585, 1496, 1457, 1415, 1347, 1262, 1221. HRMS (ESI) calculated for $C_{23}H_{17}N_5O_2$: 396.1455; found: 396.1451.

## General procedure for direct C-H arylation

DMF (3 mL) was added through a septum to an argon purged vial containing a 9-benzyl-6-phenyl-7-deazapurine **2** (143 mg, 0.5 mmol, 1 equiv.), $Pd(OAc)_2$ (5.6 mg, 0.025mmol, 5 mol %), CuI (286 mg, 1.5 mmol, 3 equiv.), Aryl halide (2 equiv.) and $Cs_2CO_3$ (408 mg, 1.25 mmol, 2.5 equiv.). Reaction mixture was heated to 160 °C for 60 h. The solvent was evaporated under reduced pressure. Products were isolated by flash column chromatography (gradient elution hexanes → ethyl acetate/hexanes 1:6).

**7-Benzyl-6-(4-methoxyphenyl)-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-6-phenyl-8-(4-methoxyphenyl)-7-deazapurine) (21a)**

Product **21a** (76 mg, 39%) was obtained as yellow solid. Crystallization in hexan/EtOAc gave yellowish crystals.

**7-Benzyl-4-phenyl-6-p-tolyl-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**(7-Benzyl-6-phenyl-8-p-tolyl-7-deazapurine) (21b)**

Product **21b** (77 mg, 41%) was obtained as yellow solid. Crystallization in hexan/EtOAc gave yellowish crystals.

**7-Benzyl-4-phenyl-6-(pyren-1-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-6-phenyl-8-(pyren-1-yl)-7-deazapurine) (21c)**

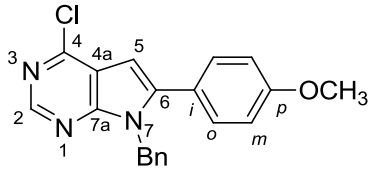
Product **21c** (85 mg, 35%) was obtained as yellow oil.

## 5.4.2 Two-step synthesis of 6,8-disubstituted 7-deazapurines – scope and limitations

**One pot C-H borylation - Suzuki coupling sequence. General procedure:**

9-Benzyl-6-chloro-7-deazapurine **7** (972 mg, 4 mmol, 1 equiv.), bispinacolatodiboron (1.524 g, 6.0 mmol, 1.5 equiv.), $[Ir(COD)OMe]_2$ (218 mg, 0.32 mmol, 8 mol %) and 4,4'-di-tert-butyl-2,2'-bipyridine (172 mg, 0.64 mmol, 16 mol %) were dissolved in dry THF (30 ml). The solution was heated at 80 °C in a septum-sealed vial and stirred under argon for 20 h. The solvent was removed under reduced pressure and the crude boronic ester was heated at 50 °C on vacuum line for 2 h to remove organic impurities. The crude boronic ester **14** was then combined with aryl halide (4.4 mmol, 1.1 equiv.), $Pd(dppf)Cl_2$ (146 mg, 0.2 mmol, 5 mol %) and $K_2CO_3$ (2211 mg, 16 mmol, 4 equiv.) in DMF (30 mL) and stirred under argon at 90 °C for 1 h. The solvent was evaporated and the residue was purified by silica gel flash chromatography to give products **22a-22c**.

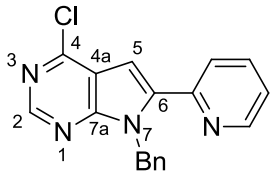
**7-Benzyl-4-chloro-6-(4-methoxyphenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-6-chloro-8-(4-methoxyphenyl)-7-deazapurine) (22a)**




Chromatography (hexane/EtOAc 7:1) was used to give product **22a** (586 mg, 42%) as white solid. Crystallization in hexan/EtOAc gave white crystals. M.p. 98-104 °C. $^1$H NMR (600 MHz, $CDCl_3$): 3.85 (s, 3H, $CH_3O$); 5.50 (s, 2H, $CH_2$); 6.61 (s, 1H, H-5); 6.938 (m, 2H, H-*m*-$C_6H_4OMe$); 6.942 (m, 2H, H-*o*-Bn); 7.20-7.25 (m, 3H, H-*m*,*p*-Bn); 7.30 (m, 2H, H-*o*-$C_6H_4OMe$); 8.65 (s, 1H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$):

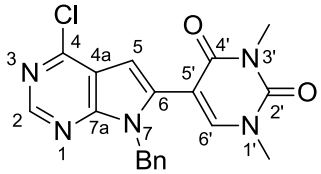
46.48 ($CH_2Ph$); 55.36 ($CH_3O$); 98.79 (CH-5); 114.19 (CH-*m*-$C_6H_4OMe$); 117.68 (C-4a); 122.98 (C-*i*-$C_6H_4OMe$); 126.54 (CH-*o*-Bn); 127.54 (CH-*p*-Bn); 128.67 (CH-*m*-Bn); 130.68 (CH-*o*-$C_6H_4OMe$); 137.04 (C-*i*-Bn); 143.25 (C-6); 150.56 (CH-2); 151.13 (C-4); 152.58 (C-7a); 160.38 (C-*p*-$C_6H_4OMe$). IR($CHCl_3$):3005, 2944, 1615, 1587, 1574, 1542, 1497, 1463, 1442, 1351, 1252, 1176, 1031, 935, 838. HRMS (ESI) calculated for $C_{20}H_{16}ClN_3O$: 350.1066; found: 350.1055. Anal. calculated for $C_{25}H_{20}N_4$ (349.81): C 68.67%, H 4.61%, N 12.01%, Cl 10.13%; found: C 68.57%, H 4.63%, N 11.85%, Cl 10.40 %.

**7-Benzyl-4-chloro-6-(pyridin-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-4-chloro-8-(pyridin-2-yl)-7-deazapurine) (22b)**




Chromatography (hexane/EtOAc 7:1) was used to give product **22b** (396 mg, 31%) as white solid. Crystallization in hexan/EtOAc gave white crystals. M.p. 153-154 °C. $^1$H NMR (600 MHz, $CDCl_3$): 3.85 (s, 3H, $CH_3O$); 5.50 (s, 2H, $CH_2$); 6.61 (s, 1H, H-5); 6.938 (m, 2H, H-*m*-$C_6H_4OMe$); 6.942 (m, 2H, H-*o*-Bn); 7.20-7.25 (m, 3H, H-*m*,*p*-Bn); 7.30 (m, 2H, H-*o*-$C_6H_4OMe$); 8.65 (s, 1H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): 46.48 ($CH_2Ph$); 55.36 ($CH_3O$); 98.79 (CH-5); 114.19 (CH-*m*-$C_6H_4OMe$); 117.68 (C-4a); 122.98 (C-*i*-$C_6H_4OMe$); 126.54 (CH-*o*-Bn); 127.54 (CH-*p*-Bn); 128.67 (CH-*m*-Bn); 130.68 (CH-*o*-$C_6H_4OMe$); 137.04 (C-*i*-Bn); 143.25 (C-6); 150.56 (CH-2); 151.13 (C-4); 152.58 (C-7a); 160.38 (C-*p*-$C_6H_4OMe$). IR($CHCl_3$): 3089, 3035, 3019, 3000, 1588, 1567, 1546, 1497, 1435, 1422, 1354, 1272, 1249, 1172, 937, 865. HRMS (ESI) calculated for $C_{18}H_{13}ClN_4$: 321.0902; found: 321.0903.

**5-(7-Benzyl-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione**
**(9-Benzyl-6-chloro-8-(1,3-dimethyluracil-5-yl)-7-deazapurine) (22c)**



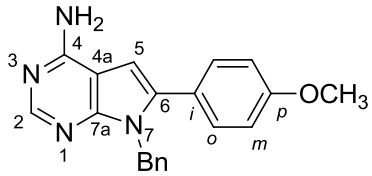

The residue was dissolved in 5 ml $CHCl_3$ and colorless crystals were formed and filtered off [excess of 5-iodo-1,3-dimethylpyrimidine-2,4(1H,3H)-dione]. The residual solution was purified by chromatography (hexane/EtOAc 7:1 to 1:1) to give product **22c** (548 mg, 36%) as white solid. M.p. 189-192 °C. $^1$H NMR (600 MHz, $CDCl_3$): 3.25 (s, 3H, $CH_3$-1′); 3.41 (s, 3H, $CH_3$-3′); 5.53 (s, 2H, $CH_2$); 6.57 (s, 1H, H-5); 6.89 (m, 2H,

H-*o*-Bn); 6.95 (s, 1H, H-6′); 7.17-7.21 (m, 3H, H-*m*,*p*-Bn); 8.66 (s, 1H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): 28.29 ($CH_3$-3′); 37.10 ($CH_3$-1′); 46.85 ($CH_2$Ph); 101.39 (CH-5); 105.25 (C-5′); 116.88 (C-4a); 126.86 (CH-*o*-Bn); 127.55 (CH-*p*-Bn); 128.56 (CH-*m*-Bn); 134.61 (C-6); 137.23 (C-*i*-Bn); 143.89 (CH-6′); 150.94 (C-2′); 151.10 (CH-2); 151.70 (C-4); 152.41 (C-7a); 161.46 (C-4′). IR($CDCl_3$): 3029, 3010, 2960, 2928, 1711, 1661, 1585, 1542, 1466, 1455, 1433, 1350, 1253, 1170, 909. HRMS (ESI) calculated for $C_{19}H_{16}ClN_5O_2$: 382.1065; found: 382.1064.

**Procedure for amination of 8-aryl-6-chloro-7-deazapurines**

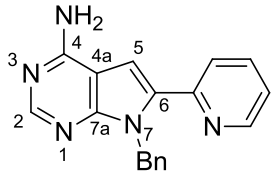
8-Aryl-9-benzyl-6-chloro-7-deazapurines **22a-22c** (0.5 mmol) were dissolved in 10-15 ml methanolic ammonia (saturated with $NH_3$ at 0 °C) and placed in an autoclave. The reaction mixture was heated at 120–130 °C overnight. The mixture was then cooled and the solvent was evaporated to provide the crude deaza adenines **23a-23c**. The residue was purified by silica gel flash chromatography (EtOAc/MeOH 20:1).

**4-Amino-7-benzyl-6-(4-methoxyphenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine (6-Amino-9-benzyl-8-(4-methoxyphenyl)-7-deazapurine) (23aa)**



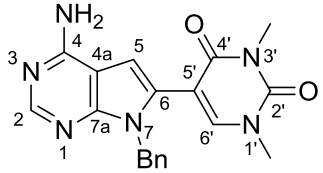

Product **23aa** (143 mg, 83%) was obtained as yellow foam. M.p. 158-162 °C. $^1$H NMR (500 MHz, $CDCl_3$): 3.83 (s, 3H, $CH_3O$); 5.44 (s, 2H, $CH_2$); 5.47 (bs, 2H, $NH_2$); 6.37 (s, 1H, H-5); 6.90 (m, 2H, H-*m*-$C_6H_4$OMe); 7.95 (m, 2H, H-*o*-Bn); 7.18-7.24 (m, 3H, H-*m*,*p*-Bn); 7.25 (m, 2H, H-*o*-$C_6H_4$OMe); 8.34 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.05 ($CH_2$Ph); 55.31 ($CH_3O$); 97.20 (CH-5); 103.20 (C-4a); 113.97 (CH-*m*-$C_6H_4$OMe); 123.99 (C-*i*-$C_6H_4$OMe); 126.44 (CH-*o*-Bn); 127.19 (CH-*p*-Bn); 128.53 (CH-*m*-Bn); 130.54 (CH-*o*-$C_6H_4$OMe); 137.84 (C-*i*-Bn); 138.85 (C-6); 151.25 (CH-2); 151.67 (C-7a); 156.02 (C-4); 159.78 (C-*p*-$C_6H_4$OMe). IR($CHCl_3$): 3523, 3414, 3009, 2967, 2840, 1619, 1589, 1562, 1550, 1497, 1467, 1455, 1350, 1302, 1291, 1252, 1177, 1031, 838. HRMS (ESI) calculated for $C_{20}H_{18}N_4O$: 331.1553; found: 331.1553.

**7-benzyl-6-(pyridin-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine (6-amino-9-benzyl-8-(pyridin-2-yl)-7-deazapurine) (23b)**



Product **23b** (128 mg, 85%) was obtained as yellowish foam. M.p. 195-199 °C. $^{1}$H NMR (500 MHz, $CDCl_3$): 5.65 (bs, 2H, $NH_2$); 6.05 (s, 2H, $CH_2$); 6.74 (s, 1H, H-5); 7.02 (m, 2H, H-*o*-Bn); 7.03-7.15 (m, 3H, H-*m*,*p*-Bn); 7.18 (ddd, 1H, $J_{5,4}$ = 7.6, $J_{5,6}$ = 4.9, $J_{5,3}$ = 1.2, H-5-py); 7.50 (ddd, 1H, $J_{3,4}$ = 7.9, $J_{3,5}$ = 1.2, $J_{3,6}$ = 1.0, H-3-py); 7.64 (ddd, 1H, $J_{4,3}$ = 7.9, $J_{4,5}$ = 7.6, $J_{4,6}$ = 1.8, H-4-py); 8.38 (s, 1H, H-2); 8.63 (ddd, 1H, $J_{6,5}$ = 4.9, $J_{6,4}$ = 1.8, $J_{6,3}$ = 1.0, H-6-py). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.34 ($CH_2$Ph); 99.70 (CH-5); 103.09 (C-4a); 122.22 (CH-5-py); 122.71 (CH-3-py); 126.87 (CH-*p*-Bn); 126.92 (CH-*o*-Bn); 128.18 (CH-*m*-Bn); 136.01 (C-6); 136.58 (CH-4-py); 138.48 (C-*i*-Bn); 149.05 (CH-6-py); 151.41 (C-2-py); 152.39 (CH-2); 152.62 (C-7a); 156.78 (C-4). IR($CHCl_3$): 3523, 3415, 3010, 2975, 2930, 2856, 1620, 1588, 1566, 1497, 1471, 1455, 1432, 1354, 1285, 1237. HRMS (ESI) calculated for $C_{18}H_{15}N_5$: 302.1400; found: 302.1401.

**5-(4-amino-7-benzyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione**
**(6-amino-9-benzyl-8-(1,3-dimethyluracil-5-yl)-7-deazapurine) (23c)**

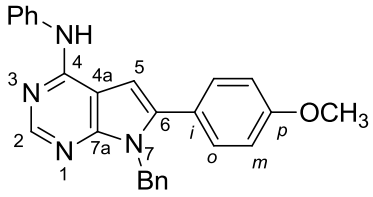


Product **23c** (143 mg, 79%) was obtained as brown foam. Crystallization in $CHCl_3$/hexane gave brownish crystals. M.p. 222-226 °C. $^{1}$H NMR (600 MHz, $CDCl_3$): 3.21 (s, 3H, $CH_3$-1′); 3.42 (s, 3H, $CH_3$-3′); 5.31 (bs, 2H, $NH_2$); 5.45 (s, 2H, $CH_2$); 6.38 (s, 1H, H-5); 6.82 (s, 1H, H-6′); 6.93 (m, 2H, H-*o*-Bn); 7.17-7.24 (m, 3H, H-*m*,*p*-Bn); 8.37 (s, 1H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): 28.35 ($CH_3$-3′); 37.04 ($CH_3$-1′); 46.38 ($CH_2$Ph); 100.15 (CH-5); 102.71 (C-4a); 105.94 (C-5′); 126.79 (CH-*o*-Bn); 127.31 (CH-*p*-Bn); 128.55 (CH-*m*-Bn); 129.53 (C-6); 138.23 (C-*i*-Bn); 143.36 (CH-6′); 151.16 (C-2′); 151.92 (C-7a); 152.36 (CH-2); 156.40 (C-4); 162.01 (C-4′). IR($CDCl_3$): 3527, 3416, 3020, 2983, 1708, 1661, 1620, 1588, 1563, 1545, 1470, 1454, 1370, 1349, 1340. HRMS (ESI) calculated for $C_{19}H_{18}N_6O_2$: 363.1564; found: 363.1563.

**Procedure for introduction of aryl/alkylamino group to 8-aryl-6-chloro-7-deazapurines**

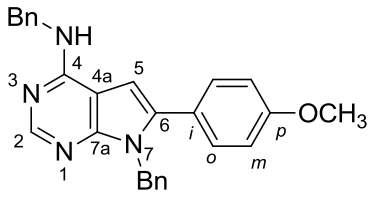
9-Benzyl-6-chloro-7-deazapurine **22a** (0.5 mmol) was refluxed with an amine (1.5 mmol) in 1-butanol (6 mL) overnight. The volatiles were evaporated in vacuum. The residue was purified by silica gel flash chromatography (hexane/EtOAc 3:1).

**7-benzyl-6-(4-methoxyphenyl)-*N*-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine (6-amino-9-benzyl-8-(4-methoxyphenyl)- *N*-phenyl-7-deazapurine) (23ab)**




Product **23ab** (132 mg, 65%) was obtained as white foam. Crystallization in hexane/EtOAc gave white crystals. M.p. 145-146 °C. $^{1}$H NMR (600 MHz, $CDCl_3$): 3.83 (s, 3H, $CH_3O$); 5.45 (s, 2H, $CH_2N$); 6.10 (s, 1H, H-5); 6.89 (m, 2H, H-*m*-$C_6H_4OMe$); 6.96 (m, 2H, H-*o*-Bn); 7.18 (m, 1H, H-*p*-Ph); 7.19-7.25 (m, 5H, H-*m*,*p*-Bn and H-*o*-$C_6H_4OMe$); 7.40 (m, 2H, H-*m*-Ph); 7.61 (m, 2H, H-*o*-Ph); 8.48 (s, 1H, H-2). $^{13}$C NMR (151 MHz, $CDCl_3$): 46.08 ($CH_2N$); 55.33 ($CH_3O$); 98.07 (CH-5); 103.65 (C-4a); 114.00 (CH-*m*-$C_6H_4OMe$); 122.55 (CH-*o*-Ph); 123.88 (C-*i*-$C_6H_4OMe$); 124.59 (CH-*p*-Ph); 126.51 (CH-*o*-Bn); 127.25 (CH-*p*-Bn); 128.57 (CH-*m*-Bn); 129.13 (CH-*m*-Ph); 130.56 (CH-*o*-$C_6H_4OMe$); 137.78 (C-*i*-Bn); 138.63 (C-*i*-Ph); 138.89 (C-6); 150.73 (CH-2); 152.04 (C-7a); 153.39 (C-4); 159.85 (C-*p*-$C_6H_4OMe$). IR($CHCl_3$):3034, 2966, 2929, 1650, 1608, 1584, 1564, 1497, 1468, 1455, 1292, 1252, 1177, 839. HRMS (ESI) calculated for $C_{26}H_{22}N_4O$: 407.1866; found: 407.1864. Anal. calculated for $C_{26}H_{22}N_4O$ (406.48): C 76.83%, H 5.46%, N 13.78%; found: C 79.50%, H 5.51%, N 13.56%.

**7-benzyl-4-(benzylamino)-6-(4-methoxyphenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (6-(benzylamino)-9-benzyl-8-(4-methoxyphenyl)-7-deazapurine) (23ac)**



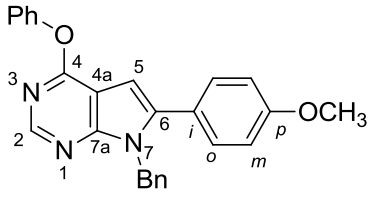

Product **23ac** (162 mg, 77%) was obtained as white foam. Crystallization in hexane/EtOAc gave white crystals. M.p. 145-149 °C. $^{1}$H NMR (500 MHz, $CDCl_3$): 3.82 (s, 3H, $CH_3O$); 4.88 (d, 2H, $J_{vic}$ = 5.6, C**H$_2$**NH); 5.31 (bs, 1H, NH); 5.44 (s, 2H, $CH_2N$); 6.33 (s, 1H, H-5); 6.88 (m, 2H, H-*m*-$C_6H_4OMe$); 6.95 (m, 2H, H-*o*-BnN); 7.16-7.22 (m, 3H, H-*m*,*p*-BnN); 7.22 (m, 2H, H-*o*-$C_6H_4OMe$); 7.30 (m, 1H, H-*p*-BnNH); 7.37 (m, 2H, H-*m*-BnNH); 7.42 (m, 2H, H-*o*-BnNH); 8.43 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 45.35 ($CH_2NH$); 46.02 ($CH_2N$); 55.31 ($CH_3O$); 97.09 (CH-5); 103.09 (C-4a); 113.98 (CH-*m*-$C_6H_4OMe$); 124.26 (C-*i*-$C_6H_4OMe$); 126.53 (CH-*o*-BnN); 127.14 (CH-*p*-BnN); 127.53 (CH-*p*-BnNH); 127.79 (CH-*o*-BnNH); 128.52 (CH-*m*-BnN); 128.76 (CH-*m*-BnNH); 130.53 (CH-*o*-$C_6H_4OMe$); 138.06 (C-*i*-BnN); 138.20 (C-6); 138.85 (C-*i*-BnNH); 151.42 (C-7a); 151.84 (CH-2); 155.77 (C-4); 159.73 (C-*p*-$C_6H_4OMe$). IR($CHCl_3$): 3010, 2966, 1654, 1601, 1564, 1497,

1467, 1454, 1343, 1291, 1251, 1177, 1030, 838. HRMS (ESI) calculated for $C_{27}H_{24}N_4O$: 421.2023; found: 421.2021. Anal. calculated for $C_{27}H_{24}N_4O$ (420.51): C 77.12%, H 5.75%, N 13.32%; found: C 76.92%, H 5.75%, N 13.23%.

**Procedure for introduction phenoxy group to 8-aryl-6-chloro-7-deazapurines**

A solution of phenol (57 mg, 0.6 mmol, 1.2 equiv.) in DMF (4 ml) was treated with KO*t*-Bu (67 mg, 0.6 mmol, 1.2 equiv.) and the mixture was stirred at rt for 2 h. The mixture was then treated with deazapurine **22a** (175 mg, 0.5 mmol, 1.0 equiv.) and $K_2CO_3$ (52 mg, 0.375 mmol, 0.75 equiv.) and heated at 110 °C for 16 h. The mixture was then cooled and the solvent was evaporated. Crude product was purified by silica gel flash chromatography (hexane/EtOAc 6:1→ 3:1) to give product **23ad** (162 mg, 77%) as white solid.

**7-Benzyl-6-(4-methoxyphenyl)-4-phenoxy-*7H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-8-(4-methoxyphenyl)-6-phenoxy-7-deazapurine) (23ad)**




M.p. 162-165 °C. $^1$H NMR (500 MHz, $CDCl_3$): 3.84 (s, 3H, $CH_3O$); 5.52 (s, 2H, $CH_2$); 6.50 (s, 1H, H-5); 6.93 (m, 2H, H-*m*-$C_6H_4$OMe); 6.99 (m, 2H, H-*o*-Bn); 7.20-7.32 (m, 8H, H-*o*,*p*-PhO, H-*m*,*p*-Bn and H-*o*-$C_6H_4$OMe); 7.47 (m, 2H, H-*m*-PhO); 8.50 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.30 ($CH_2$); 55.25 ($CH_3O$); 97.99 (CH-5); 105.84 (C-4a); 114.04 (CH-*m*-$C_6H_4$OMe); 121.75 (CH-*o*-PhO); 123.70 (C-*i*-$C_6H_4$OMe); 125.40 (CH-*p*-PhO); 126.52 (CH-*o*-Bn); 127.28 (CH-*p*-Bn); 128.53 (CH-*m*-Bn); 129.58 (CH-*m*-PhO); 130.60 (CH-*o*-$C_6H_4$OMe); 137.59 (C-*i*-Bn); 140.61 (C-6); 150.78 (CH-2); 153.00 (C-*i*-PhO); 154.28 (C-7a); 159.99 (C-*p*-$C_6H_4$OMe); 161.87 (C-4). IR($CHCl_3$): 3067, 3011, 2929, 2840, 1613, 1591, 1558, 1497, 1491, 1467, 1454, 1446, 1317, 1252, 1200, 1177, 1035, 838. HRMS (ESI) calculated for $C_{26}H_{21}N_3O$: 408.1718; found: 408.1706.

## 5.4.3 Synthesis of 8-aryl 7-deazahypoxantines and 8-aryl-7-deazaadenines

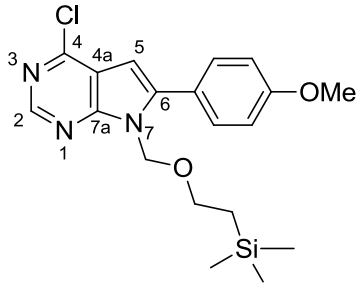
**One pot C-H borylation - Suzuki coupling sequence. General procedure:**

A 7-deazapurines **9-11** (4 mmol, 1 equiv.), bispinacolatodiboron (1.22 g, 4.8 mmol, 1.2 equiv.), $[Ir(COD)OMe]_2$ (132 mg, 0.2 mmol, 5 mol %) and 4,4'-di-tert-butyl-2,2'-bipyridine (108 mg, 0.4 mmol, 10 mol %) were dissolved in dry THF (30 ml) under Ar. The solution was heated at 80 °C in a septum sealed vial and stirred under argon for 20 h. The solvent was

removed under reduced pressure. The residue was then combined with aryl halide (4.4 mmol, 1.1 equiv.), Pd(dppf)$Cl_2$ (146 mg, 0.2 mmol, 5 mol %) and $K_2CO_3$ (2.2 g, 16 mmol, 4 equiv.) in DMF (30 mL) and stirred under Ar at 90 °C complete consumption of staring material (1-18 hours) as monitored by NMR. The solution was then cooled to room temperature, diluted with EtOAc (50 mL) and water (50 mL). Aqueous solution was then extracted three times with EtOAc and combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by flash chromatography in hexane/EtOAc.

**4-Chloro-6-(4-methoxyphenyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

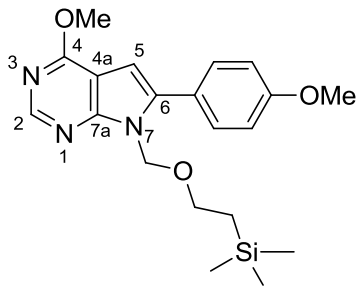
**6-Chloro-8-(4-methoxyphenyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (24a)**




Starting from **9** (1.14 g, 4 mmol) and 4-iodoanisole (1.03 g, 4.4 mmol), the reaction was performed according to the General procedure for 1 hour. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **24a** as yellowish oil (312 mg, 20%). $^1$H NMR (500 MHz, $CDCl_3$): -0.03 (s, 9H, $CH_3Si$); 0.96-0.99 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.72-3.76 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 3.88 (s, 3H, $CH_3O$); 5.61 (s, 2H, $NCH_2O$); 6.63 (s, 1H, H-5); 7.02-7.04 (m, 2H, H-*m*-Ph); 7.71-7.73 (m, 2H, H-*o*-Ph); 8.65 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 55.4 ($CH_3O$); 67.0 ($O\mathbf{C}H_2CH_2Si$); 71.0 ($NCH_2O$); 98.6 (CH-5); 114.3 (CH-*m*-Ph); 117.7 (C-4a); 122.8 (C-*i*-Ph); 130.9 (CH-*o*-Ph); 143.7 (C-6); 150.5 (CH-2); 151.0 (C-4); 153.4 (C-7a); 160.5 (C-*p*-Ph). IR (KBr): 2956, 2899, 2833, 1607, 1538, 1500, 1347, 1248, 1180, 1165, 1084, 857, 842. HRMS (ESI) calculated for $C_{19}H_{25}O_2N_3ClSi$: 390.1399; found: 390.1404.

**4-Methoxy-6-(4-methoxyphenyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

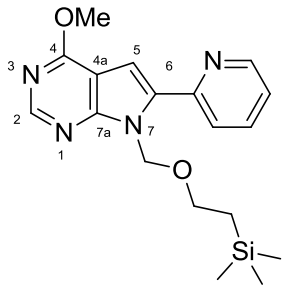
**6-Methoxy-8-(4-methoxyphenyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25a)**



Starting from **10** (1.12 g, 4 mmol) and 4-iodoanisole (1.03 g, 4.4 mmol), the reaction was performed according to the General procedure for 1 hour. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **25a** as yellowish oil (1.08 g, 70%). $^{1}$H NMR (500 MHz, $CDCl_3$): -0.03 (s, 9H, $CH_3Si$); 0.94-0.98 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.70-3.74 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 3.87 (s, 3H, $CH_3O$-*p*); 4.14 (s, 3H, $CH_3O$-4); 5.58 (s, 2H, $NCH_2O$); 6.56 (s, 1H, H-5); 6.99-7.01 (m, 2H, H-*m*-$C_6H_4OMe$); 7.67-7.68 (m, 2H, H-*o*-$C_6H_4OMe$); 8.49 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 53.7 ($CH_3O$-4); 55.3 ($CH_3O$-*p*); 66.6 ($O\mathbf{C}H_2CH_2Si$); 70.8 ($NCH_2O$); 97.8 (CH-5); 105.5 (C-4a); 114.2 (CH-*m*-$C_6H_4OMe$); 123.9 (C-*i*-$C_6H_4OMe$); 130.7 (CH-*o*-$C_6H_4OMe$); 140.2 (C-6); 150.7 (CH-2); 153.95 (C-7a); 160.0 (C-*p*-$C_6H_4OMe$); 162.5 (C-4). IR (KBr): 2995, 2950, 2893, 2833, 1613, 1595, 1565, 1500, 1476, 1419, 1353, 1320, 1284, 1251, 1213, 1183, 1072, 857, 839, 785, 764. HRMS (ESI) calculated for $C_{20}H_{27}O_3N_3NaSi$: 408.1714; found: 408.1714.

**4-Methoxy-6-(pyridin-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

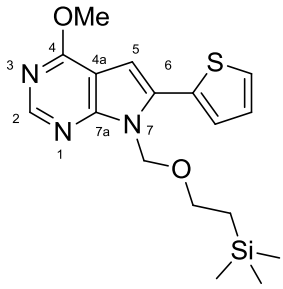
**6-Methoxy-8-(pyridin-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25b)**



Starting from **10** (1.12 g, 4 mmol) and 2-iodopyridine (0.47 mL, 4.4 mmol), the reaction was performed according to the General procedure for 18 hours. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **25b** as yellowish oil (713 g, 50%). $^{1}$H NMR (600.1 MHz, $CDCl_3$): -0.17 (s, 9H, $CH_3Si$); 0.79-0.82 (m, 2H, $SiC\mathbf{H_2}CH_2O$); 3.47-3.50 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.15 (s, 3H, $CH_3O$); 6.20 (s, 2H, $NCH_2O$); 6.95 (s, 1H, H-5); 7.27 (ddd, 1H, $J_{5,4}$ = 7.2, $J_{5,6}$ = 4.8, $J_{5,3}$ = 1.4, H-5-py); 7.77 (ddd, 1H, $J_{4,3}$ = 8.0, $J_{4,5}$ = 7.2, $J_{4,6}$ = 1.8, H-4-py); 7.80 (ddd, 1H, $J_{3,4}$ = 8.0, $J_{3,5}$ = 1.4, $J_{3,6}$ = 1.0, H-3-py); 8.45 (d, 1H, $J_{2,6}$ = 0.2, H-2); 8.69 (ddd, 1H, $J_{6,5}$ = 4.8, $J_{6,4}$ = 1.8, $J_{6,3}$ = 1.0, H-6-py). $^{13}$C NMR (150.9 MHz, $CDCl_3$): -1.6 ($CH_3Si$); 17.7 ($Si\mathbf{C}H_2CH_2O$); 53.8 ($CH_3O$); 66.1 ($O\mathbf{C}H_2CH_2Si$); 71.4 ($NCH_2O$); 101.1 (CH-5); 105.4 (C-4a); 122.5 (CH-5-py); 123.0 (CH-3-py); 136.8 (CH-4-py); 147.8 (C-6); 149.4 (CH-6-py); 151.3 (C-2-py); 151.8 (CH-2); 154.7 (C-7a); 163.2 (C-4). HRMS (ESI) calculated for $C_{18}H_{24}O_2N_4NaSi$: 379.1560; found: 379.1561.

**4-Methoxy-6-(thiophen-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

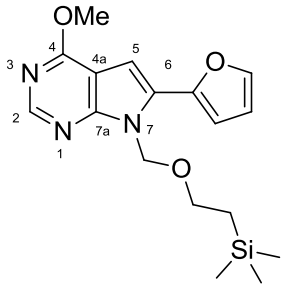
**6-Methoxy-8-(thiophen-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25c)**




Starting from **10** (1.12 g, 4 mmol) and 2-iodothiophene (0.49 mL, 4.4 mmol), the reaction was performed according to the General procedure for 1 hour. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **25c** as yellowish oil (939 mg, 65%). $^{1}$H NMR (500 MHz, $CDCl_3$): -0.05 (s, 9H, $CH_3Si$); 0.95-0.98 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.67-3.70 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.14 (s, 3H, $CH_3O$); 5.71 (s, 2H, $NCH_2O$); 6.72 (s, 1H, H-5); 7.13 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.6 Hz, H-4-thienyl); 7.39 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.59 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 8.49 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.9 ($OCH_2\mathbf{C}H_2Si$); 53.7 ($CH_3O$); 66.4 ($O\mathbf{C}H_2CH_2Si$); 70.7 ($NCH_2O$); 99.1 (CH-5); 105.4 (C-4a); 126.6 (CH-5-thienyl); 127.6 (CH-3-thienyl); 128.1 (CH-4-thienyl); 132.8 and 132.9 (C-6,C-2-thienyl); 151.2 (CH-2); 154.0 (C-7a); 162.7 (C-4). IR (KBr): 2956, 2896, 2866, 1595, 1553, 1473, 1458, 1413, 1356, 1344, 1320, 1248, 1207, 1081, 857, 833, 782, 764, 698. HRMS (ESI) calculated for $C_{17}H_{24}N_3O_2SiS$: 362.1359; found: 362.1370.

**6-(Furan-2-yl)-4-methoxy-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**8-(Furan-2-yl)-6-methoxy-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25d)**

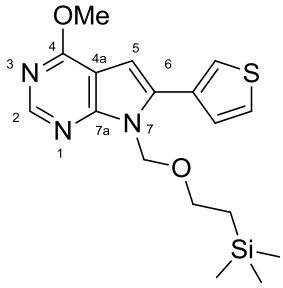



Starting from **10** (1.12 g, 4 mmol) and 2-bromofuran (0.39 mL, 4.4 mmol), the reaction was performed according to the General procedure for 18 hours. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **25d** as brown oil (621 mg, 45%). $^{1}$H NMR (500 MHz, $CDCl_3$): -0.08 (s, 9H, $CH_3Si$); 0.89-0.94 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.60-3.64 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.14 (s, 3H, $CH_3O$); 5.79 (s, 2H, $NCH_2O$); 6.53 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.84 (s, 1H, H-5); 6.93 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.8 Hz, H-3-furyl); 7.54 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.8 Hz, H-5-furyl); 8.48 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 53.7 ($CH_3O$); 66.4 ($O\mathbf{C}H_2CH_2Si$); 70.7 ($NCH_2O$); 99.1 (CH-5); 105.4 (C-4a); 126.6 (CH-5-thienyl); 127.6 (CH-3-thienyl); 128.1 (CH-4-thienyl); 132.8 and 132.9 (C-6,C-2-

thienyl); 151.2 (CH-2); 154.0 (C-7a); 162.7 (C-4). IR (KBr): 2956, 2929, 2866, 2848, 1595, 1589, 1565, 1476, 1461, 1419, 1353, 1329, 1248, 1216, 1090, 866, 839, 776. HRMS (ESI) calculated for $C_{17}H_{23}O_3N_3NaSi$: 368.1401; found: 368.1401.

**4-Methoxy-6-(thiophen-3-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

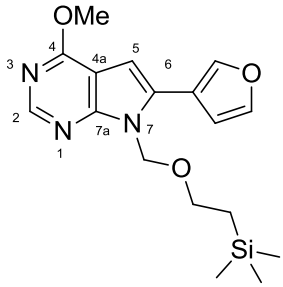
**6-Methoxy-8-(thiophen-3-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25e)**




Starting from **10** (1.12 g, 4 mmol) and 3-iodothiophene (0.45 mL, 4.4 mmol), the reaction was performed according to the General procedure for 1 hour. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **25e** as yellowish solid (1.11 g, 77%). M. p. 55°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.04 (s, 9H, $CH_3Si$); 0.96-0.99 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.72-3.76 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.18 (s, 3H, $CH_3O$); 5.70 (s, 2H, $NCH_2O$); 6.69 (s, 1H, H-5); 7.43 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.46 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 7.88 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 8.51 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 54.3 ($CH_3O$); 66.5 ($O\mathbf{C}H_2CH_2Si$); 70.9 ($NCH_2O$); 98.1 (CH-5); 105.3 (C-4a); 124.4 (CH-2-thienyl); 126.3 (CH-5-thienyl); 128.2 (CH-4-thienyl); 131.6 (C-3-thienyl); 135.6 (C-6); 150.2 (CH-2); 153.4 (C-7a); 162.4 (C-4). IR (KBr): 3102, 2953, 2902, 2857, 1601, 1571, 1562, 1470, 1413, 1392, 1347, 1317, 1299, 1257, 1230, 1204, 1078, 1054, 946, 925, 863, 836, 812, 779, 764. HRMS (ESI) calculated for $C_{17}H_{24}N_3O_2SiS$: 362.1359; found: 362.1346.

**6-(Furan-3-yl)-4-methoxy-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**8-(Furan-3-yl)-6-methoxy-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25f)**

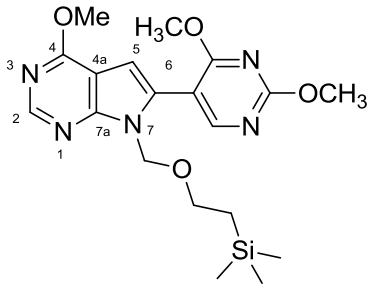



Starting from **10** (1.12 g, 4 mmol) and 3-bromofuran (0.4 mL, 4.4 mmol), the reaction was performed according to the General procedure for 1 hour. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **25f** as brown oil (802 mg, 58%). $^1$H NMR (500 MHz, $CDCl_3$): -0.05 (s, 9H, $CH_3Si$); 0.93-0.96 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.65-3.68 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.13 (s,

3H, $CH_3O$); 5.67 (s, 2H, $NCH_2O$); 6.62 (s, 1H, H-5); 6.77 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.51 (t, 1H, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, H-5-furyl); 7.99 (dd, 1H, $J_{2,5}$ = 1.5 Hz, $J_{2,4}$ = 0.9 Hz, H-2-furyl); 8.47 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 18.0 ($OCH_2$**C**$H_2Si$); 53.7 ($CH_3O$); 66.3 (O**C**$H_2CH_2Si$); 70.6 ($NCH_2O$); 97.5 (CH-5); 105.4 (C-4a); 110.5 (CH-4-furyl); 116.8 (C-3-furyl); 131.7 (C-6); 141.0 (CH-2-furyl); 143.5 (CH-5-furyl); 150.8 (CH-2); 153.9 (C-7a); 162.5 (C-4). IR (KBr): 2947, 2893, 1769, 1598, 1559, 1476, 1419, 1329, 1251, 1213, 1081, 875, 857, 836, 779, 761. HRMS (ESI) calculated for $C_{17}H_{24}N_3O_3Si$: 346.1587; found: 346.1589.

**4-Methoxy-6-(2,4-dimethoxypyrimidin-5-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**6-Methoxy-8-(2,4-dimethoxypyrimidin-5-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25g)**




Starting from **10** (1.12 g, 4 mmol) and 5-iodo-2,4-dimethoxypyrimidine (1.17 g, 4.4 mmol), the reaction was performed according to the General procedure for 18 hours. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **25g** as yellowish solid (1.1 g, 66%). M.p. 79°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.11 (s, 9H, $CH_3Si$); 0.79-0.83 (m, 2H, $OCH_2C$**H$_2$**Si); 3.45-3.48 (m, 2H, O**C**$H_2CH_2Si$); 4.00 (s, 3H, $CH_3O$-4′); 4.06 (s, 3H, $CH_3O$-2′); 4.13 (s, 3H, $CH_3O$-4); 5.53 (s, 2H, $NCH_2O$); 6.61 (s, 1H, H-5); 8.44 (s, 1H, H-6′); 8.50 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.6 ($CH_3Si$); 17.8 ($OCH_2$**C**$H_2Si$); 53.7 ($CH_3O$-4); 54.3 ($CH_3O$-2′); 55.1 ($CH_3O$-4′); 66.3 (O**C**$H_2CH_2Si$); 71.2 ($NCH_2O$); 101.4 (CH-5); 105.4 (C-4a); 107.1 (C-5′); 130.8 (C-6); 151.4 (CH-2); 153.8 (C-7a); 159.8 (CH-6′); 162.8 (C-4); 165.5 (C-2′); 168.8 (C-4′). IR (KBr): 2986, 2956, 2896, 2866, 1610, 1598, 1473, 1380, 1356, 1320, 1290, 1251, 1213, 1078, 1018, 866, 833. HRMS (ESI) calculated for $C_{19}H_{28}N_5O_4Si$: 418.1911; found: 418.1898.

**6-(3-Aminophenyl)-4-methoxy-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**8-(3-Aminophenyl)-6-methoxy-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25h)**

Starting from **10** (1.12 g, 4 mmol) and 3-iodoaniline (0.53 mL, 4.4 mmol), the reaction was performed according to the General procedure for 1 hour. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **25h** as yellowish solid (1.1 g, 74%). M.p. 113°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.04 (s, 9H, $CH_3Si$); 0.93-0.96 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.69-3.73 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.14 (s, 3H, $CH_3O$); 5.61 (s, 2H, $NCH_2O$); 6.61 (s, 1H, H-5); 6.83 (ddd, 1H, $J_{6',5'}$ = 8.0 Hz, $J_{6',2'}$ = 2.4 Hz, $J_{6',4'}$ = 1.0 Hz, H-6′); 7.14 (m, 1H, H-2′); 7.19 (ddd, 1H, $J_{4',5'}$ = 7.6 Hz, $J_{4',2'}$ = 1.6 Hz, $J_{4',6'}$ = 1.0 Hz, H-4′); 7.27 (t, 1H, $J_{5',4'} = J_{5',6'}$ = 7.8 Hz, H-5′); 8.50 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 53.8 ($CH_3O$); 66.6 ($O\mathbf{C}H_2CH_2Si$); 70.9 ($NCH_2O$); 98.5 (CH-5); 105.5 (C-4a); 116.0 (CH-6′); 116.4 (CH-2′); 120.6 (CH-4′); 129.7 (CH-5′); 132.5 (C-3′); 140.3 (C-6); 145.2 (C-1′); 150.9 (CH-2); 154.0 (C-7a); 162.7 (C-4). IR (KBr): 3434, 3318, 3207, 2956, 1592, 1556, 1476, 1329, 1207, 1072, 1057, 866, 842, 797. HRMS (ESI) calculated for $C_{19}H_{27}O_2N_4Si$: 371.1899; found: 371.1898.

**4-(Methylsulfanyl)-6-(4-methoxyphenyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

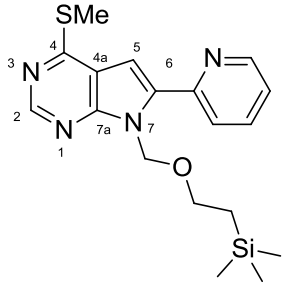
**6-(Methylsulfanyl)-8-(4-methoxyphenyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (26a)**

Starting from **11** (1.18 g, 4 mmol), 4-iodoanisole (1.03 g, 4.4 mmol) and Pd(dppf)$Cl_2$ (292 mg, 0.4 mmol, 10 mol %), the reaction was performed according to the General procedure for 1 hour. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **26a** as yellowish solid (1.27 g, 79%). M.p. 144°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.03 (s, 9H, $CH_3Si$); 0.95-0.98 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 2.72 (s, 3H, $CH_3S$); 3.71-3.74 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 3.87 (s, 3H, $CH_3O$); 5.58 (s, 2H, $NCH_2O$); 6.54 (s, 1H, H-5); 7.00-7.01 (m, 2H, H-*m*-Ph); 7.69-7.71 (m, 2H, H-*o*-Ph); 8.69 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 11.9 ($CH_3S$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 55.4 ($CH_3O$); 66.7 ($O\mathbf{C}H_2CH_2Si$); 70.6 ($NCH_2O$); 98.3 (CH-5); 114.2 (CH-*m*-Ph); 116.1 (C-4a); 123.5 (C-*i*-Ph); 130.7 (CH-*o*-Ph); 141.3 (C-6); 150.4 (C-7a); 150.8 (CH-2); 160.1 (C-*p*-Ph); 160.4 (C-4). IR (KBr): 3066, 2953, 2902, 2842, 1616,

1503, 1422, 1344, 1317, 1263, 1248, 1192, 1141, 1126, 1078, 1057, 863, 851, 836, 755, 534. HRMS (ESI) calculated for $C_{20}H_{27}O_2N_3NaSSi$: 424.1486; found: 424.1486.

**4-(Methylsulfanyl)-6-(pyridin-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

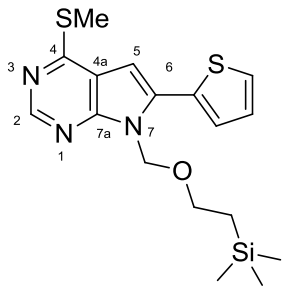
**6-(Methylsulfanyl)-8-(pyridin-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (26b)**




Starting from **11** (1.18 g, 4 mmol), 2-iodopyridine (0.47 mL, 4.4 mmol) and Pd(dppf)$Cl_2$ (292 mg, 0.4 mmol, 10 mol %), the reaction was performed according to the General procedure for 18 hours. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **26b** as yellowish oil (954 mg, 64%). $^1$H NMR (500 MHz, $CDCl_3$): -0.16 (s, 9H, $CH_3Si$); 0.80-0.83 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 2.73 (s, 3H, $CH_3S$); 3.48-3.51 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 6.17 (s, 2H, $NCH_2O$); 6.94 (s, 1H, H-5); 7.28 (ddd, 1H, $J_{5,4}$ = 7.5 Hz, $J_{5,6}$ = 4.8 Hz, $J_{5,3}$ = 1.2 Hz, H-5-py); 7.79 (btd, 1H, $J_{4,5}$ = $J_{4,3}$ = 7.7 Hz, $J_{4,6}$ = 1.8 Hz, H-4-py); 7.85 (dt, 1H, $J_{3,4}$ = 8.0 Hz, $J_{3,5}$ = $J_{3,6}$ = 1.1 Hz, H-3-py); 8.70 (ddd, 1H, $J_{6,5}$ = 4.8 Hz, $J_{6,4}$ = 1.8 Hz, $J_{6,3}$ = 1.0 Hz, H-6-py); 8.72 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.6 ($CH_3Si$); 11.9 ($CH_3S$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 66.3 ($O\mathbf{C}H_2CH_2Si$); 71.2 ($NCH_2O$); 101.4 (CH-5); 115.8 (C-4a); 122.8 (CH-5-py); 123.3 (CH-3-py); 136.8 (CH-4-py); 138.2 (C-6); 149.5 (CH-6-py); 150.9 and 151.1 (C-7a, C-2-py); 151.7 (CH-2); 161.9 (C-4). IR (KBr): 3052, 2953, 2932, 2893, 1589, 1556, 1455, 1443, 1416, 1350, 1269, 1251, 1177, 1075, 937, 917, 860, 836, 770. HRMS (ESI) calculated for $C_{18}H_{24}N_4OSSi$: 372.1440; found: 372.1442.

**4-(Methylsulfanyl)-6-(thiophen-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

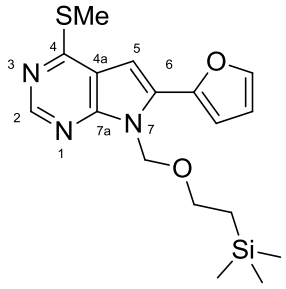
**6-(Methylsulfanyl)-8-(thiophen-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (26c)**



Starting from **11** (1.18 g, 4 mmol), 2-iodothiophene (0.49 mL, 4.4 mmol) and Pd(dppf)$Cl_2$ (292 mg, 0.4 mmol, 10 mol %), the reaction was performed according to the General procedure for 1 hour. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **26c** as yellowish solid (1.05 g, 69%). M.p. 92°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.04 (s, 9H, $CH_3Si$); 0.95-0.98 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 2.72 (s, 3H, $CH_3S$); 3.67-3.71 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.72 (s, 2H, $NCH_2O$); 6.69 (s, 1H, H-5); 7.15 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.7 Hz, H-4-thienyl); 7.42 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.63 (dd, 1H, $J_{3,4}$ = 3.7 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 8.68 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 11.9 ($CH_3S$); 17.9 ($OCH_2\mathbf{C}H_2Si$); 66.5 ($O\mathbf{C}H_2CH_2Si$); 70.5 ($NCH_2O$); 99.4 (CH-5); 115.9 (C-4a); 127.1 (CH-5-thienyl); 128.0 (CH-3-thienyl); 128.2 (CH-4-thienyl); 132.5 (C-2-thienyl); 134.0 (C-6); 150.5 (C-7a); 151.2 (CH-2); 160.9 (C-4). IR (KBr): 3081, 3066, 2953, 2926, 2893, 1559, 1485, 1458, 1440, 1407, 1356, 1260, 1248, 1174, 1057, 928, 854, 839, 785, 755, 728. HRMS (ESI) calculated for $C_{17}H_{24}ON_3S_2Si$: 378.1125; found: 378.1126.

**6-(Furan-2-yl)-4-(methylsulfanyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**8-(Furan-2-yl)-6-(methylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (26d)**

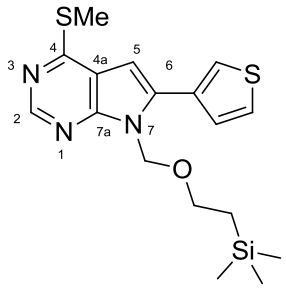


Starting from **11** (1.18 g, 4 mmol), 2-bromofuran (0.39 mL, 4.4 mmol) and Pd(dppf)$Cl_2$ (292 mg, 0.4 mmol, 10 mol %), the reaction was performed according to the General procedure for 1 hour. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **26d** as yellowish solid (897 mg, 62%). M.p. 100°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.07 (s, 9H, $CH_3Si$); 0.91-0.94 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 2.73 (s, 3H, $CH_3S$); 3.60-3.64 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.80 (s, 2H, $NCH_2O$); 6.55 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.83 (s, 1H, H-5); 6.98 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.8 Hz, H-3-furyl); 7.56 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.8 Hz, H-5-furyl); 8.67 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 11.9 ($CH_3S$); 17.8 ($OCH_2\mathbf{C}H_2Si$); 66.3 ($O\mathbf{C}H_2CH_2Si$); 70.9 ($NCH_2O$); 97.7 (CH-5); 110.1 (CH-3-furyl); 111.9 (CH-4-furyl); 115.9 (C-4a); 130.8 (C-6); 143.3 (CH-5-furyl); 145.6 (C-2-furyl); 150.4 (C-7a); 151.1 (CH-2); 161.2

(C-4). IR (KBr): 2944, 2923, 2893, 2872, 1562, 1524, 1464, 1443, 1425, 1407, 1344, 1269, 1248, 1213, 1186, 1162, 1075, 1015, 946, 928, 866, 833, 770, 761, 734. HRMS (ESI) calculated for $C_{17}H_{24}O_2N_3SSi$: 362.1353; found: 362.1354.

**4-(Methylsulfanyl)-6-(thiophen-3-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

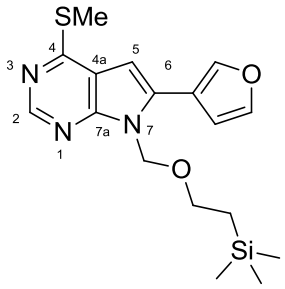
**6-(Methylsulfanyl)-8-(thiophen-3-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (26e)**




Starting from **11** (1.18 g, 4 mmol), 3-iodothiophene (0.45 mL, 4.4 mmol) and Pd(dppf)$Cl_2$ (292 mg, 0.4 mmol, 10 mol %), the reaction was performed according to the General procedure for 18 hours. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **26e** as yellowish solid (1.06 g, 70%). M.p. 99°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.03 (s, 9H, $CH_3Si$); 0.96-1.00 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 2.73 (s, 3H, $CH_3S$); 3.72-3.75 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.68 (s, 2H, $NCH_2O$); 6.64 (s, 1H, H-5); 7.44 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.49 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 7.91 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 8.68 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 11.9 ($CH_3S$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 66.6 ($O\mathbf{C}H_2CH_2Si$); 70.5 ($NCH_2O$); 98.4 (CH-5); 115.9 (C-4a); 124.7 (CH-2-thienyl); 126.3 (CH-5-thienyl); 128.2 (CH-4-thienyl); 131.5 (C-3-thienyl); 136.2 (C-6); 150.3 (C-7a); 150.9 (CH-2); 160.7 (C-4). IR (KBr): 3102, 3043, 2953, 2920, 2896, 2863, 1550, 1461, 1347, 1269, 1242, 1177, 1081, 917, 860, 836, 776. HRMS (ESI) calculated for $C_{17}H_{23}N_3OSiS_2$: 377.1052; found: 377.1053.

**6-(Furan-3-yl)-4-(methylsulfanyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

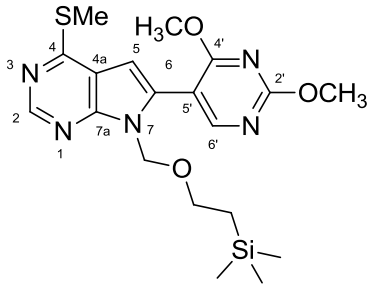
**8-(Furan-3-yl)-6-(methylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (26f)**



Starting from **11** (1.18 g, 4 mmol), 3-bromofuran (0.4 mL, 4.4 mmol) and Pd(dppf)$Cl_2$ (292 mg, 0.4 mmol, 10 mol %), the reaction was performed according to the General procedure for 18 hours. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **26f** as yellowish solid (721 mg, 50%). $^1$H NMR (500 MHz, $CDCl_3$): -0.05 (s, 9H, $CH_3Si$); 0.94-0.97 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 2.73 (s, 3H, $CH_3S$); 3.65-3.68 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.67 (s, 2H, $NCH_2O$); 6.60 (s, 1H, H-5); 6.80 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.53 (bt, 1H, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, H-5-furyl); 8.02 (dd, 1H, $J_{2,5}$ = 1.6 Hz, $J_{2,4}$ = 0.9 Hz, H-2-thienyl); 8.67 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 12.0 ($CH_3S$); 17.9 ($OCH_2\mathbf{C}H_2Si$); 66.4 ($O\mathbf{C}H_2CH_2Si$); 70.4 ($NCH_2O$); 97.9 (CH-5); 110.5 (CH-4-furyl); 116.0 (C-4a); 116.6 (C-3-furyl); 132.9 (C-6); 141.4 (CH-2-furyl); 143.6 (CH-5-furyl); 150.4 (C-7a); 150.9 (CH-2); 160.5 (C-4). HRMS (ESI) calculated for $C_{17}H_{23}N_3O_2SSi$: 361.1280; found: 361.1278.

**4-(Methylsulfanyl)-6-(2,4-dimethoxypyrimidin-5-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

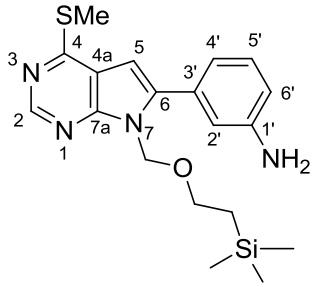
**6-(Methylsulfanyl)-8-(2,4-dimethoxypyrimidin-5-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (26g)**



Starting from **11** (1.18 g, 4 mmol), 5-iodo-2,4-dimethoxypyrimidine (1.17 g, 4.4 mmol) and Pd(dppf)$Cl_2$ (292 mg, 0.4 mmol, 10 mol %), the reaction was performed according to the General procedure for 18 hours. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **26g** as white solid (676 mg, 39%). M.p. 134°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.10 (s, 9H, $CH_3Si$); 0.80-0.83 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 2.72 (s, 3H, $CH_3S$); 3.45-3.48 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.01 (s, 3H, $CH_3O$-4′); 4.07 (s, 3H, $CH_3O$-2′); 5.53 (s, 2H, $NCH_2O$); 6.59 (s, 1H, H-5); 8.45 (s, 1H, H-6′); 8.70 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 11.9 ($CH_3S$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 54.4 ($CH_3O$-4′); 55.2 ($CH_3O$-2′); 66.4 ($O\mathbf{C}H_2CH_2Si$); 71.0 ($NCH_2O$); 101.8 (CH-5); 106.8 (C-5′); 115.9 (C-4a); 132.0 (C-6); 150.1 (C-7a); 151.3 (CH-2); 159.8 (CH-6′); 161.3 (C-4); 165.6 (C-2′); 168.7 (C-4′). IR (KBr): 2953, 2932, 1613, 1568, 1553, 1476, 1407, 1377, 1302, 1248, 1189, 1078, 1066, 863, 842. HRMS (ESI) calculated for $C_{19}H_{27}N_5O_3SSi$: 433.1604; found: 433.1602.

**6-(3-Aminophenyl)-4-(methylsulfanyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**8-(3-Aminophenyl)-6-(methylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (26h)**



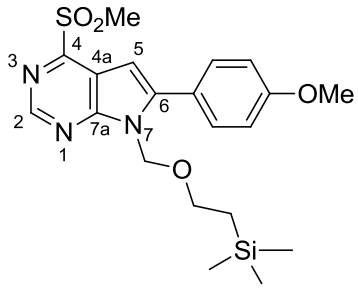

Starting from **11** (1.18 g, 4 mmol), 3-iodoaniline (0.53 mL, 4.4 mmol) and Pd(dppf)$Cl_2$ (292 mg, 0.4 mmol, 10 mol %), the reaction was performed according to the General procedure for 1 hour. Purification was performed by HPFC (hexane/EtOAc, 0–20% EtOAc) to give product **26h** as yellowish solid (1.21 g, 78%). M.p. 109°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.03 (s, 9H, $CH_3Si$); 0.93-0.97 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 2.73 (s, 3H, $CH_3S$); 3.70-3.73 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.61 (s, 2H, $NCH_2O$); 6.58 (s, 1H, H-5); 6.75 (ddd, 1H, $J_{6',5'}$ = 8.0 Hz, $J_{6',2'}$ = 2.4 Hz, $J_{6',4'}$ = 1.0 Hz, H-6′); 7.07-7.08 (m, 1H, H-2′); 7.13 (ddd, 1H, $J_{4',5'}$ = 7.6 Hz, $J_{4',2'}$ = 1.7 Hz, $J_{4',6'}$ = 0.9 Hz, H-4′); 7.25 (t, 1H, $J_{5',4'} = J_{5',6'}$ = 7.8 Hz, H-5′); 8.70 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 11.9 ($CH_3S$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 66.7 ($O\mathbf{C}H_2CH_2Si$); 70.7 ($NCH_2O$); 98.9 (CH-5); 115.6 and 115.7 (CH-2′,6′); 116.0 (C-4a); 119.7 (CH-4′); 129.7 (CH-5′); 132.1 (C-3); 141.6 (C-6); 146.6 (C-1′); 150.4 (C-7a); 150.8 (CH-2); 160.7 (C-4). IR (KBr): 3324, 2950, 1610, 1553, 1538, 1479, 1464, 1437, 1353, 1251, 1171, 1060, 851, 833, 785. HRMS (ESI) calculated for $C_{19}H_{27}ON_4SSi$: 387.1669; found: 387.1670.

**Oxidation to sulfones. General procedure:**

A 6-MeS-7-deazapurine **26a-h, 26l** (2 mmol, 1 equiv.) was dissolved in DCM (10 mL) and *m*-CPBA (900 mg, 4 mmol, 2 equiv.) was slowly added (water/ice bath during addition) and the reaction mixture was stirred at r.t. overnight. Then 1M NaOH (10 mL) was added to the mixture to remove residual *m*-CPBA. The layers were separated and the aqueous layer was extracted two times with DCM (25 mL). The combined organic layers were dried over sodium sulphate, solvents were evaporated and the residue was purified by flash chromatography (HPFC) in $CHCl_3$/MeOH (20:1).

**4-(Methylsulfonyl)-6-(4-methoxyphenyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

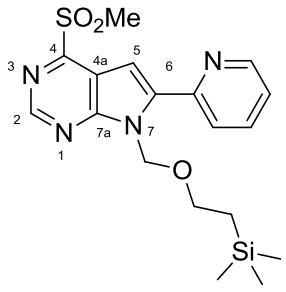
**6-(Methylsulfonyl)-8-(4-methoxyphenyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (29a)**



Starting from deazapurine **26a** (803 mg, 2 mmol) and *m*-CPBA (900 mg, 4 mmol), the reaction was performed according to the General procedure to give product **29a** (668 mg, 77%) as white solid. M.p. 147°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.01 (s, 9H, $CH_3Si$); 0.98-1.01 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.36 (s, 3H, $CH_3SO_2$); 3.74-3.78 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 3.89 (s, 3H, $CH_3O$); 5.67 (s, 2H, $NCH_2O$); 7.03-7.05 (m, 2H, H-*m*-Ph); 7.14 (s, 1H, H-5); 7.77-7.78 (m, 2H, H-*o*-Ph); 8.95 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 40.1 ($CH_3SO_2$); 55.4 $CH_3O$); 67.2 ($O\mathbf{C}H_2CH_2Si$); 70.9 ($NCH_2O$); 99.0 (CH-5); 114.4 (CH-*m*-Ph); 114.5 (C-4a); 122.3 (C-*i*-Ph); 131.0 (CH-*o*-Ph); 147.1 (C-6); 149.9 (CH-2); 153.8 (C-4); 156.0 (C-7a); 160.9 (C-*p*-Ph). IR (KBr): 3132, 3010, 2953, 2929, 2899, 1473, 1413, 1344, 1302, 1245, 1174, 1138, 1123, 1066, 1015, 869, 845, 782, 755, 761, 537. HRMS (ESI) calculated for $C_{20}H_{27}O_4N_3NaSSi$: 456.1384; found: 456.1384.

**4-(Methylsulfonyl)-6-(pyridin-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**6-(Methylsulfonyl)-8-(pyridin-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (29b)**

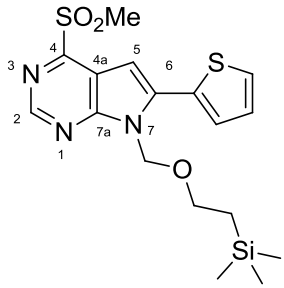


Starting from deazapurine **26b** (745 mg, 2 mmol) and *m*-CPBA (900 mg, 4 mmol), the reaction was performed according to the General procedure to give product **29b** (528 mg, 65%) as white solid. M.p. 109°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.17 (s, 9H, $CH_3Si$); 0.78-0.80 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.37 (s, 3H, $CH_3SO_2$); 3.44-3.47 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 6.34 (s, 2H, $NCH_2O$); 7.37 (ddd, 1H, $J_{5,4}$ = 7.5 Hz, $J_{5,6}$ = 4.8 Hz, $J_{5,3}$ = 1.2 Hz, H-5-py); 7.48 (s, 1H, H-5); 7.85 (btd, 1H, $J_{4,5} = J_{4,3}$ = 7.7 Hz, $J_{4,6}$ = 1.8 Hz, H-4-py); 7.91 (dt, 1H, $J_{3,4}$ = 7.9 Hz, $J_{3,5} = J_{3,6}$ = 1.1 Hz, H-3-py); 8.75 (ddd, 1H, $J_{6,5}$ = 4.8 Hz, $J_{6,4}$ = 1.8 Hz, $J_{6,3}$ = 0.9 Hz, H-6-py); 9.01 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.6 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 40.0 ($CH_3SO_2$); 66.7 ($O\mathbf{C}H_2CH_2Si$); 71.7 ($NCH_2O$); 101.9 (CH-5); 113.8 (C-4a); 123.8 (CH-5-py); 124.0 (CH-3-py); 137.1 (CH-4-py); 143.2 (C-6);

149.6 (CH-6-py); 150.1 (C-2-py); 151.0 (CH-2); 155.5 (C-4); 156.2 (C-7a). IR (KBr): 2950, 2899, 1476, 1347, 1323, 1302, 1248, 1135, 1063, 1051, 863, 791, 767, 528. HRMS (ESI) calculated for $C_{18}H_{24}N_4O_3SiS$: 404.1338; found: 404.1335.

**4-(Methylsulfonyl)-6-(thiophen-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

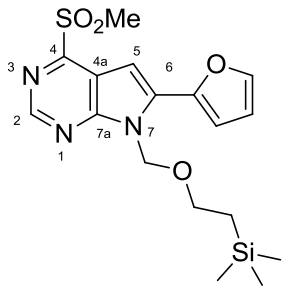
**6-(Methylsulfonyl)-8-(thiophen-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (29c)**




Starting from deazapurine **26c** (755 mg, 2 mmol) and *m*-CPBA (900 mg, 4 mmol), the reaction was performed according to the General procedure to give product **29c** (717 mg, 89%) as yellow solid. M.p. 107°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.03 (s, 9H, $CH_3Si$); 0.98-1.01 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.37 (s, 3H, $CH_3SO_2$); 3.70-3.73 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.82 (s, 2H, $NCH_2O$); 7.20 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.7 Hz, H-4-thienyl); 7.27 (s, 1H, H-5); 7.53 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.77 (dd, 1H, $J_{3,4}$ = 3.7 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 8.95 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 17.9 ($OCH_2\mathbf{C}H_2Si$); 40.1 ($CH_3SO_2$); 67.0 ($O\mathbf{C}H_2CH_2Si$); 70.8 ($NCH_2O$); 99.8 (CH-5); 114.3 (C-4a); 128.5 (CH-4-thienyl); 128.9 (CH-5-thienyl); 129.5 (CH-3-thienyl); 131.2 (C-2-thienyl); 139.9 (C-6); 150.3 (CH-2); 154.3 (C-4); 155.9 (C-7a). IR (KBr): 3004, 2959, 2929, 2893, 1544, 1485, 1413, 1353, 1302, 1248, 1138, 1123, 1069, 863, 839, 779, 764, 534. HRMS (ESI) calculated for $C_{17}H_{24}O_3N_3{}^{32}S_2{}^{28}Si$: 410.1023; found: 410.1022.

**6-(Furan-2-yl)-4-(methylsulfonyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

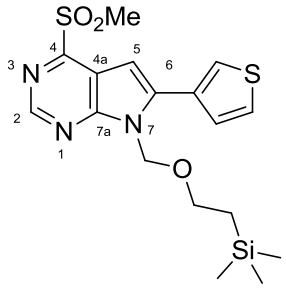
**8-(Furan-2-yl)-6-(methylsulfonyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (29d)**



Starting from deazapurine **26d** (723 mg, 2 mmol) and *m*-CPBA (900 mg, 4 mmol), the reaction was performed according to the General procedure to give product **29d** (600 mg, 76%) as yellow solid. M.p. 146°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.06 (s, 9H, $CH_3Si$); 0.93-0.96 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.36 (s, 3H, $CH_3SO_2$); 3.62-3.65 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.91 (s, 2H, $NCH_2O$); 6.60 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 7.16 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.7 Hz, H-3-furyl); 7.39 (s, 1H, H-5); 7.64 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.7 Hz, H-5-furyl); 8.93 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 40.1 ($CH_3SO_2$); 66.8 ($O\mathbf{C}H_2CH_2Si$); 71.3 ($NCH_2O$); 98.1 (CH-5); 112.3 (CH-4-furyl); 112.6 (CH-3-furyl); 114.3 (C-4a); 136.0 (C-6); 144.6 (C-2-furyl); 144.7 (CH-5-furyl); 150.2 (CH-2); 154.4 (C-4); 155.8 (C-7a). HRMS (ESI) calculated for $C_{17}H_{23}O_4N_3NaSSi$: 416.1071; found: 416.1070.

**4-(Methylsulfonyl)-6-(thiophen-3-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

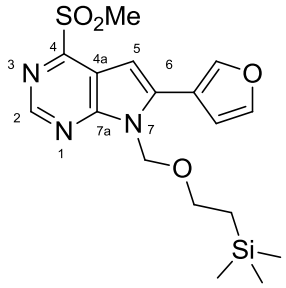
**6-(Methylsulfonyl)-8-(thiophen-3-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (29e)**



Starting from deazapurine **26e** (755 mg, 2 mmol) and *m*-CPBA (900 mg, 4 mmol), the reaction was performed according to the General procedure to give product **29e** (507 mg, 62%) as yellow solid. M.p. 178°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.02 (s, 9H, $CH_3Si$); 0.99-1.03 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.37 (s, 3H, $CH_3SO_2$); 3.74-3.77 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.78 (s, 2H, $NCH_2O$); 7.24 (s, 1H, H-5); 7.49 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.57 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 8.07 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 8.95 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 40.1 ($CH_3SO_2$); 67.1 ($O\mathbf{C}H_2CH_2Si$); 70.8 ($NCH_2O$); 99.1 (CH-5); 114.3 (C-4a); 126.6 (CH-2-thienyl); 126.9 (CH-5-thienyl); 128.2 (CH-4-thienyl); 130.5 (C-3-thienyl); 141.8 (C-6); 150.1 (CH-2); 154.3 (C-4); 155.8 (C-7a). IR (KBr): 3102, 3007, 2953, 2929, 2896, 1583, 1550, 1467, 1350, 1311, 1251, 1135, 1126, 1072, 863, 833, 776, 534. HRMS (ESI) calculated for $C_{17}H_{23}N_3O_3SiS_2$: 409.0950; found: 409.0948.

**6-(Furan-3-yl)-4-(methylsulfonyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

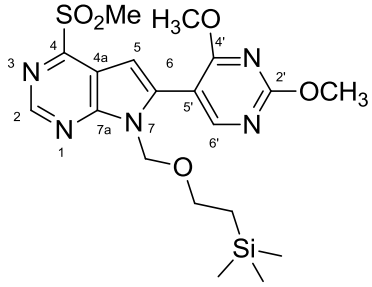
**8-(Furan-3-yl)-6-(methylsulfonyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (29f)**



Starting from deazapurine **26f** (633 mg, 1.75 mmol) and *m*-CPBA (784 mg, 3.5 mmol), the reaction was performed according to the General procedure to give product **29f** (430 mg, 62%) as white solid. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.03 (s, 9H, $CH_3Si$); 0.96-0.99 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.36 (s, 3H, $CH_3SO_2$); 3.67-3.70 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.78 (s, 2H, $NCH_2O$); 6.88 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.19 (s, 1H, H-5); 7.57 (bt, 1H, $J_{5,2} = J_{5,4}$ = 1.7 Hz, H-5-furyl); 8.15 (dd, 1H, $J_{2,5}$ = 1.5 Hz, $J_{2,4}$ = 0.9 Hz, H-2-thienyl); 8.93 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 17.9 ($OCH_2\mathbf{C}H_2Si$); 40.0 ($CH_3SO_2$); 66.9 ($O\mathbf{C}H_2CH_2Si$); 70.7 ($NCH_2O$); 98.6 (CH-5); 110.4 (CH-4-furyl); 114.3 (C-4a); 116.0 (C-3-furyl); 138.8 (C-6); 142.6 (CH-2-furyl); 144.1 (CH-5-furyl); 150.0 (CH-2); 154.1 (C-4); 155.8 (C-7a). HRMS (ESI) calculated for $C_{17}H_{23}N_3O_4SiS$: 393.1179; found: 393.1177.

**4-(Methylsulfonyl)-6-(2,4-dimethoxypyrimidin-5-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**6-(Methylsulfonyl)-8-(2,4-dimethoxypyrimidin-5-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (29g)**

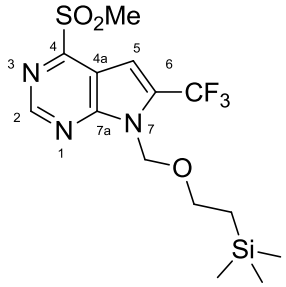


Starting from deazapurine **26g** (650 mg, 1.5 mmol) and *m*-CPBA (672 mg, 3 mmol), the reaction was performed according to the General procedure to give product **29g** (598 mg, 86%) as white solid. M.p. 122°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.08 (s, 9H, $CH_3Si$); 0.82-0.85 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.37 (s, 3H, $CH_3SO_2$); 3.48-3.51 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.03 (s, 3H, $CH_3O$-4′); 4.09 (s, 3H, $CH_3O$-2′); 5.63 (s, 2H, $NCH_2O$); 7.19 (s, 1H, H-5); 8.50 (s, 1H, H-6′); 8.98 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.8 ($OCH_2\mathbf{C}H_2Si$); 40.0 ($CH_3SO_2$); 54.5 ($CH_3O$-4′); 55.3 ($CH_3O$-2′); 67.0 ($O\mathbf{C}H_2CH_2Si$); 71.4 ($NCH_2O$); 102.7 (CH-5); 105.9 (C-4a); 114.0 (C-5′); 138.1 (C-6); 150.6 (CH-2); 155.0 (C-4); 155.3 (C-7a); 160.1 (CH-6′); 166.0 (C-2′); 168.6 (C-4′). IR (KBr): 3031, 3007, 2953, 2923, 2890, 1601, 1550,

1470, 1401, 1380, 1344, 1320, 1248, 1081, 866, 839, 776, 761, 531. HRMS (ESI) calculated for $C_{19}H_{27}N_5O_5SSi$: 465.1502; found: 465.1505.

**6-(Trifluoromethyl)-4-(methylsulfonyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**8-(Trifluoromethyl)-6-(methylsulfonyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (29l)**



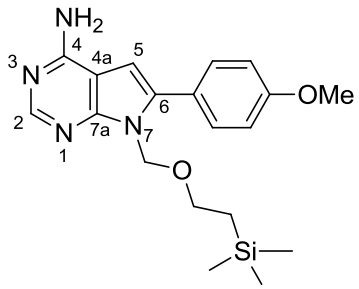

Starting from deazapurine **26l** (218 mg, 0.6 mmol) and *m*-CPBA (207 mg, 1.2 mmol), the reaction was performed according to the General procedure to give product **29l** (168 mg, 71%) as white solid. M.p. 145°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.04 (s, 9H, $CH_3Si$); 0.92-0.95 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.38 (s, 3H, $CH_3SO_2$); 3.58-3.62 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.86 (s, 2H, $NCH_2O$); 7.61 (q, 1H, $J_{5,F}$ = 1.1 Hz, CH-5); 9.11 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 39.8 ($CH_3SO_2$); 67.4 ($O\mathbf{C}H_2CH_2Si$); 72.0 ($NCH_2O$); 104.1 (q, $J_{C,F}$ = 4.3 Hz, CH-5); 111.7 (C-4a); 120.0 (q, $J_{C,F}$ = 270.2 Hz, $CF_3$); 131.8 (q, $J_{C,F}$ = 39.5 Hz, C-6); 152.9 (CH-2); 155.1 (C-7a); 158.4 (C-4). $^{19}$F NMR (470.3 MHz, $CDCl_3$): -56.86 (s, 1F, F-2). IR (KBr): 2956, 2926, 2893, 1547, 1431, 1371, 1344, 1320, 1233, 1180, 1159, 1138, 1093, 863, 836, 528. HRMS (ESI) calculated for $C_{14}H_{20}O_3N_3F_3NaSSi$: 418.0839; found: 418.0838.

**Amination of sulfones to 7-deazaadenines. General procedure:**

A 6-methylsulfonyl-7-deazapurine **29a-g**, **29l** (1 mmol) was dissolved in 1,4-dioxane (5 mL) and aq. ammonia (25% [w/w], 5 mL) was added and the reaction mixture was stirred at 50°C overnight. Then the solvents were evaporated and the residue was purified by flash chromatography (HPFC) in EtOAc/MeOH (20:1).

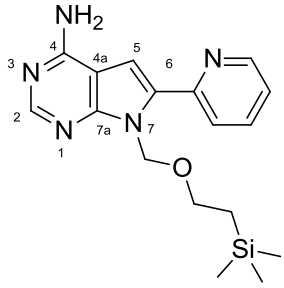
**6-(4-Methoxyphenyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

**8-(4-Methoxyphenyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazaadenine (30a)**



Starting from deazapurine **29a** (434 mg, 1 mmol), the reaction was performed according to the General procedure to give product **30a** (308 mg, 83%) as white solid. M.p. 142°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.03 (s, 9H, $CH_3Si$); 0.94-0.98 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.70-3.74 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 3.87 (s, 3H, $CH_3O$); 5.19 (bs, 2H, $NH_2$); 5.54 (s, 2H, $NCH_2O$); 6.38 (s, 1H, H-5); 6.99-7.01 (m, 2H, H-*m*-Ph); 7.65-7.67 (m, 2H, H-*o*-Ph); 8.35 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 55.3 ($CH_3O$); 66.5 ($O\mathbf{C}H_2CH_2Si$); 70.6 ($NCH_2O$); 97.1 (CH-5); 103.1 (C-4a); 114.1 (CH-*m*-Ph); 124.0 (C-*i*-Ph); 130.6 (CH-*o*-Ph); 139.2 (C-6); 151.8 (CH-2); 152.6 (C-7a); 156.0 (C-4); 159.9 (C-*p*-Ph). IR (KBr): 3324, 3138, 2950, 2917, 2899, 1664, 1592, 1553, 1455, 1440, 1314, 1248, 1222, 1084, 860, 833, 749, 737. HRMS (ESI) calculated for $C_{19}H_{27}O_2N_4Si$: 371.1898; found: 371.1898.

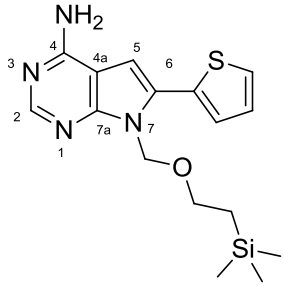
**6-(Pyridin-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**
**8-(Pyridin-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazaadenine (30b)**



Starting from deazapurine **29b** (404 mg, 1 mmol), the reaction was performed according to the General procedure to give product **30b** (320 mg, 94%) as yellowish solid. M.p. 137°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.15 (s, 9H, $CH_3Si$); 0.82-0.85 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.52-3.55 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.51 (bs, 2H, $NH_2$); 6.09 (s, 2H, $NCH_2O$); 6.85 (s, 1H, H-5); 7.26 (ddd, 1H, $J_{5,4}$ = 7.4 Hz, $J_{5,6}$ = 4.8 Hz, $J_{5,3}$ = 1.2 Hz, H-5-py); 7.76 (btd, 1H, $J_{4,5} = J_{4,3}$ = 7.7 Hz, $J_{4,6}$ = 1.8 Hz, H-4-py); 7.82 (dt, 1H, $J_{3,4}$ = 8.0 Hz, $J_{3,5} = J_{3,6}$ = 1.1 Hz, H-3-py); 8.37 (s, 1H, H-2); 8.68 (ddd, 1H, $J_{6,5}$ = 4.8 Hz, $J_{6,4}$ = 1.8 Hz, $J_{6,3}$ = 1.0 Hz, H-6-py). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.6 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 66.2 ($O\mathbf{C}H_2CH_2Si$); 71.2 ($NCH_2O$); 100.6 (CH-5); 102.9 (C-4a); 122.5 (CH-5-py); 122.8 (CH-3-py); 136.7 (C-6); 136.8 (CH-4-py); 149.5 (CH-6-py); 150.9 (C-2-py); 152.0 (CH-2); 153.2 (C-7a); 156.4 (C-4). IR (KBr): 3309, 3114, 3043, 2950, 1673, 1595, 1589, 1562, 1556, 1455, 1323, 1248, 1096, 1069, 863, 839, 761. HRMS (ESI) calculated for $C_{17}H_{23}N_5OSi$: 341.1672; found: 341.1671.

**6-(Thiophen-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

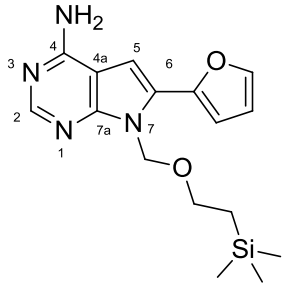
**8-(Thiophen-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazaadenine (30c)**



Starting from deazapurine **29c** (410 mg, 1 mmol), the reaction was performed according to the General procedure to give product **30c** (316 mg, 91%) as yellowish solid. M.p. 151°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.04 (s, 9H, $CH_3Si$); 0.94-0.98 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.67-3.70 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.58 (bs, 2H, $NH_2$); 5.68 (s, 2H, $NCH_2O$); 6.59 (s, 1H, H-5); 7.14 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.6 Hz, H-4-thienyl); 7.38 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.58 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 8.33 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.9 ($OCH_2\mathbf{C}H_2Si$); 66.4 ($O\mathbf{C}H_2CH_2Si$); 70.6 ($NCH_2O$); 98.7 (CH-5); 102.9 (C-4a); 126.6 (CH-5-thienyl); 127.6 (CH-3-thienyl); 128.2 (CH-4-thienyl); 132.4 (C-6); 132.6 (C-2-thienyl); 150.9 (CH-2); 152.3 (C-7a); 155.6 (C-4). IR (KBr): 3455, 3291, 3159, 3090, 2950, 2914, 1643, 1592, 1547, 1476, 1311, 1248, 1081, 863, 854, 833, 707. HRMS (ESI) calculated for $C_{16}H_{22}N_4OSiS$: 346.1284; found: 346.1286.

**6-(Furan-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

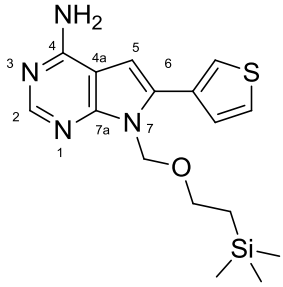
**8-(Furan-2-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazaadenine (30d)**



Starting from deazapurine **29d** (393 mg, 1 mmol), the reaction was performed according to the General procedure to give product **30d** (280 mg, 85%) as yellowish solid. M.p. 153°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.07 (s, 9H, $CH_3Si$); 0.91-0.94 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.61-3.64 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.64 (bs, 2H, $NH_2$); 5.75 (s, 2H, $NCH_2O$); 6.53 (dd, 1H, $J_{4,3}$ = 3.4 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.72 (s, 1H, H-5); 6.92 (dd, 1H, $J_{3,4}$ = 3.4 Hz, $J_{3,5}$ = 0.8 Hz, H-3-furyl); 7.53 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.8 Hz, H-5-furyl); 8.31 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.8 ($OCH_2\mathbf{C}H_2Si$); 66.2 ($O\mathbf{C}H_2CH_2Si$); 71.0 ($NCH_2O$); 96.9 (CH-5); 102.9 (C-4a); 109.2 (CH-3-furyl); 111.8 (CH-4-furyl); 129.3 (C-6); 142.9 (CH-5-furyl); 145.7 (C-2-furyl); 151.0 (CH-2); 152.2 (C-7a); 155.9 (C-4). HRMS (ESI) calculated for $C_{16}H_{23}O_2N_4Si$: 331.1585; found: 331.1585.

**6-(Thiophen-3-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

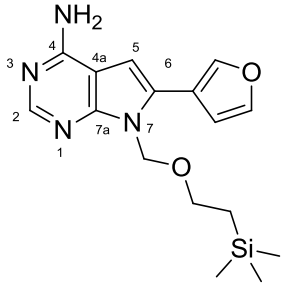
**8-(Thiophen-3-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazaadenine (30e)**



Starting from deazapurine **29e** (410 mg, 1 mmol), the reaction was performed according to the General procedure to give product **30e** (292 mg, 84%) as white solid. M.p. 159°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.04 (s, 9H, $CH_3Si$); 0.96-0.99 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.72-3.75 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.42 (bs, 2H, $NH_2$); 5.64 (s, 2H, $NCH_2O$); 6.53 (s, 1H, H-5); 7.42 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.44 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.4 Hz, H-4-thienyl); 7.84 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 8.34 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 18.0 ($OCH_2\mathbf{C}H_2Si$); 66.5 ($O\mathbf{C}H_2CH_2Si$); 70.6 ($NCH_2O$); 97.4 (CH-5); 102.9 (C-4a); 124.0 (CH-2-thienyl); 126.2 (CH-5-thienyl); 128.1 (CH-4-thienyl); 131.8 (C-3-thienyl); 134.5 (C-6); 151.2 (CH-2); 152.4 (C-7a); 155.8 (C-4). IR (KBr): 3446, 3288, 3135, 3102, 2950, 2917, 2890, 1634, 1595, 1556, 1470, 1302, 1293, 1251, 1081, 860, 836. HRMS (ESI) calculated for $C_{16}H_{22}N_4OSiS$: 346.1284; found: 346.1283.

**6-(Furan-3-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

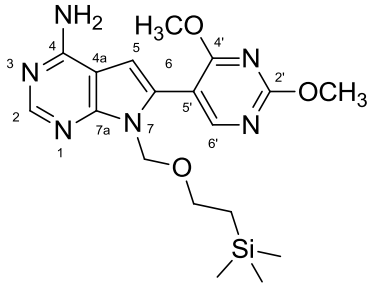
**8-(Furan-3-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazaadenine (30f)**



Starting from deazapurine **29f** (394 mg, 1 mmol), the reaction was performed according to the General procedure to give product **30f** (248 mg, 71%) as white solid. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.05 (s, 9H, $CH_3Si$); 0.93-0.97 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.65-3.69 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.57 (bs, 2H, $NH_2$); 5.63 (s, 2H, $NCH_2O$); 6.51 (s, 1H, H-5); 6.76 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.51 (t, 1H, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, H-5-furyl); 7.97 (dd, 1H, $J_{2,5}$ = 1.5 Hz, $J_{2,4}$ = 0.9 Hz, H-2-thienyl); 8.31 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.4 ($CH_3Si$); 17.9 ($OCH_2\mathbf{C}H_2Si$); 66.3 ($O\mathbf{C}H_2CH_2Si$); 70.5 ($NCH_2O$); 97.1 (CH-5); 102.9 (C-4a); 110.4 (CH-4-furyl); 116.7 (C-3-furyl); 131.1 (C-6); 141.0 (CH-2-furyl); 143.5 (CH-5-furyl); 150.6 (CH-2); 152.2 (C-7a); 155.5 (C-4). HRMS (ESI) calculated for $C_{16}H_{23}O_2N_4Si$: 331.1585; found: 331.1585.

**6-(2,4-Dimethoxypyrimidin-5-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

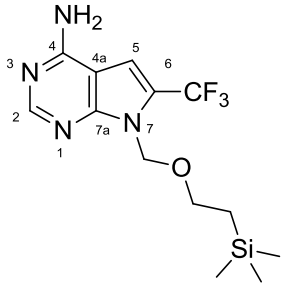
**8-(2,4-Dimethoxypyrimidin-5-yl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazaadenine (30g)**



Starting from deazapurine **29g** (465 mg, 1 mmol), the reaction was performed according to the General procedure to give product **30g** (374 mg, 93%) as white solid. M.p. 104°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.10 (s, 9H, $CH_3Si$); 0.80-0.83 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.47-3.49 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.01 (s, 3H, $CH_3O$-4′); 4.07 (s, 3H, $CH_3O$-2′); 5.50 (s, 2H, $NCH_2O$); 5.58 (bs, 2H, $NH_2$); 6.51 (s, 1H, H-5); 8.35 (s, 1H, H-2); 8.43 (s, 1H, H-6′). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.8 ($OCH_2\mathbf{C}H_2Si$); 54.4 ($CH_3O$-4′); 55.1 ($CH_3O$-2′); 66.3 ($O\mathbf{C}H_2CH_2Si$); 71.1 ($NCH_2O$); 101.0 (CH-5); 102.9 (C-4a); 107.0 (C-5′); 130.1 (C-6); 151.0 (CH-2); 152.1 (C-7a); 155.7 (C-4); 159.8 (CH-6′); 165.5 (C-2′); 168.8 (C-4′). IR (KBr): 3437, 3413, 3339, 3219, 3138, 2959, 2896, 1646, 1610, 1586, 1559, 1473, 1398, 1377, 1299, 1251, 1087, 1015, 866, 833. HRMS (ESI) calculated for $C_{18}H_{26}N_6O_3Si$: 402.1836; found: 402.1835.

**6-(Trifluoromethyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

**8-(Trifluoromethyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazaadenine (30l)**



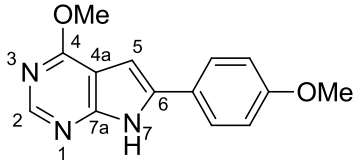
Starting from deazapurine **29l** (130 mg, 0.33 mmol), the reaction was performed according to the General procedure to give product **30l** (100 mg, 90%) as white solid. M.p. 140°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.06 (s, 9H, $CH_3Si$); 0.90-0.93 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.57-3.60 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.71 (s, 2H, $NCH_2O$); 5.80 (bs, 2H, $NH_2$); 6.96 (q, 1H, $J_{5,F}$ = 1.1 Hz, CH-5); 8.40 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.6 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 66.8 ($O\mathbf{C}H_2CH_2Si$); 71.6 ($NCH_2O$); 101.1 (C-4a); 102.5 (q, $J_{C,F}$ = 4.4 Hz, CH-5); 120.7 (q, $J_{C,F}$ = 268.7 Hz, $CF_3$); 125.1 (q, $J_{C,F}$ = 39.3 Hz, C-6); 152.5 (C-7a); 153.1 (CH-2); 157.0 (C-4). $^{19}$F NMR (470.3 MHz, $CDCl_3$): -56.03 (s, 1F, F-2). IR (KBr): 3135, 2953, 2929, 1655, 1601, 1562, 1544, 1365, 1314, 1251, 1180, 1129, 1120, 869, 836. HRMS (ESI) calculated for $C_{13}H_{20}ON_4F_3Si$: 333.1353; found: 333.1353.

**Deprotection of SEM group. General procedure:**

A SEM-protected 7-deazapurine **25a-h, 25j-l, 30a-g, 30l, 33j-l** was dissolved in trifluoroacetic acid (2 mL) and the reaction mixture was stirred at rt for 30 min. The mixture was then diluted with $NaHCO_3$ (to adjust pH=7) and EtOAc (25 mL) was added. The layers were separated and the aqueous layer was extracted two times with EtOAc. The combined organic layers were dried over sodium sulphate, and concentrated under the reduced pressure to give solid. The solid was then diluted with aq. ammonia (25% [w/w], 15 mL) and stirred at r.t. overnight to form white precipitate of product which was isolated by filtration.

**4-Methoxy-6-(4-methoxyphenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**

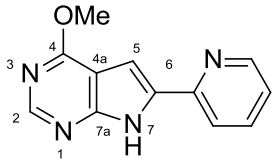
**6-Methoxy-8-(4-methoxyphenyl)-7-deazapurine (27a)**




Starting from deazapurine **25a** (772 mg, 2 mmol) the reaction was performed according to the General procedure to give product **27a** (458 mg, 90%) as white solid. M.p. 278°C. $^1$H NMR (600.1 MHz, $CDCl_3$): 3.80 (s, 3H, $CH_3O$-*p*); 4.04 (s, 3H, $CH_3O$-4); 6.83 (s, 1H, H-5); 7.01-7.03 (m, 2H, H-*m*-$C_6H_4OMe$); 7.85-7.87 (m, 2H, H-*o*-$C_6H_4OMe$); 8.36 (s, 1H, H-2); 12.41 (bs, 1H, NH). $^{13}$C NMR (150.9 MHz, $CDCl_3$): 53.5 ($CH_3O$-4); 55.4 ($CH_3O$-*p*); 93.6 (CH-5); 106.0 (C-4a); 114.6 (CH-*m*-$C_6H_4OMe$); 123.9 (C-*i*-$C_6H_4OMe$); 126.9 (CH-*o*-$C_6H_4OMe$); 136.8 (C-6); 150.3 (CH-2); 153.7 (C-7a); 159.4 (C-*p*-$C_6H_4OMe$); 161.8 (C-4). IR (KBr): 3150, 3013, 2995, 2941, 2842, 1622, 1598, 1544, 1503, 1482, 1332, 1254, 1177, 1126, 1024, 976, 890, 827, 773. HRMS (ESI) calculated for $C_{14}H_{14}O_2N_3$: 256.1081; found: 256.1081.

**4-Methoxy-6-(pyridin-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

**6-Methoxy-8-(pyridin-2-yl)-7-deazapurine (27b)**

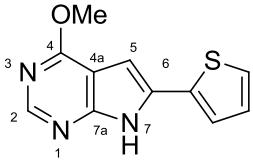



Starting from deazapurine **25b** (356 mg, 1 mmol), the reaction was performed according to the General procedure to give product **27b** (192 mg, 85%) as white solid. M.p. >350°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 4.06 (s, 3H, $CH_3O$); 7.20 (s, 1H, H-5); 7.34 (ddd, 1H, $J_{5,4}$ = 7.5 Hz, $J_{5,6}$ = 4.8 Hz, $J_{5,3}$ = 1.1 Hz, H-5-py); 7.89 (td, 1H, $J_{4,5}$ = $J_{4,3}$ = 7.8 Hz, $J_{4,6}$ = 1.8 Hz, H-4-py); 8.06 (dt, 1H, $J_{3,4}$ = 8.0 Hz, $J_{3,5}$ = $J_{3,6}$ = 1.1 Hz, H-2-furyl); 8.41 (s, 1H, H-2); 8.64 (ddd, 1H, $J_{6,5}$ = 4.8 Hz, $J_{6,4}$ = 1.8 Hz, $J_{6,3}$ = 1.0 Hz, H-6-py); 12.64 (vbs, 1H, NH). $^{13}$C NMR

(125.7 MHz, DMSO-$d_6$): 53.6 ($CH_3O$); 97.4 (CH-5); 105.8 (C-4a); 120.2 (CH-3-py); 123.0 (CH-5-py); 136.5 (C-6); 137.4 (CH-4-py); 149.7 (CH-6-py); 149.9 (C-2-py); 151.6 (CH-2); 153.6 (C-7a); 162.7 (C-4). IR (KBr): 3066, 3007, 2983, 2935, 2857, 2797, 1601, 1589, 1580, 1479, 1458, 1443, 1410, 1329, 1278, 1242, 1180, 1126, 979, 887, 842, 752. HRMS (ESI) calculated for $C_{12}H_{10}ON_4Na$: 249.0747; found: 249.0746.

**4-Methoxy-6-(thiophen-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**

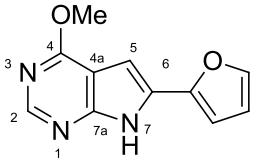
**6-Methoxy-8-(thiophen-2-yl)-7-deazapurine (27c)**




Starting from deazapurine **25c** (724 mg, 2 mmol), the reaction was performed according to the General procedure to give product **27c** (416 mg, 90%) as yellowish solid. M.p. 227°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 4.04 (s, 3H, $CH_3O$); 6.68 (s, 1H, H-5); 7.15 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.6 Hz, H-4-thienyl); 7.58 (bd, 1H, $J_{5,4}$ = 5.1 Hz, H-5-thienyl); 7.62 (bd, 1H, $J_{3,4}$ = 3.6 Hz, H-3-thienyl); 8.38 (s, 1H, H-2); 12.60 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 53.8 ($CH_3O$); 95.0 (CH-5); 106.0 (C-4a); 125.3 (CH-3-thienyl); 126.6 (CH-5-thienyl); 128.6 (CH-4-thienyl); 131.8 (C-6); 134.6 (C-2-thienyl); 151.2 (CH-2); 153.8 (C-7a); 162.3 (C-4). IR (KBr): 3210, 3123, 3069, 2988, 2947, 2875, 2842, 1610, 1592, 1562, 1485, 1407, 1344, 1329, 1299, 1216, 1183, 1123, 973, 890, 773, 695. HRMS (ESI) calculated for $C_{11}H_{10}ON_3S$: 232.0539; found: 232.0539.

**6-(Furan-2-yl)-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**8-(Furan-2-yl)-6-methoxy-7-deazapurine (27d)**

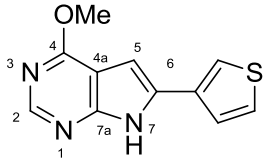



Starting from deazapurine **25d** (345 mg, 1 mmol), the reaction was performed according to the General procedure to give product **27d** (172 mg, 80%) as white solid. M.p. 243°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 4.04 (s, 3H, $CH_3O$); 6.64 (dd, 1H, $J_{4,3}$ = 3.4 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.67 (s, 1H, H-5); 6.99 (dd, 1H, $J_{3,4}$ = 3.4 Hz, $J_{3,5}$ = 0.8 Hz, H-3-furyl); 7.79 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.8 Hz, H-5-furyl); 8.38 (s, 1H, H-2); 12.59 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 53.6 ($CH_3O$); 96.7 (CH-5); 105.5 (C-4a); 107.5 (CH-3-furyl); 112.2 (CH-4-furyl); 128.4 (C-6); 143.6 (CH-5-furyl); 146.7 (C-2-furyl); 151.1 (CH-2); 153.5 (C-7a); 162.2 (C-4). IR (KBr): 3117, 3075, 2989, 2941, 2893, 2818, 1598, 1586, 1524, 1482, 1458,

1410, 1344, 1326, 1296, 1248, 1183, 1132, 1075, 1006, 973, 884, 830, 764, 740, 656. HRMS (ESI) calculated for $C_{11}H_{10}O_2N_3$: 216.0768; found: 216.0768.

**4-Methoxy-6-(thiophen-3-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**

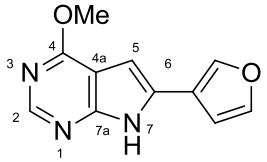
**6-Methoxy-8-(thiophen-3-yl)-7-deazapurine (27e)**




Starting from deazapurine **25e** (723 mg, 1 mmol), the reaction was performed according to the General procedure to give product **27e** (414 mg, 90%) as white solid. M.p. 232°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 4.04 (s, 3H, $CH_3O$); 6.85 (s, 1H, H-5); 7.66 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.69 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,2}$ = 1.4 Hz, H-4-thienyl); 8.00 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.4 Hz, H-2-thienyl); 8.37 (s, 1H, H-2); 12.47 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 53.4 ($CH_3O$); 94.8 (CH-5); 105.6 (C-4a); 121.1 (CH-2-thienyl); 126.1 (CH-4-thienyl); 127.5 (CH-5-thienyl); 133.0 and 133.2 (C-6,C-3-thienyl); 150.6 (CH-2); 153.4 (C-7a); 162.1 (C-4). IR (KBr): 3216, 3126, 3081, 3066, 3016, 2983, 2944, 2863, 1610, 1592, 1562, 1479, 1341, 1323, 1180, 1126, 973, 899, 878, 770, 653. HRMS (ESI) calculated for $C_{11}H_{10}ON_3S$: 232.0539; found: 232.0539.

**6-(Furan-3-yl)-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidine**

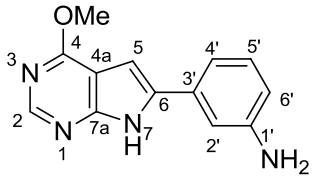
**8-(Furan-3-yl)-6-methoxy-7-deazapurine (27f)**




Starting from deazapurine **25f** (691 mg, 2 mmol), the reaction was performed according to the General procedure to give product **27f** (281 mg, 65%) as white solid. M.p. 218°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 4.04 (s, 3H, $CH_3O$); 6.79 (d, 1H, $J_{5,NH}$ = 2.1 Hz, H-5); 7.05 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.8 Hz, H-4-furyl); 7.77 (t, 1H, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, H-5-furyl); 8.21 (bdd, 1H, $J_{2,5}$ = 1.5 Hz, $J_{2,4}$ = 0.8 Hz, H-2-furyl); 8.36 (s, 1H, H-2); 12.37 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 53.4 ($CH_3O$); 94.8 (CH-5); 105.5 (C-4a); 108.4 (CH-4-furyl); 118.4 (C-3-furyl); 129.7 (C-6); 139.8 (CH-2-furyl); 144.5 (CH-5-furyl); 150.5 (CH-2); 153.4 (C-7a); 161.8 (C-4). IR (KBr): 3216, 3174, 3141, 3129, 3001, 2944, 2899, 2860, 1604, 1586, 1491, 1338, 1332, 1159, 1129, 1072, 973, 872, 767, 650, 588. HRMS (ESI) calculated for $C_{11}H_{10}O_2N_3$: 216.0768; found: 216.0768.

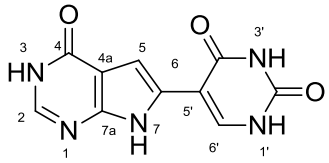
**6-(3-Aminophenyl)-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**8-(3-Aminophenyl)-6-methoxy-7-deazapurine (27h)**



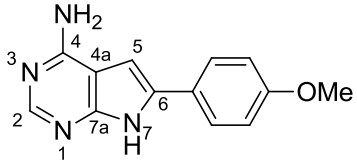

Deazapurine **25h** (1.02 g, 2.75 mmol) was used according to the General procedure. Crude product was chromatographed on silica gel $CHCl_3$/MeOH (10:1) to give product **27h** (147 mg, 22%) as yellowish solid. M.p. 296°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 4.04 (s, 3H, $CH_3O$); 5.15 (bs, 2H, $NH_2$); 6.57 (ddd, 1H, $J_{6',5'}$ = 7.8 Hz, $J_{6',2'}$ = 2.2 Hz, $J_{6',4'}$ = 1.2 Hz, H-6′); 6.71 (s, 1H, H-5); 7.02 – 7.06 (m, 2H, H-2′,4′); 7.09 (t, 1H, $J_{5',4'} = J_{5',6'}$ = 7.9 Hz, H-5′); 8.36 (s, 1H, H-2); 12.38 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 53.5 ($CH_3O$); 94.1 (CH-5); 105.8 (C-4a); 110.9 (CH-2′); 113.5 (CH-4′); 114.3 (CH-6′); 129.6 (CH-5′); 131.8 (C-3′); 137.8 (C-6); 149.2 (C-1′); 150.5 (CH-2); 153.6 (C-7a); 162.0 (C-4). IR (KBr): 3330, 3225, 3126, 1983, 2947, 1598, 1586, 1479, 1355, 1126, 776. HRMS (ESI) calculated for $C_{13}H_{13}ON_4$: 241.1084; found: 241.1084.

**5-(4-Oxo-4,7-dihydro-3*H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)pyrimidine-2,4(1*H*,3*H*)-dione (8-(uracil-5-yl)-7-deazahypoxantine) (28i)**




Deazapurine **25g** (731 mg, 1.75 mmol) was deprotected according to the General procedure directly followed by refluxing in 9 mL solution of THF: dioxane: HCl (1:1:1) for 2 hours. The reaction mixture was evaporated and ethanol (5 mL) was added. The mixture was then kept in a fridge overnight to furnish **28i** (416 mg, 97 %) as yellowish crystals. M.p. > 350°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 7.00 (d, 1H, $J_{5,NH}$ = 2.3 Hz, H-5); 7.38 (s, 1H, H-2); 7.97 (d, 1H, $J_{6',NH}$ = 6.1 Hz, H-6′); 11.31 (dd, 1H, $J_{NH,6'}$ = 6.1 Hz, $J_{NH,NH}$ = 1.8 Hz, NH-1′); 11.39 (d, 1H, $J_{NH,NH}$ = 1.8 Hz, NH-3′); 11.85 (vbs, 1H, NH-3); 11.90 (d, 1H, $J_{NH,5}$ = 2.3 Hz, NH-7). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 101.4 (CH-5); 104.9 (C-5′); 108.6 (C-4a); 126.8 (C-6); 137.7 (CH-6′); 143.9 (CH-2); 148.7 (C-7a); 150.7 (C-2′); 158.5 (C-4); 162.6 (C-4′). IR (KBr): 3261, 3219, 3183, 3156, 3114, 3063, 2908, 1706, 1682, 1583, 1565, 1524, 1416, 1257, 1227, 1192, 914, 824, 782, 555. HRMS (ESI) calculated for $C_{10}H_7O_3N_5{}^{23}Na$: 268.0441; found: 268.0442.

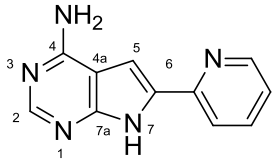
**6-(4-Methoxyphenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**
**8-(4-Methoxyphenyl)-7-deazaadenine (31a)**



Starting from deazapurine **30a** (148 mg, 0.4 mmol), the reaction was performed according to the General procedure to give product **31a** (77 mg, 80%) as white solid. M.p. 324°C. $^{1}$H NMR (500.0 MHz, DMSO-$d_6$): 3.79 (s, 3H, $CH_3O$); 6.76 (d, 1H, $J_{5,NH}$ = 2.2 Hz, H-5); 6.88 (bs, 2H, $NH_2$); 7.00-7.02 (m, 2H, H-*m*-Ph); 7.69-7.71 (m, 2H, H-*o*-Ph); 8.01 (s, 1H, H-2); 11.87 (bd, 1H, $J_{NH,5}$ = 2.0 Hz, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 55.4 ($CH_3O$); 94.8 (CH-5); 103.8 (C-4a); 114.6 (CH-*m*-Ph); 124.7 (C-*i*-Ph); 126.2 (CH-*o*-Ph); 133.8 (C-6); 151.8 (CH-2); 152.0 (C-7a); 157.1 (C-4); 158.9 (C-*p*-Ph). HRMS (ESI) calculated for $C_{13}H_{13}ON_4$: 241.1084; found: 241.1084.

**6-(Pyridin-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

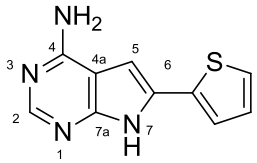
**8-(Pyridin-2-yl)-7-deazaadenine (31b)**



Starting from deazapurine **30b** (256 mg, 0.75 mmol), the reaction was performed according to the General procedure to give product **31b** (117 mg, 74%) as white solid. M.p. 326°C. $^{1}$H NMR (500.0 MHz, DMSO-$d_6$): 7.08 (bs, 2H, $NH_2$); 7.23 (bs, 1H, H-5); 7.25-7.28 (m, 1H, H-5-py); 7.82 – 7.88 (m, 2H, H-3,4-py); 8.07 (s, 1H, H-2); 8.59 (dt, 1H, $J_{6,5}$ = 4.7 Hz, $J_{6,4}$ = $J_{6,3}$ = 1.4 Hz, H-6-py); 12.08 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 99.2 (CH-5); 103.8 (C-4a); 119.1 (CH-3-py); 122.2 (CH-5-py); 133.5 (C-6); 137.3 (CH-4-py); 149.7 (CH-6-py); 150.2 (C-2-py); 152.1 (C-7a); 153.0 (CH-2); 157.9 (C-4). IR (KBr): 3398, 3078, 2971, 2923, 2845, 2809, 1637, 1622, 1595, 1580, 1464, 1443, 1359, 1284, 758. HRMS (ESI) calculated for $C_{11}H_{10}N_5$: 212.0931; found: 212.0931.

**6-(Thiophen-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

**8-(Thiophen-2-yl)-7-deazaadenine (31c)**

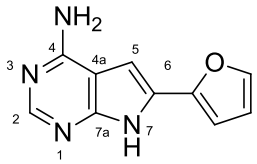


Starting from deazapurine **30c** (347 mg, 1 mmol), the reaction was performed according to the General procedure to give product **31c** (160 mg, 74%) as greyish solid. M.p. 345°C. $^{1}$H NMR (500.0 MHz, DMSO-$d_6$): 6.73 (s, 1H, H-5); 6.96 (bs, 2H, $NH_2$); 7.11 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.6 Hz, H-4-thienyl); 7.46 -7.50 (m, 2H, H-3,5-thienyl); 8.03 (s, 1H, H-2); 12.06 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 96.4 (CH-5); 103.5 (C-4a); 123.5 (CH-3-thienyl); 125.0 (CH-5-thienyl); 128.3 (CH-4-thienyl); 128.5 (C-6); 135.4 (C-2-thienyl); 151.9

(C-7a); 152.4 (CH-2); 157.2 (C-4). IR (KBr): 3464, 3300, 3117, 3108, 3096, 2988, 1637, 1586, 1556, 1485, 1314, 764, 698. HRMS (ESI) calculated for $C_{10}H_9N_4S$: 217.0542; found: 217.0543.

**6-(Furan-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

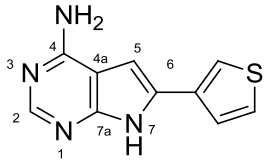
**8-(Furan-2-yl)-7-deazaadenine (31d)**



Deazapurine **30d** (248 mg, 0.75 mmol) was deprotected according to the General procedure. Crude product was chromatographed on silica gel $CHCl_3$/MeOH (10:1) to give product **31d** (119 mg, 79%) as white solid. M.p. 300°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 6.59 (dd, 1H, $J_{4,3}$ = 3.4 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.76 (d, 1H, $J_{5,NH}$ = 1.9 Hz, H-5); 6.83 (dd, 1H, $J_{3,4}$ = 3.4 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.00 (bs, 2H, $NH_2$); 7.72 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 8.03 (s, 1H, H-2); 11.99 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 95.4 (CH-5); 103.3 (C-4a); 105.8 (CH-3-furyl); 112.0 (CH-4-furyl); 125.5 (C-6); 142.8 (CH-5-furyl); 147.5 (C-2-furyl); 151.7 (C-7a); 152.4 (CH-2); 157.4 (C-4). IR (KBr): 3461, 3309, 3150, 3117, 3102, 2980, 2839, 1640, 1592, 1574, 1476, 1302, 1015, 767. HRMS (ESI) calculated for $C_{10}H_9ON_4$: 201.0771; found: 201.0771.

**6-(Thiophen-3-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

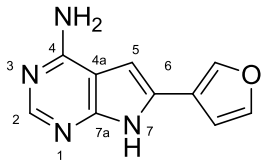
**8-(Thiophen-3-yl)-7-deazaadenine (31e)**



Deazapurine **30e** (260 mg, 0.75 mmol) was deprotected according to the General procedure. Crude product was chromatographed on silica gel $CHCl_3$/MeOH (10:1) to give product **31e** (117 mg, 72%) as white solid. M.p. > 350°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 6.74 (d, 1H, $J_{5,NH}$ = 2.2 Hz, H-5); 6.91 (bs, 2H, $NH_2$); 7.48 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 7.64 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.82 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 8.02 (s, 1H, H-2); 11.92 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 96.0 (CH-5); 103.4 (C-4a); 119.6 (CH-2-thienyl); 125.5 (CH-4-thienyl); 127.5 (CH-5-thienyl); 130.1 (C-6); 133.8 (C-3-thienyl); 151.7 (C-7a); 152.1 (CH-2); 157.3 (C-4). IR (KBr): 3467, 3297, 3111, 3087, 3025, 2905, 1646, 1595, 1562, 1485, 1320, 791, 761. HRMS (ESI) calculated for $C_{10}H_9N_4S$: 217.0542; found: 217.0543.

**6-(Furan-3-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

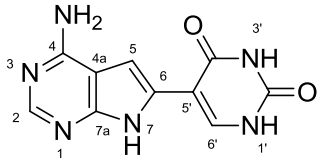
**8-(Furan-3-yl)-7-deazaadenine (31f)**



Deazapurine **30f** (247 mg, 0.75 mmol) was deprotected according to the General procedure. Crude product was chromatographed on silica gel $CHCl_3$/MeOH (10:1) to give product **31f** (98 mg, 65%) as white solid. M.p. > 350°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 6.63 (d, 1H, $J_{5,NH}$ = 2.1 Hz, H-5); 6.84 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 6.88 (bs, 2H, $NH_2$); 7.75 (t, 1H, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, H-5-furyl); 8.01 (s, 1H, H-2); 8.10 (dd, 1H, $J_{2,5}$ = 1.6 Hz, $J_{2,4}$ = 0.9 Hz, H-2-furyl); 11.81 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 95.9 (CH-5); 103.3 (C-4a); 108.6 (CH-4-furyl); 118.9 (C-3-furyl); 126.5 (C-6); 138.9 (CH-2-furyl); 144.5 (CH-5-furyl); 151.7 (C-7a); 152.0 (CH-2); 157.0 (C-4). IR (KBr): 3458, 3297, 3168, 3117, 2893, 2929, 2860, 1643, 1592, 1577, 1482, 1335, 1320, 779, 770. HRMS (ESI) calculated for $C_{10}H_9ON_4$: 201.0771; found: 201.0771.

**5-(4-Amino-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)pyrimidine-2,4(1*H*,3*H*)-dione**

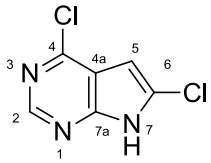
**(8-(Uracil-5-yl)-7-deazaadenine) (31i)**



Deazapurine **30g** (302 mg, 0.75 mmol) was deprotected according to the General procedure directly followed by refluxing in 9 mL solution of THF: dioxane: HCl (1:1:1) for 24 hours. The reaction mixture was evaporated and ethanol (5 mL) was added. The mixture was then kept in a fridge overnight to furnish **31i** (141 mg, 77 %) as yellowish crystals. M.p. >350°C . $^1$H NMR (500.0 MHz, DMSO-$d_6$): 7.52 (d, 1H, $J_{5,NH}$ = 2.2 Hz, H-5); 8.15 (d, 1H, $J_{6',NH}$ = 6.1 Hz, H-6′); 8.32 (s, 1H, H-2); 11.48 (d, 1H, $J_{NH,NH}$ = 1.8 Hz, NH-3′); 11.51 (dd, 1H, $J_{NH,6'}$ = 6.1 Hz, $J_{NH,NH}$ = 1.8 Hz, NH-1′); 12.81 (d, 1H, $J_{NH,5}$ = 2.2 Hz, NH-7). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 100.9 (CH-5); 102.1 (C-4a); 103.8 (C-5′); 130.7 (C-6); 139.2 (CH-6′); 142.3 (CH-2); 148.5 (C-7a); 150.4 (C-4); 150.5 (C-2′); 162.2 (C-4′). IR (KBr): 3318, 3267, 3150, 3043, 2956, 2851, 2788, 2729, 1709, 1676, 1595, 1574, 1446, 1442, 1245, 1224, 1216, 770. HRMS (ESI) calculated for $C_{10}H_9O_2N_6$: 245.0782; found: 245.0782.

**4,6-Dichloro-7*H*-pyrrolo[2,3-*d*]pyrimidine**

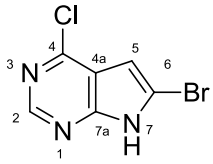
**6,8-Dichloro-7-deazapurine (34j)**



Deazapurine **33j** (318 mg, 1 mmol) was deprotected according to the general procedure. Crude product was chromatographed on silica gel $CHCl_3$/MeOH (10:1) to give product **34j** (124 mg, 66%) as white solid. M.p. 250°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 6.72 (s, 1H, H-5); 8.60 (s, 1H, H-2); 12.48 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 97.3 (CH-5); 117.3 (C-4a); 127.6 (C-6); 149.4 (C-4); 150.9 (CH-2); 151.4 (C-7a). IR (KBr): 3126, 3072,2962, 2935, 2794, 2678, 2651, 1610, 1565, 1497, 1443, 1338, 1260, 1213, 988, 872, 815. HRMS (ESI) calculated for $C_6H_3N_3Cl_2$: 186.9704; found: 186.9705.

**6-Bromo-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidine**

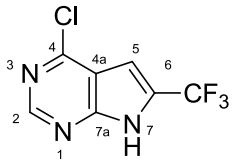
**8-Bromo-6-chloro-7-deazapurine (34k)**



Deazapurine **33k** (363 mg, 1 mmol) was deprotected according to the general procedure. Crude product was chromatographed on silica gel $CHCl_3$/MeOH (10:1) to give product **34k** (174 mg, 75%) as white solid. M.p. 258°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 6.80 (s, 1H, H-5); 8.58 (s, 1H, H-2); 13.43 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 101.2 (CH-5); 114.4 (C-6); 117.6 (C-4a); 149.1 (C-4); 150.8 (CH-2); 152.5 (C-7a). IR (KBr): 3123, 3090, 3069, 3022, 2950, 2920, 2875, 2803, 1604, 1559, 1494, 1422, 1335, 1263, 1210, 988, 866, 806. HRMS (ESI) calculated for $C_6H_3N_3ClBr$: 230.9199; found: 230.9200.

**4-Chloro-6-(trifluoromethyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**

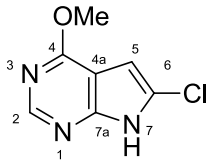
**6-Chloro-8-(trifluoromethyl)-7-deazapurine (34l)**



Deazapurine **33l** (246 mg, 0.7 mmol) was deprotected according to the general procedure. Crude product was chromatographed on silica gel $CHCl_3$/MeOH (10:1) to give product **34l** (113 mg, 73%) as white solid. M.p. 191°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 7.30 (q, 1H, $J_{5,F}$ = 1.3 Hz, H-5); 8.79 (s, 1H, H-2); 13.92 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 101.4 (bq, $J_{C,F}$ = 3.7 Hz, CH-5); 115.8 (C-4a); 120.7 (bq, $J_{C,F}$ = 268.8 Hz, $CF_3$); 127.4 (q, $J_{C,F}$ = 39.7 Hz, C-6); 152.4 (C-7a); 153.3 (CH-2); 153.4 (C-4). $^{19}$F NMR (470.3 MHz, DMSO-$d_6$): -56.66 (s, 1F, $CF_3$). IR (KBr): 3093, 3081, 2992, 2863, 2809, 2758, 2696, 1598, 1577, 1547, 1416, 1314, 1257, 1245, 1222, 1180, 1141, 979, 872. HRMS (ESI) calculated for $C_7H_3N_3ClF_3$: 220.9968; found: 220.9969.

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

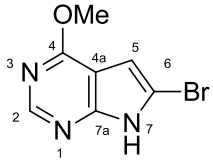
**8-Chloro-6-methoxy-7-deazapurine (27j)**




Deazapurine **25j** (471 mg, 1.5 mmol) was deprotected according to the general procedure. Crude product was chromatographed on silica gel $CHCl_3$/MeOH (10:1) to give product **27j** (150 mg, 55%) as white solid. M.p. 235°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 4.01 (s, 3H, $CH_3O$); 6.52 (s, 1H, H-5); 8.38 (s, 1H, H-2); 12.89 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 53.9 ($CH_3O$); 96.6 (CH-5); 105.3 (C-4a); 122.9 (C-6); 151.3 (CH-2); 152.1 (C-7a); 161.5 (C-4). IR (KBr): 3174, 3129, 3084, 3055, 2962, 2938, 2893, 2869, 2821, 2744, 2711, 2678, 2660, 1601, 1583, 1488, 1458, 1413, 1347, 1326, 1305, 114, 1096, 970, 940, 893, 815, 791, 653. HRMS (ESI) calculated for $C_7H_7ON_3Cl$: 184.0272; found: 184.0272.

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

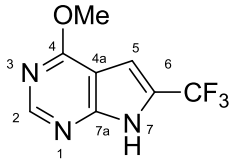
**8-Bromo-6-methoxy-7-deazapurine (27k)**




Starting from deazapurine **25k** (347 mg, 1.25 mmol), the reaction was performed according to the General procedure to give product **27k** (142 mg, 50%) as white solid. M.p. 234°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 4.01 (s, 3H, $CH_3O$); 6.60 (s, 1H, H-5); 8.36 (s, 1H, H-2); 12.84 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 53.6 ($CH_3O$); 100.1 (CH-5); 105.9 (C-4a); 109.3 (C-6); 150.8 (CH-2); 153.3 (C-7a); 160.0 (C-4). IR (KBr): 3697, 3129, 3087, 3049, 2988, 2959, 2938, 2866, 2818, 1607, 1589, 1479, 1461, 1413, 1347, 1326, 1141, 979, 896. HRMS (ESI) calculated for $C_7H_7ON_3{}^{79}Br$: 227.9767; found: 227.9768.

**6-(Trifluoromethyl)-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**8-(Trifluoromethyl)-6-methoxy-7-deazapurine (27l)**

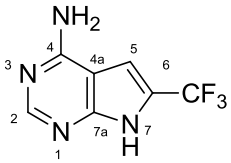



Deazapurine **25l** (420 mg, 1.2 mmol) was deprotected according to the general procedure. Crude product was chromatographed on silica gel $CHCl_3$/MeOH (10:1) to give product **27l** (198 mg, 75%) as white solid. M.p. 190°C. $^1$H NMR (500 MHz, DMSO-$d_6$): 3.44 (s, 3H, $CH_3O$); 7.10 (q, 1H, $J_{5,F}$ = 1.3 Hz, H-5); 8.54 (s, 1H, H-2); 13.36 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 54.1 ($CH_3O$); 100.6 (q, $J_{C,F}$ = 3.7 Hz, CH-5); 104.0 (C-4a); 121.2 (q, $J_{C,F}$ = 267.8 Hz, $CF_3$); 124.0 (q, $J_{C,F}$ = 39.2 Hz, C-6); 153.3 (C-7a); 153.7 (CH-2); 163.9 (C-4). $^{19}$F NMR

(470.3 MHz, DMSO-$d_6$): -56.00 (s, 1F, $CF_3$). IR (KBr): 3111, 3081, 2998, 2956, 2854, 2827, 2732, 2678, 2630, 1592, 1556, 1491, 1413, 1335, 1320, 1296, 1254, 1192, 1177, 1126, 1084, 967, 893, 845, 788, 719, 659. HRMS (ESI) calculated for $C_8H_7ON_3F_3$: 218.0536; found: 218.0534.

**6-(Trifluoromethyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine**

**8-(Trifluoromethyl)-7-deazaadenine (31l)**



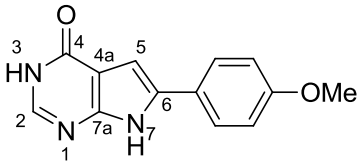
Deazapurine **30l** (100 mg, 0.3 mmol) was deprotected according to the general procedure. Crude product was chromatographed on silica gel $CHCl_3$/MeOH (10:1) to give product **31l** (55 mg, 90%) as white solid. M.p. more than 350°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 7.09 (q, 1H, $J_{5',F}$ = 1.4 Hz, H-5); 7.32 (bs, 2H, $NH_2$); 8.14 (s, 1H, H-2); 12.68 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 101.6 (C-4a); 101.7 (q, $J_{C,F}$ = 3.8 Hz, CH-5); 120.8 (q, $J_{C,F}$ = 38.8 Hz, C-6); 121.5 (q, $J_{C,F}$ = 266.9 Hz, $CF_3$); 151.9 (C-7a); 154.6 (CH-2); 158.7 (C-4). $^{19}$F NMR (470.3 MHz, DMSO-$d_6$): -55.67 (s, 1F, $CF_3$). IR (KBr): 3494, 3072, 2983, 2920, 2845, 2809, 2735, 2669, 1661, 1586, 1380, 1329, 1204, 1177, 1120, 1081. HRMS (ESI) calculated for $C_7H_6N_4F_3$: 203.0539; found: 203.0538.

**Deprotection of OMe group to 7-deazahypoxanthines. General procedure:**

To a stirred mixture of a 6-methoxy-7-deazapurine **27a-f, 27h, 27l** (0.50 mmol, 1 equiv.) and NaI (272 mg, 2.5 mmol, 5 equiv.) in dry MeCN (5 mL), TMSCl (438 μL, 2.5 mmol, 5 equiv.) was slowly added and the mixture was stirred at 80°C for 18 h. The precipitate was filtered off, washed carefully with MeCN, and dissolved in water, and pH of the solution was adjusted to 7 using solid $K_2CO_3$. The product precipitated and was filtered off.

**6-(4-Methoxyphenyl)-3*H*-pyrrolo[2,3-*d*]pyrimidin-4(7*H*)-one**

**8-(4-Methoxyphenyl)-7-deazahypoxantine (28a)**

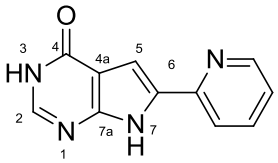


Starting from deazapurine **27a** (128 mg, 0.5 mmol), the reaction was performed according to the General procedure to give product **28a** (103 mg, 85%) as greyish solid. M.p. > 300°C. $^1$H NMR (500 MHz, $CDCl_3$): 3.78 (s, 3H, $CH_3O$); 6.79 (d, 1H, $J_{5,NH}$ = 2.4 Hz, H-5); 6.97-6.99 (m, 2H, H-*m*-$C_6H_4$OMe); 7.75-7.76 (m, 2H, H-*o*-$C_6H_4$OMe); 7.84

(bd, 1H, $J_{2,NH}$ = 3.2 Hz, H-2); 11.81 (bs, 1H, NH-3); 12.22 (bd, 1H, $J_{NH,5}$ = 2.4 Hz, NH-7). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 55.3 ($CH_3O$); 97.9 (CH-5); 109.2 (C-4a); 114.5 (CH-*m*-$C_6H_4OMe$); 124.3 (C-*i*-$C_6H_4OMe$); 126.2 (CH-*o*-$C_6H_4OMe$); 133.4 (C-6); 143.2 (CH-2); 149.2 (C-7a); 158.3 (C-4); 158.8 (C-*p*-$C_6H_4OMe$). IR (KBr): 3192, 3111, 3093, 3028, 3001, 2962, 2899, 2863, 2836, 1664, 1610, 1527, 1497, 1380, 1299, 1281, 1263, 1242, 1183, 1024, 914, 839, 809, 776, 620. HRMS (ESI) calculated for $C_{13}H_{12}O_2N_3$: 242.0924; found: 242.0925.

**6-(Pyridin-2-yl)-3*H*-pyrrolo[2,3-*d*]pyrimidin-4(7*H*)-one**

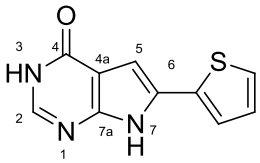
**8-(Pyridin-2-yl)-7-deazahypoxantine (28b)**



Starting from deazapurine **27b** (113 mg, 0.5 mmol), the reaction was performed according to the General procedure to give product **28b** (75 mg, 71%) as greyish solid. M.p. >300°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 7.17 (s, 1H, H-5); 7.27 (ddd, 1H, $J_{5,4}$ = 7.5 Hz, $J_{5,6}$ = 4.8 Hz, $J_{5,3}$ = 1.1 Hz, H-5-py); 7.83 (ddd, 1H, $J_{4,3}$ = 8.0 Hz, $J_{4,5}$ = 7.5 Hz, $J_{4,6}$ = 1.8 Hz, H-4-py); 7.89 (s, 1H, H-2); 7.94 (dt, 1H, $J_{3,4}$ = 8.0 Hz, $J_{3,5}$ = $J_{3,6}$ = 1.1 Hz, H-3-py); 8.58 (ddd, 1H, $J_{6,5}$ = 4.8 Hz, $J_{6,4}$ = 1.8 Hz, $J_{6,3}$ = 1.0 Hz, H-6-py); 11.89 (bs, 1H, NH-3); 12.48 (bs, 1H, NH-7). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 101.8 (CH-5); 109.4 (C-4a); 119.4 (CH-3-py); 122.3 (CH-5-py); 133.2 (C-6); 137.2 (CH-4-py); 144.5 (CH-2); 149.5 (CH-6-py); 149.7 (C-7a); 149.9 (C-2-py); 158.6 (C-4). IR (KBr): 3111, 3043, 2956, 2908, 2854, 2830, 1667, 1595, 1568, 1529, 1467, 1443, 1428, 1257, 1210, 1156, 919, 878, 836, 752. HRMS (ESI) calculated for $C_{11}H_8ON_4Na$: 235.0590; found: 235.0590.

**6-(Thiophen-2-yl)-3*H*-pyrrolo[2,3-*d*]pyrimidin-4(7*H*)-one**

**8-(Thiophen-2-yl)-7-deazahypoxantine (28c)**

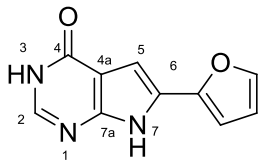


Starting from deazapurine **27c** (231 mg, 1 mmol), the reaction was performed according to the General procedure to give product **28c** (195 mg, 90%) as yellowish solid. M.p. > 350°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 6.62 (s, 1H, H-5); 7.08-7.10 (m, 1H, H-4-thienyl); 7.45 - 7.48 (m, 2H, H-3,5-thienyl); 7.86 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 99.0 (CH-5); 109.1 (C-4a); 123.4 (CH-3-thienyl); 125.0 (CH-5-thienyl); 128.2 (CH-4-thienyl); 128.6 (C-6); 135.2 (C-2-thienyl); 144.1 (CH-2); 149.6 (C-7a); 158.4 (C-4). IR (KBr): 3198, 3138, 3105,

3072, 3037, 2959, 2911, 2845, 1673, 1589, 1535, 1494, 1431, 1386, 1254, 1195, 919, 856, 770, 683. HRMS (ESI) calculated for $C_{10}H_6ON_3S$: 216.0237; found: 216.0239.

**6-(Furan-2-yl)-3*H*-pyrrolo[2,3-*d*]pyrimidin-4(7*H*)-one**

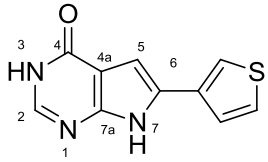
**8-(Furan-2-yl)-7-deazahypoxantine (28d)**



Starting from deazapurine **27d** (65 mg, 0.3 mmol), the reaction was performed according to the General procedure to give product **28d** (55 mg, 92%) as greyish solid. M.p. > 350°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 6.57 (dd, 1H, $J_{4,3}$ = 3.4 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.61 (s, 1H, H-5); 7.79 (dd, 1H, $J_{3,4}$ = 3.4 Hz, $J_{3,5}$ = 0.8 Hz, H-3-furyl); 7.69 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.8 Hz, H-5-furyl); 7.84 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 97.9 (CH-5); 105.3 (CH-3-furyl); 108.9 (C-4a); 112.0 (CH-4-furyl); 125.8 (C-6); 142.4 (CH-5-furyl); 144.4 (CH-2); 147.8 (C-2-furyl); 149.9 (C-7a); 159.1 (C-4). IR (KBr): 3189, 3120, 3078, 3040, 2971, 2914, 2890, 2833, 2818, 2773, 2708, 1652, 1595, 1565, 1518, 1431, 1389, 1257, 1216, 1012, 919, 890, 839, 773, 731, 620. HRMS (ESI) calculated for $C_{10}H_7O_2N_3Na$: 224.0430; found: 224.0431.

**6-(Thiophen-3-yl)-3*H*-pyrrolo[2,3-*d*]pyrimidin-4(7*H*)-one**

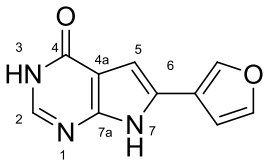
**8-(Thiophen-3-yl)-7-deazahypoxantine (28e)**



Starting from deazapurine **27e** (231 mg, 1 mmol), the reaction was performed according to the General procedure to give product **28e** (152 mg, 70%) as greyish solid. M.p. > 350°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 6.80 (s, 1H, H-5); 7.60 (dd, 1H, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.5 Hz, H-4-thienyl); 7.61 (dd, 1H, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 2.7 Hz, H-5-thienyl); 7.84 (dd, 1H, $J_{2,5}$ = 2.7 Hz, $J_{2,4}$ = 1.5 Hz, H-2-thienyl); 7.86 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 99.2 (CH-5); 109.0 (C-4a); 119.3 (CH-2-thienyl); 125.9 (CH-4-thienyl); 127.2 (CH-5-thienyl); 129.8 (C-6); 133.6 (C-3-thienyl); 144.1 (CH-2); 149.3 (C-7a); 158.8 (C-4). IR (KBr): 3201, 3186, 3174, 3129, 3081, 3060, 2989, 2914, 2854, 1673, 1655, 1586, 1568, 1541, 1446, 1422, 1245, 1207, 1186, 1084, 961, 917, 857, 761, 600. HRMS (ESI) calculated for $C_{10}H_6ON_3S$: 216.0237; found: 216.0238.

**6-(Furan-3-yl)-3*H*-pyrrolo[2,3-*d*]pyrimidin-4(7*H*)-one**

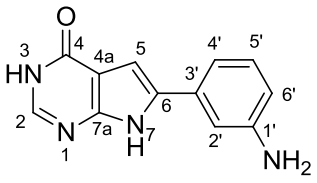
**8-(Furan-3-yl)-7-deazahypoxantine (28f)**



Starting from deazapurine **27f** (215 mg, 1 mmol), the reaction was performed according to the General procedure to give product **28f** (160 mg, 80%) as greyish solid. M.p. > 350°C. $^{1}$H NMR (500.0 MHz, DMSO-$d_6$): 6.69 (s, 1H, H-5); 6.97 (dd, 1H, $J_{4,5}$ = 1.9 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.72 (t, 1H, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, H-5-furyl); 7.84 (s, 1H, H-2); 8.10 (dd, 1H, $J_{2,5}$ = 1.5 Hz, $J_{2,4}$ = 0.9 Hz, H-2-furyl). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 99.1 (CH-5); 108.8 (CH-4-furyl); 108.8 (C-4a); 118.6 (C-3-furyl); 126.4 (C-6); 138.8 (CH-2-furyl); 143.7 (CH-2); 144.3 (CH-5-furyl); 149.0 (C-7a); 158.3 (C-4). IR (KBr): 3105, 3037, 2965, 2848, 2806, 2717, 2663, 1679, 1562, 1601, 1559, 1425, 1389, 1242, 1213. HRMS (ESI) calculated for $C_{10}H_7N_3O_2$: 201.0538; found: 201.0540.

**6-(3-Aminophenyl)-3*H*-pyrrolo[2,3-*d*]pyrimidin-4(7*H*)-one**

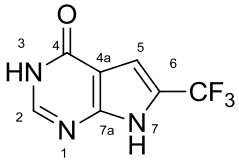
**8-(3-Aminophenyl)-7-deazahypoxantine (28h)**



Starting from deazapurine **27h** (120 mg, 0.5 mmol), the reaction was performed according to the General procedure to give product **28h** (85 mg, 75%) as greyish solid. M.p. > 350°C. $^{1}$H NMR (500.0 MHz, DMSO-$d_6$): 5.10 (bs, 2H, $NH_2$); 6.50 (ddd, 1H, $J_{6',5'}$ = 7.9 Hz, $J_{6',2'}$ = 2.2 Hz, $J_{6',4'}$ = 1.1 Hz, H-6′); 6.67 (d, 1H, $J_{5,NH}$ = 2.2 Hz, H-5); 6.94 – 6.97 (m, 2H, H-2′,4′); 7.05 (t, 1H, $J_{5',4'}$ = $J_{5',6'}$ = 8.0 Hz, H-5′); 7.84 (s, 1H, H-2); 11.82 (bs, 1H, NH-3); 12.19 (bs, 1H, NH-7). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 98.4 (CH-5); 109.1 (C-4a); 110.3 (CH-2′); 112.8 (CH-4′); 113.6 (CH-6′); 129.5 (CH-5′); 132.1 (C-3′); 134.3 (C-6); 143.6 (CH-2); 149.1 and 149.2 (C-1′,7a); 158.4 (C-4). IR (KBr): 3401, 3321, 3219, 3147, 3028, 2959, 2899, 2854, 1673, 1613, 1595, 1482, 1263, 1239, 919, 773. HRMS (ESI) calculated for $C_{12}H_{11}ON_4$: 227.0927; found: 227.0930.

**6-(Trifluoromethyl)-3*H*-pyrrolo[2,3-*d*]pyrimidin-4(7*H*)-one**

**8-(Trifluoromethyl)-7-deazahypoxantine (28l)**



Starting from deazapurine **27l** (163 mg, 0.75 mmol), the reaction was performed according to the General procedure to give product **28l** (45 mg, 30%) as greyish solid. M.p. >350°C. $^{1}$H NMR (500.0 MHz, DMSO-

$d_6$): 6.88 (s, 1H, H-5); 7.88 (s, 1H, H-2); 11.76 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 103.1 (CH-5); 107.9 (C-4a); 122.2 (bq, $J_{C,F}$ = 266.8 Hz, $CF_3$); 123.2 (m, C-6); 144.6 (m, CH-2); 151.6 (m, C-7a); 158.9 (C-4). $^{19}$F NMR (470.3 MHz, $CDCl_3$): -55.36 (s, 1F, F-2). IR (KBr): 3075, 2995, 2920, 2830, 1691, 1592, 1532, 1389, 1219, 1207, 1177, 1123. HRMS (ESI) calculated for $C_7H_4ON_3F_3Na$: 226.0199; found: 226.0198.

### 5.4.4 One-pot C–H borylation/Cu-catalyzed substitution

**One pot C-H borylation – substitution sequence. General procedures:**

Procedure A: A 7-deazapurines **2, 9, 10** (2 mmol, 1 equiv.), bispinacolatodiboron (0.61 g, 2.4 mmol, 1.2 equiv.), $[Ir(COD)OMe]_2$ (66 mg, 0.1 mmol, 5 mol %) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (54 mg, 0.2 mmol, 10 mol %) were dissolved in dry THF (15 ml) under Ar. The solution was heated at 80 °C in a septum sealed vial and stirred under argon for 20 h. The solvent was removed under reduced pressure. The crude mixture was then dissolved in acetone (10 mL). A solution of $CuCl_2$ (807 mg, 6.0 mmol, 3 equiv.) in water (10 mL) was then added to the reaction mixture, which was heated for 4 hours at 80 °C. The solution was then cooled to room temperature, diluted with EtOAc (25 mL) and with saturated aq. solution of $NH_4Cl$ (25 mL). Aqueous solution was then extracted three times with EtOAc and combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by flash chromatography (HPFC) in hexane/EtOAc.

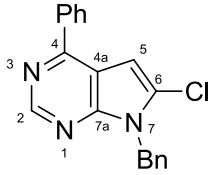
Procedure B: The same as Procedure A, only using $CuBr_2$ (1.34 g, 6.0 mmol, 3 equiv.) instead of $CuCl_2$.

Procedure C: A 7-deazapurines **2, 9, 10, 11** (2 mmol, 1 equiv.), bispinacolatodiboron (0.61 g, 2.4 mmol, 1.2 equiv.), $[Ir(COD)OMe]_2$ (66 mg, 0.1 mmol, 5 mol %) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (54 mg, 0.2 mmol, 10 mol %) were dissolved in dry THF (10 mL) under Ar. The solution was heated at 80 °C in a septum sealed vial and stirred under argon for 20 h. The solvent was removed under reduced pressure. The crude mixture was then dissolved in DCM (8 mL). The solution was transferred by a syringe into an oven-dried sealed bomb that was placed with CuTc (38 mg, 0.2 mmol, 10 mol%), 1,10-phenanthroline (72 mg, 0.4 mmol, 20 mol%), $LiOH.H_2O$ (168 mg, 4 mmol, 2 equiv.) and Togni's reagent (726 mg, 2.2 mmol, 1.1 equiv.) under Ar. The reaction system was quickly degassed through three freeze-pump-thaw

cycles and refilled with Ar. The reaction was stirred at 45 °C for 18 hours. The solution was then cooled to room temperature, diluted with DCM (25 mL) and saturated solution of $NH_4Cl$ (25 mL). Aqueous solution was then extracted two times with DCM and the combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by flash chromatography (HPFC) in hexane/EtOAc.

Procedure D: 7-Deazapurine **2** (0.5 mmol, 1 equiv.), bispinacolatodiboron (152 mg, 0.6 mmol, 1.2 equiv.), $[Ir(COD)OMe]_2$ (17 mg, 0.025 mmol, 5 mol %) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (13 mg, 0.05 mmol, 10 mol %) were dissolved in dry THF (5 mL) under Ar. The solution was heated at 80 °C in a septum sealed vial and stirred under argon for 20 h. The solvent was removed under reduced pressure. The residue was then dissolved in MeOH (10 mL) and $Cu(NO_3)_2 \bullet {}_3H_2O$ (242 mg, 1 mmol, 2 equiv.), $Zn(CN)_2$ (176 mg, 1,5 mmol, 3 equiv.), and CsF (76 mg, 0.5 mmol, 1 equiv.) were added to the reaction vessel followed by $H_2O$ (4 mL). The flask was sealed with a Teflon-lined cap, and the green suspension was stirred vigorously at 100 ºC for 3 h. The solution was then cooled to r.t., diluted with EtOAc (15 mL) and with saturated solution of $NH_4Cl$ (15 mL). Aqueous solution was then extracted three times with EtOAc and the combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by flash chromatography (HPFC) in hexan/EtOAc.

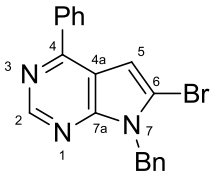
**7-Benzyl-6-chloro-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-8-chloro-6-phenyl-7-deazapurine) (32j)**




Starting from **2** (285 mg, 1 mmol), the reaction was performed according to the General procedure A to give product **32j** (146 mg, 46%) as yellowish solid. M.p. 118°C. $^1$H NMR (500 MHz, $CDCl_3$): 5.58 (s, 2H, $CH_2$-Bn); 6.82 (s, 1H, H-5); 7.26 – 7.34 (m, 5H, H-*o*,*m*,*p*-Bn); 7.48 – 7.58 (m, 3H, H-*m*,*p*-Ph); 8.06-8.08 (m, 2H, H-*o*-Ph); 8.98 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 45.7 ($CH_2$-Bn); 99.0 (CH-5); 115.2 (C-4a); 127.4 (CH-*o*-Bn); 127.9 (CH-*p*-Bn); 128.6 (C-6); 128.7 (CH-*o*-Ph); 128.7 (CH-*m*-Bn); 128.9 (CH-*m*-Ph); 130.2 (CH-*p*-Ph); 136.3 (C-*i*-Bn); 137.8 (C-*i*-Ph); 151.5 (C-7a); 151.8 (CH-2); 156.3 (C-4). HRMS (ESI) calculated for $C_{19}H_{15}N_3Cl$: 320.0949; found: 320.0949.

**7-Benzyl-6-bromo-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (26k)**

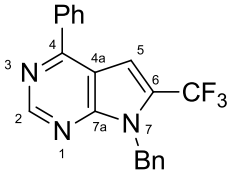
**(9-Benzyl-8-bromo-6-phenyl-7-deazapurine) (32k)**



Starting from **2** (285 mg, 1 mmol), the reaction was performed according to the General procedure B to give product **32k** (229 mg, 63%) as yellowish solid. M.p. 110°C. $^{1}$H NMR (499.8 MHz, $CDCl_3$): 5.60 (s, 2H, $CH_2Ph$); 6.98 (s, 1H, H-5); 7.26-7.33 (m, 5H, H-*o*,*m*,*p*-Bn); 7.51-7.58 (m, 3H, H-*m*,*p*-Ph); 8.08-8.10 (m, 2H, H-*o*-Ph); 8.97 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.9 ($CH_2Ph$); 103.4 (CH-5); 116.0 (C-6); 116.9 (C-4a); 127.4 (CH-*o*-Bn); 127.9 (CH-*p*-Bn); 128.8 (CH-*m*-Bn); 128.9 (CH-*o*-Ph); 129.0 (CH-*m*-Ph); 130.4 (CH-*p*-Ph); 136.0 (C-*i*-Bn); 151.2 (CH-2); 152.1 (C-7a); (C-4 and C-*i*-Ph not detected). HRMS (ESI) calculated for $C_{19}H_{15}N_3Br$: 364.0444; found: 364.0444.

**7-Benzyl-4-phenyl-6-(trifluoromethyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**

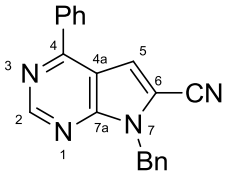
**(9-Benzyl-8-(trifluoromethyl)-6-phenyl-7-deazapurine) (32l)**



Starting from **2** (285 mg, 1 mmol), the reaction was performed according to the General procedure C to give product **32l** (120 mg, 34%) as white solid. $^{1}$H NMR (499.8 MHz, $CDCl_3$): 5.68 (s, 2H, $CH_2Ph$); 7.18-7.19 (m, 2H, H-*o*-Bn); 7.26-7.31 (m, 3H, H-*m*,*p*-Bn); 7.30 (q, 1H, $J_{H,F}$ = 1.1, H-5); 7.54-7.61 (m, 3H, H-*m*,*p*-Ph); 8.10-8.12 (m, 2H, H-*o*-Ph); 9.10 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.8 ($CH_2Ph$); 103.7 (q, $J_{C,F}$ = 4.3, CH-5); 116.9 (C-4a); 120.7 (q, $J_{C,F}$ = 269.2, $CF_3$); 126.9 (CH-*o*-Bn); 127.8 (CH-*p*-Bn); 128.1 (q, $J_{C,F}$ = 38.1, C-6); 128.6 (CH-*m*-Bn); 128.9 (CH-*o*-Ph); 129.0 (CH-*m*-Ph); 130.8 (CH-*p*-Ph); 136.3 (C-*i*-Bn); 137.2 (C-*i*-Ph); 153.2 (C7a); 154.1 (CH-2); 160.2 (C-4). $^{19}$F{$^{1}$H} NMR (470.3 MHz, $CDCl_3$): -55.79. HRMS (ESI) calculated for $C_{20}H_{15}N_3F_3$: 354.1213; found: 354.1214.

**7-Benzyl-4-phenyl-6-cyano-7*H*-pyrrolo[2,3-*d*]pyrimidine**

**(9-Benzyl-8-carbonitrile-6-phenyl-7-deazapurine) (32m)**

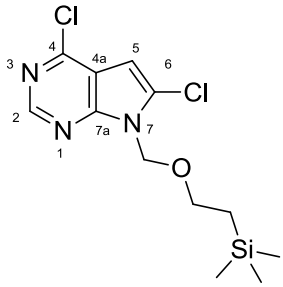


Starting from **2** (143 mg, 0.5 mmol), the reaction was performed according to the General procedure D to give product **32m** (90 mg, 58%) as white solid. M.p. 123°C. $^{1}$H NMR (499.8 MHz, $CDCl_3$): 5.65 (s, 2H, $CH_2Ph$); 7.31-7.33 (m, 1H, H-*p*-Bn); 7.35-7.36 (m, 2H, H-*m*-Bn); 7.42-7.44 (m, 2H, H-*o*-Bn); 7.49 (s, 1H, H-5); 7.56-7.59 (m, 3H, H-*m*,*p*-Ph); 8.06-8.08 (m, 2H, H-*o*-Ph); 9.14 (s,

1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 47.6 ($CH_2Ph$); 111.2 (C-6); 112.4 (CH-5); 112.5 (CN); 114.0 (C-4a); 128.2 (CH-*o*-Bn); 128.50 (CH-*p*-Bn); 128.95 (CH-*m*-Bn); 128.98 (CH-*o*-Ph); 129.12 (CH-*m*-Ph); 131.1 (CH-*p*-Ph); 135.5 (C-*i*-Bn); 136.8 (C-*i*-Ph); 151.8 (C-7a); 154.9 (CH-2); 160.7 (C-4). HRMS (ESI) calculated for $C_{20}H_{15}N_4$: 311.1291; found: 311.1290.

**4,6-Dichloro-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

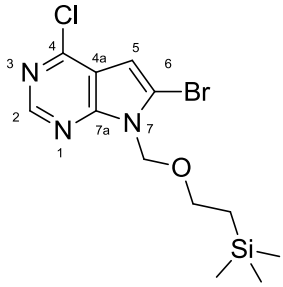
**6,8-Dichloro-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (33j)**



Starting from **9** (568 mg, 2 mmol), the reaction was performed according to the General procedure A to give product **33j** (350 mg, 55%) as colourless oil. $^1$H NMR (500 MHz, $CDCl_3$): -0.06 (s, 9H, $CH_3Si$); 0.90-0.94 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.58-3.61 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.70 (s, 2H, $NCH_2O$); 6.62 (s, 1H, H-5); 8.65 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 67.1 ($O\mathbf{C}H_2CH_2Si$); 70.8 ($NCH_2O$); 99.0 (CH-5); 117.1 (C-4a), 129.2 (C-6); 150.9 (C-4); 151.7 (CH-2); 154.5 (C-7a). IR (KBr): 3114, 2950, 2920, 2896, 2866, 1592, 1577, 1541, 1503, 1455, 1446, 1419, 1383, 1344, 1254, 1248, 1207, 1186, 1126, 1093, 911, 860, 839, 779, 755. HRMS (ESI) calculated for $C_{12}H_{17}ON_3Cl_2NaSi$: 340.0410; found: 340.0410.

**6-Bromo-4-chloro-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

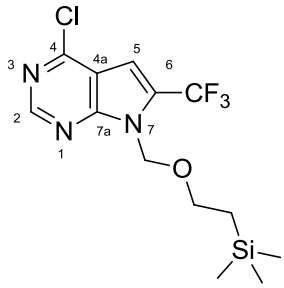
**8-Bromo-6-chloro-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (33k)**



Starting from **9** (568 mg, 2 mmol), the reaction was performed according to the General procedure B to give product **33k** (403 mg, 56%) as white solid. M.p. 49°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.06 (s, 9H, $CH_3Si$); 0.90-0.94 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.57-3.60 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.71 (s, 2H, $NCH_2O$); 6.77 (s, 1H, H-5); 8.64 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 67.0 ($O\mathbf{C}H_2CH_2Si$); 71.9 ($NCH_2O$); 103.1 (CH-5); 116.6 (C-6), 118.0 (C-4a); 150.8 (C-4); 151.2 (CH-2); 152.2 (C-7a). IR (KBr): 3105, 2956, 2917, 2902, 2881, 2866, 1583, 1541, 1485, 1458, 1434, 1416, 1386, 1350, 1257, 1248, 1180, 1090, 1075, 1033, 911, 860, 839, 779, 749. HRMS (ESI) calculated for $C_{12}H_{18}ON_3BrClSi$: 362.0086; found: 362.0086.

**4-Chloro-6-(trifluoromethyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

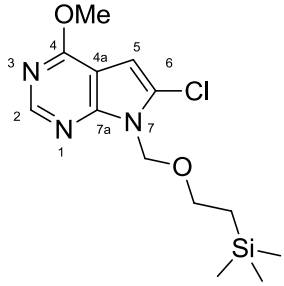
**6-Chloro-8-(trifluoromethyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (33l)**



Starting from **9** (568 mg, 2 mmol), the reaction was performed according to the General procedure C to give product **33l** (264 mg, 38 %) as colourless oil. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.06 (s, 9H, $CH_3Si$); 0.91-0.94 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.57-3.61 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.79 (s, 2H, $NCH_2O$); 7.12 (q, 1H, $J_{5,F}$ = 1.1 Hz, CH-5); 8.79 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.6 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 67.2 ($O\mathbf{C}H_2CH_2Si$); 72.0 ($NCH_2O$); 103.6 (q, $J_{C,F}$ = 4.4 Hz, CH-5); 115.6 (C-4a); 120.2 (q, $J_{C,F}$ = 269.3 Hz, $CF_3$); 129.0 (q, $J_{C,F}$ = 39.7 Hz, C-6); 154.0 (C-7a); 153.4 (CH-2); 154.6 (C-4). $^{19}$F NMR (470.3 MHz, $CDCl_3$): -56.61 (s, 1F, F-2). IR (KBr): 3950, 2929, 2899, 1592, 1553, 1544, 1446, 1431, 1413, 1371, 1353, 1248, 1189, 1147, 1096, 860, 842. HRMS (ESI) calculated for $C_{13}H_{18}ON_3ClF_3Si$: 352.0854; found: 352.0855.

**6-Chloro-4-methoxy-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

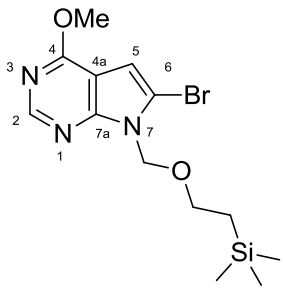
**8-Chloro-6-methoxy-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25j)**



Starting from **10** (1116 mg, 4 mmol), the reaction was performed according to the General procedure A to give product **25j** (590 mg, 47%) as white solid. M.p. 80°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.07 (s, 9H, $CH_3Si$); 0.90-0.93 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.57-3.60 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.10 (s, 3H, $CH_3O$); 5.66 (s, 2H, $NCH_2O$); 6.51 (s, 1H, H-5); 8.47 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 53.8 ($CH_3O$); 66.6 ($O\mathbf{C}H_2CH_2Si$); 70.5 ($NCH_2O$); 97.8 (CH-5); 105.0 (C-4a); 124.8 (C-6); 151.3 (CH-2); 152.1 (C-7a); 161.9 (C-4). IR (KBr): 3261, 3102, 3060, 3001, 2953, 2923, 2899, 2869, 1712, 1685, 1661, 1595, 1559, 1503, 1479, 1464, 1410, 1377, 1314, 1245, 1230, 1099, 1060, 917, 860, 839, 794, 755.. HRMS (ESI) calculated for $C_{13}H_{20}O_2N_3ClNaSi$: 336.0906; found: 336.0906.

**6-Bromo-4-methoxy-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

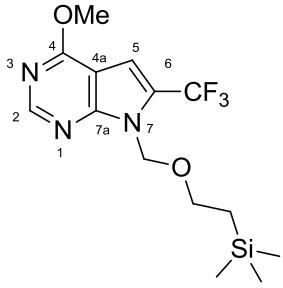
**8-Bromo-6-methoxy-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25k)**




Starting from **10** (1116 mg, 4 mmol), the reaction was performed according to the General procedure B to give product **25k** (490 mg, 34%) as white solid. M.p. 82°C. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.06 (s, 9H, $CH_3Si$); 0.90-0.93 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.56-3.60 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.11 (s, 3H, $CH_3O$); 5.67 (s, 2H, $NCH_2O$); 6.65 (s, 1H, H-5); 8.45 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.5 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 53.8 ($CH_3O$); 66.6 ($O\mathbf{C}H_2CH_2Si$); 71.6 ($NCH_2O$); 102.1 (CH-5); 106.0 (C-4a); 111.8 (C-6); 151.3 (CH-2); 152.9 (C-7a); 161.7 (C-4). IR (KBr): 3099, 2953, 2914, 1896, 1863, 1595, 1473, 1461, 1416, 1383, 1353, 1317, 1242, 1227, 1093, 911, 842. HRMS (ESI) calculated for $C_{13}H_{20}O_2N_3BrNaSi$: 380.0400; found: 380.0401.

**4-Methoxy-6-(trifluoromethyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

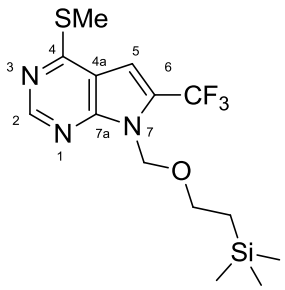
**6-Methoxy-8-(trifluoromethyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (25l)**




Starting from **10** (1116 mg, 4 mmol), the reaction was performed according to the General procedure C to give product **25l** (472 mg, 34%) as colourless oil. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.07 (s, 9H, $CH_3Si$); 0.90-0.93 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.56-3.59 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.14 (s, 3H, $CH_3O$); 5.75 (s, 2H, $NCH_2O$); 7.02 (q, 1H, $J_{5,F}$ = 1.2 Hz, H-5); 8.58 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.6 ($CH_3Si$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 54.0 ($CH_3O$); 66.7 ($O\mathbf{C}H_2CH_2Si$); 71.6 ($NCH_2O$); 102.9 (q, $J_{C,F}$ = 4.5 Hz, CH-5); 103.8 (C-4a); 120.7 (q, $J_{C,F}$ = 268.7 Hz, $CF_3$); 125.9 (q, $J_{C,F}$ = 39.2 Hz, C-6); 153.7 (CH-2); 153.9 (C-7a); 164.2 (C-4). $^{19}$F NMR (470.3 MHz, $CDCl_3$): -56.07 (s, 1F, F-2). HRMS (ESI) calculated for $C_{14}H_{21}O_2N_3F_3Si$: 348.1350; found: 348.1351.

**6-(Trifluoromethyl)-4-(methylsulfanyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine**

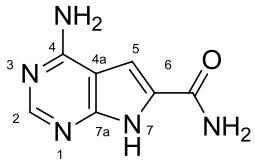
**8-(Trifluoromethyl)-6-(methylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (26l)**



Starting from **11** (1116 mg, 4 mmol), the reaction was performed according to the General procedure C to give product **26l** (472 mg, 34%) as colourless oil. $^{1}$H NMR (500 MHz, $CDCl_3$): -0.06 (s, 9H, $CH_3Si$); 0.90-0.93 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 2.72 (s, 3H, $CH_3S$); 3.56-3.59 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.75 (s, 2H, $NCH_2O$); 7.01 (q, 1H, $J_{5,F}$ = 1.1 Hz, CH-5); 8.76 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.6 ($CH_3Si$); 11.9 ($CH_3S$); 17.7 ($OCH_2\mathbf{C}H_2Si$); 66.8 ($O\mathbf{C}H_2CH_2Si$); 71.5 ($NCH_2O$); 103.1 (q, $J_{C,F}$ = 4.3 Hz, CH-5); 113.8 (C-4a); 120.6 (q, $J_{C,F}$ = 269.1 Hz, $CF_3$); 126.5 (q, $J_{C,F}$ = 39.2 Hz, C-6); 150.4 (C-7a); 153.2 (CH-2); 164.7 (C-4). $^{19}$F NMR (470.3 MHz, $CDCl_3$): -56.20 (s, 1F, F-2). IR (KBr): 2953, 2923, 2890, 1556, 1443, 1368, 1275, 1251, 1183, 1153, 1129, 1090, 860, 833. HRMS (ESI) calculated for $C_{14}H_{21}ON_3F_3SSi$: 364.1121; found: 364.1123.

**4-Amino-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxamide**

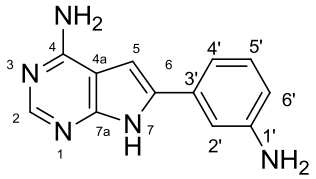
**8-Carboxamide-7-deazaadenine (31m)**



A solution of **34l** (111 mg, 0.5 mmol) and aq. ammonia (25% [w/w], 5 mL) in dioxane (5 mL) was stirred in autoclave at 120 °C for 18 h. Then the solvents were evaporated and the residue was purified by flash chromatography (HPFC) in $CHCl_3$/MeOH (5:1) to give product **31m** (45 mg, 50%) as white powder. M.p. > 350°C. $^{1}$H NMR (500.0 MHz, DMSO-$d_6$): 7.08 (s, 1H, H-5); 7.16 (bs, 2H, $NH_2$-4); 7.35 and 7.70 (2×bs, 2×1H, $CONH_2$); 8.07 (s, 1H, H-2); 11.82 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 103.05 (C-4a and CH-5); 128.4 (C-6); 151.4 (C-7a); 154.2 (CH-2); 158.9 (C-4); 162.5 (CO). IR (KBr): 3428, 3404, 3330, 3177, 3108, 2995, 2908, 2782, 1694, 1655, 1628, 1598, 1538, 1437, 1386, 1335. HRMS (ESI) calculated for $C_7H_8ON_5$: 178.0723; found: 178.0721.

**6-(3-Aminophenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine**

**8-(3-Aminophenyl)-7-deazaadenine (31h)**



A mixture of 7-deazahypoxanthine **28h** (57 mg, 0.25 mmol), benzyltriethylammonium chloride (114 g, 0.5 mmol), *N*,*N*-dimethylaniline (35 μL, 0.275 mmol) in dry MeCN (2.5 mL) was stirred at r.t. and then phosphorus oxychloride (115 μL, 1.25 mmol) was added. The mixture was then stirred at 100 °C for 6 hours. Solvents were evaporated

under reduced pressure, the residue was diluted with water and neutralized with aqueous ammonia to pH 7. Crude intermediate was filtered, washed with cold water, then with hydrochloric acid and again with cold water. After drying under reduced pressure, the intermediate was placed in steel bomb and aq ammonia (25% [w/w], 2 mL) in dioxane (2 mL) was added and stirred at 120 °C for 18 h. Then the solvents were evaporated and the residue was purified by flash chromatography (HPFC) in $CHCl_3$/MeOH (5:1) to give product **31h** (22 mg, 40%) as brown solid. M.p. more than 350°C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 6.53 (ddd, 1H, $J_{6',5'}$ = 8.0 Hz, $J_{6',2'}$ = 2.2 Hz, $J_{6',4'}$ = 1.0 Hz, H-6′); 6.83 (d, 1H, $J_{5,NH}$ = 1.9 Hz, H-5); 6.92 – 6.96 (m, 2H, H-2′,4′); 7.08 (bt, 1H, $J_{5',4'} = J_{5',6'}$ = 7.9 Hz, H-5′); 7.32 (bs, 2H, $NH_2$-4); 8.09 (s, 1H, H-2); 12.07 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 96.1 (CH-5); 103.5 (C-4a); 110.3 (CH-2′); 112.9 (CH-4′); 113.9 (CH-6′); 129.6 (CH-5′); 132.2 (C-3′); 135.5 (C-6); 149.2 (C-1′); 149.8 (CH-2); 151.3 (C-7a); 155.7 (C-4). IR (KBr): 3348, 3120, 2956, 2926, 2851, 1673, 1619, 1601, 1538, 1488, 1317, 1287, 764. HRMS (ESI) calculated for $C_{12}H_{12}N_5$: 226.1087; found: 226.1086.

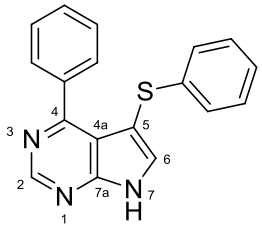
# 5.5 C-H sulfenylation of purines and deazapurines

## 5.5.1 Sulfenytion of 7-deazapurines

**General Procedure:**

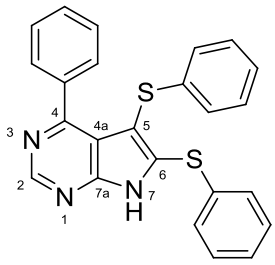
A mixture of 7-deazapurines **2, 3, 8, 35** (2 mmol), disulphides (1.5 mmol), and CuI (0.2 mmol, 10 mol %) in DMF (20 mL) was stirred at 110°C under air atmosphere for 18 hours until complete consumption of staring material as monitored by TLC. The solution was then cooled to room temperature, diluted with EtOAc (30 mL), washed with 1M solution of sodium salt of EDTA (20 mL). Aqueous solution was then extracted three times with EtOAc and combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel.

**4-Phenyl-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Phenyl-7-(phenylsulfanyl)-7-deazapurine) (36a)**



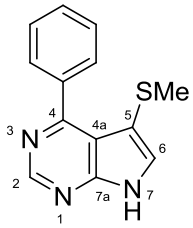
6-Phenyl-7-deazapurine **3** (390 mg, 2 mmol) and diphenyldisulfide (328 mg , 1.5 mmol) were used as starting compounds to give products **36a** (582 mg, 96%) a **37a** (25 mg, 3%) as white solids after chromatography eluting with hexane/EtOAc 5:1 to 1:1. Crystallization in hexan/EtOAc gave white needles. M.p. 184-186 °C. $^{1}$H NMR (499.8 MHz, DMSO-$d_6$): 6.70 (m, 2H, H-*o*-SPh); 6.99 (m, 1H, H-*p*-SPh); 7.06 (m, 2H, H-*m*-SPh); 7.27 (m, 2H, H-*m*-Ph); 7.38 (m, 1H, H-*p*-Ph); 7.53 (m, 2H, H-*o*-Ph); 8.05 (d, 1H, $J_{6,NH}$ = 2.5, H-6); 8.88 (s, 1H, H-2); 12.86 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 99.90 (C-5); 115.26 (C-4a); 125.25 (CH-*p*-SPh); 126.04 (CH-*o*-SPh); 127.29 (CH-*m*-Ph); 128.80 (CH-*m*-SPh); 129.23 (CH-*p*-Ph); 129.86 (CH-*o*-Ph); 135.69 (CH-6); 137.04 (C-*i*-Ph); 138.47 (C-*i*-SPh); 151.53 (CH-2); 153.55 (C-7a); 159.40 (C-4). IR(KBr): 3104, 3059, 2988, 2862, 2818, 1598, 1581, 1551, 1478, 1435, 1322. HRMS (ESI) calculated for $C_{18}H_{14}N_3S$: 304.0902; found: 304.0901. Anal. calculated for $C_{18}H_{13}N_3S$ (303.08): C 71.26%, H 4.32%, N 13.85%, S 10.57%; found: C 71.07%, H 4.15%, N 13.57%, S 10.47%.

**4-Phenyl-5,6-bis(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Phenyl-7,8-bis(phenylsulfanyl)-7-deazapurine) (37a)**



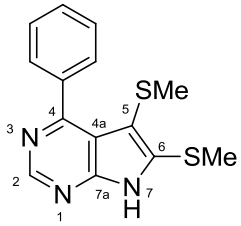
M.p. 231-233 °C. $^{1}$H NMR (500.0 MHz, $CDCl_3$): 6.68 (m, 2H, H-*o*-SPh-5); 6.95 (m, 1H, H-*p*-SPh-5); 6.98 (m, 2H, H-*m*-SPh-5); 7.23 (m, 2H, H-*m*-Ph); 7.28-7.365 (m, 3H, H-*p*-Ph, H-*m*,*p*-SPh-6); 7.45 (m, 2H, H-*o*-SPh-6); 7.49 (m, 2H, H-*o*-Ph); 8.62 (s, 1H, H-2); 10.33 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 104.40 (C-5); 117.30 (C-4a); 125.40 (CH-*p*-SPh-5); 126.82 (CH-*o*-SPh-5); 127.46 (CH-*m*-Ph); 128.61 (CH-*m*-SPh-5); 129.04 (CH-*p*-Ph); 129.39 (CH-*p*-SPh-6); 129.87 (CH-*o*-Ph); 130.09 (CH-*m*-SPh-6); 131.02 (C-*i*-SPh-6); 132.24 (CH-*o*-SPh-6); 136.50 (C-*i*-Ph); 137.17 (C-*i*-SPh-5); 140.40 (C-6); 151.31 (CH-2); 153.27 (C-7a); 159.77 (C-4). IR(KBr): 3430, 3073, 2489, 1581, 1559, 1477, 1327. HRMS (ESI) calculated for $C_{24}H_{18}N_3S_2$: 412.0935; found: 412.0936.

**5-(Methylsulfanyl)-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(7-(Methylsulfanyl)-6-phenyl-7-deazapurine) (36b)**



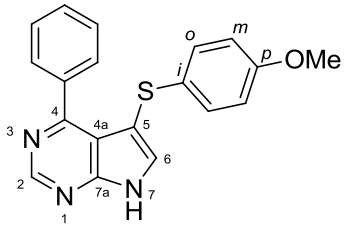

6-Phenyl-7-deazapurine **3** (390 mg, 2 mmol) and dimethyldisulfide (0.9 mL, 10 mmol) were used as starting compounds to give products **36b** (343 mg, 71%) a **37b** (86 mg, 15%) as yellow solids after chromatography with hexane/EtOAc 5:1 to 1:1. M.p. 174-175 °C. $^{1}$H NMR (600.1 MHz, $CDCl_3$): 1.92 (s, 3H, $CH_3S$); 7.37 (d, 1H, *J* = 2.1, H-6); 7.53 (m, 3H, H-*m*,*p*-Ph); 7.91 (m, 2H, H-*o*-Ph); 9.01 (s, 1H, H-2); 11.12 (bs, 1H, NH). $^{13}$C NMR (150.9 MHz, $CDCl_3$): 18.99 ($CH_3S$); 108.89 (C-5); 115.85 (C-4a); 126.78 (CH-6); 127.84 (CH-*m*-Ph); 129.76 (CH-*p*-Ph); 129.93 (CH-*o*-Ph); 137.27 (C-*i*-Ph); 151.29 (CH-2); 153.17 (C-7a); 160.54 (C-4). IR($CDCl_3$): 3452, 3114, 2924, 2855, 1579, 1553, 1453, 1442, 1325. HRMS (ESI) calculated for $C_{13}H_{12}N_3S$: 242.0746; found: 242.0746.

**5,6-Bis(methylsulfanyl)-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(7,8- Bis(methylsulfanyl)-6-phenyl-7-deazapurine) (37b)**




M.p. 139-141 °C. $^{1}$H NMR (499.8 MHz, DMSO-$d_6$): 1.70 (s, 3H, $CH_3S$-5); 2.66 (s, 3H, $CH_3S$-6); 7.48-7.55 (m, 3H, H-*m*,*p*-Ph); 7.80 (m, 2H, H-*o*-Ph); 8.81 (s, 1H, H-2); 12.86 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 15.74 ($CH_3S$-6); 19.33 ($CH_3S$-5); 103.91 (C-5); 116.72 (C-4a); 127.51 (CH-*m*-Ph); 129.49 (CH-*p*-Ph); 129.95 (CH-*m*-Ph); 136.69 (C-*i*-Ph); 142.14 (C-6); 149.87 (CH-2); 153.67 (C-7a); 156.20 (C-4). IR(KBr): 2920, 2857, 1739, 1577, 1550, 1464, 1458, 1437, 1317, 1254, 770, 704. HRMS (ESI) calculated for $C_{14}H_{14}N_3S_2$: 288.0624; found: 288.0624.

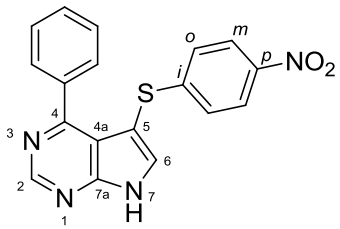
**5-[(4-Methoxyphenyl)sulfanyl]-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(7-[(4-Methoxyphenyl)sulfanyl]-6-phenyl-7-deazapurine) (36c)**




6-Phenyl-7-deazapurine **3** (390 mg, 2 mmol) and bis(4-methoxyphenyl) disulphide (418 mg, 1.5 mmol) were used as starting compounds to give product **36c** (608 mg, 91%) as white solids after chromatography eluting with hexane/EtOAc 5:1 to 1:1. Crystallization from hexan/EtOAc gave white needles. M.p. 192-196 °C. $^{1}$H NMR (499.8 MHz, $CDCl_3$): 3.71 (s, 3H, $CH_3O$); 6.59 (m, 2H, H-*m*-$SC_6H_4OMe$); 6.74 (m, 2H, H-*o*-$SC_6H_4OMe$); 7.42 (m, 2H, H-*m*-Ph); 7.47 (m, 1H, H-*p*-Ph);

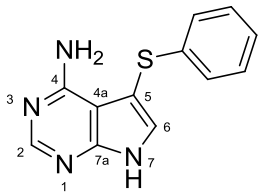
7.54(s, 1H, H-6); 7.68 (m, 2H, H-*o*-Ph); 9.00 (s, 1H, H-2); 11.13 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 55.29 ($CH_3O$); 106.46 (C-5); 114.30 (CH-*m*-$SC_6H_4OMe$); 115.56 (C-4a); 127.29 (C-*i*-$SC_6H_4OMe$); 127.61 (CH-*m*-Ph); 129.53 (CH-*p*-Ph); 130.09 (CH-*o*-Ph); 130.67 (CH-*o*-$SC_6H_4OMe$); 131.02 (CH-6); 136.82 (C-*i*-Ph); 151.35 (CH-2); 153.33 (C-7a); 158.39 (C-*p*-$SC_6H_4OMe$); 160.94 (C-4). IR(KBr): 3099, 2982, 2959, 2835, 1595, 1552, 1493, 1249, 1026. HRMS (ESI) calculated for $C_{19}H_{16}ON_3S$: 334.1009; found: 334.1008.

**5-[(4-Nitrophenyl)sulfanyl]-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(7-[(4-Nitrophenyl)sulfanyl]-6-phenyl-7-deazapurine) (36d)**




6-Phenyl-7-deazapurine **3** (390 mg, 2 mmol) and 4-nitrophenyl disulphide (463 mg, 1.5 mmol) were used as starting compounds to give product **36d** (328 mg, 47%) as green solids after chromatography eluting with hexane/EtOAc 5:1 to 1:1. M.p. 253-261 °C. $^1$H NMR (499.8 MHz, DMSO-$d_6$): 6.88 (m, 2H, H-*o*-$SC_6H_4NO_2$); 7.22 (m, 2H, H-*m*-Ph); 7.32 (m, 1H, H-*p*-Ph); 7.47 (m, 2H, H-*o*-Ph); 7.88 (m, 2H, H-*m*-$SC_6H_4NO_2$); 8.16 (s, 1H, H-6); 8.92 (s, 1H, H-2); 13.03 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 97.21 (C-5); 115.06 (C-4a); 123.79 (CH-*m*-$SC_6H_4NO_2$); 125.47 (CH-*o*-$SC_6H_4NO_2$); 127.29 (CH-*m*-Ph); 129.28 (CH-*p*-Ph); 129.63 (CH-*o*-Ph); 136.31 (CH-6); 136.71 (C-*i*-Ph); 144.53 (C-*p*-$SC_6H_4NO_2$); 149.10 (C-*i*-$SC_6H_4NO_2$); 151.84 (CH-2); 153.69 (C-7a); 159.56 (C-4). IR(KBr): 2986, 2862, 2821, 1600, 1580, 1553, 1502, 1342, 1320, 1085. HRMS (ESI) calculated for $C_{18}H_{13}O_2N_4S$: 349.0754; found: 349.0753.

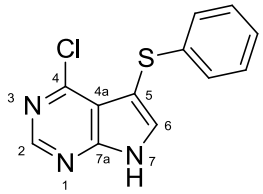
**5-(Phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidin-4-amine**
**(7-(Phenylsulfanyl)-7-deazaadenine) (36e)**




6-Amino-7-deazapurine **35** (268 mg, 2 mmol) and diphenyldisulfide (1.1 g, 5 mmol) were used as starting compounds to give product **36f** (384 mg, 79%) as white solids after chromatography eluting DCM/MeOH 10:0 to 7:3 with 1% $Et_3N$. M.p. 268-299 °C $^1$H NMR (500.0 MHz, DMSO-$d_6$): 6.52 (bs, 2H, $NH_2$); 7.09 (m, 2H, H-*o*-Ph); 7.13 (m, 1H, H-*p*-Ph); 7.27 (m, 2H, H-*m*-Ph); 7.58 (s, 1H, H-8); 8.10 (s, 1H, H-2); 12.16 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 98.03 (C-7); 102.87 (C-5); 125.67 (CH-*p*-Ph); 125.79 (CH-*o*-Ph);

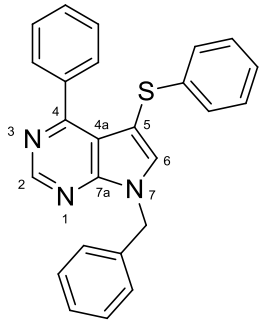
129.35 (CH-*m*-Ph); 129.91 (CH-8); 138.94 (C-*i*-Ph); 151.83 (C-4); 152.79 (CH-2); 157.52 (C-6). IR(KBr):3456, 3100, 3066, 1644,1611, 1597, 1582, 1479, 1318. HRMS (ESI) calculated for $C_{12}H_{11}N_4S$: 243.0699; found: 243.0699

**4-Chloro-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Chloro-7-(phenylsulfanyl)-7-deazapurine) (44a)**




6-Chloro-7-deazapurine **8** (307 mg, 2 mmol) and diphenyldisulfide (2.2 g, 10 mmol) were used as starting compounds to give product **44a** (472 mg, 90%) as white solids. Diphenyldisulfide was divided into five portions and each one was added every 10 hours until complete consumption of staring material as monitored by TLC. Chromatography was started with pure hexane (to remove excess of diphenyldisulfide) and followed by hexane/EtOAc 5:1 to 1:1. Crystallization in hexan/EtOAc gave white crystals. M.p. 184-186 °C $^1$H NMR (499.8 MHz, DMSO-$d_6$): 7.06 (m, 2H, H-*o*-Ph); 7.12 (m, 1H, H-*p*-Ph); 7.24 (m, 2H, H-*m*-Ph); 8.12 (d, 1H, $J$ = 2.6, H-6); 8.65 (s, 1H, H-2); 13.11 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 99.70 (C-5); 116.29 (C-4a); 125.49 (CH-*p*-Ph); 125.90 (CH-*o*-Ph); 129.25 (CH-*m*-Ph); 136.32 (CH-6); 139.13 (C-*i*-Ph); 150.98 (C-4); 151.44 (CH-2); 153.31 (C-7a). IR(KBr): 3072, 2963, 2813, 1596, 1551, 1478, 1439, 1338, 1228, 975, 844, 734. HRMS (ESI) calculated for $C_{12}H_9N_3ClS$: 262.0200; found: 262.0200.

**7-Benzyl-4-phenyl-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-6-phenyl-7-(phenylsulfanyl)-7-deazapurine) (53a)**




7-Benzyl-6-phenyl-7-deazapurine **2** (570 mg, 2 mmol) and diphenyldisulfide (1.1 g, 5 mmol) was used as starting compound and after 18 h the reaction give product **53a** (157 mg, 20%) as white solids after chromatography eluting with hexane/EtOAc 10:1 to 4:1. Crystallization in hexan/EtOAc gave white crystals. Recovery of starting compound **2** was found (405 mg, 71%). M.p. 91-94 °C $^1$H NMR (500.0 MHz, $CDCl_3$): 5.55 (s, 2H, $CH_2$Ph); 6.71 (m, 2H, H-*o*-SPh); 6.98 (m, 1H, H-*p*-SPh); 6.99 (m, 2H, H-*m*-SPh); 7.29 (m, 2H, H-*m*-Bn); 7.33 (m, 2H, H-*o*-Bn); 7.35-7.40 (m, 4H, H-*m*,*p*-Ph, H-*p*-Bn); 7.48 (s, 1H, H-6); 7.52 (m, 2H, H-*o*-Ph); 9.01 (s, 1H, H-2). $^{13}$C NMR (125.7

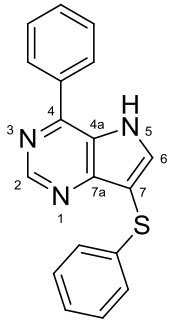
MHz, $CDCl_3$): 48.23 ($CH_2Ph$); 102.82 (C-5); 115.90 (C-4a); 125.25 (CH-*p*-SPh); 126.80 (CH-*o*-SPh); 127.38 (CH-*m*-Bn); 127.85 (CH-*o*-Bn); 128.28 (CH-*p*-Bn); 128.45 (CH-*m*-SPh); 129.03 (CH-*m*-Ph); 129.20 (CH-*p*-Ph); 129.80 (CH-*o*-Ph); 135.25 (CH-6); 136.14 (C-*i*-Ph); 136.78 (C-*i*-Bn); 137.81 (C-*i*-SPh); 151.93 (CH-2); 152.66 (C-7a); 160.93 (C-4). IR(KBr): 1552, 1451, 1414, 1330, 983. HRMS (ESI) calculated for $C_{25}H_{20}N_3S$: 394.1372; found: 394.1371. Anal. calculated for $C_{25}H_{19}N_3S$ (393.13): C 76.31%, H 4.87%, N 10.68%, S 8.15%; found: C 76.13%, H 4.69%, N 10.43%, S 8.02%.

## 5.5.2 Sulfenytion of 9-deazapurines

**General Procedure:**

A mixture of CuI (0.2 mmol, 10 mol %) and 2,2'-bipyridine (0.4 mmol, 20 mol %) in DMF (10 mL) was stirred at rt for 15 minutes and then was added to mixture of 9-deazapurines **38-40** (2 mmol), disulphides (3 mmol) in DMF (20 mL) and then was stirred at 110°C under air atmosphere for 48 hours until complete consumption of staring material as monitored by TLC. The solution was then cooled to room temperature, diluted with EtOAc (30 mL), washed with 1M solution of sodium salt of EDTA (20 mL). Aqueous solution was then extracted three times with EtOAc and combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel.

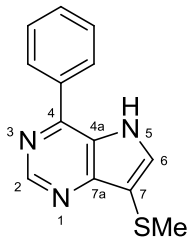
**4-Phenyl-7-(phenylsulfanyl)-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(6-Phenyl-9-(phenylsulfanyl)-9-deazapurine) (41a)**




6-Phenyl-9-deazapurine **38** (390 mg, 2 mmol) and diphenyldisulfide (656 mg, 3 mmol) were used as starting compounds to give product **41a** (596 mg, 98%) as white solids after chromatography eluting with hexane/EtOAc 5:1 to 1:2. Crystallization in hexan/EtOAc gave white needles. M.p. 210-216 °C. $^1$H NMR (499.8 MHz, DMSO-$d_6$): 7.10 (m, 3H, H-*o*,*p*-SPh); 7.22 (m, 2H, H-*m*-SPh); 7.61 (m, 1H, H-*p*-Ph); 7.63 (m, 2H, H-*m*-Ph); 8.11 (m, 2H, H-*o*-Ph); 8.29 (s, 1H, H-6); 8.95 (s, 1H, H-2); 12.56 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 101.28 (C-7); 124.83 (C-4a); 125.30 (CH-*p*-SPh); 126.02 (CH-*o*-SPh); 128.99 (CH-*o*-Ph); 129.10, 129.15 (CH-*m*-Ph, CH-*m*-SPh); 130.61 (CH-*p*-Ph); 135.77 (C-*i*-Ph); 138.63 (C-*i*-SPh); 140.37

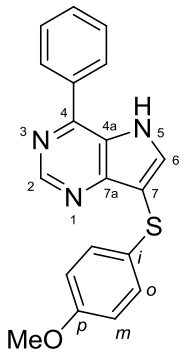
(CH-6); 148.88 (C-4); 151.29 (CH-2); 151.43 (C-7a). IR(KBr): 3066, 2835, 1594, 1542, 1505, 1490, 1480, 1429. HRMS (ESI) calculated for $C_{18}H_{14}N_3S$: 304.0902; found: 304.0902.

**7-(Methylsulfanyl)-4-phenyl-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(9-(Methylsulfanyl)-6-phenyl-9-deazapurine) (41b)**



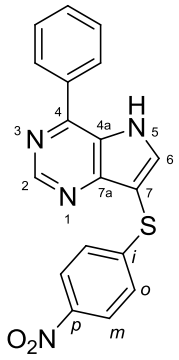

6-Phenyl-9-deazapurine **38** (390 mg, 2 mmol) and dimethyldisulfide (1.26 mL, 14 mmol) was used as starting compounds to give product **41b** (145 mg, 30%) as yellow solids after chromatography with hexane/EtOAc 5:1 to 1:2. M.p. 196-206 °C. $^1$H NMR (499.8 MHz, DMSO-$d_6$): 2.46 (s, 3H, $CH_3S$); 7.59 (m, 1H, H-*p*-Ph); 7.61 (m, 2H, H-*m*-Ph); 7.94 (s, 1H, H-6); 8.07 (m, 2H, H-*o*-Ph); 8.94 (s, 1H, H-2); 12.15 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 18.12 ($CH_3S$); 107.46 (C-7); 124.55 (C-4a); 128.88 (CH-*o*-Ph); 129.17 (CH-*m*-Ph); 130.54 (CH-*p*-Ph); 135.06 (CH-6); 135.99 (C-*i*-Ph); 148.42 (C-4); 150.50 (CH-2); 150.54 (C-7a). IR(KBr): 3053, 2988, 2924, 2824, 1604, 1592, 1537, 1502, 1486, 1471, 1421, 1115, 866, 771. HRMS (ESI) calculated for $C_{13}H_{12}N_3S$: 242.0746; found: 242.0746.

**7-((4-Methoxyphenyl)sulfanyl)-4-phenyl-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(9-((4-Methoxyphenyl)sulfanyl)-6-phenyl-9-deazapurine) (41c)**



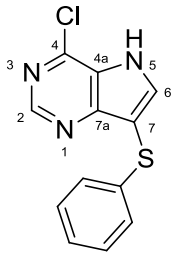

6-Phenyl-9-deazapurine **38** (390 mg, 2 mmol) and bis(4-methoxyphenyl) disulphide (836 mg, 3 mmol) were used as starting compounds to give product **10c** (566 mg, 85%) as yellow crystals after chromatography eluting with hexane/EtOAc 5:1 to 1:2. M.p. 175-177 °C. $^1$H NMR (600.1 MHz, $CDCl_3$): 3.63 (s, 3H, $CH_3O$); 6.63 (m, 2H, H-*m*-$SC_6H_4OMe$); 7.03 (m, 2H, H-*m*-$SC_6H_4OMe$); 7.20 (m, 2H, H-*m*-Ph); 7.26 (m, 1H, H-*p*-Ph); 7.72 (d, 1H, $J$ = 3.0, H-6); 7.86 (m, 2H, H-*o*-Ph); 8.66 (s, 1H, H-2); 12.59 (bs, 1H, NH). $^{13}$C NMR (150.9 MHz, $CDCl_3$): 55.10 ($CH_3O$); 104.13 (C-7); 114.33 (CH-*m*-$SC_6H_4OMe$); 125.56 (C-4a); 128.15 (C-*i*-$SC_6H_4OMe$); 128.50 (CH-*o*-Ph); 128.60 (CH-*m*-Ph); 128.71 (CH-*o*-$SC_6H_4OMe$); 130.16 (CH-*p*-Ph); 135.34 (C-*i*-Ph); 139.05 (CH-6); 149.91 (C-4); 150.56 (C-7a); 150.77 (CH-2); 157.91 (C-*p*-$SC_6H_4OMe$). IR($CDCl_3$): 3453, 3066, 2838, 2231, 1671, 1595, 1537, 1493, 1464, 1287, 1244, 1182, 1034. HRMS (ESI) calculated for $C_{19}H_{16}ON_3S$: 334.1009; found: 334.1008.

**7-((4-Nitrophenyl)sulfanyl)-4-phenyl-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(9-((4-Nitrophenyl)sulfanyl)-6-phenyl-9-deazapurine) (41d)**



6-Phenyl-9-deazapurine **38** (390 mg, 2 mmol) and 4-nitrophenyl disulphide (926 mg, 3 mmol) were used as starting compounds to give product **41d** (348 mg, 50%) as yellow crystals after chromatography eluting with hexane/EtOAc 5:1 to 1:2. M.p. 114-118 °C. $^{1}$H NMR (600.1 MHz, DMSO-$d_6$): 7.25 (m, 2H, H-*o*-$SC_6H_4NO_2$); 7.64 (m, 1H, H-*p*-Ph); 7.65 (m, 2H, H-*m*-Ph); 8.07 (m, 2H, H-*m*-$SC_6H_4NO_2$); 8.13 (m, 2H, H-*o*-Ph); 8.41 (s, 1H, H-6); 8.96 (s, 1H, H-2); 12.75 (bs, 1H, NH). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 98.61 (C-7); 124.20 (CH-*m*-$SC_6H_4NO_2$); 125.11 (C-4a); 125.56 (CH-*o*-$SC_6H_4NO_2$); 129.01 (CH-*o*-Ph); 129.18 (CH-*m*-Ph); 130.72 (CH-*p*-Ph); 135.65 (C-*i*-Ph); 140.90 (CH-6); 144.80 (C-*p*-$SC_6H_4NO_2$); 149.09 (C-*i*-$SC_6H_4NO_2$); 149.17 (C-4); 151.18 (C-7a); 151.49 (CH-2). IR(KBr): 3095, 3065, 1596, 1580, 1540, 1506, 1322, 1115, 1089, 854. HRMS (ESI) calculated for $C_{18}H_{13}O_2N_4S$:349.0754; found: 349.0753.

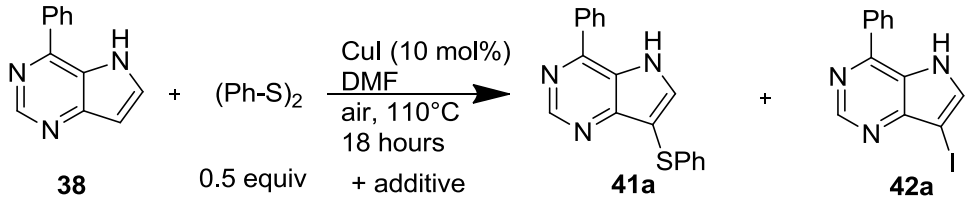
**4-Chloro-7-(phenylsulfanyl)-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(6-Chloro-9-(phenylsulfanyl)-9-deazapurine) (41e)**



6-Chloro-9-deazapurine **40** (307 mg, 2 mmol) and diphenyldisulfide (3.1 g, 14 mmol) were used as starting compounds to give product **41e** (471 mg, 90%) as white solids. Diphenyldisulfide was divided into seven portions and each one was added every 10 hours until complete consumption of staring material as monitored by TLC. Chromatography was started with hexane (to remove excess of diphenyldisulfide) and followed by hexane/EtOAc 5:1 to 1:2. Crystallization in hexan/EtOAc gave white crystals. [Do not excess the reaction time (80 hours) to avoid forming mixture of products.] M.p. 224-226 °C $^{1}$H NMR (499.8 MHz, DMSO-$d_6$):7.06 (m, 2H, H-*o*-Ph); 7.10 (m, 1H, H-*p*-Ph); 7.21 (m, 2H, H-*m*-Ph); 8.39 (s, 1H, H-6); 8.69 (s, 1H, H-2); 13.08 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 102.28 (C-7); 125.36 (C-4a); 125.48 (CH-*p*-Ph); 126.11 (CH-*o*-Ph); 129.16 (CH-*m*-Ph); 138.12 (C-*i*-Ph); 140.98 (CH-6); 142.99 (C-4); 150.43 (CH-2); 151.38 (C-7a). IR(KBr): 3072, 1796, 1612, 1584, 1524, 1494, 1478, 1422, 1393, 1215, 868. HRMS (ESI) calculated for $C_{12}H_9N_3ClS$: 262.0200; found: 262.0200.

**Optimization of bypirydine ligand**

A mixture of CuI (0.1 mmol, 10 mol %) and bypiridine ligand (10-100 mol%) in DMF (5 mL) was stirred at rt for 15 minutes and then was added to mixture of 9-deazapurines **7** (195 mg, 1 mmol) and diphenyl disulphides (110 mg, 0.5 mmol) in DMF (5 mL) and then was stirred at 110°C under air atmosphere for 18 hours. The solution was then cooled to room temperature, diluted with EtOAc (10 mL), washed with 1M solution of sodium salt of EDTA (5 mL). Aqueous solution was then extracted three times with EtOAc and combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum and NMR of reaction mixture was measured.




NMR conversion

| **additive** | **7** | **10a** | **11a** |
|---|---|---|---|
| bpy (10 mol%) | 54% | 43% | 3% |
| bpy (20 mol%) | 55% | 45% | 0% |
| bpy (50 mol%) | 22% | 78% | 0% |
| bpy (100 mol%) | 15% | 85% | 0% |
| dtbpy (10 mol%) | 35% | 63% | 2% |
| dtbpy (20 mol%) | 29% | 71% | 0% |
| dtbpy (50 mol%) | 21% | 79% | 0% |
| dtbpy (100 mol%) | 0% | 100% | 0% |

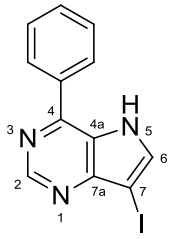
As the most economical ligand was chosen bpy (20 mol%) for substrates **41a-d** and the time was prolonged until complete conversion (generally 48 hours). To avoid mixture of products

for substrate **41e** was used as a ligand more effective dtbpy (20 mol%) to finish reaction up to 80 hours.

**Halogenation of 9-deazapurines. General Procedure:**

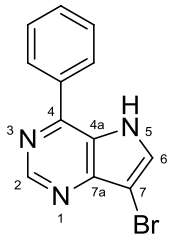
A mixture of 9-deazapurine **38** or **40** (0.5 mmol) and $CuX_2$ (I, $Br_2$) (0.6 mmol) in DMF (5 mL) was stirred at 110°C under air atmosphere for 18 hours until complete consumption of staring material as monitored by TLC. The solution was then cooled to room temperature, diluted with EtOAc (15 mL), washed with 1M solution of sodium salt of EDTA (10 mL). Aqueous solution was then extracted three times with EtOAc and combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel.

**7-Iodo-4-phenyl-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(9-Iodo-6-phenyl-9-deazapurine) (42a)**



6-Phenyl-9-deazapurine **38** (98 mg, 0.5 mmol) and CuI (115 mg, 0.6 mmol) were used as starting compound to give product **42a** (130 mg, 81%) as white solid after chromatography eluting with hexane/EtOAc 5:1 to 1:2. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 7.60 (m, 3H, H-*m*,*p*-Ph); 8.09 (m, 2H, H-*o*-Ph); 8.11 (s, 1H, H-6); 8.97 (s, 1H, H-2); 12.43 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 58.43 (C-7); 124.08 (C-4a); 128.90 (CH-*o*-Ph); 129.07 (CH-*m*-Ph); 130.54 (CH-*p*-Ph); 135.57 (C-*i*-Ph); 137.73 (CH-6); 148.48 (C-4); 150.95 (CH-2); 151.19 (C-7a). IR(KBr): 3434, 1605, 1595, 1539, 1504, 1486. HRMS (ESI) calculated for $C_{12}H_9N_3I$: 321.9836; found: 321.9835

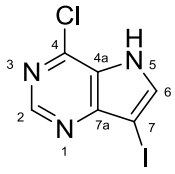
**7-Bromo-4-phenyl-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(9-Bromo-6-phenyl-9-deazapurine) (42b)**



6-Phenyl-9-deazapurine **38** (98 mg, 0.5 mmol) and $CuBr_2$ (134 mg, 0.6 mmol) were used as starting compound to give product **42b** (123 mg, 75%) as white solid after chromatography eluting with hexane/EtOAc 5:1 to 1:2. M.p. 264 - 294 °C. $^1$H NMR (499.8 MHz, DMSO-$d_6$): 7.59 (m, 1H, H-*p*-Ph); 7.62 (m, 2H, H-*m*-Ph); 8.08 (m, 2H, H-*o*-Ph); 8.15 (d, 1H, $J$ = 3.1, H-6); 8.98 (s, 1H, H-2); 12.40 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 89.68 (C-7); 123.66 (C-4a); 128.96

(CH-*o*-Ph); 129.14 (CH-*m*-Ph); 130.68 (CH-*p*-Ph); 133.44 (CH-6); 135.53 (C-*i*-Ph); 147.88 (C-7a); 148.77 (C-4); 150.98 (CH-2). IR(KBr): 3438, 3054, 2929, 2788, 1607, 1597, 1545, 1508, 1490,1432, 1184. HRMS (ESI) calculated for $C_{12}H_9N_3Br$: 273.9974; found: 273.9974.

**4-Chloro-7-iodo-*5H*-pyrrolo[3,2-*d*]pyrimidine**
**(6-Chloro-9-iodo-9-deazapurine) (42c)**

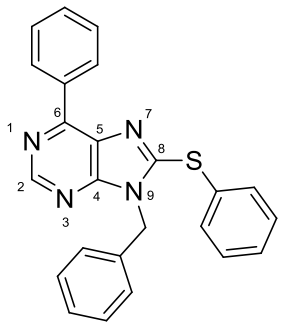


6-Chloro-9-deazapurine **40** (77 mg, 0.5 mmol) and CuI (115 mg, 0.6 mmol) were used as starting compound to give product **42c** (91 mg, 65%) as white solid after chromatography eluting with hexane/EtOAc 5:1 to 1:2. $^1$H NMR (499.8 MHz, DMSO-$d_6$): 8.20 (s, 1H, H-6); 8.71 (s, 1H, H-2); 12.95 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 58.68 (C-7); 124.59 (C-4a); 138.45 (CH-6); 142.30 (C-4); 150.00 (CH-2); 151.13 (C-7a). IR(KBr): 3436, 3120, 3092, 2972, 1609, 1527, 1494, 1417, 1354, 1245, 1177, 898, 860. HRMS (ESI) calculated for $C_6H_4N_3ClI$: 279.9133; found: 279.9133.

## 5.5.3 Sulfenytion of 9-benzyl-6-phenyl-*9H*-purine

A 20 mL sealable tube equipped with a magnetic stirring bar was charged with all solid reaction components, 9-benzyl-6-phenyl-*9H*-purine **1** (286 mg, 1 mmol), disulphide (2.5 mmol), *t*BuOLi (240 mg, 3 mmol) and 1,4-dioxane (2 mL) via a syringe. The vessel was close by Teflon-coated screw cap under Ar and was placed in a pre-heated oil bath at 130 °C and stirred until complete consumption of staring material as monitored by TLC, approx. 130 hours. It was cooled to room temperature and diluted with ethyl acetate (15 mL). The resulting solution was directly filtered through a filter paper and concentrated under reduced pressure.

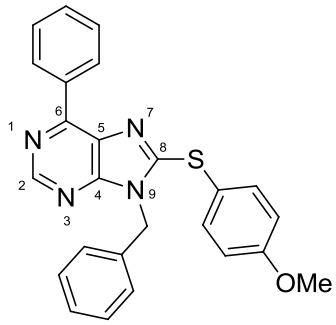
**9-Benzyl-6-phenyl-8-(phenylsulfanyl)-*9H*-purine (43a)**



Diphenyldisulfide (546 mg, 2.5 mmol) was used as starting compound to give product **43a** (237 mg, 60%) as white crystals after chromatography eluting with hexane/EtOAc 5:1 to 1:2. M.p. 101 - 104 °C. $^1$H NMR (499.8 MHz, $CDCl_3$): 5.50 (s, 2H, $CH_2$Ph); 7.27-7.35 (m, 5H, H-*o*,*m*,*p*-Bn); 7.37-7.41 (m, 5H, H-*m*,*p*-PhS); 7.45-7.50 (m, 3H, H-*m*,*p*-Ph); 7.59 (m, 2H, H-*o*-PhS); 8.74 (m, 2H, H-*o*-Ph); 8.96 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.59 ($CH_2$Ph); 127.75 (CH-*o*-Bn); 128.18 (CH-*p*-Bn);

128.50 (CH-*m*-Ph); 128.68 (C-*i*-PhS); 128.82 (CH-*m*-Bn); 129.03 (CH-*p*-PhS); 129.37 (CH-*m*-PhS); 129.68 (CH-*o*-Ph); 130.78 (CH-*p*-Ph); 131.16 (C-5); 132.91 (CH-*o*-PhS); 135.24 (C-*i*-Bn); 135.54 (C-*i*-Ph); 151.95 (CH-2); 152.37 (C-6); 152.92 (C-8); 154.46 (C-4). IR(KBr): 2921, 2851, 1580, 1561, 1495, 1459, 1429, 1258, 764. HRMS (ESI) calculated for $C_{24}H_{19}N_4S$: 395.1325; found: 395.1323.

**9-Benzyl-8-[(4-methoxyphenyl)sulfanyl]-6-phenyl-*9H*-purine (43b)**




Bis(4-methoxyphenyl) disulphide (696 mg, 2.5 mmol) was used as starting compound to give product **43b** (238 mg, 56% ) as white crystals after chromatography eluting with hexane/EtOAc 5:1 to 1:2. M.p. 124-127 °C. $^1$H NMR (500.0 MHz, $CDCl_3$): 3.85 (s, 3H, $CH_3O$); 5.49 (s, 2H, $CH_2Ph$); 6.94 (m, 2H, H-*m*-$SC_6H_4OMe$); 7.28-7.36 (m, 5H, H-*o,m,p*-Bn); 7.45-7.50 (m, 3H, H-*m,p*-Ph); 7.56 (m, 2H, H-*o*-$SC_6H_4OMe$); 8.73 (m, 2H, H-*o*-Ph); 8.95 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.47 ($CH_2Ph$); 55.43 ($CH_3O$); 114.96 (CH-*m*-$SC_6H_4OMe$); 118.00 (C-*i*-$SC_6H_4OMe$); 127.73 (CH-*o*-Bn); 128.16 (CH-*p*-Bn); 128.47 (CH-*m*-Ph); 128.81 (CH-*m*-Bn); 129.65 (CH-*o*-Ph); 130.73 (CH-*p*-Ph); 131.10 (C-5); 135.21 (C-*i*-Bn); 135.39 (C-*i*-Ph); 135.84 (CH-*o*-$SC_6H_4OMe$); 151.47 (CH-2); 151.61 (C-6); 154.67 (C-4,8); 160.76 (C-*p*-$SC_6H_4OMe$). IR (KBr): 3066, 3022, 2953, 2923, 2854, 1586, 1559, 1494, 1542, 1443, 1323, 1302, 1245, 1171, 1030, 833, 770, 725, 692. HRMS (ESI) calculated for $C_{25}H_{21}ON_4S$: 425.1431; found: 425.1429.

## 5.6 C-H sulfenylation in synthesis of substituted 7-deazapurine bases and ribonucleosides

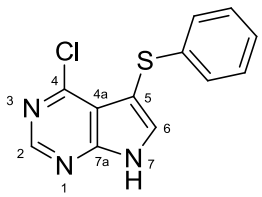
The synthetic approach to target 7-arylsulfanyl-7-deazapurines was based on recently developed direct C-H sulfenylation[119] of 6-chloro-7-deazapurine **8** catalysed by CuI and dtbpy under oxygen atmosphere. This modified procedure (oxygen atmosphere and dtbpy) gave better results than previously published methods developed for related heterocycles.[119]

**Sulfenytion of 7-deazapurines. General Procedure:**

A mixture of 6-chlor-7-deazapurine (15.36 g, 100 mmol), disulphides (100 mmol), CuI (1.9 g, 10 mmol) and dtbpy (5.37 g, 20 mmol) in DMF (300 mL) was stirred at 110°C under oxygen

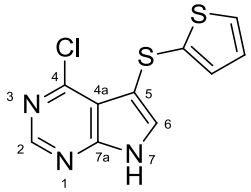
for 18 hours until complete consumption of staring material as monitored by TLC. The solution was then cooled to room temperature, diluted with EtOAc (200 mL), washed with 1M solution of sodium salt of EDTA (100 mL). Aqueous solution was then extracted three times with EtOAc and combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel.

**4-Chloro-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Chloro-7-(phenylsulfanyl)-7-deazapurine) (44a)**




Diphenyldisulfide (21.83 g, 100 mmol) was used as starting compounds to give product **44a** (22.25 g, 85%) as yellowish solids. Chromatography was started with pure hexane (to remove excess of disulphide) and followed by hexane/EtOAc 5:1 to 1:1. Crystallization in ethanol gave white crystals. $^1$H NMR was compared with published data.[119]

**4-Chloro-5-(thiophen-2-ylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Chloro-7-(thiophen-2-ylsulfanyl)-7-deazapurine) (45a)**



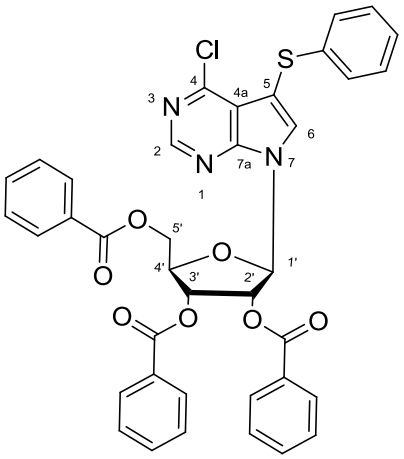

2-Thienyl disulphide (23.04 g, 100 mmol) was used as starting compounds to give product **45a** (25.5 g, 95%) as white solids. Chromatography was started with pure hexane (to remove excess of disulphide) and followed by hexane/EtOAc 5:1 to 1:1. M.p. 176 °C. $^1$H NMR (500 MHz, DMSO-$d_6$): 6.98 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-thienyl); 7.21 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-thienyl); 7.51 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-thienyl); 8.06 (s, 1H, H-6); 8.59 (s, 1H, H-2); 13.03 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 104.01 (C-5); 115.45 (C-4a); 128.03 (CH-4-thienyl); 129.25 (CH-5-thienyl); 130.61 (CH-3-thienyl); 134.76 (CH-6); 136.71 (C-2-thienyl); 150.92 (C-4); 151.40 (CH-2); 152.76 (C-7a). IR (KBr): 3066, 2944, 2809, 2770, 1601, 1556, 1446, 1401, 1401, 1332, 1239, 1216, 1003, 973, 848, 716, 623. HRMS (ESI) calculated for $C_{10}H_7N_3ClS_2$: 267.9767; found: 267.9764.

**Glycosylation of 7-sulfanyl-7-deazapurines. General Procedure:**

7-Sulfanyl-7-deazapurine **44a-45a** (40 mmol) was suspended in acetonitrile (200 ml) and BSA (10.4 ml, 40 mmol) was added. Reaction mixture was stirred for 15 min at rt (during this time clear solution was formed). Then TMSOTf (14.46 ml, 80 mmol) and protected ribofuranose (20.2 g, 40 mmol) were added. Mixture was heated to 80 °C for 6 h. After cooling to rt, the mixture was extracted with EtOAc and water, organic layer was washed with $NaHCO_3$ and again with water, dried over $MgSO_4$ and evaporated under reduced pressure. Crude product was purified using column chromatography with chloroform.

**4-Chloro-5-(phenylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-d-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

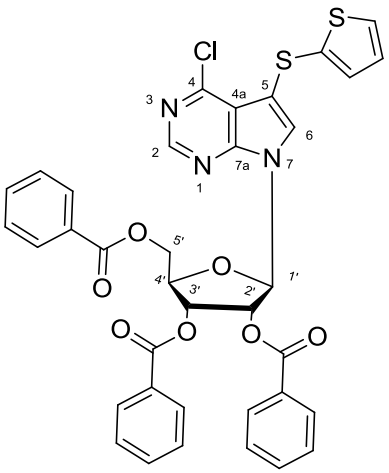
**(6-Chloro-7-(phenylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-d-ribofuranosyl)-7-deazapurine) (46a)**




Reaction of **44a** (10.4 g, 40 mmol) according to the general procedure afforded compound **46a** (13.84 g, 49%) as yellowish foam. M.p. 89 °C. $^1$H NMR (600.1 MHz, $CDCl_3$): 4.71 (dd, 1H, $J_{gem}$ = 12.3, $J_{5'b,4'}$ = 3.8, H-5'b); 4.82 (ddd, 1H, $J_{4',3'}$ = 4.7, $J_{4',5'}$ = 3.8, 3.1, H-4'); 4.89 (dd, 1H, $J_{gem}$ = 12.3, $J_{5'a,4'}$ = 3.1, H-5'a); 6.14 (dd, 1H, $J_{3',2'}$ = 5.8, $J_{3',4'}$ = 4.7, H-3'); 6.23 (dd, 1H, $J_{2',3'}$ = 5.8, $J_{2',1'}$ = 5.4, H-2'); 6.66 (d, 1H, $J_{1',2'}$ = 5.4, H-1'); 7.12 (m, 2H, H-*o*-Ph); 7.13 (m, 1H, H-*p*-Ph); 7.21 (m, 2H, H-*m*-Ph); 7.37, 7.41, 7.42 (3 × m, 3 × 2H, H-*m*-Bz); 7.55, 7.59 (2 × m, 3H, H-*p*-Bz); 7.64 (s, 1H, H-6); 7.93, 8.01, 8.08 (3 × m, 3 × 2H, H-*o*-Bz); 8.58 (s, 1H, H-2). $^{13}$C NMR (150.9 MHz, $CDCl_3$): 63.47 ($CH_2$-5'); 71.43 (CH-3'); 74.09 (CH-2'); 80.64 (CH-4'); 87.17 (CH-1'); 105.38 (C-5); 117.87 (C-4a); 125.92 (CH-*p*-Ph); 127.26 (CH-*o*-Ph); 128.38 (C-*i*-Bz); 128.53, 128.57 (CH-*m*-Bz); 128.67 (C-*i*-Bz); 128.68 (CH-*m*-Bz); 128.99 (CH-*m*-Ph); 129.21 (C-*i*-Bz); 129.66, 129.83, 129.84 (CH-*o*-Bz); 132.79 (CH-6); 133.52, 133.77, 133.81 (CH-*p*-Bz); 137.52 (C-*i*-Ph); 151.81 (CH-2); 152.48 (C-7a); 153.22 (C-4); 165.04, 165.35, 166.12 (CO-Bz). IR (KBr): 3123, 3058, 3028, 3004, 2947, 1727, 1601, 1574, 1541, 1452, 1263, 1123, 1090, 707. HRMS (ESI) calculated for $C_{38}H_{28}O_7N_3ClNaS$: 728.1229; found: 728.1233.

**4-Chloro-5-(2-thienylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-d-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

**(6-Chloro-7-(2-thienylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-d-ribofuranosyl)-7-deazapurine) (47a)**



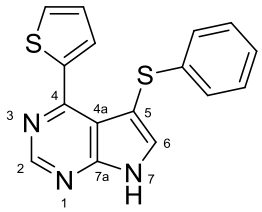
To form clear solution double amount of BSA (20.8 ml, 80 mmol) was added. Reaction of **45a** (10.71 g, 40 mmol) according to the general procedure afforded compound **47a** (8.5 g, 30%) as white foam. M.p. 72 °C. $^{1}$H NMR (500 MHz, $CDCl_3$): 4.67 (dd, 1H, $J_{gem}$ = 12.2 Hz, $J_{5'a,4'}$ = 3.9 Hz, H-5′a); 4.79 (m, 1H, H-4′); 4.86 (dd, 1H, $J_{gem}$ = 12.2 Hz, $J_{5'b,4'}$ = 3.1 Hz, H-5′b); 6.12 (dd, 1H, $J_{3',2'}$ = 5.8 Hz, $J_{3',4'}$ = 4.5 Hz, H-3'); 6.20 (t, 1H, $J_{2',1'} = J_{2',3'}$ = 5.7 Hz, H-2'); 6.61 (d, 1H, $J_{1',2'}$ = 5.6 Hz, H-1'); 6.89 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.15 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.25 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.36 and 7.40 (2×m, 2×2H, CH-*m*-Bz); 7.44 (s, 1H, H-6); 7.48 (m, 2H, H-*m*-Bz); 7.51 – 7.64 (m, 3H, H-*p*-Bz); 7.92, 7.99 and 8.10 (3×m, 3×2H, H-*o*-Bz); 8.57 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 63.62 ($CH_2$-5′); 71.41 (CH-3′); 74.01 (CH-2′); 80.59 (CH-4′); 87.04 (CH-1′); 109.91 (C-5); 117.06 (C-4a); 127.56 (CH-4-Sthienyl); 128.40 (C-*i*-Bz); 128.49 and 128.53 (CH-*m*-Bz); 128.68 (C-*i*-Bz); 128.70 (CH-*m*-Bz); 128.28 (C-*i*-Bz); 129.53 (CH-5-Sthienyl); 129.73, 129.80 and 129.82 (CH-*o*-Bz); 130.00 (CH-6); 132.70 (CH-3-Sthienyl); 133.52, 133.72 and 133.75 (CH-*p*-Bz); 133.86 (C-2-Sthienyl); 151.63 (CH-2); 151.97 (C-7a); 152.90 (C-4); 165.02, 165.32 and 166.09 (CO-Bz). IR (KBr): 3102, 3087, 3066, 3031, 3007, 2950, 1730, 1601, 1583, 1538, 1452, 1314, 1263, 1219, 1120, 1096, 1069, 707. HRMS (ESI) calculated for $C_{36}H_{26}O_7N_3ClNaS_2$: 734.0796; found: 734.0793.

## 5.6.1 Modification at position 6

### General procedure for the Stille coupling

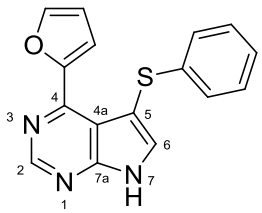
Compound **44a-47a** (1 equiv.), tributylstannane (1.2 equiv.) and $PdCl_2(PPh_3)_2$ (5 mol%) under argon atmosphere were dissolved in anhydrous DMF and heated to 100 °C for 8h. Then, solvent was evaporated under reduced pressure and crude product was purified using HPFC.

**5-(Phenylsulfanyl)-4-(thiophen-2-yl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (7-(Phenylsulfanyl)-6-(thiophen-2-yl)-7-deazapurine) (44b)**



Deazapurine **44a** (523 mg, 2 mmol), 2-(tributylstannyl)thiophene (0.762 mL, 2.4 mmol) and 15 mL DMF were used according to the general procedure. Crude product was purified using HPFC (hexane/EtOAc, 0–50% EtOAc) and product **44b** was obtained as yellowish solid (496 mg, 80%). Crystallization in ethanol/$H_2O$ gave yellowish needles. M.p. 240 °C. $^1$H NMR (600.1 MHz, DMSO-$d_6$): 6.92 (m, 2H, H-*o*-Ph); 7.03 (m, 1H, H-*p*-Ph); 7.07 (dd, 1H, $J_{4,5}$ = 5.1, $J_{4,3}$ = 3.8, H-4-thienyl); 7.15 (m, 2H, H-*m*-Ph); 7.69 (dd, 1H, $J_{5,4}$ = 5.1, $J_{5,3}$ = 1.1, H-5-thienyl); 8.10 (s, 1H, H-6); 8.39 (dd, 1H, $J_{3,4}$ = 3.8, $J_{3,5}$ = 1.1, H-3-thienyl); 8.78 (s, 1H, H-2); 12.93 (bs, 1H, NH). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 98.90 (C-5); 113.95 (C-4a); 128.11 (CH-*p*-Ph); 125.64 (CH-*o*-Ph); 128.11 (CH-4-thienyl); 129.18 (CH-*m*-Ph); 130.66 (CH-5-thienyl); 131.87 (CH-3-thienyl); 136.84 (CH-6); 139.19 (C-*i*-Ph); 141.57 (C-2-thienyl); 151.15 (CH-2); 152.10 (C-4); 154.33 (C-7a). IR (KBr): 3105, 2986, 2869, 2827, 1595, 1541, 1479, 1431, 1308, 1260, 806, 740, 707. HRMS (ESI) calculated for $C_{16}H_{12}N_3S_2$: 310.0468; found: 310.0467. Anal. calculated for $C_{16}H_{11}N_3S_2 \cdot 0.15H_2O$: C, 61.57; H, 3.65; N, 13.46; S, 20.54. Found: C, 61.85; H, 3.55; N, 13.39; S, 20.26.

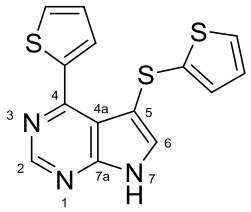
**4-(Furan-2-yl)-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-(Furan-2-yl)-7-(phenylsulfanyl)-7-deazapurine) (44c)**



Deazapurine **44a** (523 mg, 2 mmol), 2-(tributylstannyl)furane (0.755 mL, 2.4 mmol) and 15 mL DMF were used according to the general procedure. Crude product was purified using HPFC (hexane/EtOAc, 0–50% EtOAc) and product **44c** was obtained as yellowish solid (510 mg, 87%). Crystallization in ethanol/$H_2O$ gave yellowish needles. M.p. 234 °C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 7.58 (dd, 1H, $J_{4,3}$ = 3.4, $J_{4,5}$ = 1.7, H-4-furyl); 6.99 (m, 2H, H-*o*-Ph); 7.03 (m, 1H, H-*p*-Ph); 7.16 (m, 2H, H-*m*-Ph); 7.40 (dd, 1H, $J_{3,4}$ = 3.4, $J_{3,5}$ = 0.8, H-3-furyl); 7.70 (dd, 1H, $J_{5,4}$ = 1.7, $J_{5,3}$ = 0.8, H-5-furyl); 8.05 (s, 1H, H-6); 8.81 (s, 1H, H-2); 12.87 (bs, 1H, NH). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 99.51 (C-5); 112.27 (CH-4-furyl); 113.48 (C-4a); 114.77 (CH-3-furyl); 125.14 (CH-*p*-Ph); 125.65 (CH-*o*-Ph); 129.01 (CH-*m*-Ph); 136.57 (CH-6); 139.69 (C-*i*-Ph); 145.53 (CH-5-furyl); 147.73 (C-4); 150.92 (C-2-furyl); 151.32 (CH-2);

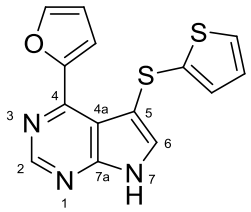
154.33 (C-7a). IR (KBr): 3108, 2989, 2869, 2821, 1580, 1541, 1479, 1443, 1314, 827, 731. HRMS (ESI) calculated for $C_{16}H_{12}ON_3S$: 294.0696; found: 294.0696. Anal. calculated for $C_{16}H_{11}N_3OS \cdot 0.25H_2O$: C, 64.52; H, 3.89; N, 14.11; S, 10.76. Found: C, 64.65; H, 3.73; N, 13.99; S, 10.47.

**4-(Thiophen-2-yl)-5-(thiophen-2-ylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-(Thiophen-2-yl)-7-(thiophen-2-ylsulfanyl)-7-deazapurine) (45b)**



Deazapurine **45a** (535 mg, 2 mmol), 2-(tributylstannyl)thiophene (0.762 mL, 2.4 mmol) and 15 mL DMF were used according to the general procedure. Crude product was purified using HPFC (EtOAc/MeOH, 0–5% MeOH) and product **45b** was obtained as yellowish solid (360 mg, 57%). M.p. 224 °C. $^1$H NMR (500 MHz, DMSO-d$_6$): 6.78 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 6.84 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.29 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.7 Hz, H-4-thienyl); 7.39 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.84 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.1 Hz, H-5-thienyl); 8.07 (s, 1H, H-6); 8.44 (dd, 1H, $J_{3,4}$ = 3.7 Hz, $J_{3,5}$ = 1.1 Hz, H-3-thienyl); 8.76 (s, 1H, H-2); 12.83 (bs, 1H, NH). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 103.50 (C-5); 113.19 (C-4a); 127.76 (CH-4-Sthienyl); 128.21 (CH-4-thienyl); 129.08 (CH-5-Sthienyl); 129.85 (CH-3-Sthienyl); 160.73 (CH-5-thienyl); 132.46 (CH-3-thienyl); 135.19 (CH-6); 137.15 (C-2-Sthienyl); 141.41 (C-2-thienyl); 151.16 (CH-2); 152.01 (C-4); 153.80 (C-7a). IR (KBr): 2977, 2860, 2812, 1598, 1547, 1443, 1320, 809, 701. HRMS (ESI) calculated for $C_{14}H_{10}N_3S_3$: 316.0031; found: 316.0033.

**4-(Furan-2-yl)-5-(thiophen-2-ylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-(Furan-2-yl)-7-(thiophen-2-ylsulfanyl)-7-deazapurine) (45c)**

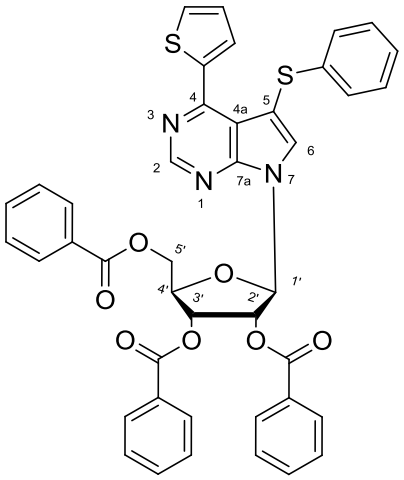


Deazapurine **45a** (535 mg, 2 mmol), 2-(tributylstannyl)furane (0.755 mL, 2.4 mmol) and 15 mL DMF were used according to the general procedure. Crude product was purified using HPFC (EtOAc/MeOH, 0–5% MeOH) and product **45c** was obtained as yellowish solid (434 mg, 72%). M.p. 201°C. $^1$H NMR (500 MHz, DMSO-d$_6$): 6.76 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.7 Hz, H-4-furyl); 6.92 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 6.99 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.45 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.48

(dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.8 Hz, H-3-furyl); 7.84 (s, 1H, H-6); 8.02 (dd, 1H, $J_{5,4}$ = 1.7 Hz, $J_{5,3}$ = 0.8 Hz, H-5-furyl); 8.77 (s, 1H, H-2); 12.70 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 104.76 (C-5); 112.39 (C-4a); 112.56 (CH-4-furyl); 114. 86 (CH-3-furyl); 127.86 (CH-4-Sthienyl); 129.24 (CH-5-Sthienyl); 130.57 (CH-3-Sthienyl); 133.65 (CH-6); 136.87 (C-2-Sthienyl); 145.80 (CH-5-furyl); 147.52 (C-4); 151.18 (C-2-furyl); 151.26 (CH-2); 153.75 (C-7a). IR (KBr): 3105, 2989, 2860, 2830, 1601, 1586, 1532, 1317, 824, 749. HRMS (ESI) calculated for $C_{14}H_{10}ON_3S_2$: 300.0260; found: 300.0261.

**5-(Phenylsulfanyl)-4-(thiophen-2-yl)-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

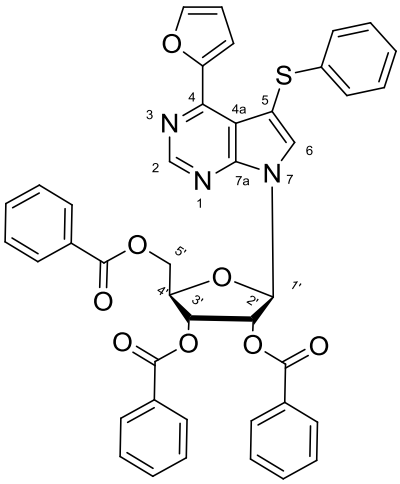
**(7-(Phenylsulfanyl)-6-(thiophen-2-yl)-9-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-7-deazapurine) (46b)**



Nucleoside **46a** (706 mg, 1 mmol), 2-(tributylstannyl)thiophene (0.381 mL, 1.2 mmol) and 10 mL DMF were used according to the general procedure. Crude product was purified using HPFC (hexane/EtOAc, 0–20% EtOAc) and product **46b** was obtained as yellowish solid (540 mg, 72%). M.p. 76 °C. $^1$H NMR (500.0 MHz, $CDCl_3$): 4.73 (dd, 1H, $J_{gem}$ = 12.2, $J_{5'b,4'}$ = 3.7, H-5'b); 4.83 (ddd, 1H, $J_{4',3'}$ = 4.6, $J_{4',5'}$ = 3.7, 3.1, H-4'); 4.90 (dd, 1H, $J_{gem}$ = 12.2, $J_{5'a,4'}$ = 3.1, H-5'a); 6.16 (dd, 1H, $J_{3',2'}$ = 5.8, $J_{3',4'}$ = 4.6, H-3'); 6.26 (dd, 1H, $J_{2',3'}$ = 5.8, $J_{2',1'}$ = 5.6, H-2'); 6.80 (d, 1H, $J_{1',2'}$ = 5.6, H-1'); 6.90 (m, 2H, H-*o*-Ph); 7.01 (dd, 1H, $J_{4,5}$ = 5.1, $J_{4,3}$ = 3.8, H-4-thienyl); 7.02 (m, 1H, H-*p*-Ph); 7.07 (m, 2H, H-*m*-Ph); 7.36, 7.39, 7.41 (3 × m, 3 × 2H, H-*m*-Bz); 7.42 (dd, 1H, $J_{5,4}$ = 5.1, $J_{5,3}$ = 1.1, H-5-thienyl); 7.54, 7.55, 7.59 (3 × m, 3 × 1H, H-*p*-Bz); 7.71 (s, 1H, H-6); 7.95, 8.02, 8.10 (3 × m, 3 × 2H, H-*o*-Bz); 8.20 (dd, 1H, $J_{3,4}$ = 3.8, $J_{3,5}$ = 1.1, H-3-thienyl); 8.84 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 63.63 ($CH_2$-5'); 71.50 (CH-3'); 74.04 (CH-2'); 80.48 (CH-4'); 86.54 (CH-1'); 104.35 (C-5); 115.63 (C-4a); 125.55 (CH-*p*-Ph); 126.70 (CH-*o*-Ph); 127.68 (CH-4-thienyl); 128.49, 128.53, 128.65 (C-*i*-Bz, CH-*m*-Bz); 128.78 (CH-*m*-Ph); 129.23 (C-*i*-Bz); 129.66, 129.83, 129.85 (CH-*o*-Bz); 129.93 (CH-5-thienyl); 132.57 (CH-3-thienyl); 133.24 (CH-6); 133.44, 133.72 (CH-*p*-Bz); 137.57 (C-*i*-Ph); 140.15 (C-2-thienyl);

151.64 (CH-2); 153.48 (C-7a); 154.15 (C-4); 165.07, 165.37, 166.15 (CO-Bz). IR (KBr): 3055, 3040, 3004, 2950, 2923, 1730, 1541, 1452, 1440, 1317, 1263, 1126, 1093, 1069, 1024, 704. HRMS (ESI) calculated for $C_{42}H_{32}O_7N_3S_2$: 754.1676; found: 754.1682.

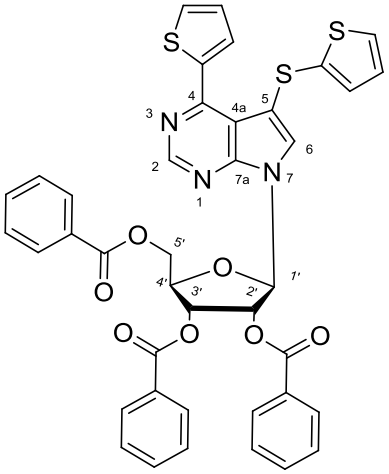
**4-(Furan-2-yl)-5-(phenylsulfanyl)-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-(Furan-2-yl)-7-(phenylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-7-deazapurine) (46c)**



Nucleoside **46a** (706 mg, 1 mmol), 2-(tributylstannyl)furane (0.378 mL, 1.2 mmol) and 10 mL DMF were used according to the general procedure. Crude product was purified using HPFC (hexane/EtOAc, 0–20% EtOAc) and product **46c** was obtained as yellowish solid (677 mg, 92%). M.p. 67 °C. $^1$H NMR (500.0 MHz, $CDCl_3$): 4.72 (dd, 1H, $J_{gem}$ = 12.2 Hz, $J_{5'a,4'}$ = 3.8 Hz, H-5′a); 4.82 (bdt, 1H, $J_{4',3'}$ = 4.6 Hz, $J_{4',5'a}$ = $J_{4',5'b}$ = 3.4 Hz, H-4′); 4.88 (dd, 1H, $J_{gem}$ = 12.2 Hz, $J_{5'b,4'}$ = 3.1 Hz, H-5′b); 6.15 (bdd, 1H, $J_{3',2'}$ = 5.9 Hz, $J_{3',4'}$ = 4.6 Hz, H-3'); 6.25 (t, 1H, $J_{2',1'}$ = $J_{2',3'}$ = 5.7 Hz, H-2'); 6.45 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.7 Hz, H-4-furyl); 6.77 (d, 1H, $J_{1',2'}$ = 5.5 Hz, H-1'); 7.01 (m, 2H, H-*o*-SPh); 7.04 (m, 1H, H-*p*-SPh); 7.12 (m, 2H, H-*m*-SPh); 7.34 – 7.44 (m, 6H, CH-*m*-Bz); 7.45 (dd, 1H, $J_{5,4}$ = 1.7 Hz, $J_{5,3}$ = 0.8 Hz, H-5-furyl); 7.57 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.8 Hz, H-3-furyl); 7.50 – 7.61 (m, 3H, H-*p*-Bz); 7.67 (s, 1H, H-6); 7.94, 8.01 and 8.09 (3×m, 3×2H, H-*o*-Bz); 8.87 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 63.62 ($CH_2$-5′); 71.48 (CH-3′); 74.05 (CH-2′); 80.44 (CH-4′); 86.60 (CH-1′); 104.34 (C-5); 112.04 (CH-4-furyl); 144.95 (C-4a); 116.15 (CH-3-furyl); 125.43 (CH-*p*-SPh); 126.46 (CH-*o*-SPh); 128.48 (C-*i*-Bz); 128.49, 128.54 and 128.64 (CH-*m*-Bz); 128.72 (C-*i*-Bz); 128.81 (CH-*m*-SPh); 129.23 (C-*i*-Bz); 129.66, 129.83 and 129.85 (CH-*o*-Bz); 133.39 (CH-6); 133.42, 133.71 and 133.72 (CH-*p*-Bz); 138.27 (C-*i*-SPh); 145.11 (CH-5-furyl); 149.26 (C-4); 150.26 (C-2-furyl); 151.84 (CH-2); 153.59 (C-7a); 165.06, 165.37 and 166.16 (CO-Bz).IR (KBr): 3117, 3063, 3031, 2959, 2920, 2857, 1730, 1538, 1452, 1317, 1263, 1120, 1093, 707. HRMS (ESI) calculated for $C_{42}H_{32}O_8N_3S$: 738.1905; found: 738.1908.

**4-(Thiophen-2-yl)-5-(thiophen-2-ylsulfanyl)-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

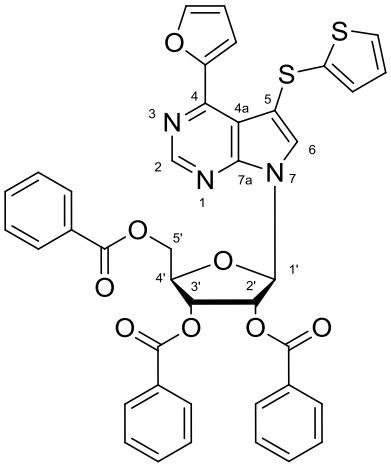
**(6-(Thiophen-2-yl)-7-(thiophen-2-ylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-7-deazapurine) (47b)**



Nucleoside **47a** (712 mg, 1 mmol), 2-(tributylstannyl)thiophene (0.381 mL, 1.2 mmol) and 10 mL DMF were used according to the general procedure. Crude product was purified using HPFC with pure DCM and product **47b** was obtained as yellowish solid (595 mg, 78%). M.p. 77 °C. $^{1}$H NMR (500 MHz, $CDCl_3$): 4.70 (dd, 1H, $J_{gem}$ = 12.2 Hz, $J_{5'a,4'}$ = 3.9 Hz, H-5′a); 4.81 (m, 1H, H-4′); 4.87 (dd, 1H, $J_{gem}$ = 12.2 Hz, $J_{5'b,4'}$ = 3.1 Hz, H-5′b); 6.12 (dd, 1H, $J_{3',2'}$ = 5.8 Hz, $J_{3',4'}$ = 4.3 Hz, H-3'); 6.18 (t, 1H, $J_{2',1'} = J_{2',3'}$ = 5.8 Hz, H-2'); 6.67 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 6.73 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 6.76 (d, 1H, $J_{1',2'}$ = 5.8 Hz, H-1'); 7.13 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.24 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.7 Hz, H-4-thienyl); 7.37, 7.41 and 7.49 (3×m, 3×2H, H-*m*-Bz); 7.52 – 7.65 (m, 4H, H-*p*-Bz, H-5-thienyl); 7.58 (s, 1H, H-6); 7.93, 8.00 and 8.14 (3×m, 3×2H, H-*o*-Bz); 8.26 (dd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 8.86 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 63.78 ($CH_2$-5′); 71.53 (CH-3′); 74.07 (CH-2′); 80.63 (CH-4′); 86.42 (CH-1′); 109.61 (C-5); 114.89 (C-4a); 127.33 (CH-4-Sthienyl); 127.94 (CH-4-thienyl); 128.42 (C-*i*-Bz); 128.51 and 128.55 (CH-*m*-Bz); 128.71 (C-*i*-Bz); 128.76 (CH-*m*-Bz); 129.32 (C-*i*-Bz); 129.42 (CH-5-Sthienyl); 129.77, 129.84 and 129.87 (CH-*o*-Bz); 130.77 (CH-5-thienyl); 131.07 (CH-6); 132.19 (CH-3-Sthienyl); 133.45 (CH-3-thienyl); 133.54, 133.74 and 133.76 (CH-*p*-Bz); 133.5 (C-2-thienyl); 134.09 (C-2-Sthienyl); 150.91 (CH-2); 153.03 (C-4,7a); 165.08, 165.38 and 166.14 (CO-Bz). IR (KBr): 3108, 3060, 3037, 3007, 2953, 2926, 2851, 1727, 1550, 1455, 1317, 1269, 1126, 1090, 1066, 1030, 713. HRMS (ESI) calculated for $C_{40}H_{30}O_7N_3S_3$: 760.1240; found: 760.1243.

**4-(Furan-2-yl)-5-(thiophen-2-ylsulfanyl)-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

**(6-(Furan-2-yl)-7-(thiophen-2-ylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-7-deazapurine) (47c)**

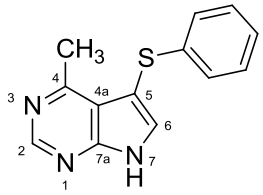


Nucleoside **47a** (712 mg, 1 mmol), 2-(tributylstannyl)furane (0.378 mL mg, 1.2 mmol) and 10 mL DMF were used according to the general procedure Crude product was purified using HPFC with pure DCM and product **47c** obtained as yellowish solid (303 mg, 41%). M.p. 64 °C. $^{1}$H NMR (500 MHz, $CDCl_3$): 4.67 (dd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'a,4'}$ = 3.9 Hz, H-5′a); 4.78 (m, 1H, H-4′); 4.81 (dd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'b,4'}$ = 3.2 Hz, H-5′b); 6.12 (dd, 1H, $J_{3',2'}$ = 5.8 Hz, $J_{3',4'}$ = 4.4 Hz, H-3'); 6.19 (t, 1H, $J_{2',1'} = J_{2',3'}$ = 5.7 Hz, H-2'); 6.64 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.70 (d, 1H, $J_{1',2'}$ = 5.7 Hz, H-1'); 6.81 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 6.93 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.18 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.34 (s, 1H, H-6); 7.36, 7.40 and 7.48 (3×m, 3×2H, H-*m*-Bz); 7.51 - 7.62 (m, 3H, H-*p*-Bz); 7.60 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.74 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 7.93, 7.99 and 8.12 (3×m, 3×2H, H-*o*-Bz); 8.83 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 63.88 ($CH_2$-5′); 71.53 (CH-3′); 73.99 (CH-2′); 80.39 (CH-4′); 86.44 (CH-1′); 110.33 (C-5); 112.30 (CH-4-furyl); 113.79 (C-4a); 115.70 (CH-3-furyl); 127.47 (CH-4-Sthienyl); 128.45 and 128.51 (CH-*m*-Bz); 128.57 (C-*i*-Bz); 128.67 (CH-*m*-Bz); 128.80 (C-*i*-Bz); 129.16 (CH-6); 129.40 (C-*i*-Bz); 129.49 (CH-5-Sthienyl); 129.79, 129.82 and 129.86 (CH-*o*-Bz); 131.61 (CH-3-Sthienyl); 133.42 and 133.65 (CH-*p*-Bz); 134.30 (C-2-Sthienyl); 145.11 (CH-5-furyl); 148.86 (C-4); 150.90 (C-2-furyl); 151.70 (CH-2); 153.18 (C-7a); 165.05, 165.35 and 166.13 (CO-Bz). IR (KBr): 3102, 3055, 3034, 3004, 2956, 2926, 2866, 2851, 1733, 1562, 1535, 1452, 1269, 1123, 1099, 713. HRMS (ESI) calculated for $C_{40}H_{30}O_8N_3S_2$: 744.1469; found: 744.1471.

**General procedure for methylation**

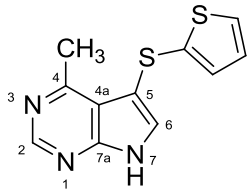
$Me_3Al$ (3 equiv., 2 M in toluene) was added to solution of compound **44a-47a** (1 equiv.), and $Pd(PPh_3)_4$ (5 mol%) in THF. The reaction mixture was stirred at 70 °C for 12 h. Then the solution was dropped in water (decomposition of $Me_3Al$) and extracted three times with EtOAc and combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by HPFC.

**4-Methyl-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Methyl-7-(phenylsulfanyl)-7-deazapurine) (44d)**



Deazapurine **44a** (523 mg, 2 mmol), $Me_3Al$ (3 mL, 6 mmol, 2 M in toluene) and 40 mL THF were used according to the general procedure. Crude product was purified using HPFC (hexane/EtOAc, 0–50% EtOAc) and product **44d** was obtained as yellowish solid (355 mg, 73%). Crystallization in ethanol/$H_2O$ gave yellowish needles. M.p. 230 °C. $^1$H NMR (500.0 MHz, DMSO-$d_6$): 2.60 (s, 3H, $CH_3$); 7.03 (m, 2H, H-*o*-Ph); 7.12 (m, 1H, H-*p*-Ph); 7.25 (m, 2H, H-*m*-Ph); 7.95 (s, 1H, H-6); 8.66 (s, 1H, H-2); 12.64 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 20.89 ($CH_3$); 98.18 (C-5); 117.17 (C-4a); 125.46 (CH-*o*-Ph); 125.49 (CH-*p*-Ph); 129.44 (CH-*m*-Ph); 134.49 (CH-6); 139.52 (C-*i*-Ph); 151.82 (CH-2); 152.26 (C-7a); 159.36 (C-4). IR (KBr): 3123, 2986, 2842, 1577, 1473, 1434, 1332, 1263, 1227, 737. HRMS (ESI) calculated for $C_{13}H_{12}N_3S$: 242.0746; found: 242.0747. Anal. calculated for $C_{13}H_{11}N_3S \cdot 0.25H_2O$: C, 63.52; H, 4.72; N, 17.09; S, 13.04. Found: C, 63.48; H, 4.49; N, 16.93; S, 13.28.

**4-Methyl-5-(thiophen-2-ylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Methyl-7-(thiophen-2-ylsulfanyl)-7-deazapurine) (45d)**

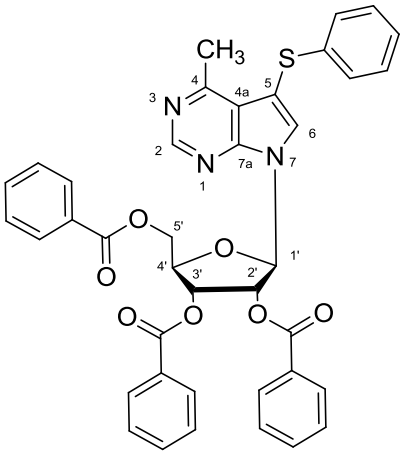


Deazapurine **45a** (535 mg, 2 mmol), $Me_3Al$ (3 mL, 6 mmol, 2 M in toluene) and 40 mL THF were used according to the general procedure. Crude product was purified using HPFC (EtOAc/MeOH, 0–5% MeOH) and product **45d** was obtained as yellowish solid (325 mg, 66%). M.p. 198 °C. $^1$H NMR (500 MHz, DMSO-$d_6$): 2.81 (s, 3H, $CH_3$-4); 6.98 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.12 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.47 (dd,

1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.94 (s, 1H, H-6); 8.64 (s, 1H, H-2); 12.55 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 21.54 ($CH_3$-4); 103.13 (C-5); 116.39 (C-4a); 128.08 (CH-4-Sthienyl); 128.37 (CH-5-Sthienyl); 128.77 (CH-3-Sthienyl); 133.34 (CH-6); 138.22 (C-2-Sthienyl); 151.72 (C-7a); 151.74 (CH-2); 159.23 (C-4). IR (KBr): 3075, 2962, 2803, 2773, 2753, 2702, 2576, 1598, 2574, 1434, 1410, 1338, 1132, 1006, 696, 626. HRMS (ESI) calculated for $C_{11}H_{10}N_3S_2$: 248.0311; found: 248.0311.

**4-Methyl-5-(phenylsulfanyl)-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

**(6-Methyl-7-(phenylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-7-deazapurine) (46d)**

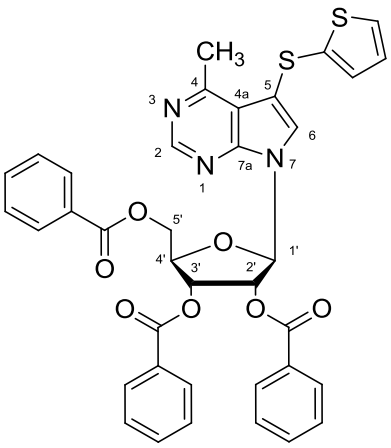


Nucleoside **46a** (706 mg, 1 mmol), $Me_3Al$ (1.5 mL, 3 equiv., 2 M in toluene) and 20 mL THF were used according to the general procedure. Crude product was purified using HPFC (hexane/EtOAc, 0–20% EtOAc) and product **46d** was obtained as white foam (380 mg, 55%). M.p. 61 °C. $^1$H NMR (500 MHz, $CDCl_3$): 2.69 (s, 3H, $CH_3$); 4.71 (dd, 1H, $J_{gem}$ = 12.2 Hz, $J_{5'a,4'}$ = 3.9 Hz, H-5′a); 4.81 (bdt, 1H, $J_{4',3'}$ = 4.7 Hz, $J_{4',5'a}$ = $J_{4',5'b}$ = 3.6 Hz, H-4′); 4.89 (dd, 1H, $J_{gem}$ = 12.2 Hz, $J_{5'b,4'}$ = 3.2 Hz, H-5′b); 6.16 (dd, 1H, $J_{3',2'}$ = 5.9 Hz, $J_{3',4'}$ = 4.7 Hz, H-3'); 6.24 (t, 1H, $J_{2',1'}$ = $J_{2',3'}$ = 5.7 Hz, H-2'); 6.71 (d, 1H, $J_{1',2'}$ = 5.5 Hz, H-1'); 7.05 (m, 2H, H-*o*-SPh); 7.11 (m, 1H, H-*p*-SPh); 7.20 (m, 2H, H-*m*-SPh); 7.37, 7.40 and 7.41 (3×m, 3×2H, H-*m*-Bz); 7.53, 7.55 and 7.58 (3×m, 3×1H, H-*p*-Bz); 7.61 (s, 1H, H-6); 7.94, 8.01 and 8.07 (3×m, 3×2H, H-*o*-Bz); 8.73 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 21.24 ($CH_3$); 63.59 ($CH_2$-5′); 71.50 (CH-3′); 74.10 (CH-2′); 80.44 (CH-4′); 86.71 (CH-1′); 104.19 (C-5); 118.59 (C-4a); 125.56 (CH-*p*-SPh); 126.14 (CH-*o*-SPh); 128.50 (CH-*m*-Bz); 128.52 (C-*i*-Bz); 128.54 and 128.64 (CH-*m*-Bz); 128.877 (C-*i*-Bz); 129.09 (CH-*m*-SPh); 129.31 (C-*i*-Bz); 129.69, 129.84 and 129.86 (CH-*o*-Bz); 132.14 (CH-6); 133.43, 133.71 and 133.73 (CH-*p*-Bz); 138.34 (C-*i*-SPh); 151.82 (C-7a); 152.28 (CH-2); 161.52 (C-4); 165.09, 165.38 and 166.17 (CO-Bz). IR (KBr): 3058, 3028, 3007, 2956, 2926, 2869, 2854, 1730, 1571, 1449,

1263, 1120, 1096, 1069, 1027, 707. HRMS (ESI) calculated for $C_{39}H_{32}O_7N_3S$: 686.1956; found: 686.1958.

**4-Methyl-5-(thiophen-2-ylsulfanyl)-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

**(6-Methyl-7-(thiophen-2-ylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-7-deazapurine) (47d)**

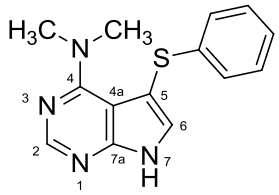


Nucleoside **47a** (712 mg, 1 mmol), $Me_3Al$ (1.5 mL, 3 equiv., 2 M in toluene) and 20 mL THF were used according to the general procedure. Crude product was purified using HPFC (DCM/MeOH, 0–5% MeOH) and product **47d** was obtained as white foam (469 mg, 67%). M.p. 59 °C. $^1$H NMR (500 MHz, $CDCl_3$): 2.92 (s, 3H, $CH_3$); 4.69 (dd, 1H, $J_{gem}$ = 12.2 Hz, $J_{5'a,4'}$ = 3.9 Hz, H-5′a); 4.79 (m, 1H, H-4′); 4.87 (dd, 1H, $J_{gem}$ = 12.2 Hz, $J_{5'b,4'}$ = 3.2 Hz, H-5′b); 6.15 (dd, 1H, $J_{3',2'}$ = 5.9 Hz, $J_{3',4'}$ = 4.5 Hz, H-3'); 6.21 (t, 1H, $J_{2',1'} = J_{2',3'}$ = 5.7 Hz, H-2'); 6.68 (d, 1H, $J_{1',2'}$ = 5.5 Hz, H-1'); 6.88 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 6.99 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.20 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.36, 7.40 and 7.47 (3×m, 3×2H, H-*m*-Bz); 7.53 (s, 1H, H-6); 7.51 – 7.62 (m, 3H, H-*p*-Bz); 7.93, 7.99 and 8.12 (3×m, 3×2H, H-*o*-Bz); 8.72 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 21.94 ($CH_3$); 63.71 ($CH_2$-5′); 71.51 (CH-3′); 74.05 (CH-2′); 80.43 (CH-4′); 86.60 (CH-1′); 108.20 (C-5); 118.00 (C-4a); 127.51 (CH-4-Sthienyl); 128.19 (CH-5-Sthienyl); 128.46 and 128.52 (CH-*m*-Bz); 128.56 (C-*i*-Bz); 128.67 (CH-*m*-Bz); 128.80 and 129.41 (C-*i*-Bz); 129.76, 129.83 and 129.85 (CH-*o*-Bz); 130.06 (CH-6); 130.34 (CH-3-Sthienyl); 133.44 and 133.67 (CH-*p*-Bz); 136.26 (C-2-Sthienyl); 151.38 (C-7a); 152.18 (CH-2); 161.21 (C-4); 165.07, 165.36 and 166.15 (CO-Bz). IR (KBr): 3111, 3066, 3028, 3007, 2932, 2851, 1730, 1568, 1452, 1317, 1269, 1177, 1123, 1093, 1069, 1024, 713. HRMS (ESI) calculated for $C_{37}H_{30}O_7N_3S_2$: 692.1520; found: 692.1521.

**General procedure for dimethyl amination**

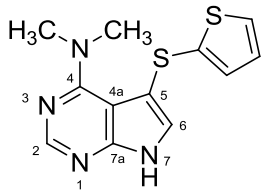
Dimethylamine (3 equiv., 2M in THF) was added to solution of compound **44a-47a** (1 equiv.), in propan-2-ol (25 mL) and the reaction mixture was stirred at 70 °C for 24 h. Volatiles were removed under reduced pressure and crude product was purified by HPFC.

**4-(N,N-Dimethylamino)-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-(N,N-Dimethylamino)-7-(phenylsulfanyl)-7-deazapurine) (44e)**



Deazapurine **44a** (523 mg, 2 mmol) was used according to the general procedure. Crude product was purified using HPFC (hexane/EtOAc, 0–50% EtOAc) and product **44e** was obtained as yellowish solid (454 mg, 84%). Crystallization in ethanol/$H_2O$ gave white needles. M.p. 201 °C. $^1$H NMR (600.1 MHz, DMSO-$d_6$): 3.11 (s, 6H, $(CH_3)_2N$); 7.00 (m, 2H, H-*o*-Ph); 7.09 (m, 1H, H-*p*-Ph); 7.23 (m, 2H, H-*m*-Ph); 7.66 (s, 1H, H-6); 8.21 (s, 1H, H-2); 12.36 (bs, 1H, NH). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 41.23 ($(CH_3)_2N$); 98.32 (C-5); 104.52 (C-4a); 125.15 (CH-*o*-Ph); 125.21 (CH-*p*-Ph); 129.22 (CH-*m*-Ph); 131.94 (CH-6); 140.13 (C-*i*-Ph); 150.85 (CH-2); 153.58 (C-7a); 159.41 (C-4). IR (KBr): 3090, 2968, 2863, 2818, 1589, 1559, 1488, 1416, 1398, 1063, 922, 860 743. HRMS (ESI) calculated for $C_{14}H_{15}N_4S$: 271.1012; found: 271.1012. Anal. calculated for: $C_{14}H_{14}N_4S$: C, 62.20; H, 5.22; N, 20.72; S, 11.86; found: C, 61.97; H, 5.18; N, 20.64; S, 11.73.

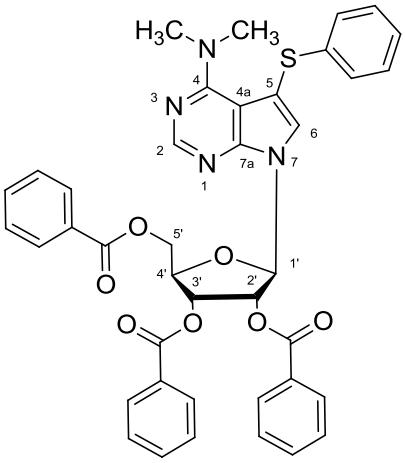
**4-(N,N-Dimethylamino)-5-(thiophen-2-ylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-(N,N-Dimethylamino)-7-(thiophen-2-ylsulfanyl)-7-deazapurine) (45e)**



Deazapurine **45a** (535 mg, 2 mmol) was used according to the general procedure. Crude product was purified using HPFC (EtOAc/MeOH, 0–5% MeOH) and product **45e** was obtained as brownish solid (346 mg, 63%). M.p. 185 °C. $^1$H NMR (401 MHz, DMSO-$d_6$): 3.22 (s, 6H, $(CH_3)_2N$); 6.95 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.07 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.44 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.62 (s, 1H, H-6); 8.19 (s, 1H, H-2); 12.23 (bs, 1H, NH). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 41.45 ($(CH_3)_2N$); 103.09 (C-5); 103.91 (C-4a); 127.95 (CH-4-Sthienyl); 128.47 (CH-5-Sthienyl); 129.14 (CH-3-Sthienyl); 130.17 (CH-6); 138.47 (C-2-Sthienyl); 150.82 (CH-2); 153.12 (C-

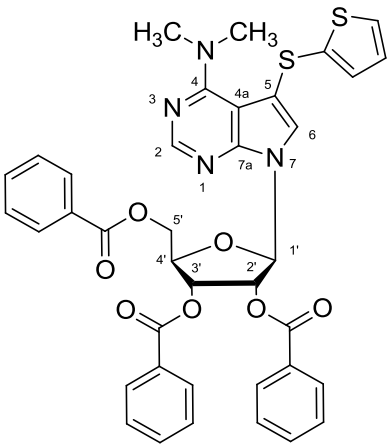
7a); 159.48 (C-4). IR (KBr): 3081, 2941, 2860, 2806, 1589, 1559, 1416, 1401, 1060, 928, 848, 692. HRMS (ESI) calculated for $C_{12}H_{13}N_4S_2$: 277.0576; found: 277.0576.

**4-(N,N-Dimethylamino)-5-(phenylsulfanyl)-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-(N,N-Dimethylamino)-7-(phenylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-7-deazapurine) (46e)**



Nucleoside **46a** (706 mg, 1 mmol) was used according to the general procedure. Crude product was purified using HPFC (hexane/EtOAc, 0–20% EtOAc) and product **46e** was obtained as white foam (624 mg, 88%). M.p. 67 °C. $^1$H NMR (500 MHz, $CDCl_3$): 3.17 (s, 6H, $(CH_3)_2N$); 4.70 (dd, 1H, $J_{gem}$ = 12.1 Hz, $J_{5'a,4'}$ = 3.8 Hz, H-5′a); 4.78 (bdt, 1H, $J_{4',3'}$ = 4.6 Hz, $J_{4',5'a}$ = $J_{4',5'b}$ = 3.5 Hz, H-4′); 4.85 (dd, 1H, $J_{gem}$ = 12.1 Hz, $J_{5'b,4'}$ = 3.2 Hz, H-5′b); 6.11 (dd, 1H, $J_{3',2'}$ = 5.9 Hz, $J_{3',4'}$ = 4.6 Hz, H-3'); 6.18 (t, 1H, $J_{2',1'}$ = $J_{2',3'}$ = 5.8 Hz, H-2'); 6.75 (d, 1H, $J_{1',2'}$ = 5.6 Hz, H-1'); 7.01 (m, 2H, H-*o*-SPh); 7.08 (m, 1H, H-*p*-SPh); 7.17 (m, 2H, H-*m*-SPh); 7.33 – 7.42 (m, 6H, CH-*m*-Bz); 7.45 (s, 1H, H-6); 7.48 – 7.60 (m, 3H, H-*p*-Bz); 7.95, 7.98 and 8.08 (3×m, 3×2H, H-*o*-Bz); 8.33 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 41.17 ($(CH_3)_2N$); 63.54 ($CH_2$-5′); 71.32 (CH-3′); 73.79 (CH-2′); 80.03 (CH-4′); 85.94 (CH-1′); 102.88 (C-5); 105.52 (C-4a); 125.21 (CH-*p*-SPh); 125.70 (CH-*o*-SPh); 128.44, 128.48 and 128.58 (CH-*m*-Bz); 128.64 and 128.81 (C-*i*-Bz); 128.88 (CH-*m*-SPh); 129.35 (CH-6); 129.67, 129.83 and 129.88 (CH-*o*-Bz); 133.30 and 133.61 (CH-*p*-Bz); 138.79 (C-*i*-SPh); 151.13 (CH-2); 152.95 (C-7a); 159.55 (C-4); 164.83, 165.14 and 165.94 (CO-Bz). IR (KBr): 3123, 3058, 3031, 3010, 2950, 2926, 2881, 2806, 1727, 1565, 1544, 1455, 1419, 1401, 1317, 1263, 1126, 1096, 1072, 1027, 707.. HRMS (ESI) calculated for $C_{40}H_{35}O_7N_4S$: 715.2221; found: 715.2223.

**4-(N,N-Dimethylamino)-5-(thiophen-2-ylsulfanyl)-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-(N,N-Dimethylamino)-7-(thiophen-2-ylsulfanyl)-9-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-7-deazapurine) (47e)**

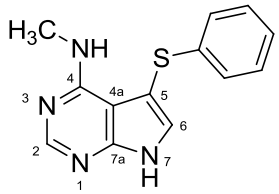


Nucleoside **47a** (712 mg, 1 mmol was used according to the general procedure. Crude product was purified using HPFC (DCM/MeOH, 0–5% MeOH) and product **47e** was obtained as white foam (634 mg, 88%). M.p. 81 °C. $^{1}$H NMR (500 MHz, $CDCl_3$): 3.29 (s, 6H, $(CH_3)_2N$); 4.67 (dd, 1H, $J_{gem}$ = 12.1 Hz, $J_{5'a,4'}$ = 3.9 Hz, H-5′a); 4.75 (m, 1H, H-4′); 4.82 (dd, 1H, $J_{gem}$ = 12.1 Hz, $J_{5'b,4'}$ = 3.2 Hz, H-5′b); 6.09 (dd, 1H, $J_{3',2'}$ = 5.8 Hz, $J_{3',4'}$ = 4.4 Hz, H-3'); 6.15 (t, 1H, $J_{2',1'} = J_{2',3'}$ = 5.8 Hz, H-2'); 6.70 (d, 1H, $J_{1',2'}$ = 5.7 Hz, H-1'); 6.83 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 6.93 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.16 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.32 (s, 1H, H-6); 7.36, 7.38 and 7.47 (3×m, 3×2H, H-*m*-Bz); 7.53, 7.56 and 7.59 (3×m, 3×1H, H-*p*-Bz); 7.95, 7.96 and 8.14 (3×m, 3×2H, H-*o*-Bz); 8.33 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 41.64 $(CH_3)_2N$); 63.94 ($CH_2$-5′); 71.55 (CH-3′); 73.98 (CH-2′); 80.23 (CH-4′); 86.05 (CH-1′); 105.34 (C-5); 107.91 (C-4a); 126.92 (CH-6); 127.38 (CH-4-Sthienyl); 128.13 (CH-5-Sthienyl); 128.42, 128.46 and 128.65 (CH-*m*-Bz); 128.70, 128.84 and 129.48 (C-*i*-Bz); 129.79, 129.82 and 129.89 (CH-*o*-Bz); 130.28 (CH-3-Sthienyl); 133.35 and 133.58 (CH-*p*-Bz); 136.59 (C-2-Sthienyl); 151.37 (CH-2); 152.82 (C-7a); 160.04 (C-4); 165.07, 165.37 and 166.18 (CO-Bz). IR (KBr): 3066, 2926, 2887, 2854, 1724, 1562, 1544, 1449, 1407, 1317, 1266, 1123, 1096, 1069, 1024, 710. HRMS (ESI) calculated for $C_{38}H_{33}O_7N_4S_2$: 721.1785; found: 721.1787.

**General procedure for methylamination**

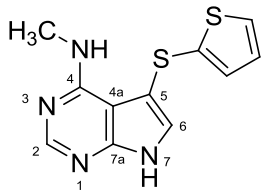
Compound **44a-47a** (1 equiv.), as methylamine (40% [w/w], 5 mL) in dioxane (5 mL) was stirred at autoclave at 120 °C for 18h. Solvent was then evaporated under reduced pressure and crude products were purified using RP-HPFC (0→100% of MeOH in $H_2O$).

**4-(N-Methylamino)-5-(phenylsulfanyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (6-(N-Methylamino)-7-(phenylsulfanyl)-7-deazapurine) (44f)**



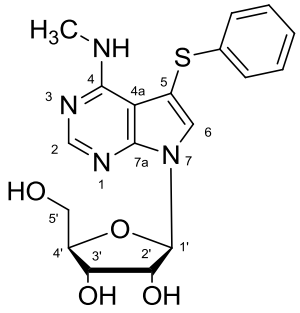
Reaction of deazapurine **44a** (523 mg, 2 mmol) according to the general procedure afforded compound **44f** as brownish solid (423 mg, 83 %). Crystallization in ethanol/$H_2O$ gave yellowish needles. M.p. 230 °C. $^1$H NMR (500 MHz, DMSO-$d_6$): 2.90 (d, 3H, $J_{CH3,NH}$ = 4.8 Hz, C**H**$_3$NH); 6.48 (q, 1H, $J_{NH,CH3}$ = 4.8 Hz, $CH_3$N**H**); 7.09 (m, 2H, H-*o*-Ph); 7.13 (m, 1H, H-*p*-Ph); 7.26 (m, 2H, H-*m*-Ph); 7.55 (s, 1H, H-6); 8.19 (s, 1H, H-2); 12.19 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 27.62 ($CH_3$NH); 97.87 (C-5); 103.25 (C-4a); 125.71 (CH-*p*-Ph); 126.02 (CH-*o*-Ph); 129.33 (CH-*m*-Ph); 129.59 (CH-6); 139.07 (C-*i*-Ph); 150.99 (C-7a); 152.67 (CH-2); 157.08 (C-4). IR (KBr): 3374, 3099, 3058, 2962, 2902, 2860, 2812, 1607, 1586, 1491, 1485, 1383, 881, 737. HRMS (ESI) calculated for $C_{13}H_{13}N_4S$: 257.0855 ; found: 257.0855. Anal. calculated for $C_{13}H_{12}N_4S$: C, 60.91; H, 4.72; N, 21.86; S, 12.51 ; found: C, 60.66; H, 4.71; N, 21.75; S, 12.17.

**4-(N-Methylamino)-5-(thiophen-2-ylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-(N-Methylamino)-7-(thiophen-2-ylsulfanyl)-7-deazapurine) (45f)**



Reaction of deazapurine **45a** (535 mg, 2 mmol) according to the general procedure afforded compound **45f** as brownish solid (303 mg, 58 %). M.p. 212 °C. $^1$H NMR (401 MHz, DMSO-$d_6$): 3.01 (d, 3H, $J_{CH3,NH}$ = 4.8 Hz, C**H**$_3$NH); 6.71 (q, 1H, $J_{NH,CH3}$ = 4.8 Hz, $CH_3$N**H**); 6.97 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.24 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.49 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.54 (s, 1H, H-6); 8.17 (s, 1H, H-2); 12.10 (bs, 1H, NH). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 27.74 ($CH_3$NH); 102.26 (C-5); 102.53 (C-4a); 127.97 (CH-4-Sthienyl); 128.50 (CH-6); 129.19 (CH-5-Sthienyl); 129.92 (CH-3-Sthienyl); 137.86 (C-2-Sthienyl); 150.46 (C-7a); 152.43 (CH-2); 156.76 (C-4). IR (KBr): 3392, 3102, 3060, 2995, 2965, 2905, 2863, 2788, 1607, 1595, 1488, 1413, 1383, 1350, 1314, 881, 626. HRMS (ESI) calculated for $C_{11}H_{11}N_4S_2$: 263.0420 ; found: 263.0420.

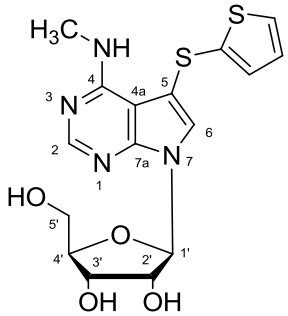
**4-(N-Methylamino)-5-(phenylsulfanyl)-7-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-(N-Methylamino)-7-(phenylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (50f)**



Reaction of nucleoside **46a** (706 mg, 1 mmol) according to the general procedure afforded compound **50f** as white solid (352 mg, 90 %). Crystallization in MeOH/$H_2O$ gave white foam. M.p. 157 °C. $[\alpha]_D$ −57.9 (0.21). $^1$H NMR (600.1 MHz, DMSO-$d_6$): 2.91 (d, 3H, $J_{CH3,NH}$ = 4.8 Hz, C**H**$_3$NH); 3.55 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'a,OH}$ = 6.2 Hz, $J_{5'a,4'}$ = 3.7 Hz, H-5′a); 3.65 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'b,OH}$ = 5.0 Hz, $J_{5'b,4'}$ = 3.7 Hz, H-5′b); 3.92 (q, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 3.5 Hz, H-4′); 4.10 (td, 1H, $J_{3',2'} = J_{3',OH}$ = 5.0 Hz, $J_{3',4'}$ = 3.2 Hz, H-3'); 4.43 (td, 1H, $J_{2',1'} = J_{2',OH}$ = 6.2 Hz, $J_{2',3'}$ = 5.1 Hz, H-2'); 5.14 (d, 1H, $J_{OH,3'}$ = 4.9 Hz, OH-3′); 5.21 (dd, 1H, $J_{OH,5'a}$ = 6.2 Hz, $J_{OH,5'b}$ = 5.0 Hz, OH-5′); 5.37 (d, 1H, $J_{OH,2'}$ = 6.3 Hz, OH-2′); 6.08 (d, 1H, $J_{1',2'}$ = 6.0 Hz, H-1'); 6.59 (q, 1H, $J_{NH,CH3}$ = 4.8 Hz, $CH_3$N**H**); 7.13 (m, 2H, H-*o*-SPh); 7.16 (m, 1H, H-*p*-SPh); 7.29 (m, 2H, H-*m*-SPh); 7.87 (s, 1H, H-6); 8.23 (s, 1H, H-2). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 27.74 ($CH_3$NH); 61.65 ($CH_2$-5′); 70.63 (CH-3′); 74.25 (CH-2′); 85.46 (CH-4′); 87.63 (CH-1′); 99.16 (C-5); 103.82 (C-4a); 125.95 (CH-*p*-SPh); 126.24 (CH-*o*-SPh); 129.44 (CH-*m*-SPh); 129.96 (CH-6); 138.39 (C-*i*-SPh); 150.33 (C-7a); 152.62 (CH-2); 157.10 (C-4). IR (KBr): 3398, 3180, 3126, 2941, 2917, 2905, 2896, 2866, 1613, 1562, 1488, 1389, 1099, 1060, 740, 629. HRMS (ESI) calculated for $C_{18}H_{21}O_4N_4S$: 389.1278; found: 389.1281. Anal. calculated for $C_{18}H_{20}N_4O_4S \cdot 1.25H_2O$: C, 52.61; H, 5.52; N, 13.63; S, 7.8; found: C, 52.79; H, 5.35; N, 13.46; S, 7.98.

**4-(N-Methylamino)-5-(thiophen-2-ylsulfanyl)-7-β-D-ribofuranosyl-*7H*-pyrrolo[2,3-*d*]pyrimidine**

**(6-(N-Methylamino)-7-(thiophen-2-ylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (51f)**



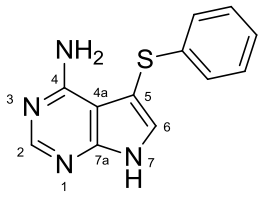
Reaction of nucleoside **47a** (712 mg, 1 mmol) according to the general procedure afforded compound **51f** as white solid (297 mg, 75 %). M.p. 187 °C. $[\alpha]_D$ −51.7 (0.23). $^1$H NMR (401.0 MHz, DMSO-$d_6$): 3.03 (d, 3H, $J_{CH3,NH}$ = 4.8 Hz, C**H**$_3$NH); 3.54 (dd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'a,4'}$ = 3.7 Hz, H-5′a); 3.65 (dd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'b,4'}$ = 3.7 Hz, H-5′b); 3.91 (q, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 3.6 Hz, H-4′); 4.09 (dd, 1H, $J_{3',2'}$ = 5.1 Hz, $J_{3',4'}$ = 3.4 Hz, H-3'); 4.39 (dd, 1H, $J_{2',1'}$ = 6.0 Hz, $J_{2',3'}$ = 5.1 Hz, H-2'); 5.02 – 5.50 (m, 3H, OH-2′,3′,5′); 6.03 (d, 1H, $J_{1',2'}$ = 6.0 Hz, H-1'); 6.80 (q, 1H, $J_{NH,CH3}$ = 4.8 Hz,

$CH_3N\mathbf{H}$); 6.99 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.27 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.53 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.87 (s, 1H, H-6); 8.20 (s, 1H, H-2). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 27.80 ($CH_3NH$); 61.68 ($CH_2$-5′); 70.61 (CH-3′); 74.20 (CH-2′); 85.47 (CH-4′); 87.66 (CH-1′); 103.17 and 103.33 (C-4a,5); 128.04 (CH-4-Sthienyl); 128.87 (CH-6); 129.62 (CH-5-Sthienyl); 130.57 (CH-3-Sthienyl); 136.89 (C-2-Sthienyl); 149.88 (C-7a); 152.59 (CH-2); 156.95 (C-4). IR (KBr): 3503, 3404, 3279, 3126, 3099, 2929, 2869, 1613, 1568, 1491, 1416, 1398, 1338, 1308, 1126, 1084, 1048, 701. HRMS (ESI) calculated for $C_{16}H_{19}O_4N_4S_2$: 395.0842; found: 395.0842.

**General procedure for amination**

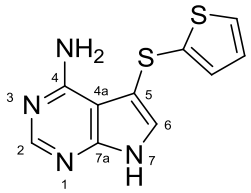
Compound **44a-47a** (1 equiv.), aq ammonia (25% [w/w], 5 mL) in dioxane (5 mL) was stirred at autoclave at 120 °C for 18h. After cooling to rt precipitate was formed and filtrated.

**4-Amino-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Amino-7-(phenylsulfanyl)-7-deazapurine) (36e)**



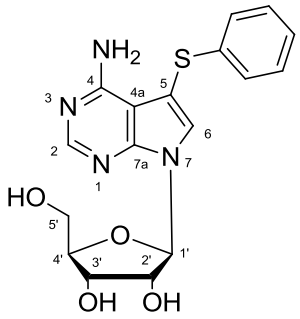

Reaction of deazapurine **44a** (523 mg, 2 mmol) according to the general procedure afforded compound **36e** (411 g, 85%) as white powder. $^1$H NMR was compared with published data.[119]

**4-Amino-5-(thiophen-2-ylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Amino-7-(thiophen-2-ylsulfanyl)-7-deazapurine) (45g)**



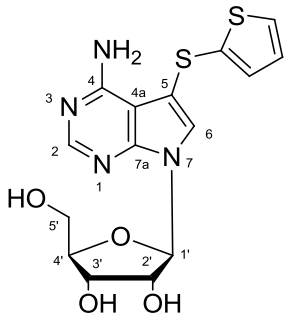

Reaction of deazapurine **45a** (535 mg, 2 mmol) according to the general procedure afforded compound **45g** (425 mg, 85%) as white powder. M.p. 281 °C. $^1$H NMR (500 MHz, DMSO-$d_6$): 6.70 (bs, 2H, $NH_2$); 6.97 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.20 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.49 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.57 (s, 1H, H-6); 8.08 (s, 1H, H-2); 12.01 (vbs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 102.18 and 102.22 (C-5,4a); 128.00 (CH-4-Sthienyl); 128.84 (CH-6); 128.88 (CH-5-Sthienyl); 129.35 (CH-3-Sthienyl); 137.99 (C-2-Sthienyl); 151.42 (C-7a); 152.76 (CH-2); 157.43 (C-4). IR (KBr): 3099, 3069, 2980, 2806, 2672, 1643, 1583, 1320, 719, 686. HRMS (ESI) calculated for $C_{10}H_9N_4S_2$: 249.0263; found: 249.0264.

**4-amino-5-(phenylsulfanyl)-7-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-amino-7-(phenylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (50g)**



Reaction of nucleoside **46a** (706 mg, 1 mmol) according to the general procedure afforded compound **50g** (321 mg, 86%) as white powder. M.p. 214 °C. $[\alpha]_D$ −62.8 (0.21). $^1$H NMR (600.1 MHz, DMSO-$d_6$): 3.55 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'a,OH}$ = 6.2 Hz, $J_{5'a,4'}$ = 3.7 Hz, H-5′a); 3.65 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'b,OH}$ = 5.0 Hz, $J_{5'b,4'}$ = 3.7 Hz, H-5′b); 3.93 (q, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 3.6 Hz, H-4′); 4.11 (td, 1H, $J_{3',2'} = J_{3',OH}$ = 4.9 Hz, $J_{3',4'}$ = 3.3 Hz, H-3'); 4.34 (td, 1H, $J_{2',1'} = J_{2',OH}$ = 6.2 Hz, $J_{2',3'}$ = 5.1 Hz, H-2'); 5.15 (d, 1H, $J_{OH,3'}$ = 4.8 Hz, OH-3′); 5.22 (dd, 1H, $J_{OH,5'a}$ = 6.3 Hz, $J_{OH,5'b}$ = 5.0 Hz, OH-5′); 5.39 (d, 1H, $J_{OH,2'}$ = 6.3 Hz, OH-2′); 6.09 (d, 1H, $J_{1',2'}$ = 6.1 Hz, H-1'); 7.12 (m, 2H, H-*o*-SPh); 7.16 (m, 1H, H-*p*-SPh); 7.29 (m, 2H, H-*m*-SPh); 7.90 (s, 1H, H-6); 8.14 (s, 1H, H-2). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 61.67 ($CH_2$-5′); 70.67 (CH-3′); 74.23 (CH-2′); 85.49 (CH-4′); 87.58 (CH-1′); 99.34 (C-5); 103.39 (C-4a); 125.94 (CH-*p*-SPh); 126.01 (CH-*o*-SPh); 129.50 (CH-*m*-SPh); 130.28 (CH-6); 138.29 (C-*i*-SPh); 151.21 (C-7a); 152.77 (CH-2); 157.65 (C-4). IR (KBr): 3407, 3282, 3147, 3087, 1646, 1586, 1556, 1473, 1440, 1329, 1317, 1144, 1015, 749. HRMS (ESI) calculated for $C_{17}H_{19}O_4N_4S$: 375.1122; found: 375.1123. Anal. calculated for: $C_{17}H_{18}N_4O_4S \cdot 0.60H_2O$: C, 53; H, 5.02; N, 14.54; S, 8.32; found: C, 52.77; H, 4.72; N, 14.29; S, 8.54.

**4-Amino-5-(thiophen-2-ylsulfanyl)-7-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-Amino-7-(thiophen-2-ylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (51g)**



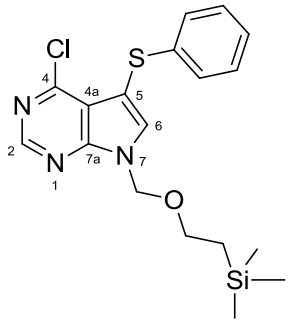
Reaction of nucleoside **47a** (712 mg, 1 mmol) was performed according to the general procedure. Precipitate was not formed. Solvent was then evaporated under reduced pressure and crude products were purified using RP-HPFC (0→100% of MeOH in $H_2O$) and product **51g** was obtained as white powder (267 mg, 70 %). M.p. 178 °C. $[\alpha]_D$ −49.5 (0.23). $^1$H NMR (401.0 MHz, DMSO-$d_6$): 3.55 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'a,OH}$ = 6.2 Hz, $J_{5'a,4'}$ = 3.7 Hz, H-5′a); 3.65 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'b,OH}$ = 4.9 Hz, $J_{5'b,4'}$ = 3.7 Hz, H-5′b); 3.91 (bq, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 3.5 Hz, H-4′); 4.09 (td, 1H, $J_{3',2'} = J_{3',OH}$ = 4.9 Hz, $J_{3',4'}$ = 3.3 Hz, H-3'); 4.40 (td, 1H, $J_{2',1'} = J_{2',OH}$ = 6.2

Hz, $J_{2',3'}$ = 5.1 Hz, H-2'); 5.13 (d, 1H, $J_{OH,3'}$ = 4.8 Hz, OH-3′); 5.23 (dd, 1H, $J_{OH,5'a}$ = 6.2 Hz, $J_{OH,5'b}$ = 4.9 Hz, OH-5′); 5.35 (d, 1H, $J_{OH,2'}$ = 6.4 Hz, OH-2′); 6.03 (d, 1H, $J_{1',2'}$ = 6.1 Hz, H-1'); 6.88 (vbs, 2H, $NH_2$); 6.99 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.24 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.53 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.90 (s, 1H, H-6); 8.11 (s, 1H, H-2). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 61.68 ($CH_2$-5′); 70.63 (CH-3′); 74.17 (CH-2′); 85.47 (CH-4′); 87.60 (CH-1′); 102.77 (C-4a); 103.45 (C-5); 128.09 (CH-4-Sthienyl); 129.23 (CH-6); 129.37 (CH-5-Sthienyl); 130.10 (CH-3-Sthienyl); 136.95 (C-2-Sthienyl); 150.74 (C-7a); 152.70 (CH-2); 157.58 (C-4). IR (KBr): 3285, 3102, 1625, 1589, 1556, 1479, 1437, 1344, 1311, 1129, 1045, 701. HRMS (ESI) calculated for $C_{15}H_{17}O_4N_4S_2$: 381.0686; found: 381.0687.

## 5.6.2 Methylation

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

**(6-Chloro-7-(phenylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (48a)**

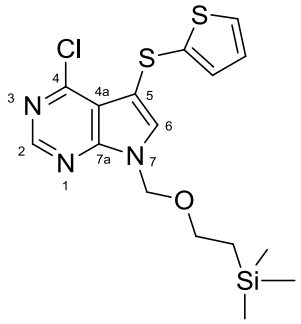



To a flask was added **44a** (1.044 g, 4 mmol) and DMF (10 mL). The mixture was cooled to – 5 °C in an ice/brine bath. Sodium hydride (NaH, 60 wt%, 178 mg, 4.4 mmol, 1.1 equiv.) was added in portions as a solid. The solution darkened over 15 minutes. 2-(Trimethylsilyl)ethoxymethyl chloride (SEM-Cl, 0.78 mL, 4.4 mmol, 1.1 equiv.) was added slowly via syringe at a rate such that the temperature did not exceed 5 °C. The reaction was stirred for 30 minutes, determined to be complete by TLC. Water (25 mL) was slowly added to quench the reaction. The mixture was then diluted with water (100 mL) and ether (200 mL). The layers were separated and the aqueous layer was extracted with ether (200 mL). The combined organic layers were washed with water (2 x 100 mL) and brine (100 mL), dried over sodium sulphate ($Na_2SO_4$), and concentrated under the reduced pressure. Crude product was purified using by HPFC (hexane/EtOAc, 0–20% EtOAc) and product **48a** (1.25 g, 80%) was obtained as a pale yellow oil which solidified upon standing at room temperature. M.p. 107 °C. $^1$H NMR (500 MHz, $CDCl_3$): -0.04 (s, 9H, $CH_3Si$); 0.93 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.57 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.67 (s, 2H, $NCH_2O$); 7.13 – 7.18 (m, 3H, H-*o*,*p*-SPh); 7.23 (m, 2H, H-*m*-SPh); 7.60 (s, 1H, H-6); 8.68

(bs, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.46 ($CH_3Si$); 17.74 ($OCH_2\mathbf{C}H_2Si$); 67.15 ($O\mathbf{C}H_2CH_2Si$); 73.38 ($NCH_2O$); 104.42 (C-5); 116.9 (C-4a); 125.95 (CH-*p*-SPh); 127.25 (CH-*o*-SPh); 129.02 (CH-*m*-SPh); 134.96 (CH-6); 137.86 (C-*i*-SPh); 151.84 (CH-2); 152.82 (C-7a); 153.01 (C-4). IR (KBr): 3060, 3004, 2953, 2923, 1586, 1541, 1452, 1368, 1335, 1248, 1227, 1090, 979, 863, 830, 734, 629. HRMS (ESI) calculated for $C_{18}H_{23}ON_3ClSSi$: 392.1014; found: 392.1015.

**4-Chloro-5-(thiophen-2-ylsulfanyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

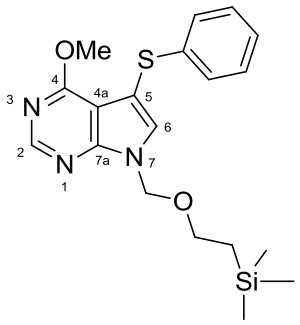
**(6-Chloro-7-(thiophen-2-ylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (49a)**




Compound **49a** was prepared as described for **48a** from 6-chloro-7-(thiophen-2-ylsulfanyl)-7-deazapurine (**45a**) (1.107 g, 4 mmol) to give protected deazapurine **49a** (1.09 g, 69%) as a pale yellow oil which solidified upon standing at room temperature. M.p. 57°C. $^1$H NMR (500 MHz, $CDCl_3$): -0.06 (s, 9H, $CH_3Si$); 0.89 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.51 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 5.60 (s, 2H, $NCH_2O$); 6.97 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.26 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.33 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.41 (s, 1H, H-6); 8.65 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.48 ($CH_3Si$); 17.68 ($OCH_2\mathbf{C}H_2Si$); 67.03 ($O\mathbf{C}H_2CH_2Si$); 73.26 ($NCH_2O$); 108.87 (C-5); 116.09 (C-4a); 127.64 (CH-4-Sthienyl); 129.44 (CH-5-Sthienyl); 132.25 (CH-6); 132.49 (CH-3-Sthienyl); 134.53 (C-2-Sthienyl); 151.65 (CH-2); 152.30 (C-7a); 152.66 (C-4). IR (KBr): 3090, 3060, 2950, 2896, 1571, 1538, 1452, 1440, 1422, 1401, 1356, 1332, 1251, 1216, 1180, 1096, 979, 866, 836, 713, 689, 632. HRMS (ESI) calculated for $C_{16}H_{21}ON_3ClS_2Si$: 398.0578; found: 398.0579.

**4-Methoxy-5-(phenylsulfanyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

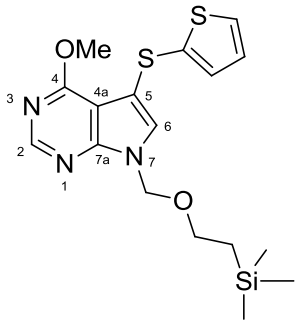
**(6-Methoxy-7-(phenylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (48h)**



Protected deazapurine **48a** (950 mg, 2.5 mmol, 1 equiv.) was dissolved in acetone (10 mL) and 1 M solution of MeONa in MeOH (5 mL, 2 equiv.) was added. Reaction mixture was stirred at rt overnight. Solvents were evaporated under reduced pressure and the mixture was then diluted with water (25 mL) and EtOAc (25 mL). The layers were separated and the aqueous layer was extracted two times with EtOAc (25 mL). The combined organic layers were dried over sodium sulphate ($Na_2SO_4$), and concentrated under the reduced pressure to give product **48h** (1.01 g, 99%) was as yellow oil which solidified upon standing at room temperature. M.p. 286 °C. $^1$H NMR (500 MHz, $CDCl_3$): -0.05 (s, 9H, $CH_3Si$); 0.91 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.56 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 3.97 (s, 3H, $CH_3O$-4); 5.61 (s, 2H, $NCH_2O$); 7.13 (m, 1H, H-*p*-SPh); 7.19 – 7.24 (m, 4H, H-*o*,*m*-SPh); 7.33 (s, 1H, H-6); 8.48 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): -1.47 ($CH_3Si$); 17.74 ($OCH_2\mathbf{C}H_2Si$); 53.75 ($CH_3O$-4); 66.69 ($O\mathbf{C}H_2CH_2Si$); 73.17 ($NCH_2O$); 104.00 (C-5); 106.33 (C-4a); 125.72 (CH-*p*-SPh); 127.74 and 128.74 (CH-*m*,*o*-SPh); 130.67 (CH-6); 138.19 (C-*i*-SPh); 152.11 (CH-2); 153.28 (C-7a); 163.65 (C-4). IR (KBr): 3087, 3052, 2992, 2947, 2935, 2896, 1589, 1562, 1476, 1407, 1338, 1323, 1248, 1222, 1093, 863, 842, 743. HRMS (ESI) calculated for $C_{19}H_{25}O_2N_3NaSSi$: 410.1329; found: 410.1331.

**4-Methoxy-5-(thiophen-2-ylsulfanyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

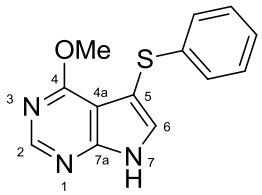
**(6-Methoxy-7-(thiophen-2-ylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine) (49h)**



Compound **49h** was prepared as described for **48h** from 6-methoxy-7-(thiophen-2-ylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (**49a**) (995 mg, 2.5 mmol) to give 6-methoxy deazapurine **49h** (930 mg, 95%) as a pale yellow oil which solidified upon standing at room temperature. M.p. 101 °C. $^1$H NMR (500 MHz, $CDCl_3$): -0.07 (s, 9H, $CH_3Si$); 0.88 (m, 2H, $OCH_2C\mathbf{H_2}Si$); 3.50 (m, 2H, $OC\mathbf{H_2}CH_2Si$); 4.15 (s, 3H, $CH_3O$); 5.54 (s, 2H, $NCH_2O$); 6.96 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.16 (s, 1H, H-6); 7.24 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.31 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 8.46 (s, 1H, H-2). $^{13}$C

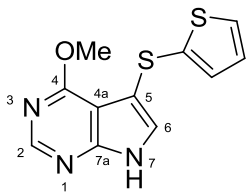
NMR (125.7 MHz, $CDCl_3$): -1.48 ($CH_3Si$); 17.70 ($OCH_2\mathbf{C}H_2Si$); 53.70 ($CH_3O$); 66.60 ($O\mathbf{C}H_2CH_2Si$); 73.06 ($NCH_2O$); 105.45 (C-4a); 108.19 (C-5); 127.39 (CH-4-Sthienyl); 128.13 (CH-6); 129.26 (CH-5-Sthienyl); 132.73 (CH-3-Sthienyl); 135.02 (C-2-Sthienyl); 151.98 (CH-2); 152.87 (C-7a); 163.53 (C-4). IR (KBr):3087, 3004, 2953, 2890, 1589, 1562, 1479, 1410, 1341, 1326, 1248, 1224, 1174, 1096, 1078, 866, 833. HRMS (ESI) calculated for $C_{17}H_{24}O_2N_3S_2Si$: 394.1074; found: 394.1074.

**4-Methoxy-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Methoxy-7-(phenylsulfanyl)-7-deazapurine) (44h)**




Protected deazapurine **48h** (774 mg, 2.0 mmol, 1 equiv.) was dissolved in trifluoroacetic acid (2 mL) and the reaction mixture was stirred at rt overnight. The mixture was then diluted with $NaHCO_3$ (check pH=7!) and EtOAc (25 mL). The layers were separated and the aqueous layer was extracted two times with EtOAc (25 mL). The combined organic layers were dried over sodium sulphate ($Na_2SO_4$), and concentrated under the reduced pressure to give white solid. The solid was then diluted with aq ammonia (25% [w/w], 15 mL) and stirred at rt overnight to form white precipitate. The precipitate was filtered to give product **44h** (460 mg, 90%) as a white powder. M.p. 200 °C. $^1$H NMR (600.1 MHz, DMSO-$d_6$): 3.86 (s, 3H, $CH_3O$); 7.07 (m, 2H, H-*o*-SPh); 7.10 (m, 1H, H-*p*-SPh); 7.23 (m, 2H, H-*m*-SPh); 7.71 (s, 1H, H-6); 8.41 (s, 1H, H-2); 12.54 (bs, 1H, NH). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 53.57 ($CH_3O$); 99.54 (C-5); 105.71 (C-4a); 125.30 (CH-*p*-SPh); 126.20 (CH-*o*-SPh); 129.04 (CH-*m*-SPh); 131.31 (CH-6); 139.40 (C-*i*-SPh); 151.51 (CH-2); 153.58 (C-7a); 162.90 (C-4). IR (KBr): 3096, 2974, 2941, 2896, 2851, 2821, 1598, 1583, 1485, 1434, 1398, 1335, 1326, 1093, 878, 737. HRMS (ESI) calculated for $C_{13}H_{12}ON_3S$: 258.0696; found: 258.0696.

**4-Methoxy-5-(thiophen-2-ylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Methoxy-7-(thiophen-2-ylsulfanyl)-7-deazapurine) (45h)**




Compound **45h** was prepared as described for **44h** from 6-chloro-7-(thiophen-2-ylsulfanyl)-9-((2-(trimethylsilyl)ethoxy)methyl)-7-deazapurine (**49h**) (787 mg, 2.0 mmol) to give nonprotected 6-methoxy deazapurine **45h** (462 mg, 88%) as a white powder. M.p. 167 °C. $^1$H

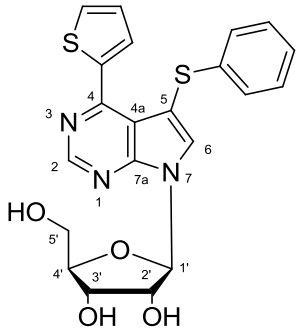
NMR (401 MHz, DMSO-$d_6$): 4.03 (s, 3H, $CH_3O$); 6.98 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.20 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.50 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.60 (s, 1H, H-6); 8.39 (s, 1H, H-2); 12.41 (bs, 1H, NH). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 53.56 ($CH_3O$); 104.10 (C-5); 104.91 (C-4a); 127.84 (CH-4-Sthienyl); 129.25 (CH-6); 129.46 (CH-5-Sthienyl); 131.46 (CH-3-Sthienyl); 136.58 (C-2-Sthienyl); 151.52 (CH-2); 153.07 (C-7a); 162.81 (C-4). IR (KBr):3096, 2992, 2947, 2899, 2857, 2824, 1595, 1583, 1476, 1395, 1338, 1317, 1102, 713, 626. HRMS (ESI) calculated for $C_{11}H_{10}ON_3S_2$: 264.0260; found: 264.0261.

## 5.6.3 Deprotection of 7-substituted nucleosides

**General procedure:**

Protected nucleoside **46b-46e** or **47b-47e** (1 equiv.) was dissolved in methanol and 1 M solution of MeONa in MeOH (1.5 equiv.) was added. Reaction mixture was stirred at rt overnight. Solvent was evaporated under reduced pressure and crude products were purified using RP-HPFC (0→100% of MeOH in $H_2O$).

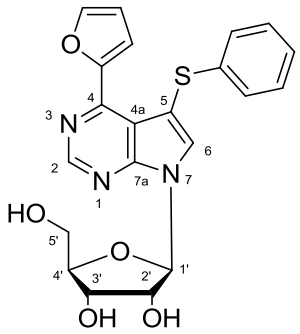
**5-(Phenylsulfanyl)-4-(thiophen-2-yl)-7-β-D-ribofuranosyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (7-(Phenylsulfanyl)-6-(thiophen-2-yl)-9-β-D-ribofuranosyl)-7-deazapurine) (50b)**




Deprotection of **46b** (376 mg, 0.5 mmol) according to the general procedure afforded compound **50b** (164 mg, 75%) as yellow solid. Crystallization in MeOH/$H_2O$ gave yellow foam. M.p. 77 °C $[\alpha]_D$ −49.3 (0.19). $^1$H NMR (401.0 MHz, DMSO-$d_6$): 3.59 (dd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'a,4'}$ = 3.7 Hz, H-5′a); 3.69 (dd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'b,4'}$ = 3.7 Hz, H-5′b); 3.97 (q, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 3.7 Hz, H-4′); 4.15 (dd, 1H, $J_{3',2'}$ = 5.0 Hz, $J_{3',4'}$ = 3.6 Hz, H-3'); 4.46 (bt, 1H, $J_{2',1'} = J_{2',3'}$ = 5.4 Hz, H-2'); 5.06 – 5.64 (m, 3H, OH-2′,3′,5′); 6.33 (d, 1H, $J_{1',2'}$ = 5.8 Hz, H-1'); 6.93 (m, 2H, H-*o*-SPh); 7.04 (m, 1H, H-*p*-SPh); 7.08 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.8 Hz, H-4-thienyl); 7.16 (m, 2H, H-*m*-SPh); 7.71 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.1 Hz, H-5-thienyl); 8.35 (dd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,5}$ = 1.1 Hz, H-3-thienyl); 8.41 (s, 1H, H-6); 8.84 (s, 1H, H-2). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 61.37 ($CH_2$-5′); 70.51 (CH-3′); 74.60 (CH-2′); 85.56 (CH-4′); 87.26 (CH-1′); 100.37 (C-5); 114.66 (C-4a); 125.67 (CH-*p*-SPh); 125.83 (CH-*o*-

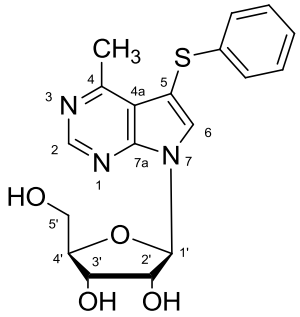
SPh); 128.20 (CH-4-thienyl); 129.27 (CH-*m*-SPh); 131.08 (CH-5-thienyl); 132.28 (CH-3-thienyl); 136.12 (CH-6); 138.44 (C-*i*-SPh); 140.89 (C-2-thienyl); 151.22 (CH-2); 152.62 (C-4); 153.50 (C-7a). IR (KBr): 3117, 3052, 2923, 2869, 1559, 1482, 1437, 1404, 1195, 1105, 1081, 1048, 1021, 737.. HRMS (ESI) calculated for $C_{21}H_{20}O_4N_3S_2$: 442.0890; found: 442.0890.

**4-(Furan-2-yl)-5-(phenylsulfanyl)-7-β-D-ribofuranosyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-(Furan-2-yl)-7-(phenylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (50c)**



Deprotection of **46c** (552 mg, 0.75 mmol) according to the general procedure afforded compound **50c** (248 mg, 78%) as yellow solid. Crystallization in MeOH/$H_2O$ gave yellow foam. M.p. 120 °C $[\alpha]_D$ −39.3 (0.19). $^1$H NMR (500 MHz, DMSO-$d_6$): 3.59 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'a,OH}$ = 5.5 Hz, $J_{5'a,4'}$ = 3.7 Hz, H-5′a); 3.68 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'b,OH}$ = 5.3 Hz, $J_{5'b,4'}$ = 3.9 Hz, H-5′b); 3.97 (q, 1H, $J_{4',5'a}$ = $J_{4',5'b}$ = $J_{4',3'}$ = 3.7 Hz, H-4′); 4.15 (td, 1H, $J_{3',2'}$ = $J_{3',OH}$ = 5.0 Hz, $J_{3',4'}$ = 3.6 Hz, H-3'); 4.46 (td, 1H, $J_{2',1'}$ = $J_{2',OH}$ = 6.0 Hz, $J_{2',3'}$ = 5.0 Hz, H-2'); 5.13 (t, 1H, $J_{OH,5'a}$ = $J_{OH,5'b}$ = 5.4 Hz, OH-5′); 5.22 (d, 1H, $J_{OH,3'}$ = 5.0 Hz, OH-3′); 5.50 (d, 1H, $J_{OH,2'}$ = 6.1 Hz, OH-2′); 6.32 (d, 1H, $J_{1',2'}$ = 5.8 Hz, H-1'); 6.59 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.7 Hz, H-4-furyl); 7.01 (m, 2H, H-*o*-SPh); 7.05 (m, 1H, H-*p*-SPh); 7.18 (m, 2H, H-*m*-SPh); 7.42 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 7.71 (dd, 1H, $J_{5,4}$ = 1.7 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 8.38 (s, 1H, H-6); 8.87 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 61.39 ($CH_2$-5′); 70.54 (CH-3′); 74.54 (CH-2′); 85.55 (CH-4′); 87.09 (CH-1′); 100.90 (C-5); 112.43 (CH-4-furyl); 114.11 (C-4a); 115.27 (CH-3-furyl); 125.36 (CH-*p*-SPh); 125.76 (CH-*o*-SPh); 129.11 (CH-*m*-SPh); 135.98 (CH-6); 139.03 (C-*i*-SPh); 145.91 (CH-5-furyl); 148.09 (C-4); 150.63 (C-2-furyl); 151.41 (CH-2); 153.57 (C-7a). IR (KBr): 3294, 3135, 3117, 2947, 2920, 2902, 1580, 1556, 1482, 1440, 1326, 1204, 1108, 988, 734. HRMS (ESI) calculated for $C_{21}H_{20}O_5N_3S$: 426.1118; found: 426.1118. Anal. calculated for $C_{21}H_{19}N_3O_5S \cdot 0.75H_2O$: C, 57.46; H, 4.71; N, 9.57; S, 7.3; found: C, 57.77; H, 4.56; N, 9.21; S, 7.17.

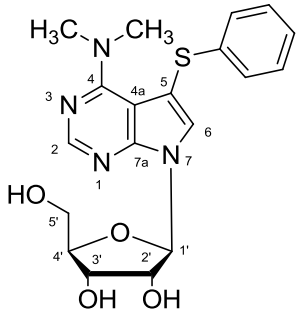
**4-Methyl-5-(phenylsulfanyl)-7-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-Methyl-7-(phenylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (50d)**



Deprotection of **46d** (274 mg, 0.4 mmol) according to the general procedure afforded compound **50d** (130 mg, 87%) as white solid. Crystallization in MeOH/$H_2O$ gave white foam. M.p. 182 °C $[\alpha]_D$ −54.5 (0.21). $^1$H NMR (600.1 MHz, DMSO-$d_6$): 2.60 (s, 3H, $CH_3$-4); 3.58 (ddd, 1H, $J_{gem}$ = 11.9 Hz, $J_{5'a,OH}$ = 5.5 Hz, $J_{5'a,4'}$ = 3.7 Hz, H-5′a); 3.67 (ddd, 1H, $J_{gem}$ = 11.9 Hz, $J_{5'b,OH}$ = 5.2 Hz, $J_{5'b,4'}$ = 3.9 Hz, H-5′b); 3.95 (q, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 3.7 Hz, H-4′); 4.14 (td, 1H, $J_{3',2'} = J_{3',OH}$ = 4.9 Hz, $J_{3',4'}$ = 3.4 Hz, H-3'); 4.45 (td, 1H, $J_{2',1'} = J_{2',OH}$ = 6.0 Hz, $J_{2',3'}$ = 5.0 Hz, H-2'); 5.11 (t, 1H, $J_{OH,5'a} = J_{OH,5'b}$ = 5.4 Hz, OH-5′); 5.20 (d, 1H, $J_{OH,3'}$ = 4.9 Hz, OH-3′); 5.45 (d, 1H, $J_{OH,2'}$ = 6.1 Hz, OH-2′); 6.25 (d, 1H, $J_{1',2'}$ = 5.9 Hz, H-1'); 7.07 (m, 2H, H-*o*-SPh); 7.15 (m, 1H, H-*p*-SPh); 7.28 (m, 2H, H-*m*-SPh); 8.27 (s, 1H, H-6); 8.73 (s, 1H, H-2). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 20.81 ($CH_3$-4); 61.46 ($CH_2$-5′); 70.56 (CH-3′); 74.44 (CH-2′); 85.53 (CH-4′); 87.10 (CH-1′); 100.54 (C-5); 117.80 (C-4a); 125.58 (CH-*o*-SPh); 125.69 (CH-*p*-SPh); 129.15 (CH-*m*-SPh); 134.14 (CH-6); 138.79 (C-*i*-SPh); 151.62 (C-7a); 151.79 (CH-2); 159.62 (C-4). IR (KBr): 3455, 3422, 3225, 3072, 2953, 2914, 2881, 2839, 1580, 1568, 1470, 1428, 1338, 1213, 1054, 1042, 740, 629. HRMS (ESI) calculated for $C_{18}H_{20}O_4N_3S$: 374.1169; found: 374.1170. Anal. calculated for $C_{18}H_{19}N_3O_4S \cdot 0.3\ H_2O$: C, 57.07; H, 5.21; N, 11.09; S, 8.46; found: C, 57.12; H, 5.16; N, 10.92; S, 8.29.

**4-(N,N-Dimethylamino)-5-(phenylsulfanyl)-7-β-D-ribofuranosyl-*7H*-pyrrolo[2,3-*d*]pyrimidine**

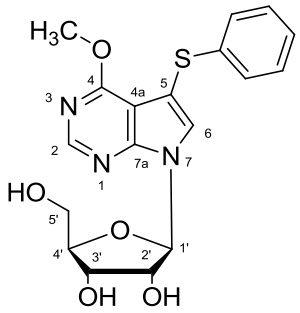
**(6-(N,N-Dimethylamino)-7-(phenylsulfanyl)-9-β-D-ribofuranosyl-7-deazapurine) (50e)**



Deprotection of **46e** (535 mg, 0.75 mmol) according to the general procedure afforded compound **50e** (302 mg, 87%) as white solid. Crystallization in MeOH/$H_2O$ gave white foam. M.p. 112 °C $[\alpha]_D$ −44.4 (0.18). $^1$H NMR (600.1 MHz, DMSO-$d_6$): 3.12 (s, 6H, $(CH_3)_2$N); 3.55 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'a,OH}$ = 5.7 Hz, $J_{5'a,4'}$ = 3.7 Hz, H-5′a); 3.65 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'b,OH}$ = 4.9 Hz, $J_{5'b,4'}$ = 3.7 Hz, H-5′b); 3.92 (q, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 3.6 Hz, H-4′); 4.10 (m, 1H, H-3'); 4.41 (m, 1H, H-2'); 5.13 – 5.17 (m, 2H, OH-3′,5′); 5.39 (m, 1H, OH-2′); 6.18 (d, 1H, $J_{1',2'}$ = 5.9 Hz, H-1'); 7.03 (m, 2H, H-*o*-SPh); 7.12 (m, 1H, H-*p*-SPh); 7.26 (m, 2H, H-*m*-SPh); 8.01 (s, 1H, H-6);

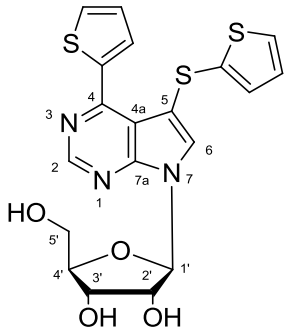
8.25 (s, 1H, H-2). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 41.26 ($(CH_3)_2N$); 61.51 ($CH_2$-5′); 70.53 (CH-3′); 74.30 (CH-2′); 85.32 (CH-4′); 87.33 (CH-1′); 99.61 (C-5); 104.95 (C-4a); 125.31 (CH-*o*-SPh); 125.45 (CH-*p*-SPh); 129.32 (CH-*m*-SPh); 131.82 (CH-6); 139.39 (C-*i*-SPh); 150.78 (CH-2); 152.83 (C-7a); 159.39 (C-4). IR (KBr): 3515, 3407, 3192, 3114, 3052, 2941, 2902, 2863, 1571, 1547, 1491, 1416, 1296, 1096, 1057, 1030,740. HRMS (ESI) calculated for $C_{19}H_{23}O_4N_4S$: 403.1435; found: 403.1436. Anal. calculated for $C_{19}H_{22}N_4O_4S \cdot 1.15H_2O$: C, 53.93; H, 5.79; N, 13.24; S, 7.58; found: C, 54.14; H, 5.72; N, 13.03; S, 7.48.

**4-Methoxy-5-(phenylsulfanyl)-7-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-Methoxy-7-(phenylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (50h)**



Deprotection and methoxylation of **46a** (706 mg, 1 mmol) according to the general procedure (4 equiv. of NaOMe were used) afforded compound **50h** (290 mg, 75%) as white solid. Crystallization in MeOH/$H_2O$ gave white foam. M.p. 162 °C $[\alpha]_D$ −55.1 (0.18). $^1$H NMR (600.1 MHz, DMSO-$d_6$): 3.56 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'a,OH}$ = 5.7 Hz, $J_{5'a,4'}$ = 3.8 Hz, H-5′a); 3.65 (ddd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'b,OH}$ = 5.2 Hz, $J_{5'b,4'}$ = 3.9 Hz, H-5′b); 3.87 (s, 3H, $CH_3O$-4); 3.93 (q, 1H, $J_{4',5'a}$ = $J_{4',5'b}$ = $J_{4',3'}$ = 3.7 Hz, H-4′); 4.11 (td, 1H, $J_{3',2'}$ = $J_{3',OH}$ = 4.9 Hz, $J_{3',4'}$ = 3.4 Hz, H-3'); 4.42 (m, 1H, H-2'); 5.10 (t, 1H, $J_{OH,5'a}$ = $J_{OH,5'b}$ = 5.4 Hz, OH-5′); 5.18 (d, 1H, $J_{OH,3'}$ = 4.8 Hz, OH-3′); 5.42 (d, 1H, $J_{OH,2'}$ = 6.0 Hz, OH-2′); 6.18 (d, 1H, $J_{1',2'}$ = 6.0 Hz, H-1'); 7.11 (m, 2H, H-*o*-SPh); 7.13 (m, 1H, H-*p*-SPh); 7.26 (m, 2H, H-*m*-SPh); 8.04 (s, 1H, H-6); 8.48 (s, 1H, H-2). $^{13}$C NMR (150.9 MHz, DMSO-$d_6$): 53.83 ($CH_3O$-4); 61.52 ($CH_2$-5′); 70.59 (CH-3′); 74.44 (CH-2′); 85.53 (CH-4′); 87.40 (CH-1′); 101.02 (C-5); 106.28 (C-4a); 125.61 (CH-*p*-SPh); 126.51 (CH-*o*-SPh); 129.14 (CH-*m*-SPh); 131.09 (CH-6); 138.61 (C-*i*-SPh); 151.73 (CH-2); 152.96 (C-7a); 162.97 (C-4). IR (KBr): 3225, 3150, 3058, 3016, 3001, 2941, 2908, 2869, 2848, 1589, 1556, 1479, 1449, 1419, 1344, 1299, 1072, 1051, 737. HRMS (ESI) calculated for $C_{18}H_{20}O_5N_3S$: 390.1118; found: 390.1119.

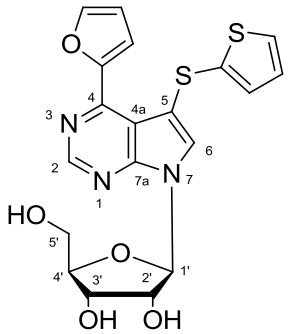
**4-(Thiophen-2-yl)-5-(thiophen-2-ylsulfanyl)-7-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-(Thiophen-2-yl)-7-(thiophen-2-ylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (51b)**



Deprotection of **47b** (462 mg, 0.65 mmol) according to the general procedure afforded compound **51b** (171 mg, 59%) as yellowish solid. M.p. 165 °C $[\alpha]_D$ −31.2 (0.19). $^1$H NMR (401.0 MHz, DMSO-$d_6$): 3.60 (dd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'a,4'}$ = 3.8 Hz, H-5′a); 3.70 (dd, 1H, $J_{gem}$ = 12.0 Hz, $J_{5'b,4'}$ = 3.8 Hz, H-5′b); 3.97 (q, 1H, $J_{4',5'a}$ = $J_{4',5'b}$ = $J_{4',3'}$ = 3.7 Hz, H-4′); 4.15 (dd, 1H, $J_{3',2'}$ = 5.0 Hz, $J_{3',4'}$ = 3.6 Hz, H-3'); 4.43 (bt, 1H, $J_{2',1'}$ = $J_{2',3'}$ = 5.4 Hz, H-2'); 4.96 – 5.66 (m, 3H, OH-2′,3′,5′); 6.28 (d, 1H, $J_{1',2'}$ = 5.7 Hz, H-1'); 6.79 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 6.85 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.30 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.7 Hz, H-4-thienyl); 7.41 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.86 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.1 Hz, H-5-thienyl); 8.38 (s, 1H, H-6); 8.40 (dd, 1H, $J_{3,4}$ = 3.7 Hz, $J_{3,5}$ = 1.1 Hz, H-3-thienyl); 8.82 (s, 1H, H-2). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 61.41 ($CH_2$-5′); 70.51 (CH-3′); 74.56 (CH-2′); 85.57 (CH-4′); 87.29 (CH-1′); 104.92 (C-5); 113.99 (C-4a); 127.83 (CH-4-Sthienyl); 128.31 (CH-4-thienyl); 129.54 (CH-5-Sthienyl); 130.56 (CH-3-Sthienyl); 131.15 (CH-5-thienyl); 132.91 (CH-3-thienyl); 134.53 (CH-6); 136.03 (C-2-Sthienyl); 140.81 (C-2-thienyl); 151.21 (CH-2); 152.52 (C-4); 152.94 (C-7a). IR (KBr): 3291, 3111, 2932, 2869, 1556, 1443, 1401, 1192, 1099, 1075, 1045, 803, 716, 629. HRMS (ESI) calculated for $C_{19}H_{18}O_4N_3S_3$: 448.0454; found: 448.0453.

**4-(Furan-2-yl)-5-(thiophen-2-ylsulfanyl)-7-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

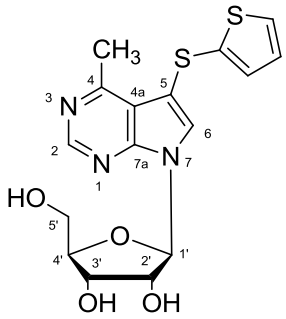
**(6-(Furan-2-yl)-7-(thiophen-2-ylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (51c)**



Deprotection of **47c** (260 mg, 0.35 mmol) according to the general procedure afforded compound **51c** (85 mg, 57%) as yellow solid. M.p. 172 °C $[\alpha]_D$ −41.7 (0.21). $^1$H NMR (401.0 MHz, DMSO-$d_6$): 3.56 (dd, 1H, $J_{gem}$ = 11.9 Hz, $J_{5'a,4'}$ = 3.8 Hz, H-5′a); 3.66 (dd, 1H, $J_{gem}$ = 11.9 Hz, $J_{5'b,4'}$ = 3.8 Hz, H-5′b); 3.95 (q, 1H, $J_{4',5'a}$ = $J_{4',5'b}$ = $J_{4',3'}$ = 3.7 Hz, H-4′); 4.11 (dd, 1H, $J_{3',2'}$ = 5.0 Hz, $J_{3',4'}$ = 3.6 Hz, H-3'); 4.39 (bt, 1H, $J_{2',1'}$ = $J_{2',3'}$ = 5.4 Hz, H-2'); 4.96 – 5.67 (m, 3H, OH-2′,3′,5′); 6.25 (d, 1H, $J_{1',2'}$ = 5.8 Hz, H-1'); 6.78 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.93 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.02 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-

Sthienyl); 7.48 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.50 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 8.05 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 8.17 (s, 1H, H-6); 8.83 (s, 1H, H-2). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 61.44 ($CH_2$-5′); 70.55 (CH-3′); 74.51 (CH-2′); 85.52 (CH-4′); 87.16 (CH-1′); 106.19 (C-5); 112.74 (CH-4-furyl); 113.10 (C-4a); 115.42 (CH-3-furyl); 127.95 (CH-4-Sthienyl); 129.71 (CH-5-Sthienyl); 131.25 (CH-3-Sthienyl); 133.07 (CH-6); 135.74 (C-2-Sthienyl); 146.18 (CH-5-furyl); 147.87 (C-4); 150.87 (C-2-furyl); 151.33 (CH-2); 152.96 (C-7a). IR (KBr): 3252, 3162, 3138, 2944, 2914, 2872, 1586, 1562, 1532, 1461, 1338, 1198, 1096, 1054, 1024, 979, 812, 752, 704. HRMS (ESI) calculated for $C_{19}H_{17}O_5N_3NaS_2$: 454.0502; found: 454.0502.

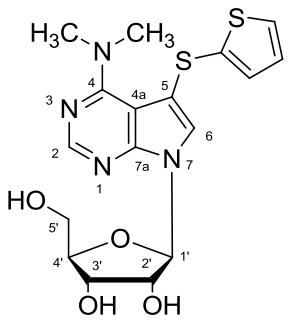
**4-Methyl-5-(thiophen-2-ylsulfanyl)-7-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-Methyl-7-(thiophen-2-ylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (51d)**




Deprotection of **47d** (415 mg, 0.6 mmol) according to the general procedure afforded compound **51d** (146 mg, 64%) as white solid. M.p. 140 °C $[\alpha]_D$ −53.0 (0.22). $^1$H NMR (401.0 MHz, DMSO-$d_6$): 2.83 (s, 3H, $CH_3$); 3.57 (dd, 1H, $J_{gem}$ = 11.9 Hz, $J_{5'a,4'}$ = 3.8 Hz, H-5′a); 3.68 (dd, 1H, $J_{gem}$ = 11.9 Hz, $J_{5'b,4'}$ = 3.9 Hz, H-5′b); 3.94 (q, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 3.7 Hz, H-4′); 4.12 (dd, 1H, $J_{3',2'}$ = 5.1 Hz, $J_{3',4'}$ = 3.5 Hz, H-3'); 4.41 (dd, 1H, $J_{2',1'}$ = 5.9 Hz, $J_{2',3'}$ = 5.1 Hz, H-2'); 5.00 – 5.55 (m, 3H, OH-2′,3′,5′); 6.20 (d, 1H, $J_{1',2'}$ = 5.9 Hz, H-1'); 7.00 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.16 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.51 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 8.27 (s, 1H, H-6); 8.71 (s, 1H, H-2). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 21.60 ($CH_3$); 61.50 ($CH_2$-5′); 70.55 (CH-3′); 74.45 (CH-2′); 85.54 (CH-4′); 87.18 (CH-1′); 104.53 (C-5); 117.14 (C-4a); 128.20 (CH-4-Sthienyl); 128.85 (CH-5-Sthienyl); 129.50 (CH-3-Sthienyl); 133.11 (CH-6); 137.12 (C-2-Sthienyl); 151.10 (C-7a); 151.76 (CH-2); 159.90 (C-4). IR (KBr): 3425, 3282, 3108, 2950, 2932, 2881, 2842, 1583, 1562, 1416, 1407, 1338, 1219, 1207, 1117, 1096, 1057, 1039, 976, 848, 710, 695, 626. HRMS (ESI) calculated for $C_{16}H_{17}O_4N_3NaS_2$: 402.0553; found: 402.0553.

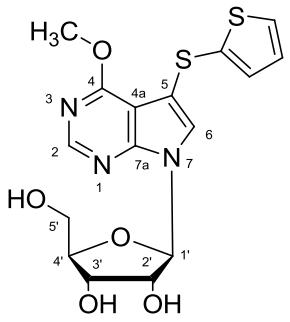
**4-(N,N-Dimethylamino)-5-(thiophen-2-ylsulfanyl)-7-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**

**(6-(N,N-Dimethylamino)-7-(thiophen-2-ylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (51e)**



Deprotection of **47e** (540 mg, 0.75 mmol) according to the general procedure afforded compound **51e** (197 mg, 65%) as white solid. M.p. 199 °C $[\alpha]_D$ −41.8 (0.19). $^1$H NMR (401.0 MHz, DMSO-$d_6$): 3.24 (s, 6H, $(CH_3)_2N$); 3.55 (dd, 1H, $J_{gem}$ = 11.9 Hz, $J_{5'a,4'}$ = 3.7 Hz, H-5′a); 3.65 (dd, 1H, $J_{gem}$ = 11.9 Hz, $J_{5'b,4'}$ = 3.7 Hz, H-5′b); 3.91 (q, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 3.7 Hz, H-4′); 4.09 (dd, 1H, $J_{3',2'}$ = 5.1 Hz, $J_{3',4'}$ = 3.6 Hz, H-3'); 4.36 (dd, 1H, $J_{2',1'}$ = 5.8 Hz, $J_{2',3'}$ = 5.1 Hz, H-2'); 5.00 – 5.51 (m, 3H, OH-2′,3′,5′); 6.11 (d, 1H, $J_{1',2'}$ = 5.8 Hz, H-1'); 6.97 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.10 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.48 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 8.23 (s, 1H, H-6); 8.30 (s, 1H, H-2). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 41.54 ($(CH_3)_2N$); 61.57 ($CH_2$-5′); 70.54 (CH-3′); 74.32 (CH-2′); 85.33 (CH-4′); 87.44 (CH-1′); 104.37 and 104.47 (C-4a,5); 128.05 (CH-4-Sthienyl); 128.93 (CH-5-Sthienyl); 129.82 (CH-3-Sthienyl); 130.12 (CH-6); 137.39 (C-2-Sthienyl); 150.76 (CH-2); 152.35 (C-7a); 159.53 (C-4). IR (KBr):3494, 3282, 3222, 3117, 2941, 2887, 1577, 1538, 1497, 1437, 1419, 1404, 1299, 1219, 1135, 1030, 698. HRMS (ESI) calculated for $C_{17}H_{21}O_4N_4S_2$: 409.0999; found: 409.1002.

**4-Methoxy-5-(thiophen-2-ylsulfanyl)-7-β-D-ribofuranosyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (6-Methoxy-7-(thiophen-2-ylsulfanyl)-9-β-D-ribofuranosyl)-7-deazapurine) (51h)**



Deprotection and methoxylation of **47a** (712 mg, 1 mmol) according to the general procedure (4 equiv. of NaOMe were used) afforded compound **51h** (305 mg, 77%) as white solid. M.p. 194 °C $[\alpha]_D$ −51.1 (0.17). $^1$H NMR (401.0 MHz, DMSO-$d_6$): 3.55 (dd, 1H, $J_{gem}$ = 11.9 Hz, $J_{5'a,4'}$ = 3.8 Hz, H-5′a); 3.64 (dd, 1H, $J_{gem}$ = 11.9 Hz, $J_{5'b,4'}$ = 3.8 Hz, H-5′b); 3.91 (q, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 3.6 Hz, H-4′); 4.06 (s, 3H, $CH_3O$); 4.09 (dd, 1H, $J_{3',2'}$ = 5.1 Hz, $J_{3',4'}$ = 3.4 Hz, H-3'); 4.37 (dd, 1H, $J_{2',1'}$ = 6.1 Hz, $J_{2',3'}$ = 5.1 Hz, H-2'); 4.98 – 5.52 (m, 3H, OH-2′,3′,5′); 6.12 (d, 1H, $J_{1',2'}$ = 6.1 Hz, H-1'); 7.00 (dd, 1H, $J_{4,5}$ = 5.3 Hz, $J_{4,3}$ = 3.6 Hz, H-4-Sthienyl); 7.24 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{3,5}$ = 1.3 Hz, H-3-Sthienyl); 7.55 (dd, 1H, $J_{5,4}$ = 5.3 Hz, $J_{5,3}$ = 1.3 Hz, H-5-Sthienyl); 7.93 (s, 1H, H-6); 8.45

(s, 1H, H-2). $^{13}$C NMR (100.8 MHz, DMSO-$d_6$): 53.83 ($CH_3O$); 61.55 ($CH_2$-5′); 70.60 (CH-3′); 74.36 (CH-2′); 85.54 (CH-4′); 87.39 (CH-1′); 105.39 and 105.53 (C-4a,5); 127.93 (CH-4-Sthienyl); 129.13 (CH-6); 129.96 (CH-5-Sthienyl); 132.18 (CH-3-Sthienyl); 135.41 (C-2-Sthienyl); 151.73 (CH-2); 152.47 (C-7a); 162.89 (C-4). IR (KBr): 3512, 3285, 3025, 2992, 2935, 2920, 2869, 1589, 1556, 1482, 1443, 1407, 1338, 1326, 1302, 1138, 1081, 1036, 704. HRMS (ESI) calculated for $C_{16}H_{18}O_5N_3S_2$: 396.0682; found: 396.0682.

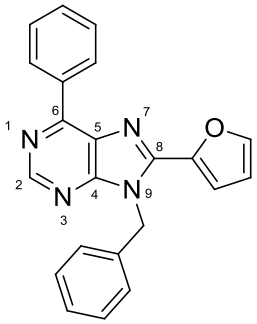
## 5.7 Reactivity of sulfanyl deazapurine and purine bases

**Liebeskind-Srogl cross-coupling of 9-benzyl-6-phenyl-8-(phenylsulfanyl)-*9H*-purine**

**a) Reaction with stannanes**

To the mixture of CuMeSal (47 mg, 0.22 mmol, 2.2 equiv.), $Pd(PPh_3)_4$ (5.8 mg, 0.005 mmol, 0.05 equiv.) and 9-benzyl-6-phenyl-8-(phenylthio)-*9H*-purine **43a** (39 mg, 0.1 mmol, 1.0 equiv.) and stannane (0.12 mmol, 1.2 equiv.) in THF (2 mL). The reaction mixture was stirred under nitrogen at 50 °C for 18 h, and then 10% aqueous $NH_4OH$ (10 mL) was added and the mixture was stirred for an additional 10 min. The reaction mixture was filtered through a plug of Celite, and the filtrate was extracted with ethyl acetate (3 × 15 mL). The organic layer was washed with brine (5 mL), dried over $NaSO_4$, and evaporated. The crude product was purified by column chromatography on silica gel.

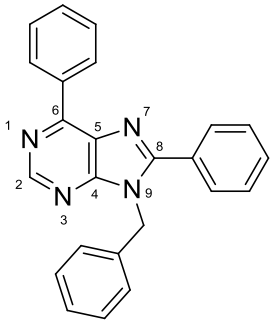
**9-Benzyl-8-(furan-2-yl)-6-phenyl-*9H*-purine (52a)**



2-(Tri-n-butylstannyl)furan (38 μL, 0.12 mmol, 1.2 equiv.) was used as starting compound to give product **52a** (25 mg, 70%) as white crystals after chromatography eluting with hexane/EtOAc 5:1 to 2:1. M.p. 135 - 141 °C. $^1$H NMR (500.0 MHz, $CDCl_3$): 5.86 (s, 2H, $CH_2Ph$); 6.59 (dd, 1H, $J_{4,3}$ = 3.6, $J_{4,5}$ = 1.8, H-4-furyl); 7.22 (m, 2H, H-*o*-Bn); 7.26 (m, 1H, H-*p*-Bn); 7.28 (m, 2H, H-*m*-Bn); 7.29 (dd, 1H, $J_{3,4}$ = 3.6, $J_{3,5}$ = 0.8, H-3-furyl); 7.52 (m, 1H, H-*p*-Ph); 7.58 (m, 2H, H-*m*-Ph); 7.64 (dd, 1H, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.8, H-5-furyl); 8.88 (m, 2H, H-*o*-Ph); 9.02 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 46.96 ($CH_2Ph$); 112.34 (CH-4-furyl); 114.88 (CH-3-furyl);126.85 (CH-*o*-Bn); 127.84 (CH-*p*-Bn); 128.62 (CH-*m*-Ph); 128.76 (CH-*m*-Bn); 129.79 (CH-*o*-Ph); 130.82 (CH-*p*-Ph); 131.05 (C-5); 135.75 (C-*i*-Ph); 136.16 (C-*i*-Bn); 144.70 (C-2-furyl); 144.93 (CH-5-furyl); 145.47 (C-8);

152.27 (CH-2); 153.64 (C-6); 154.18 (C-4). IR(KBr): 3068, 1605, 1603, 1562, 1497, 1454, 1334, 1321, 1016. HRMS (ESI) calculated for $C_{22}H_{17}ON_4$: 353.1397; found: 353.1397

**9-Benzyl-6,8-diphenyl-*9H*-purine (52b)**

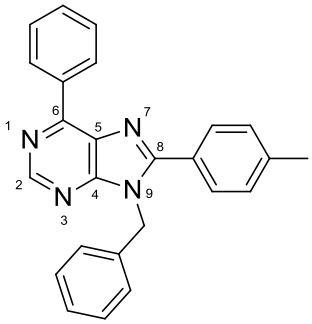


Tributylphenylstannane (39 μL, 0.12 mmol, 1.2 equiv.) was used as starting compound to give product **52b** (30 mg, 83%) as white crystals after chromatography eluting with hexane/EtOAc 5:1 to 2:1. $^1$H NMR was checked by published data.[99]

**b) Reaction with boronic acid**

9-Benzyl-6-phenyl-8-(phenylsulfanyl)-*9H*-purine **43a** (39 mg, 0.1 mmol), Cu (I) thiophene-2-carboxylate (23 mg, 0.12 mmol), *p*-tolylboronic acid (21 mg, 0.15 mmol), $Pd_2dba_3$ (4 mg, 0.004 mmol) and tris-2-furylphosphine (4 mg, 0.016 mmol) were placed in reaction vessel that was flushed with argon. THF (1 mL) was added and the mixture was stirred for 18 h at 50 °C. EtOAc (5 mL) was added and the suspension was washed with 10% aq. $NH_4OH$ (10 mL). The aqueous layer was extracted with ethyl acetate (3 × 15 mL). The combined organic phase was dried over anhydrous $Na_2SO_4$ and filtered, and all of the volatiles were removed under reduced pressure. The crude product was purified by column chromatography on silica gel to give product **52c** (20 mg, 54%) as white crystals after chromatography eluting with hexane/EtOAc 5:1 to 2:1.

**9-Benzyl-6-phenyl-8-(p-tolyl)-*9H*-purine (52c)**

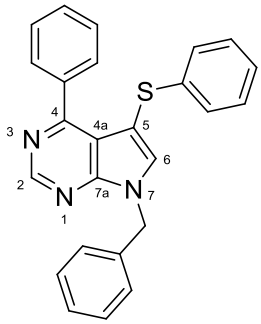


$^1$H NMR was checked by published data.[99]

**General procedure for benzylation:**

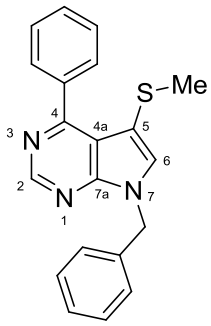
Dry DMF was added to a stirred solution of deazapurine **36a-36d, 44a** (1 equiv.) and potassium carbonate (1.1 equiv.). After 20 min, benzyl chloride (1.05 equiv.) was added and the resulting mixture was stirred overnight at rt until complete consumption of staring material as monitored by TLC. The solution was then diluted with EtOAc and washed with water. Aqueous solution was then extracted two times with EtOAc and combined organic layers were dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by HPFC (hexane/EtOAc, 0–20% EtOAc).

**7-Benzyl-4-phenyl-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-6-phenyl-7-(phenylsulfanyl)-7-deazapurine) (53a)**



Benzylation of 6-phenyl-7-(phenylsulfanyl)-7-deazapurine **36a** (606 mg, 2 mmol) according to the general procedure afforded compound **53a** (708 mg, 90 %) as yellow solid. $^1$H NMR was compared with published data.[119]

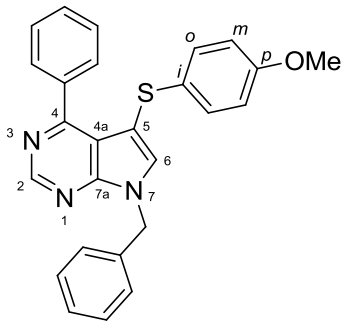
**7-Benzyl-5-(methylsulfanyl)-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-7-(methylsulfanyl)-6-phenyl-7-deazapurine) (53b)**



Benzylation of 7-(methylsulfanyl)-6-phenyl-7-deazapurine **36b** (483 mg, 2 mmol) according to the general procedure afforded compound **53b** (563 mg, 85 %) as yellow solid. M.p. 63-66 °C. $^1$H NMR (600.0 MHz, $CDCl_3$): 1.85 (s, 3H, $CH_3S$); 5.47 (s, 2H, $CH_2Ph$); 7.16 (s, 1H, H-6); 7.28 (m, 2H, H-*o*-Bn); 7.30 (m, 1H, H-*p*-Bn); 7.34 (m, 2H, H-*m*-Bn); 7.51 (m, 3H, H-*m*,*p*-Ph); 7.89 (m, 2H, H-*o*-Ph); 8.99 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 18.90 ($CH_3S$); 47.90 ($CH_2Ph$); 108.22 (C-5); 115.72 (C-4a); 127.72 (CH-*o*-Bn, CH-*m*-Ph); 128.05 (CH-*p*-Bn); 128.85 (CH-*m*-Bn); 129.33 (CH-6); 129.52 (CH-*p*-Ph); 129.85 (CH-*o*-Ph); 136.32 (C-*i*-Bn); 137.35 (C-*i*-Ph); 151.63 (CH-2); 152.17 (C-7a); 160.08 (C-4). IR(KBr): 2915, 1554, 1509, 1496, 1463, 1456, 1435, 1332, 1180, 1141, 976, 765. HRMS (ESI)

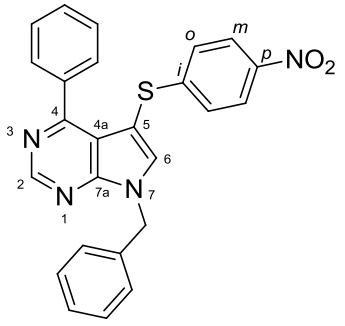
calculated for $C_{20}H_{18}N_3S$: 332.1216; found: 332.1215. Anal. calculated for $C_{20}H_{17}N_3S$ (331.11): 72.48; H, 5.17; N, 12.68; S, 9.67; found: C, 72.24; H, 5.07; N, 12.47; S, 9.35.

**7-Benzyl-5-((4-methoxyphenyl)sulfanyl)-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-7-((4-methoxyphenyl)sulfanyl)-6-phenyl-7-deazapurine) (53c)**




Benzylation of 7-((4-methoxyphenyl)sulfanyl)-6-phenyl-7-deazapurine **36c** (667 mg, 2 mmol) according to the general procedure afforded compound **53c** (763 mg, 90 %) as yellowish solid. M.p. 113-116°C. $^1$H NMR (499.8 MHz, $CDCl_3$): 3.70 (s, 3H, $CH_3O$); 5.51 (s, 2H, $CH_2Ph$); 6.56 (m, 2H, H-*m*-$SC_6H_4OMe$); 6.67 (m, 2H, H-*o*-$SC_6H_4OMe$); 7.29 (m, 2H, H-*o*-Bn); 7.34 (m, 1H, H-*p*-Bn); 7.37 (m, 2H, H-*m*-Bn); 7.38 (s, 1H, H-6); 7.39 (m, 2H, H-*m*-Ph); 7.44 (m, 1H, H-*p*-Ph); 7.65 (m, 2H, H-*o*-Ph); 8.98 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 48.16 ($CH_2Ph$); 55.27 ($CH_3O$); 105.56 (C-5); 114.25 (CH-*m*-$SC_6H_4OMe$); 115.57 (C-4a); 127.46 (C-*i*-$SC_6H_4OMe$); 127.54 (CH-*m*-Ph); 127.78 (CH-*o*-Bn); 128.23 (CH-*p*-Bn); 128.99 (CH-*m*-Bn); 129.40 (CH-*p*-Ph); 130.08 (CH-*o*-Ph); 130.35 (CH-*o*-$SC_6H_4OMe$); 133.95 (CH-6); 136.17 (C-*i*-Bn); 136.76 (C-*i*-Ph); 151.60 (CH-2); 152.50 (C-7a); 158.27 (C-*p*-$SC_6H_4OMe$); 160.48 (C-4). IR(KBr): 1595, 1580, 1556, 1493, 1454, 1327, 1290, 1246, 1185, 1176,1033. 825, 762, 695.HRMS (ESI) calculated for $C_{26}H_{22}ON_3S$: 424.1478; found: 424.1477. Anal. calculated for $C_{26}H_{21}ON_3S$ (423.14): C, 73.73; H, 5.00; N, 9.92; S, 7.57; found: C, 73.56; H, 4.96; N, 9.66; S, 7.61.

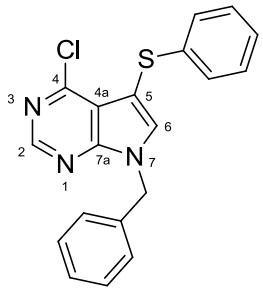
**7-Benzyl-5-((4-nitrophenyl)sulfanyl)-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-7-((4-nitrophenyl)sulfanyl)-6-phenyl-7-deazapurine) (53d)**




Benzylation of 7-((4-nitrophenyl)sulfanyl)-6-phenyl-7-deazapurine **36d** (348 mg, 1 mmol) according to the general procedure afforded compound **53d** (350 mg, 80 %) as yellowish solid. M.p. 169-171°C. $^1$H NMR (499.8 MHz, $CDCl_3$): 5.58 (s, 2H, $CH_2Ph$); 6.71 (m, 2H, H-*o*-$SC_6H_4NO_2$); 7.22 (m, 2H, H-*m*-Ph); 7.30 (m, 1H, H-*p*-Ph); 7.34-7.42 (m, 5H, H-*o*,*m*,*p*-Bn); 7.50 (m, 2H, H-*o*-Ph); 7.55 (s, 1H, H-6); 7.79 (m, 2H, H-*m*-$SC_6H_4NO_2$); 9.06 (s, 1H, H-2). $^{13}$C

NMR (125.7 MHz, $CDCl_3$): 48.44 ($CH_2Ph$); 99.68 (C-5); 115.45 (C-4a); 123.43 (CH-*m*-$SC_6H_4NO_2$); 125.50 (CH-*o*-$SC_6H_4NO_2$); 127.40 (CH-*m*-Ph); 128.00 (CH-*o*-Bn); 128.52 (CH-*p*-Bn); 129.14 (CH-*m*-Bn); 129.42 (CH-*p*-Ph); 129.59 (CH-*o*-Ph); 135.77 (C-*i*-Bn); 135.80 (CH-6); 136.19 (C-*i*-Ph); 144.93 (C-*p*-$SC_6H_4NO_2$); 148.07 (C-*i*-$SC_6H_4NO_2$); 152.35 (CH-2); 152.79 (C-7a); 160.94 (C-4). IR(KBr): 3441, 2926, 1575, 1509, 1456, 1413, 1336, 1188, 1109, 1086, 985, 853, 839, 747, 669. HRMS (ESI) calculated for $C_{25}H_{19}O_2N_4S$: 439.1223; found: 439.1223. Anal. calculated for $C_{25}H_{18}O_2N_4S$ (438.12): C, 68.48; H, 4.14; N, 12.78; S, 7.31; found: C, 68.36; H, 4.08; N, 12.49; S, 7.23.

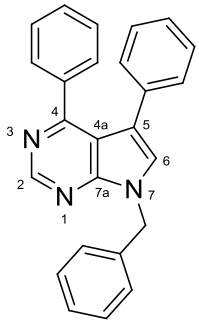
**7-Benzyl-4-chloro-5-(phenylsulfanyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-6-chloro-7-(phenylsulfanyl)-7-deazapurine) (54a)**




Benzylation of 6-chloro-7-(phenylsulfanyl)-7-deazapurine **44a** (534 mg, 2 mmol) according to the general procedure afforded compound **54a** (633 mg, 90 %) as white solid. M.p. 122-123 °C. $^1$H NMR (500.0 MHz, $CDCl_3$): 5.48 (s, 2H, $CH_2Ph$); 7.11 (m, 2H, H-*o*-SPh); 7.12 (m, 1H, H-*p*-SPh); 7.21 (m, 2H, H-*m*-SPh); 7.26 (m, 2H, H-*o*-Bn); 7.34 (m, 1H, H-*p*-Bn); 7.35 (m, 2H, H-*m*-Bn); 7.45 (s, 1H, H-6); 8.70 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 48.64 ($CH_2Ph$); 102.94 (C-5); 117.04 (C-4a); 125.65 (CH-*p*-SPh); 126.73 (CH-*o*-SPh); 127.81 (CH-*o*-Bn); 128.46 (CH-*p*-Bn); 128.91 (CH-*m*-SPh); 129.08 (CH-*m*-Bn); 135.45 (CH-6); 135.51 (C-*i*-Bn); 138.34 (C-*i*-Ph); 151.59 (CH-2); 152.30 (C-7a); 152.84 (C-4). IR(KBr): 1580, 1541, 1510, 1495, 1478, 1446, 1413, 1336, 1207, 990, 773. HRMS (ESI) calculated for $C_{19}H_{15}N_3ClS$: 352.0669; found: 352.0669. Anal. calculated for $C_{19}H_{14}ClN_3S$ (351.06): C, 64.86; H, 4.01; Cl, 10.08; N, 11.94; S, 9.11; found: C, 64.98; H, 4.09; Cl, 9.72; N, 11.64; S, 9.12.

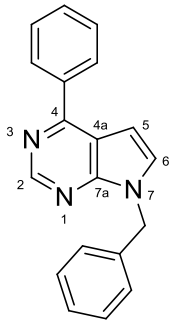
**Kumada coupling:**

**7-Benzyl-4,5-diphenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-6,7-diphenyl-7-deazapurine) (55)**



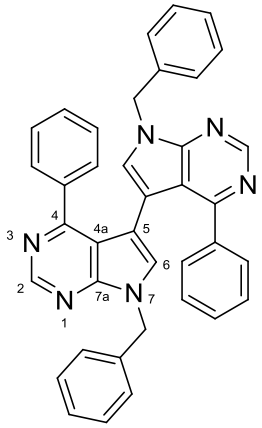
2M solution PhMgCl in THF (1.25 mL, 2.5 mmol, 2.5 equiv.) was added to solution of 9-benzyl-6-phenyl-7-(phenylsulfanyl)-7-deazapurine **53a** (393 mg, 1 mmol, 1 equiv.) with $NiCp_2$ (9.5 mg, 0.05 mmol, 5% mol) in THF (5 mL) under Ar and the solution was shaken gently at 70°C. After 15 min the mixture was quenched aqueous solution ammonium chloride and mixture were three times extracted with EtOAc and dried over $Na_2SO_4$. The crude product was purified by HPFC (hexane/EtOAc, 0–60% EtOAc) to give products **55** (181 mg, 50%) as white solid, the product of desulfenylation **2** (31 mg, 11%) as white solid and the product of dimerization **56** (71 mg, 13 %) as yellowish solid. M.p. 71-83°C. $^1$H NMR (500.0 MHz, $CDCl_3$): 5.57 (s, 2H, $CH_2Ph$); 6.94 (m, 2H, H-*o*-Ph-5); 7.05 (m, 2H, H-*m*-Ph-5); 7.10-7.15 (m, 3H, H-*p*-Ph-5, H-*m*-Ph-4); 7.26 (s, 1H, H-6); 7.27 (m, 1H, H-*p*-Ph-4); 7.29-7.38 (m, 5H, H-*o*,*m*,*p*-Bn); 7.41 (m, 2H, H-*o*-Ph-4); 9.05 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 48.03 ($CH_2Ph$); 113.65 (C-4a); 117.63 (C-5); 126.30 (CH-*p*-Ph-5); 126.97 (CH-6); 127.54 (CH-*m*-Ph-4); 127.62 (CH-*m*-Ph-5); 127.88 (CH-*o*-Bn); 128.08 (CH-*p*-Bn); 128.91 (CH-*m*-Bn); 128.98 (CH-*p*-Ph-4); 129.16 (CH-*o*-Ph-5); 129.74 (CH-*o*-Ph-4); 133.92 (C-*i*-Ph-5); 136.61 (C-*i*-Bn); 137.58 (C-*i*-Ph-4); 151.43 (CH-2); 152.03 (C-7a); 159.73 (C-4). IR(KBr): 3053, 3032, 2926, 2852, 1583, 1552, 1530, 1496, 1464, 1455, 1444, 1431, 1347, 1179, 759, 704. HRMS (ESI) calculated for $C_{25}H_{20}N_3$: 362.1652; found: 362.1651.

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



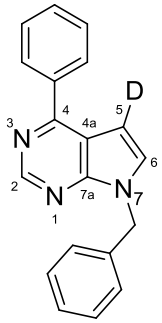
$^1$H NMR was compared with published data.[124]

**7,7'-Dibenzyl-4,4'-diphenyl-*7H*,*7'H*-5,5'-bipyrrolo[2,3-*d*]pyrimidine**
**(9,9'-Dibenzyl-6,6'-diphenyl-7,7'-bisdeazapurine) (56)**



M.p.183°C. $^{1}$H NMR (600.1 MHz, $CDCl_3$): 5.42 (s, 2H, $CH_2Ph$); 6.85 (m, 2H, H-*m*-Ph); 6.93 (s, 1H, H-6); 7.03 (m, 1H, H-*p*-Ph); 7.14 (m, 2H, H-*o*-Ph); 7.32 (m, 2H, H-*o*-Bn); 7.33 (m, 1H, H-*p*-Bn); 7.37 (m, 2H, H-*m*-Bn); 8.82 (s, 1H, H-2). $^{13}$C NMR (150.9 MHz, $CDCl_3$): 47.90 ($CH_2Ph$); 108.97 (C-5); 115.62 (C-4a); 126.76 (CH-*m*-Ph); 127.61 (CH-6); 128.01 (CH-*o*-Bn); 128.20 (CH-*p*-Bn); 128.91 (CH-*m*-Bn); 129.04 (CH-*p*-Ph); 129.78 (CH-*o*-Ph); 136.38 (C-*i*-Ph); 136.62 (C-*i*-Bn); 151.07 (CH-2); 151.34 (C-7a); 159.31 (C-4). IR(KBr): 3060,3031, 2974, 2926, 1589, 1553, 1532, 1518, 1506, 1494, 1458, 1443, 1356, 1317, 1177, 1159, 1021, 764, 722, 701. HRMS (ESI) calculated for $C_{38}H_{29}N_6$: 569.2448; found: 569.2446.

**7-Benzyl-5-deuterium-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(9-Benzyl-7-deuterium-6-phenyl-7-deazapurine) (57)**

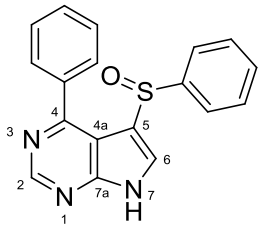


2M solution PhMgCl in THF (0.25 mL, 0.5 mmol, 2.5 equiv.) was added to solution of 9-benzyl-6-phenyl-7-(phenylsulfanyl)-7-deazapurine (79 mg, 0.2 mmol, 1 equiv.) with $NiCl_2$(dppp) (5.5 mg, 0.01 mmol, 5% mol) in THF (1 mL) under Ar and the solution was shaken gently at 70°C. After 15 min the mixture was quenched with $D_2O$ and mixture were three times extracted with EtOAc and dried over $Na_2SO_4$. The crude product was purified by HPFC (hexane/EtOAc, 0–60% EtOAc) to give products **55** (30 mg, 41%) as white solid, **57** (20 mg, 35%) as white solid and **56** (11 mg, 5 %) as yellowish solid. $^{1}$H NMR (500.0 MHz, $CDCl_3$): 5.52 (s, 2H, $CH_2$); 7.26 (m, 2H, H-*o*-Bn); 7.28 (s, 1H, H-6); 7.32 (m, 1H, H-*p*-Bn); 7.35 (m, 2H, H-*m*-Bn); 7.55 (m, 1H, H-*p*-Ph); 7.57 (m, 2H, H-*m*-Ph); 8.15 (m, 2H, H-*o*-Ph); 9.04 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 48.15 ($CH_2Ph$); 101.07 (t, $J_{C,D}$ = 27.4, C-5); 115.43 (C-4a); 127.66 (CH-*o*-Bn); 128.10 (CH-*p*-Bn); 128.92 (CH-*m*-Ph, CH-*m*-Bn); 129.00 (CH-*o*-Ph); 129.32 (CH-6); 130.46 (CH-*p*-Ph); 136.50 (C-*i*-Bn); 136.99 (C-*i*-Ph); 150.86 (CH-2); 151.72 (C-7a); 156.80 (C-4). $^{2}$H NMR (76.7 MHz, $CDCl_3$): 6.97. IR(KBr): 3114, 3084, 3063, 3049, 3043, 3028, 2926, 1559, 1550, 1506, 1461, 1437, 1413, 1335, 1207, 1192, 919, 767, 719, 695. HRMS (ESI) calculated for $C_{19}H_{15}{}^{2}HN_3$: 287.1402; found: 287.1403.

**Oxidation of sulfanyldeazapurines. General procedure:**

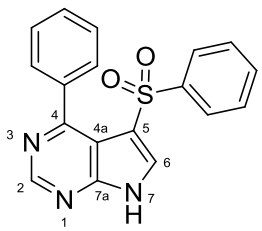
To a solution of *m*-CPBA (75%, 10 equiv.) in 1,4-dioxane cooled to 0 °C was added an NaOH (1M, 10 equiv.) aqueous solution, followed by addition of sulfanyldeazapurine **36a**, **53a**, **53d** (1 equiv.). The ratio of 1,4-dioxane/$H_2O$ was 9:1. The suspension was shaken gently at room temperature. After 16 h the mixture was quenched brine and mixture were extracted with EtOAc and dried over $Na_2SO_4$. The crude product was purified by HPFC (hexane/EtOAc, 0–20% EtOAc).

**4-Phenyl-5-(phenylsulfinyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Phenyl-7-(phenylsulfinyl)-7-deazapurine) (36aa)**



Oxidation of **36a** (304 mg, 1 mmol) according to the general procedure gave products **36aa** (239 mg, 75%) as white solid and **36ab** (50 mg, 15%) as white solid. M.p. 213-215°C. $^1$H NMR (499.8 MHz, $CDCl_3$): 6.97 (m, 2H, H-*o*-$SO_2$Ph); 7.17 (m, 2H, H-*m*-$SO_2$Ph); 7.27 (m, 1H, H-*p*-$SO_2$Ph); 7.53 (m, 2H, H-*m*-Ph); 7.56 (m, 1H, H-*p*-Ph); 7.68 (m, 2H, H-*o*-Ph); 7.99 (s, 1H, H-6); 9.03 (s, 1H, H-2); 12.20 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 112.95 (C-4a); 119.20 (C-5); 125.43 (CH-*o*-$SO_2$Ph); 128.39 (CH-6); 128.76 (CH-*m*-Ph); 128.99 (CH-*m*-$SO_2$Ph); 129.41 (CH-*o*-Ph); 130.36 (CH-*p*-Ph); 131.14 (CH-*p*-$SO_2$Ph); 138.23 (C-*i*-Ph); 144.06 (C-*i*-SPh); 151.95 (CH-2); 153.71 (C-7a); 159.78 (C-4). IR(KBr): 3191, 3101, 3051, 2837, 1589, 1580, 1557, 1455, 1442, 1429, 1401, 1335, 1246, 1231, 1082, 1028, 989, 753, 747, 688. HRMS (ESI) calculated for $C_{18}H_{14}ON_3S$: 320.0852; found: 320.0851.

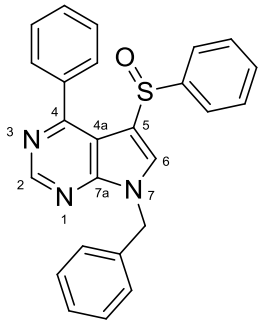
**4-Phenyl-5-(phenylsulfonyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine**
**(6-Phenyl-7-(phenylsulfonyl)-7-deazapurine) (36ab)**



$^1$H NMR (499.8 MHz, DMSO-$d_6$): 7.20 (m, 2H, H-*o*-$SO_2$Ph); 7.23 (m, 2H, H-*o*-Ph); 7.33 (m, 2H, H-*m*-Ph); 7.34 (m, 2H, H-*m*-$SO_2$Ph); 7.50 (m, 1H, H-*p*-Ph); 7.52 (m, 1H, H-*p*-$SO_2$Ph); 8.59 (s, 1H, H-6); 8.90 (s, 1H, H-2); 13.52 (bs, 1H, NH). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 111.44 (C-4a); 114.54 (C-5); 126.57 (CH-*o*-$SO_2$Ph); 127.68 (CH-*m*-Ph); 129.07 (CH-*m*-$SO_2$Ph); 129.27 (CH-*p*-Ph); 129.39 (CH-*o*-Ph); 132.85 (CH-*p*-$SO_2$Ph); 136.87

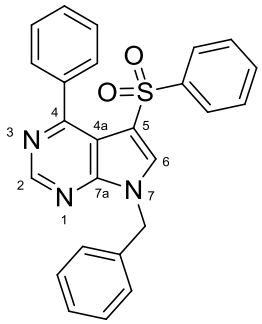
(CH-6); 138.41 (C-*i*-Ph); 141.72 (C-*i*-SPh); 152.20 (CH-2); 153.74 (C-7a); 160.01 (C-4). IR(KBr): 3106, 3065, 1598, 1567, 1513, 1458, 1324, 1140, 1026, 812, 769, 743, 704, 562. HRMS (ESI) calculated for $C_{18}H_{14}O_2N_3S$: 336.0801; found: 336.0800.

**7-Benzyl-4-phenyl-5-(phenylsulfinyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-6-phenyl-7-(phenylsulfinyl)-7-deazapurine) (53aa)**



Oxidation of **53a** (1.18 g, 3 mmol) according to the general procedure gave products **53aa** (169 mg, 13%) as white solid and **53ab** (932 mg, 73%) as white solid. M.p. 130-135°C. $^1$H NMR (500.0 MHz, $CDCl_3$): 5.47, 5.62 (2 × d, 2 × 2H, $J_{gem}$ = 14.9, $CH_2Ph$); 6.86 (m, 2H, H-*o*-SPh); 7.13 (m, 2H, H-*m*-SPh); 7.24 (m, 1H, H-*p*-SPh); 7.31 (m, 2H, H-*o*-Bn); 7.35 (m, 1H, H-*p*-Bn); 7.37 (m, 2H, H-*m*-Bn); 7.53 (m, 2H, H-*m*-Ph); 7.57 (m, 1H, H-*p*-Ph); 7.65 (m, 2H, H-*o*-Ph); 7.92 (s, 1H, H-6); 9.01 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 48.81 ($CH_2Ph$); 112.81 (C-4a); 119.12 (C-5); 125.37 (CH-*o*-SPh); 128.01 (CH-*o*-Bn); 128.51 (CH-*p*-Bn); 128.77 (CH-*m*-Ph); 128.95 (CH-*m*-SPh); 129.09 (CH-*m*-Bn); 129.47 (CH-*o*-Ph); 130.37 (CH-*p*-Ph); 130.51 (CH-6); 131.08 (CH-*p*-SPh); 135.52 (C-*i*-Bn); 138.01 (C-*i*-Ph); 144.40 (C-*i*-SPh); 152.03 (CH-2); 152.89 (C-7a); 159.23 (C-4). IR(KBr): 3104, 3081, 3033,3002, 2945, 1583, 1539, 1506, 1475, 1453, 1444, 1437, 1416, 1344, 1388, 1252, 1207, 1197, 1184, 1081, 1039, 979, 750, 703, 690, 625, 619, 509. HRMS (ESI) calculated for $C_{25}H_{20}ON_3S$: 410.1322; found: 410.1322.

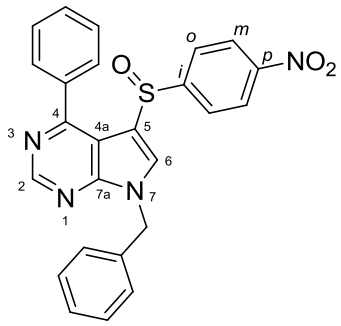
**7-Benzyl-4-phenyl-5-(phenylsulfonyl)-*7H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-6-phenyl-7-(phenylsulfonyl)-7-deazapurine) (53ab)**



M.p. 130-132°C. $^1$H NMR (499.8 MHz, $CDCl_3$): 5.57 (s, 2H, $CH_2Ph$); 7.09 (m, 2H, H-*o*-SPh); 7.17 (m, 2H, H-*m*-SPh); 7.35-7.44 (m, 10H, H-*o,m,p*-Bn, H-*o,m*-Bn, H-*p*-SPh); 7.51 (m, 1H, H-*p*-Ph); 8.23 (s, 1H, H-6); 9.01 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 48.97 ($CH_2Ph$); 112.23 (C-4a); 116.34 (C-5); 126.93 (CH-*o*-SPh); 127.91 (CH-*m*-Bn); 128.26 (CH-*o*-Bn); 128.60 (CH-*m*-SPh); 128.82 (CH-*p*-Bn); 129.27 (CH-*m*-Ph); 129.59 (CH-*o,p*-Ph); 132.41 (CH-*p*-SPh); 134.86 (C-*i*-Bn); 136.49 (CH-6); 137.53 (C-*i*-Ph); 141.03 (C-*i*-SPh); 152.23 (CH-2); 152.73 (C-7a); 161.15 (C-4). IR(KBr):

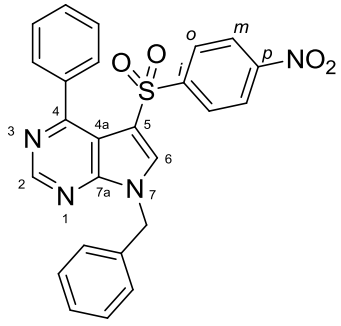
3437, 3063, 3032, 1557, 1514, 1445, 1393, 1335, 1304, 1165, 1152, 1138, 985, 750, 725, 695, 688, 593. HRMS (ESI) calculated for $C_{25}H_{20}O_2N_3S$: 426.1271; found: 426.1270. Anal. calculated for $C_{25}H_{19}O_2N_3S$ (425.12): C, 70.57; H, 4.50; N, 9.88; S, 7.54; found: C, 70.48; H, 4.53; N, 9.63; S, 7.56.

**7-Benzyl-5-((4-nitrophenyl)sulfinyl)-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-6-phenyl-7-((4-nitrophenyl)sulfinyl)-7-deazapurine) (53da)**



Oxidation of **53d** (219 mg, 0.5 mmol) according to the general procedure gave products **53da** (46 mg, 20%) as white solid and **53db** (159 mg, 68%) as white solid. M.p. 188-189°C. $^1$H NMR (499.8 MHz, $CDCl_3$): 5.50, 5.62 (2 × d, 2 × 1H, $J_{gem}$ = 14.8, $CH_2Ph$); 6.97 (m, 2H, H-*o*-$SOC_6H_4NO_2$); 7.33 (m, 2H, H-*o*-Bn); 7.37 (m, 3H, H-*m*,*p*-Bn); 7.59 (m, 2H, H-*m*-Ph); 7.62 (m, 1H, H-*p*-Ph); 7.71 (m, 2H, H-*o*-Ph); 7.95 (s, 1H, H-6); 7.96 (m, 2H, H-*m*-$SOC_6H_4NO_2$); 9.05 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 49.32 ($CH_2Ph$); 112.19 (C-4a); 119.01 (C-5); 124.12 (CH-*m*-$SOC_6H_4NO_2$); 125.96 (CH-*o*-$SOC_6H_4NO_2$); 128.09 (CH-*o*-Bn); 128.92 (CH-*p*-Bn); 129.28, 129.29 (CH-*m*-Ph, CH-*m*-Bn); 129.94 (CH-*o*-Ph); 131.59 (CH-*p*-Ph); 132.41 (CH-6); 134.73 (C-*i*-Bn); 135.61 (C-*i*-Ph); 148.99 (C-*p*-$SOC_6H_4NO_2$); 150.87 (CH-2); 151.27 (C-*i*-$SOC_6H_4NO_2$); 152.95 (C-7a); 157.74 (C-4). IR(KBr): 3106, 3062, 1603, 1557, 1523, 1441, 1344, 1076, 1047, 852, 769, 743, 704. HRMS (ESI) calculated for $C_{25}H_{18}O_3N_4NaS$: 477.0991; found: 477.0992.

**7-Benzyl-5-((4-nitrophenyl)sulfonyl)-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine (9-Benzyl-6-phenyl-7-((4-nitrophenyl)sulfonyl)-7-deazapurine) (53db)**

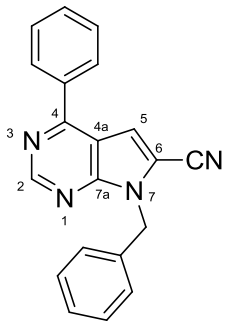


M.p. 194-195°C. $^1$H NMR (499.8 MHz, $CDCl_3$): 5.58 (s, 2H, $CH_2Ph$); 7.22 (m, 2H, H-*o*-$SO_2C_6H_4NO_2$); 7.37-7.45 (m, 9H, H-*o*,*m*-Ph, H-*o*,*m*,*p*-Bn); 7.55 (m, 1H, H-*p*-Ph); 7.97 (m, 2H, H-*m*-$SC_6H_4NO_2$); 8.27 (s, 1H, H-6); 9.03 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, $CDCl_3$): 48.90 ($CH_2Ph$); 111.91 (C-4a); 114.46 (C-5); 123.46 (CH-*m*-$SO_2C_6H_4NO_2$); 127.76 (CH-*m*-Ph); 128.10, 128.13 (CH-*o*-$SO_2C_6H_4NO_2$, CH-*o*-Bn); 128.74 (CH-*p*-Bn); 129.11 (CH-*m*-Bn); 129.44 (CH-

*o*-Ph); 129.60 (CH-*p*-Ph); 134.39 (C-*i*-Bn); 136.74 (CH-6); 137.43 (C-*i*-Ph); 146.36 (C-*i*-$SO_2C_6H_4NO_2$); 149.32 (C-*p*-$SO_2C_6H_4NO_2$); 152.54 (CH-2); 152.59 (C-7a); 160.89 (C-4). IR(KBr): 3127, 3102, 3062, 3033, 1565, 1523, 1390, 1350, 1321, 1164, 1140, 992, 851, 753, 748, 597. HRMS (ESI) calculated for $C_{25}H_{18}O_4N_4NaS$: 493.0941; found: 493.0942.

**C-nucleophiles**

**7-Benzyl-4-phenyl-*7H*-pyrrolo[2,3-*d*]pyrimidine-6-carbonitrile (9-Benzyl-8-carbonitrile-6-phenyl-7-deazapurine) (32m)**




Solution of 9-benzyl-6-phenyl-7-(phenylsulfonyl)-7-deazapurine **53ab** (425 mg, 1 mmol) and NaCN (147 mg, 3 mmol) in DMF (10 mL) was stirred overnight at 110 °C until complete consumption of staring material as monitored by TLC. The crude product was purified by HPFC (hexane/EtOAc, 0–20% EtOAc) to give **32m** (280 mg, 90%) as a white solid. $^1$H NMR was compared with published data.[125]

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