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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

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Keywords: Synthetic methods / Cross-coupling / C–H activation / Nitrogen heterocycles / Nucleobases / Deazapurines

A general access to 4-substituted 6-arylpyrrolo[2,3-*d*]-pyrimidine (6-substituted 8-aryl-7-deazapurine derivatives) was developed based on iridium-catalyzed C–H borylations of pyrrolo[2,3-*d*]pyrimidines at the 6-position followed by the Suzuki cross-coupling reactions or other functional group transformations of the boronates. Biologically relevant 6-aryl-pyrrolo[2,3-*d*]pyrimidin-4-amines (8-aryl-7-deazaadenines) and pyrrolo[2,3-*d*]pyrimidin-4-ones (–7-deazahypoxanthines) were synthesized starting from SEM-protected 4-methylsulfanyl- or 4-methoxypyrrolo[2,3-*d*]pyrimidine. The one-pot borylation/Suzuki coupling reactions were followed either by demethylation and deprotection to yield deaza-hypoxanthine bases, or by oxidation of sulfide to sulfone, amination and deprotection to give deazaadenines. In addition, the boronate intermediates were converted into 6-halo- or 6-(trifluoromethyl)pyrrolo[2,3-*d*]pyrimidine (8-halo- or 8-trifluoromethyl-7-deazapurine) derivatives.

Introduction

Pyrrolo[2,3-*d*]pyrimidines (7-deazapurines)[1] are important carba-analogues of biogenic purine bases (to refer to parent natural purines, we will also use the "purine" nomenclature and numbering for comparison). Derivatives bearing multiple substituents at the 2-, 4-, 5-, 6-, and/or 7-positions of pyrrolo[2,3-*d*]pyrimidine (2-, 6-, 7-, 8-, and/or 9-positions of 7-deazapurine) have recently attracted significant attention as synthetic targets, and many of them display promising biological effects. 6,7-Disubstituted 7-deazapurine ribonucleosides are potent cytostatics,[2] whereas 7,8-diaryl-7-deazaadenine derivatives are potent inhibitors of ACK1 kinase[3] and 7-alkyl-8-arylsulfanyl-7-deazapurines are inhibitors of dihydrofolate reductase.[4] 6-Substituted 8-aryl-7-deazapurine bases (Figure 1) also showed important biological activities: TWS119 was identified as directing the differentiation of neuronal cells in mice by GSK-3b inhibition,[5] whereas PKI166 and related compounds display antitumor activity through inhibition of EGFR-tyrosine kinase[6] or Bruton's tyrosine kinase.[7] Known methods for the synthesis of substituted pyrrolo[2,3-*d*]pyrimidines mostly involve cross-coupling reactions and/or heterocyclizations. Regioselective cross-coupling reactions were used in the synthesis of 2,4-disubstituted pyrrolo[2,3-*d*]pyrimidines[8] and, in combination with C–H arylation, for the synthesis of 2,4,6-triarylpyrrolo[2,3-*d*]pyrimidines.[9] A combination of palladium- and copper-assisted heterocyclization, followed by halogenation at the 5-position and Suzuki coupling was used for 4,5,6-trisubstituted derivatives.[10] We have recently reported[11] a chemoselective synthesis of 4,5-diarylpyrrolo[2,3-*d*]pyrimidines by using a combination of the Liebeskind–Srogl and Suzuki coupling reactions. For the synthesis of 4-substituted 6-arylpyrrolo[2,3-*d*]pyrimidines (6-substituted 8-aryl-7-deazapurines), palladium-catalyzed heterocyclizations of 5-alkynyl-6-aminopyrimidines[12] or heterocyclizations of arylpyrroles[13] were mostly utilized. The heterocyclization approaches[12,13] are more laborious for the synthesis of larger series of derivatives because several steps are typically needed for the preparation of each compound. On the other hand, regio- or chemoselective cross-coupling reactions,[7–11] either alone or in combina-

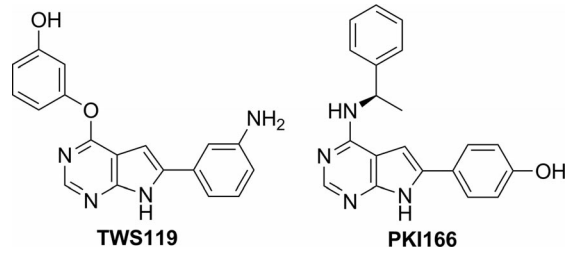

Figure 1. Examples of biologically active 4,6-disubstituted pyrrolo[2,3-*d*]pyrimidines.

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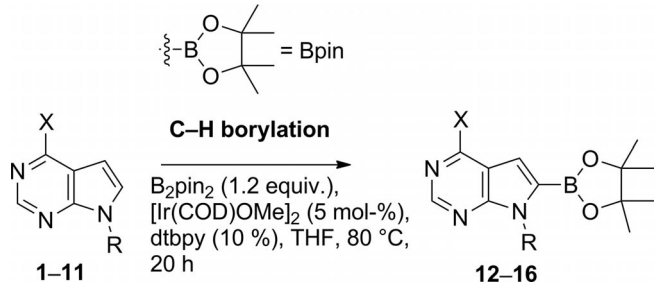
tion with C–H activations, enable late-stage diversification of the substituents in these important heterocycles and thus deserve further development.

C–H activation reactions are currently one of the hottest fields in organic synthesis and they are becoming an indispensable tool in the modification of heterocycles including nucleobases.[14] Recently, we combined C–H arylations with cross-couplings in the synthesis of substituted[15] or fused[16] purines and developed C–H borylation,[17] C–H sulfenylation,[18] and C–H amination[19] of 7-deazapurines. Iridium-catalyzed C–H borylation can be combined with the Suzuki reaction for the synthesis of 4,6-disubstituted pyrrolo[2,3-*d*]-pyrimidines (6,8-disubstituted 7-deazapurines) as demonstrated by several proof-of-principle examples in our previous preliminary communication.[17] However, the application of the borylation–coupling approach for the synthesis of biologically relevant deazapurine derivatives, i.e., 7-deazaadenine or 7-deazahypoxanthine bases, and the possibility of applying other transformations of boronates to other functional groups (aryl, CF_3, halogen) remained to be addressed. Herein, we report on these issues in this full-paper.

Results and Discussion

Iridium-catalyzed C–H borylation of arenes is an efficient single-step method to generate aryl boronates.[20] In our previous work,[17] we reported that the C–H borylation of purines did not proceed, presumably because of the strong coordination of iridium-catalysts to N7 nitrogen of purine, which prevented the catalytic activity. On the other hand, the reaction was successful[17] in some pyrrolo[2,3-*d*]-pyrimidines (7-deazapurines, lacking this chelating nitrogen). Previously reported[17] and new results of a systematic study of borylation of a series of model pyrrolo[2,3-*d*]pyrimidines **1**–**11** are summarized in Scheme 1 and Table 1. Previously, we found[17] that 4-phenyl-7-benzylpyrrolo[2,3-*d*]pyrimidine **1** undergoes the iridium-catalyzed borylation to give 6-borylated product **12** in good yield. However, now we found that neither 7-unsubstituted 4-phenylpyrrolo[2,3-*d*]pyrimidine **2** nor nucleoside **3**[21] formed the desired boronates. 7-Benzylpyrrolo[2,3-*d*]pyrimidin-4-amine (7-deazaadenine) **4** as well as its *N*-(dimethylamino)methylidene-protected derivative **5** also did not give any C–H borylation products. 7-Benzyl-4-chloropyrrolo[2,3-*d*]pyrimidine **6** gave the desired 6-borylated product **13** in moderate yield (53%), whereas the 7-unprotected 4-chloropyrrolo[2,3-*d*]pyrimidine **7** did not undergo the borylation. Apparently, the iridium-catalyzed C–H borylation only works on 7-substituted pyrrolo[2,3-*d*]pyrimidines bearing functional groups lacking any acidic protons and/or coordinating nitrogen atoms. On the other hand, we have no plausible explanation for the lack of reactivity of nucleoside **3**.



Scheme 1. Borylation of a series of model pyrrolo[2,3-*d*]pyrimidines **1**–**11**.

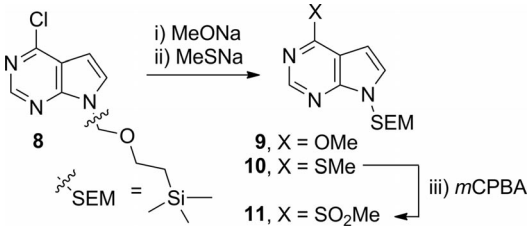
To access the biologically relevant substituted 7-deazaadenine or 7-deazahypoxanthine bases, a protecting group must be introduced at the 7-position of the pyrrolo[2,3-*d*]-pyrimidine moiety and a suitable functional group must be placed at the 4-position. The protecting group must not interfere with the borylation but must be sufficiently stable and easily removable at the end. Based on our previous experience with the difficult removal of the *N*-benzyl group from pyrrolo[2,3-*d*]pyrimidines, we choose to use the (trimethylsilyl)ethoxymethyl (SEM) group, which is easily removed by treatment with trifluoroacetic acid (TFA) followed by ammonia. As possible transformable or leaving groups at the 4-position, we considered Cl, OCH_3, SCH_3, and SO_2CH_3, which should be prone to either nucleophilic substitutions or demethylations. The SEM-protected 4-chloropyrrolo[2,3-*d*]pyrimidine **8** was prepared according to a reported procedure[22] and was converted into 4-methoxy- and 4-methylsulfanyl derivatives **9** and **10** by nucleophilic substitution with MeONa or MeSNa, respectively (Scheme 2). The sulfide **10** was oxidized to sulfone **11** by *m*CPBA. The corresponding 7-SEM-4-substituted pyrrolo-[2,3-*d*]pyrimidine derivatives **8**–**11** were then tested in the

Table 1. Direct C–H borylations of pyrrolo[2,3-*d*]pyrimidines **1**–**11**.

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

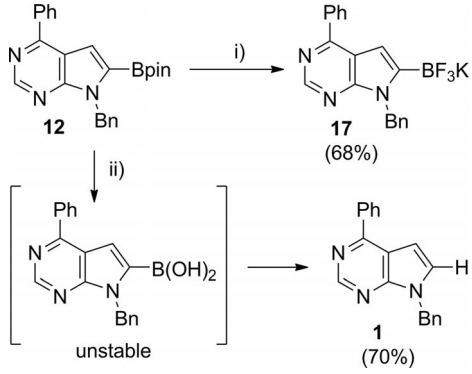
[a] Results previously reported in ref.[17]

iridium-catalyzed C–H borylation under the conditions described above (Table 1, entries 8–11). The 4-chloro-, 4-methoxy-, and 4-methylsulfanyl-pyrrolo[2,3-*d*]pyrimidines reacted well to give the corresponding boronates **14**–**16** in good yields (78–83%), whereas sulfone **11** did not give any reaction under these conditions.



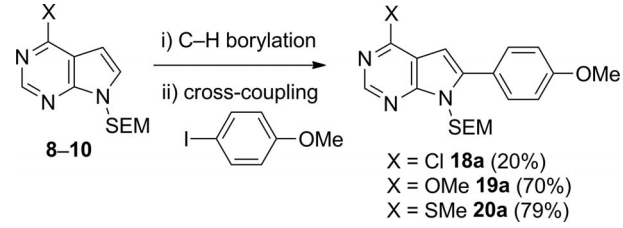
Scheme 2. Reagents and conditions: (i) 1 M MeONa in MeOH (2 equiv.), acetone, room temp., 18 h; (ii) MeSNa (1.5 equiv.), MeOH, room temp., 1 h; (iii) *m*CPBA (2 equiv.), CH_2Cl_2, room temp., 18 h.

We also explored the possible conversion of boronate **12** into either free boronic acids or trifluoroborates[23] (Scheme 3). The reaction of **12** with KHF_2 under standard conditions[24] gave the desired trifluoroborate **17** in acceptable yield (68%). However, the oxidation followed by hydrolysis under reported conditions,[24] which was expected to give the boronic acid, gave only 6-unsubstituted pyrrolo[2,3-*d*]pyrimidine **1** as a product of protodeborylation. This indicates that the corresponding pyrrolo[2,3-*d*]pyrimidine-6-boronic acid deazapurine-8-boronic acid is too unstable to be isolated under these reaction conditions.



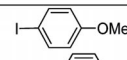
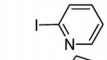
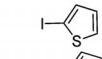
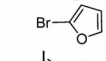
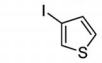
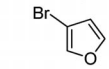
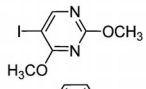
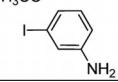
Scheme 3. Reagents and conditions: (i) KHF_2 (6 equiv.), THF/H_2O (5:3), room temp., 5 h; (ii) $NaIO_4$ (4 equiv.), THF/H_2O (4:1), 1 M HCl, room temp., 1 h.

Having confirmed the reactivity of the SEM-protected pyrrolo[2,3-*d*]pyrimidines **8**–**10** in C–H borylations (Table 1, entries 8–10), we tested a two-step, one-pot reaction sequence: C–H borylation/Suzuki cross-coupling with 4-iodoanisole. The borylation was performed as described above and was directly followed by the Suzuki coupling under the previously[17] optimized conditions [Pd(dppf)Cl_2 and K_2CO_3 in *N*,*N*-dimethylformamide (DMF); Scheme 4]. Unfortunately, the borylation/Suzuki reaction of 4-chloropyrrolo[2,3-*d*]pyrimidine **8** gave only low yield (20%) of the desired 6-aryl derivative **18a** because the Suzuki cross-coupling step was accompanied by competitive deborylation back to starting compound **8** (25%) and some other side-reactions. Therefore, we focused on the one-pot borylation/arylation of 4-methoxy and 4-methylsulfanyl derivatives **9** and **10**. These reactions proceeded smoothly and efficiently to give the desired SEM-protected 6-arylated pyrrolo[2,3-*d*]-pyrimidines **19a** (70%) and **20a** (79%).

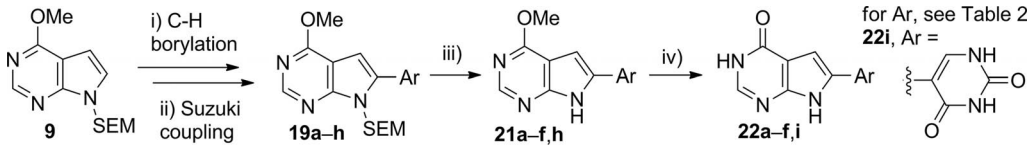


Scheme 4. Reagents and conditions: (i) B_2pin_2 (1.2 equiv.), $[Ir(COD)OMe]_2$ (5 mol-%), dtbpy (10 mol-%), THF, 80 °C, 20 h; (ii) Ar-I (1.1 equiv.), Pd(dppf)Cl_2 (5 mol-%; 10 mol-% in case of **20a**), K_2CO_3 (4 equiv.), DMF, 90 °C, 1 h.

Table 2. Synthesis of 6-arylpyrrolo[2,3-*d*]pyrimidin-4-ones (8-aryl-7-deazahypoxanthines).

Entry	Ar–X	Product **19** (yield)	Product **21** (yield)	Product **22** (yield)
1		**19a** (70%)	**21a** (90%)	**22a** (85%)
2		**19b** (50%)[b]	**21b** (85%)	**22b** (71%)
3		**19c** (65%)	**21c** (90%)	**22c** (90%)
4		**19d** (45%)[b]	**21d** (80%)	**22d** (92%)
5		**19e** (77%)	**21e** (90%)	**22e** (70%)
6		**19f** (58%)	**21f** (65%)	**22f** (80%)
7		**19g** (66%)[b]	–	**22i** (97%)[a]
8		**19h** (74%)	**21h** (22%)	**22h** (75%)

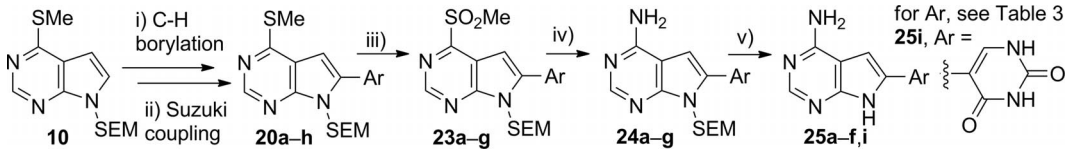
[a] Overall yield for two steps from **19g**. [b] Reaction time 18 h.



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

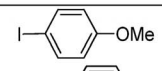
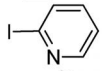
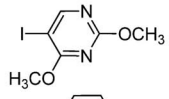
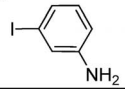
Encouraged by these successful reactions, we envisaged the use of the one-pot borylation/arylation of 6-methoxypyrrolo[2,3-*d*]pyrimidine **9** in combination with O-demethylation and SEM-deprotection for the synthesis of 6-aryl-pyrrolo[2,3-*d*]pyrimidin-4-ones (8-aryl-7-deazahypoxanthine bases). We performed a series of one-pot borylation/Suzuki coupling reactions of methoxypyrrolo[2,3-*d*]pyrimidine **9** with several aryl iodides (Scheme 5, Table 2). Generally, the reactions proceeded very well to give the desired SEM-protected 6-(het)aryl-4-methoxypyrrolo[2,3-*d*]-pyrimidines **19a**–**h** in high yields (Scheme 5, Table 2). In several cases, the reaction time for the Suzuki reaction was increased to 18 h to reach complete conversion. Deprotection[25] of the SEM group treatment with TFA followed by aqueous ammonia furnished free 6-(hetero)aryl-4-methoxypyrrolo[2,3-*d*]pyrimidines **21a**–**f** in good yields (65–90%) (Scheme 5, Table 2). In deprotection of aminophenyl-derivative **19h**, the isolated yield of pyrrolo[2,3-*d*]pyrimidine base **21h** was low (22%) due to difficult separation of the highly polar derivative by column chromatography. In the case of compound **19g**, deprotection of the SEM group was directly followed by acid hydrolysis[26] to the free 6-(uracil-5-yl)pyrrolo[2,3-*d*]pyrimidin-4-one **22i**. The final cleavage of methyl ethers **21a**–**h** was performed with iodotrimethylsilane[27] generated in situ in acetonitrile to give 6-(hetero)-arylpyrrolo[2,3-*d*]pyrimidin-4-ones [8-(hetero)aryl-7-deaza-hypoxanthines] **22a**–**h** in high yields.

To synthesize the corresponding 6-arylpyrrolo[2,3-*d*]pyrimidin-4-amines (8-aryl-7-deazaadenine bases), we started by an analogous one-pot, two-step borylation/arylation of SEM-protected 4-(methylsulfanyl)pyrrolo[2,3-*d*]pyrimidine **10**. The presence of sulfur meant that 10 mol-% 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, resulting in high yields of the desired 6-(hetero)aryl products **20a**–**h** (Scheme 6, Table 3). In several cases, the reaction time for the Suzuki reaction was again increased to 18 h to reach complete conversion. The second step was the oxidation[28] of methylsulfanyl derivatives **20a**–**h** to methylsulfones **23a**–**g** (which are more reactive electrophiles for nucleophilic substitution). The reactions proceeded well with the exception of derivative **20h** (entry 8), which gave an inseparable complex mixture. The original procedure (NH_3/MeOH) for amination of sulfones[28] was modified to NH_3/dioxane (to avoid formation of methyl ethers observed in methanol), which gave the desired SEM-protected 6-arylpyrrolo[2,3-*d*]pyrimidin-4-amines **24a**–**f** in good yields. Deprotection of the



Scheme 6. Reagents and conditions: (i) B_2pin_2 (1.2 equiv.), $[Ir(COD)OMe]_2$ (5 mol-%), dtbpy (10 mol-%), THF, 80 °C, 20 h; (ii) Ar-X (1.1 equiv.), $Pd(dppf)Cl_2$ (10 mol-%), K_2CO_3 (4 equiv.), DMF, 90 °C, 1 h (or 18 h); (iii) *m*CPBA (2 equiv.), CH_2Cl_2, room temp., 1 h; (iv) aq. ammonia (25% w/w), dioxane, 50 °C, 18 h; (v) TFA (2 mL), room temp., 1 h, followed by aq. ammonia (25% w/w), room temp., 18 h.

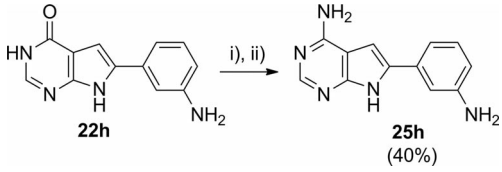
Table 3. Synthesis of 6-arylpyrrolo[2,3-*d*]pyrimidin-4-amines (8-aryl-7-deazaadenines).

Entry	Ar–X	Product **20** (yield)	Product **23** (yield)	Product **24** (yield)	Product **25** (yield)
1		**20a** (79%)	**23a** (77%)	**24a** (83%)	**25a** (80%)
2		**20b** (64%)[b]	**23b** (65%)	**24b** (94%)	**25b** (74%)
3		**20c** (69%)	**23c** (89%)	**24c** (91%)	**25c** (74%)
4		**20d** (62%)	**23d** (76%)	**24d** (85%)	**25d** (79%)
5		**20e** (70%)[b]	**23e** (62%)	**24e** (84%)	**25e** (72%)
6		**20f** (50%)[b]	**23f** (62%)	**24f** (71%)	**25f** (65%)
7		**20g** (39%)[b]	**23g** (86%)	**24g** (93%)	**25i** (77%)[a]
8		**20h** (78%)	complex mixture	–	–

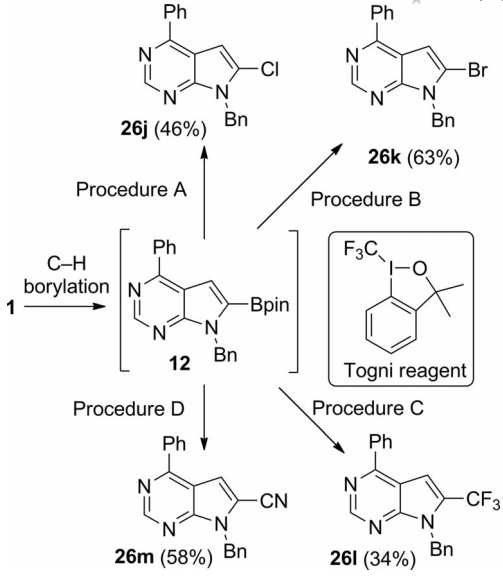
[a] Overall yield after acidic deprotection to **25i**. [b] 18 h.

SEM group using TFA followed by aqueous ammonia furnished free 6-substituted pyrrolo[2,3-*d*]pyrimidin-4-amines (8-substituted 7-deazaadenines) **21a**–**f** in 65–80% yield. In the case of compound **24g**, deprotection of the SEM group was directly followed by acid hydrolysis to give the free 6-(uracil-5-yl)-pyrrolo[2,3-*d*]pyrimidin-4-amine [8-(uracil-5-yl)-7-deazaadenine] (**25i**).

Given that the above reaction sequence did not work for the preparation 6-(3-aminophenyl)pyrrolo[2,3-*d*]pyrimidin-4-amine (**25h**), we used an alternative synthetic protocol. The corresponding pyrrolo[2,3-*d*]pyrimidin-4-one derivative **22h** was first chlorinated with $POCl_3$ followed by amination (NH_3 in dioxane) to give the desired pyrrolo[2,3-*d*]pyrimidin-4-amine (deazaadenine) **25h** in 40% overall yield (Scheme 7).



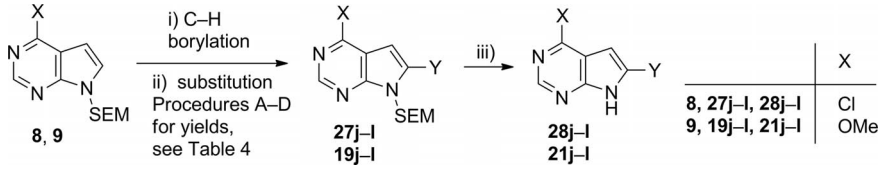
Scheme 7. Reagents and conditions: (i) $POCl_3$ (5 equiv.), $BnEt_3N^+Cl$ (2 equiv.), $PhNMe_2$ (1.1 equiv.), MeCN, reflux, 4 h; (ii) aq. ammonia (25% w/w), dioxane, 120 °C, 18 h.



Scheme 8. Reagents and conditions: (A) $CuCl_2$ (3 equiv.), acetone/H_2O (1:1), 80 °C, 3 h; (B) $CuBr_2$ (3 equiv.), acetone/H_2O (1:1), 80 °C, 3 h; (C) Togni reagent (1.1 equiv.), CuTC (10 mol-%), 1,10-phenanthroline (20 mol-%), 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, 2.5 h.

Having developed easy access to 6-borylated pyrrolo[2,3-*d*]pyrimidines, we also explored the possibility of their conversion into other functional groups. We tested the reactions of the 6-borylated 7-benzyl-pyrrolo[2,3-*d*]pyrimidine **12** generated in situ from **1** and directly functionalized by copper-catalyzed substitutions (Scheme 8). Halogenation[29] of boronate **12** with cupric chloride formed 6-chloropyrrolo[2,3-*d*]pyrimidine **26j** (46%), whereas analogous bromination with cupric bromide gave 6-bromo-derivative **26k** (63%). This two-step halogenation at the 6-position is complementary to electrophilic halogenation, which proceeds at the 5-position.[30] Boronate **12** was also converted into 6-trifluoromethyl derivative **26l** by treatment with the Togni reagent [(3,3-dimethyl-1-trifluoromethyl)-1,2-benziodoxole], CuTC [copper(I)-thiophene-2-carboxylate], and 1,10-phenanthroline,[31] but the yield was only 34% because of competitive protodeborylation. Treatment of **12** with $Zn(CN)_2$ in the presence of $Cu(NO_3)_2$ and CsF[32] gave 6-cyano derivative **26m** in 58% yield.

This one-pot, two-step reaction sequence of C–H borylation/Cu-catalyzed substitution was then applied on SEM-protected 4-chloro- and 4-methoxypyrrolo[2,3-*d*]pyrimidine **8** and **9**. The halogenations and trifluoromethyl-



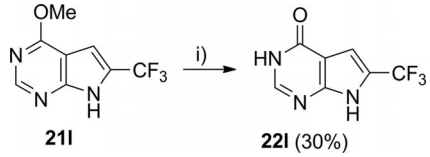
Scheme 9. Reagents and conditions: (i) B_2pin_2 (1.2 equiv.), $[Ir(COD)OMe]_2$ (5 mol-%), dtbpy (10 mol-%), THF, 80 °C, 20 h; (ii) A. $CuCl_2$ (3 equiv.), acetone/H_2O (1:1), 80 °C, 3 h; B. $CuBr_2$ (3 equiv.), acetone/H_2O (1:1), 80 °C, 3 h; C. Togni reagent (1.1 equiv.), CuTC (10 mol-%), 1,10-phenanthroline (20 mol-%), 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), room temp., 1 h, followed by aq. ammonia (25% w/w, room temp., 18 h).

Table 4. One-pot C–H borylation/Cu-catalyzed substitution of SEM-protected pyrrolo[2,3-*d*]pyrimidines followed by deprotection.

Entry	Starting compd.	Procedure	X	Y	Product yield (%)	Product yield (%)
1	**8**	A	Cl	Cl	**27j** (55)	**28j** (66)
2	**8**	B	Cl	Br	**27k** (56)	**28k** (75)
3	**8**	C	Cl	CF_3	**27l** (38)	**28l** (73)
4	**8**	D	Cl	CN	no reaction	–
5	**9**	A	OMe	Cl	**19j** (47)	**21j** (55)
6	**9**	B	OMe	Br	**19k** (34)	**21k** (50)
7	**9**	C	OMe	CF_3	**19l** (32)	**21l** (75)
8	**9**	D	OMe	CN	no reaction	–

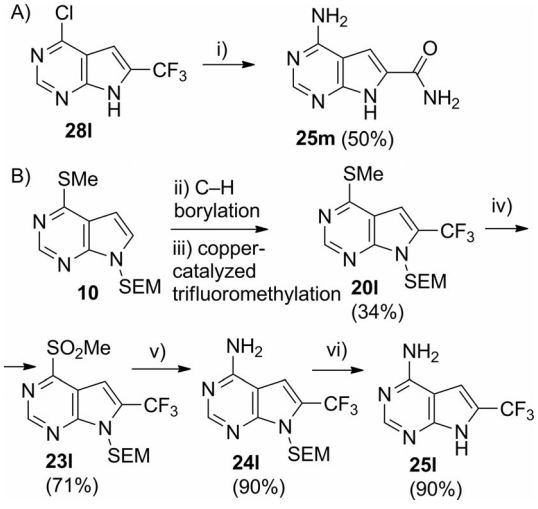
ations proceeded with modest conversions (probably due to partial protodeborylation) to give the desired 6-substituted products **19j–l** and **27j–l** in 32–56% yield (Scheme 9, Table 4). On the other hand, the cyanation did not proceed at all, and only the recovered starting material was observed. Cleavage of SEM groups using TFA followed by aqueous ammonia furnished the corresponding free 6-substituted pyrrolo[2,3-*d*]pyrimidines (8-substituted 7-deazapurine bases) **21j–l** and **28j–l** (Scheme 9, Table 4).

The last goal was the preparation of 6-trifluoromethylpyrrolo[2,3-*d*]pyrimidin-4-one (8-trifluoromethyl-7-deazahypoxanthine) (**22l**) and 6-trifluoromethyl-pyrrolo[2,3-*d*]-pyrimidin-4-amine (8-trifluoromethyl-7-deazaadenine) (**25l**). The former was easily prepared by cleavage of methyl ether **21l** with iodotrimethylsilane generated in situ (from TMSCl and NaI) in acetonitrile. The desired compound **22l** was isolated in low yield (30%; Scheme 10).



Scheme 10. Reagents and conditions: (i) TMSCl (5 equiv.), NaI (5 equiv.), MeCN, 80 °C, 18 h.

More difficult was the preparation of the corresponding 6-trifluoromethyl-pyrrolo[2,3-*d*]pyrimidin-4-amine **25l** (Scheme 11). An obvious way was through amination of 4-chloro derivative **28l**. However, the reaction did not proceed under mild conditions, whereas at 120 °C the formation of unexpected amide **25m** was observed due to hydrolysis/ammonolysis of the CF_3 group. Therefore, we used a longer sequence starting by borylation/trifluoromethylation of **10**, followed by oxidation and amination of sulfone **23l** under mild conditions to give SEM-protected pyrrolo[2,3-*d*]pyrimidin-4-amine **24l** in good yield. Final standard deprotection gave the desired compound **25l** in 90% yield.



Scheme 11. 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 mol-%), dtbpy (10 mol-%), THF, 80 °C, 20 h; (iii) Togni reagent (1.1 equiv.), CuTc (10 mol-%), 1,10-phenanthroline (20 mol-%), $LiOH·H_2O$ (2 equiv.), CH_2Cl_2, 45 °C, 18 h; (iv) *m*CPBA (2 equiv.), CH_2Cl_2, room temp., 1 h; (v) aq. ammonia (25% w/w), dioxane, 50 °C, 18 h; (vi) TFA (2 mL), room temp., 1 h, followed by aq. ammonia (25% w/w), room temp., 18 h.

Conclusions

We have developed a general approach for the synthesis of biologically relevant 4,6-disubstituted pyrrolo[2,3-*d*]pyrimidines (6,8-disubstituted 7-deazapurines). The approach was based on one-pot, two-step iridium-catalyzed C–H borylation of 7-substituted or SEM-protected 4-chloro-, 4-methoxy-, or 4-methylsulfanylpyrrolo[2,3-*d*]pyrimidines followed by palladium-catalyzed Suzuki coupling with aryl halides. Manipulation of substituents at the 4-position, i.e., demethylation of 4-methoxypyrrolo[2,3-*d*]pyrimidine or oxidation of 4-(methylsulfanyl)pyrrolo[2,3-*d*]pyrimidine derivatives to sulfones followed by amination, gave the desired 6-arylpyrrolo[2,3-*d*]pyrimidin-4-ones (8-aryl-7-deazahypoxanthines) or pyrrolo[2,3-*d*]pyrimidin-4-amines (8-aryl-7-deazaadenines), respectively, after cleavage of the SEM protection group. The 6-pinacolboronate intermediates were also converted into 6-chloro-, 6-bromo, and 6-trifluoromethylpyrrolo[2,3-*d*]pyrimidines (8-chloro-, 8-bromo, and 8-trifluoromethyl-7-deazapurines) by copper-catalyzed displacements. The approach gives easy access to an underexplored group of biologically relevant modified pyrrolo[2,3-*d*]pyrimidine (7-deazapurine) bases, which could be further *N*-alkylated or glycosylated to give a variety of nucleoside and nucleotide analogues. Application of this methodology to the synthesis of these derivatives and nucleosides and biological profiling of the products is underway.

Experimental Section

General: 4-Chloro-7*H*-pyrrolo[2,3-*d*]pyrimidine (**7**) was purchased from a commercial supplier and used without any further purification. 4-Chloro-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine[22] (**8**) and 4-methyl-7-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine[21] (**3**) were prepared according to reported procedures. Anhydrous DMF and THF were used as received. All compounds were fully characterized by NMR and spectra were recorded with a 600 MHz (^1H at 600.1 MHz, ^{13}C at 150.9 MHz), a 500 MHz (499.8 or 500.0 MHz for ^1H and 125.7 MHz for ^{13}C), or a 400 MHz (^1H at 400 MHz, ^{13}C at 100.6 MHz) spectrometer. ^1H and ^{13}C resonances were assigned based on H,C-HSQC and H,C-HMBC spectra. The samples were measured in $CDCl_3$ or $[D_6]$DMSO and chemical shifts (in ppm, δ-scale) are referenced to solvent signal [$\delta(^1H)$ = 7.26 ppm, $\delta(^1H)$ = 77.0 ppm] or in DMSO [$\delta(^1H)$ = 2.50 ppm, $\delta(^1H)$ = 39.43 ppm] Coupling constants (*J*) are given in Hz. High-performance flash chromatography (HPFC) was performed on KP-Sil columns. IR spectra (wavenumbers in cm^{-1}) were recorded by using the ATR technique. High-resolution mass spectra were measured by using the EI ionization technique.

4-Methoxy-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]-pyrimidine (9): Protected pyrrolo[2,3-*d*]pyrimidine **8** (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 room temp. 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 with EtOAc (2 × 150 mL). The combined organic layers were dried with sodium sulfate (Na_2SO_4), filtered, and concentrated under reduced pressure to give **9** (24.94 g, 99%) as a yellow oil. ^{1}H NMR (499.8 MHz, [D$_6$]DMSO): δ = –0.11 (s, 9 H, CH_3Si), 0.79–0.83 (m, 2 H, $SiCH_2CH_2O$), 3.48–3.51 (m, 2 H, OCH_2CH_2Si), 4.05 (s, 3 H, CH_3O), 5.58 (s, 2 H, NCH_2O), 6.57 (d, $J_{5,6}$ = 3.6 Hz, 1 H, H-5), 7.54 (dd, $J_{6,5}$ = 3.6, $J_{6,2}$ = 0.2 Hz, 1 H, H-6), 8.45 (d, $J_{2,6}$ = 0.2 Hz, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = –1.2 (CH_3Si), 17.3 ($SiCH_2CH_2O$), 53.7 (CH_3O), 65.7 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 2950, 2923, 2896, 1592, 1559, 1512, 1476, 1416, 1314, 1236, 1096, 1078, 1060, 863, 842, 764, 731, 647 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (10): Protected pyrrolo[2,3-*d*]pyrimidine **8** (27 g, 95 mmol, 1 equiv.) was dissolved in methanol (150 mL) and MeSNa (10 g, 142.5 mmol, 1.5 equiv.) was added. The reaction mixture was stirred at room temp. for 1 h, then the solvents were evaporated under reduced pressure and the mixture was diluted with water (150 mL) and EtOAc (150 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 150 mL). The combined organic layers were dried with sodium sulfate (Na_2SO_4), solvents were evaporated, and the residue was purified by flash chromatography (CH_2Cl_2/EtOAc, 20:1) to give **10** (25 g, 89%) as a yellowish solid, m.p. 55 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.07 (s, 9 H, CH_3Si), 0.88–0.91 (m, 2 H, OCH_2CH_2Si), 2.71 (s, 3 H, CH_3S), 3.49–3.52 (m, 2 H, OCH_2CH_2Si), 5.61 (s, 2 H, NCH_2O), 6.56 (d, $J_{5,6}$ = 3.7 Hz, 1 H, H-5), 7.23 (d, $J_{6,5}$ = 3.7 Hz, 1 H, H-6), 8.69 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 11.8 (CH_3S), 17.7 (OCH_2CH_2Si), 66.4 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3105, 3087, 3052, 2956, 2935, 2899, 2875, 1550, 1506, 1464, 1446, 1413, 1344, 1251, 1213, 1162, 1096, 1084, 394, 922, 860, 842, 758, 743 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (11): 4-Methylsulfanyl-7*H*-pyrrolo[2,3-*d*]pyrimidine **10** (1.48 g, 5 mmol, 1 equiv.) was dissolved in CH_2Cl_2 (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 room temp. 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 with CH_2Cl_2 (2 × 15 mL). The combined organic layers were dried with sodium sulfate, solvents were evaporated, and the residue was purified by flash chromatography (HPFC; $CHCl_3$/MeOH, 20:1) to give **11** (1.28 g, 78%) as a white solid, m.p. 91 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.05 (s, 9 H, CH_3Si), 0.90–0.93 (m, 2 H, OCH_2CH_2Si), 3.36 (s, 3 H, CH_3SO_2), 3.51–3.54 (m, 2 H, OCH_2CH_2Si), 5.71 (s, 2 H, NCH_2O), 7.16 (d, $J_{5,6}$ = 3.7 Hz, 1 H, H-5), 7.59 (d, $J_{6,5}$ = 3.7 Hz, 1 H, H-6), 8.98 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.7 (OCH_2CH_2Si), 39.9 (CH_3SO_2), 67.0 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{13}H_{22}O_3N_3SSi$ 328.1146; found 328.1147.

Borylation of Deazapurines; General Procedure: A pyrrolo[2,3-*d*]pyrimidine **8**–**11** (1 mmol, 1 equiv.), bispinacolatodiboron (0.305 g, 1.2 mmol, 1.2 equiv.), [Ir(COD)OMe]$_2$ (33 mg, 0.05 mmol, 5 mol-%), and 4,4′-di-*tert*-butyl-2,2′-bipyridine (27 mg, 0.1 mmol, 10 mol-%) were dissolved in anhydrous THF (5 mL) under Ar. The solution was heated at 80 °C in a septum-sealed flask for 20 h. The solvent was evaporated and the residue was purified by flash chromatography in pure dichloromethane. Finally, the crude product was rinsed with hexanes and heated at 60 °C under vacuum (6 mTorr) to remove residual pinacol.

4-Chloro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (14): Starting from **8** (284 mg, 1 mmol), product **14** (322 mg, 78%) was obtained as brownish solid, m.p. 99 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.08 (s, 9 H, CH_3Si), 0.85–0.89 (m, 2 H, OCH_2CH_2Si), 1.38 [s, 12 H, $(CH_3)_2C$], 3.50–3.53 (m, 2 H, OCH_2CH_2Si), 5.89 (s, 2 H, NCH_2O), 7.23 (s, 1 H, H-5), 8.68 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.8 (OCH_2CH_2Si), 24.8 [$(CH_3)_2C$], 66.3 (OCH_2CH_2Si), 72.6 (NCH_2O), 84.7 [$(CH_3)_2C$], 112.6 (CH-5), 117.5 (C-4a), 133.0 (C-6), 152.2 (CH-2), 153.3 (C-4), 154.0 (C-7a) ppm. IR (KBr): $\tilde{\nu}$ = 2989, 2956, 2914, 2893, 1580, 1538, 1428, 1365, 1326, 1254, 1180, 1141, 1087, 866, 827, 746 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (15): Starting from **9** (279 mg, 1 mmol), product **15** (328 mg, 81%) was obtained as a brownish oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.09 (s, 9 H, CH_3Si), 0.85–0.88 (m, 2 H, OCH_2CH_2Si), 1.36 [s, 12 H, $(CH_3)_2C$], 3.50–3.54 (m, 2 H, OCH_2CH_2Si), 4.11 (s, 3 H, CH_3O), 5.86 (s, 2 H, NCH_2O), 7.17 (s, 1 H, H-5), 8.52 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 17.8 (OCH_2CH_2Si), 24.8 [$(CH_3)_2C$], 53.7 (CH_3O), 65.9 (OCH_2CH_2Si), 72.4 (NCH_2O), 84.1 [$(CH_3)_2C$], 105.7 (C-4a), 112.3 (CH-5), 129.3 (C-6), 152.6 (CH-2), 155.1 (C-7a), 163.7 (C-7a) ppm. IR (KBr): $\tilde{\nu}$ = 2977, 2950, 2893, 1682, 1595, 1553, 1524, 1479, 1425, 1374, 1331, 1320, 1260, 1222, 1147, 1090, 970, 860, 836, 797, 761 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{19}H_{33}O_4N_3BSi$ 406.2328; found 406.2331.

4-(Methylsulfanyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (16): Starting from **10** (295 mg, 1 mmol), product **16** (350 mg, 83%) was obtained as a brownish oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.08 (s, 9 H, CH_3Si), 0.85–0.88 (m, 2 H, OCH_2CH_2Si), 1.37 [s, 12 H, $(CH_3)_2C$], 2.69 (s, 3 H, CH_3S), 3.50–3.53 (m, 2 H, OCH_2CH_2Si), 5.86 (s, 2 H, NCH_2O), 7.17 (s, 1 H, H-5), 8.70 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 11.8 (CH_3S), 17.8 (OCH_2CH_2Si), 24.8 [$(CH_3)_2C$], 66.0 (OCH_2CH_2Si), 72.3 (NCH_2O), 84.3 [$(CH_3)_2C$], 112.4 (CH-5), 116.0 (C-4a), 130.1 (C-6), 151.4 (C-7a), 152.2 (CH-2), 163.2 (C-4) ppm. IR (KBr): $\tilde{\nu}$ = 2974, 2950, 2929, 2893, 1553, 1527, 1458, 1425, 1371, 1314, 1263, 1222, 1180, 1141, 1084, 857, 839 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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-yltrifluoroborate (Potassium Salt) (17): To a flask containing **12** (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; EtOAc/MeOH, 9:1) to give product **17** (266 mg, 68%) as a white solid, m.p. > 300 °C. ^{1}H NMR (500 MHz, CD_3OD): δ = 5.67 (s, 2 H, CH_2), 6.86 (H-5),

7.14–7.15 (m, 1 H, H-*p*-Bn), 7.18–7.25 (m, 4 H, H-*o*,*m*-Bn), 7.52–7.53 (m, 1 H, H-*p*-Ph), 7.56–7.58 (m, 2 H, H-*m*-Ph), 8.06–8.07 (m, 2 H, H-*o*-Ph), 8.63 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, CD_3OD): δ = 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) ppm, C-6 was not detected. ^{19}F NMR (470.3 MHz, CD_3OD): δ = –137.91 ppm. ^{11}B NMR (160.4 MHz, CD_3OD): δ = 1.96 ppm. IR (KBr): $\tilde{\nu}$ = 3428, 3254, 3062, 3031, 2949, 1617, 1584, 1562, 1550, 1497, 1474, 1455, 1432, 1148, 1028, 1007, 937, 761, 697 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{19}H_{15}N_3BF_3Na$ 376.1203; found 376.1205.

One-Pot C–H Borylation/Suzuki Coupling Sequence; General Procedure: Pyrrolo[2,3-*d*]pyrimidine **8**–**10** (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 anhydrous 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 until complete consumption of staring material (1–18 h) was observed, as monitored by NMR spectroscopy. The solution was then cooled to room temperature, and EtOAc (50 mL) and water (50 mL) were added. The aqueous solution was then extracted with EtOAc (×3) and the combined organic layers were dried with Na_2SO_4, filtered, and the solvents were evaporated under vacuum. The crude product was purified by flash chromatography (hexane/EtOAc).

4-Chloro-6-(4-methoxyphenyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (18a): Starting from **8** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **18a** (312 mg, 20%) as a yellowish oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.03 (s, 9 H, CH_3Si), 0.96–0.99 (m, 2 H, OCH_2CH_2Si), 3.72–3.76 (m, 2 H, OCH_2CH_2Si), 3.88 (s, 3 H, CH_3O), 5.61 (s, 2 H, NCH_2O), 6.63 (s, 1 H, H-5), 7.02–7.04 (m, 2 H, H-*m*-Ph), 7.71–7.73 (m, 2 H, H-*o*-Ph), 8.65 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 18.0 (OCH_2CH_2Si), 55.4 (CH_3O), 67.0 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 2956, 2899, 2833, 1607, 1538, 1500, 1347, 1248, 1180, 1165, 1084, 857, 842 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (19a): Starting from **9** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **19a** (1.08 g, 70%) as a yellowish oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.03 (s, 9 H, CH_3Si), 0.94–0.98 (m, 2 H, OCH_2CH_2Si), 3.70–3.74 (m, 2 H, OCH_2CH_2Si), 3.87 (s, 3 H, CH_3O-*p*), 4.14 (s, 3 H, CH_3O-4), 5.58 (s, 2 H, NCH_2O), 6.56 (s, 1 H, H-5), 6.99–7.01 (m, 2 H, H-*m*-C_6H_4OMe), 7.67–7.68 (m, 2 H, H-*o*-C_6H_4OMe), 8.49 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 18.0 (OCH_2CH_2Si), 53.7 (CH_3O-4), 55.3 (CH_3O-*p*), 66.6 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 2995, 2950, 2893, 2833, 1613, 1595, 1565, 1500, 1476, 1419, 1353, 1320, 1284, 1251, 1213, 1183, 1072, 857, 839, 785, 764 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (19b): Starting from **9** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **19b** (713 g, 50%) as a yellowish oil. ^{1}H NMR (600.1 MHz, $CDCl_3$): δ = –0.17 (s, 9 H, CH_3Si), 0.79–0.82 (m, 2 H, $SiCH_2CH_2O$), 3.47–3.50 (m, 2 H, OCH_2CH_2Si), 4.15 (s, 3 H, CH_3O), 6.20 (s, 2 H, NCH_2O), 6.95 (s, 1 H, H-5), 7.27 (ddd, $J_{5,4}$ = 7.2, $J_{5,6}$ = 4.8, $J_{5,3}$ = 1.4 Hz, 1 H, H-5-py), 7.77 (ddd, $J_{4,3}$ = 8.0, $J_{4,5}$ = 7.2, $J_{4,6}$ = 1.8 Hz, 1 H, H-4-py), 7.80 (ddd, $J_{3,4}$ = 8.0, $J_{3,5}$ = 1.4, $J_{3,6}$ = 1.0 Hz, 1 H, H-3-py), 8.45 (d, $J_{2,6}$ = 0.2 Hz, 1 H, H-2), 8.69 (ddd, $J_{6,5}$ = 4.8, $J_{6,4}$ = 1.8, $J_{6,3}$ = 1.0 Hz, 1 H, H-6-py) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = –1.6 (CH_3Si), 17.7 ($SiCH_2CH_2O$), 53.8 (CH_3O), 66.1 (OCH_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) ppm. HRMS (ESI): *m*/*z* calcd. 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 (19c): Starting from **9** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **19c** (939 mg, 65%) as a yellowish oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.05 (s, 9 H, CH_3Si), 0.95–0.98 (m, 2 H, OCH_2CH_2Si), 3.67–3.70 (m, 2 H, OCH_2CH_2Si), 4.14 (s, 3 H, CH_3O), 5.71 (s, 2 H, NCH_2O), 6.72 (s, 1 H, H-5), 7.13 (dd, $J_{4,5}$ = 5.1, $J_{4,3}$ = 3.6 Hz, 1 H, H-4-thienyl), 7.39 (dd, $J_{5,4}$ = 5.1, $J_{5,3}$ = 1.2 Hz, 1 H, H-5-thienyl), 7.59 (dd, $J_{3,4}$ = 3.6, $J_{3,5}$ = 1.2 Hz, 1 H, H-3-thienyl), 8.49 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.9 (OCH_2CH_2Si), 53.7 (CH_3O), 66.4 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 2956, 2896, 2866, 1595, 1553, 1473, 1458, 1413, 1356, 1344, 1320, 1248, 1207, 1081, 857, 833, 782, 764, 698 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (19d): Starting from **9** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give product **19d** (621 mg, 45%) as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.08 (s, 9 H, CH_3Si), 0.89–0.94 (m, 2 H, OCH_2CH_2Si), 3.60–3.64 (m, 2 H, OCH_2CH_2Si), 4.14 (s, 3 H, CH_3O), 5.79 (s, 2 H, NCH_2O), 6.53 (dd, $J_{4,3}$ = 3.5, $J_{4,5}$ = 1.8 Hz, 1 H, H-4-furyl), 6.84 (s, 1 H, H-5), 6.93 (dd, $J_{3,4}$ = 3.5, $J_{3,5}$ = 0.8 Hz, 1 H, H-3-furyl), 7.54 (dd, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.8 Hz, 1 H, H-5-furyl), 8.48 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 18.0 (OCH_2CH_2Si), 53.7 (CH_3O), 66.4 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 2956, 2929, 2866, 2848, 1595, 1589, 1565, 1476, 1461, 1419, 1353, 1329, 1248, 1216, 1090, 866, 839, 776 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (19e): Starting from **9** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **19e** (1.11 g, 77%) as a yellowish solid, m.p. 55 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.04 (s, 9 H, CH_3Si), 0.96–0.99 (m, 2 H, OCH_2CH_2Si), 3.72–3.76 (m, 2 H, OCH_2CH_2Si), 4.18 (s, 3 H, CH_3O), 5.70 (s, 2 H, NCH_2O), 6.69 (s, 1 H, H-5), 7.43 (dd, $J_{5,4}$ = 5.0, $J_{5,2}$ = 2.9 Hz, 1 H, H-5-thienyl), 7.46 (dd, $J_{4,5}$ = 5.0, $J_{4,2}$ = 1.3 Hz, 1 H, H-4-thienyl), 7.88 (dd, $J_{2,5}$ = 2.9, $J_{2,4}$ = 1.3 Hz, 1 H, H-2-thienyl), 8.51 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 18.0 (OCH_2CH_2Si), 54.3 (CH_3O), 66.5 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (19f): Starting from **9** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **19f** (802 mg, 58%) as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.05 (s, 9 H, CH_3Si), 0.93–0.96 (m, 2 H, OCH_2CH_2Si), 3.65–3.68 (m, 2 H, OCH_2CH_2Si), 4.13 (s, 3 H, CH_3O), 5.67 (s, 2 H, NCH_2O), 6.62 (s, 1 H, H-5), 6.77 (dd, $J_{4,5}$ = 1.9, $J_{4,2}$ = 0.9 Hz, 1 H, H-4-furyl), 7.51 (t, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, 1 H, H-5-furyl), 7.99 (dd, $J_{2,5}$ = 1.5, $J_{2,4}$ = 0.9 Hz, 1 H, H-2-furyl), 8.47 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 18.0 (OCH_2CH_2Si), 53.7 (CH_3O), 66.3 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 2947, 2893, 1769, 1598, 1559, 1476, 1419, 1329, 1251, 1213, 1081, 875, 857, 836, 779, 761 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (19g): Starting from **9** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **19g** (1.1 g, 66%) as a yellowish solid, m.p. 79 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.11 (s, 9 H, CH_3Si), 0.79–0.83 (m, 2 H, OCH_2CH_2Si), 3.45–3.48 (m, 2 H, OCH_2CH_2Si), 4.00 (s, 3 H, CH_3O-4′), 4.06 (s, 3 H, CH_3O-2′), 4.13 (s, 3 H, CH_3O-4), 5.53 (s, 2 H, NCH_2O), 6.61 (s, 1 H, H-5), 8.44 (s, 1 H, H-6′), 8.50 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.6 (CH_3Si), 17.8 (OCH_2CH_2Si), 53.7 (CH_3O-4), 54.3 (CH_3O-2′), 55.1 (CH_3O-4′), 66.3 (OCH_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′) ppm. IR (KBr): $\tilde{\nu}$ = 2986, 2956, 2896, 2866, 1610, 1598, 1473, 1380, 1356, 1320, 1290, 1251, 1213, 1078, 1018, 866, 833 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (19h): Starting from **9** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **19h** (1.1 g, 74%) as a yellowish solid, m.p. 113 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.04 (s, 9 H, CH_3Si), 0.93–0.96 (m, 2 H, OCH_2CH_2Si), 3.69–3.73 (m, 2 H, OCH_2CH_2Si), 4.14 (s, 3 H, CH_3O), 5.61 (s, 2 H, NCH_2O), 6.61 (s, 1 H, H-5), 6.83 (ddd, $J_{6',5'}$ = 8.0, $J_{6',2'}$ = 2.4 Hz, $J_{6',4'}$ = 1.0 Hz, 1 H, H-6′), 7.14 (m, 1 H, H-2′), 7.19 (ddd, $J_{4',5'}$ = 7.6, $J_{4',2'}$ = 1.6 Hz, $J_{4',6'}$ = 1.0 Hz, 1 H, H-4′), 7.27 (t, $J_{5',4'}$ = $J_{5',6'}$ = 7.8 Hz, 1 H, H-5′), 8.50 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 18.0 (OCH_2CH_2Si), 53.8 (CH_3O), 66.6 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3434, 3318, 3207, 2956, 1592, 1556, 1476, 1329, 1207, 1072, 1057, 866, 842, 797 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{19}H_{27}O_2N_4Si$ 371.1899; found 371.1898.

6-(4-Methoxyphenyl)-4-(methylsulfanyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (20a): Starting from **10** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **20a** (1.27 g, 79%) as a yellowish solid, m.p. 144 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.03 (s, 9 H, CH_3Si), 0.95–0.98 (m, 2 H, OCH_2CH_2Si), 2.72 (s, 3 H, CH_3S), 3.71–3.74 (m, 2 H, OCH_2CH_2Si), 3.87 (s, 3 H, CH_3O), 5.58 (s, 2 H, NCH_2O), 6.54 (s, 1 H, H-5), 7.00–7.01 (m, 2 H, H-*m*-Ph), 7.69–7.71 (m, 2 H, H-*o*-Ph), 8.69 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 11.9 (CH_3S), 18.0 (OCH_2CH_2Si), 55.4 (CH_3O), 66.7 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3066, 2953, 2902, 2842, 1616, 1503, 1422, 1344, 1317, 1263, 1248, 1192, 1141, 1126, 1078, 1057, 863, 851, 836, 755, 534 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (20b): Starting from **10** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **20b** (954 mg, 64%) as a yellowish oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.16 (s, 9 H, CH_3Si), 0.80–0.83 (m, 2 H, OCH_2CH_2Si), 2.73 (s, 3 H, CH_3S), 3.48–3.51 (m, 2 H, OCH_2CH_2Si), 6.17 (s, 2 H, NCH_2O), 6.94 (s, 1 H, H-5), 7.28 (ddd, $J_{5,4}$ = 7.5, $J_{5,6}$ = 4.8, $J_{5,3}$ = 1.2 Hz, 1 H, H-5-py), 7.79 (btd, $J_{4,5}$ = $J_{4,3}$ = 7.7, $J_{4,6}$ = 1.8 Hz, 1 H, H-4-py), 7.85 (dt, $J_{3,4}$ = 8.0, $J_{3,5}$ = $J_{3,6}$ = 1.1 Hz, 1 H, H-3-py), 8.70 (ddd, $J_{6,5}$ = 4.8, $J_{6,4}$ = 1.8 Hz, $J_{6,3}$ = 1.0 Hz, 1 H, H-6-py), 8.72 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.6 (CH_3Si), 11.9 (CH_3S), 17.7 (OCH_2CH_2Si), 66.3 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3052, 2953, 2932, 2893, 1589, 1556, 1455, 1443, 1416, 1350, 1269, 1251, 1177, 1075, 937, 917, 860, 836, 770 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (20c): Starting from **10** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **20c** (1.05 g, 69%) as a yellowish solid, m.p. 92 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.04 (s, 9 H, CH_3Si), 0.95–0.98 (m, 2 H, OCH_2CH_2Si), 2.72 (s, 3 H, CH_3S), 3.67–3.71 (m, 2 H, OCH_2CH_2Si), 5.72 (s, 2 H, NCH_2O), 6.69 (s, 1 H, H-5), 7.15 (dd, $J_{4,5}$ = 5.1, $J_{4,3}$ = 3.7 Hz, 1 H, H-4-thienyl), 7.42 (dd, $J_{5,4}$ = 5.1, $J_{5,3}$ = 1.2 Hz, 1 H, H-5-thienyl), 7.63

(dd, $J_{3,4}$ = 3.7, $J_{3,5}$ = 1.2 Hz, 1 H, H-3-thienyl), 8.68 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 11.9 (CH_3S), 17.9 (OCH_2CH_2Si), 66.5 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3081, 3066, 2953, 2926, 2893, 1559, 1485, 1458, 1440, 1407, 1356, 1260, 1248, 1174, 1057, 928, 854, 839, 785, 755, 728 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (20d): Starting from **10** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **20d** (897 mg, 62%) as a yellowish solid, m.p. 100 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.07 (s, 9 H, CH_3Si), 0.91–0.94 (m, 2 H, OCH_2CH_2Si), 2.73 (s, 3 H, CH_3S), 3.60–3.64 (m, 2 H, OCH_2CH_2Si), 5.80 (s, 2 H, NCH_2O), 6.55 (dd, $J_{4,3}$ = 3.5, $J_{4,5}$ = 1.8 Hz, 1 H, H-4-furyl), 6.83 (s, 1 H, H-5), 6.98 (dd, $J_{3,4}$ = 3.5, $J_{3,5}$ = 0.8 Hz, 1 H, H-3-furyl), 7.56 (dd, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.8 Hz, 1 H, H-5-furyl), 8.67 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 11.9 (CH_3S), 17.8 (OCH_2CH_2Si), 66.3 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (20e): Starting from **10** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **20e** (1.06 g, 70%) as a yellowish solid, m.p. 99 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.03 (s, 9 H, CH_3Si), 0.96–1.00 (m, 2 H, OCH_2CH_2Si), 2.73 (s, 3 H, CH_3S), 3.72–3.75 (m, 2 H, OCH_2CH_2Si), 5.68 (s, 2 H, NCH_2O), 6.64 (s, 1 H, H-5), 7.44 (dd, $J_{5,4}$ = 5.0, $J_{5,2}$ = 2.9 Hz, 1 H, H-5-thienyl), 7.49 (dd, $J_{4,5}$ = 5.0, $J_{4,2}$ = 1.3 Hz, 1 H, H-4-thienyl), 7.91 (dd, $J_{2,5}$ = 2.9, $J_{2,4}$ = 1.3 Hz, 1 H, H-2-thienyl), 8.68 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 11.9 (CH_3S), 18.0 (OCH_2CH_2Si), 66.6 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3102, 3043, 2953, 2920, 2896, 2863, 1550, 1461, 1347, 1269, 1242, 1177, 1081, 917, 860, 836, 776 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (20f): Starting from **10** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **20f** (721 mg, 50%) as a yellowish solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.05 (s, 9 H, CH_3Si), 0.94–0.97 (m, 2 H, OCH_2CH_2Si), 2.73 (s, 3 H, CH_3S), 3.65–3.68 (m, 2 H, OCH_2CH_2Si), 5.67 (s, 2 H, NCH_2O), 6.60 (s, 1 H, H-5), 6.80 (dd, $J_{4,5}$ = 1.9, $J_{4,2}$ = 0.9 Hz, 1 H, H-4-furyl), 7.53 (bt, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, 1 H, H-5-furyl), 8.02 (dd, $J_{2,5}$ = 1.6, $J_{2,4}$ = 0.9 Hz, 1 H, H-2-thienyl), 8.67 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 12.0 (CH_3S), 17.9 (OCH_2CH_2Si), 66.4 (OCH_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) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{23}N_3O_2SSi$ 361.1280; found 361.1278.

6-(2,4-Dimethoxypyrimidin-5-yl)-4-(methylsulfanyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (20g): Starting from **10** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **20g** (676 mg, 39%) as a white solid, m.p. 134 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.10 (s, 9 H, CH_3Si), 0.80–0.83 (m, 2 H, OCH_2CH_2Si), 2.72 (s, 3 H, CH_3S), 3.45–3.48 (m, 2 H, OCH_2CH_2Si), 4.01 (s, 3 H, CH_3O-4′), 4.07 (s, 3 H, CH_3O-2′), 5.53 (s, 2 H, NCH_2O), 6.59 (s, 1 H, H-5), 8.45 (s, 1 H, H-6′), 8.70 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 11.9 (CH_3S), 17.7 (OCH_2CH_2Si), 54.4 (CH_3O-4′), 55.2 (CH_3O-2′), 66.4 (OCH_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′) ppm. IR (KBr): $\tilde{\nu}$ = 2953, 2932, 1613, 1568, 1553, 1476, 1407, 1377, 1302, 1248, 1189, 1078, 1066, 863, 842 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (20h): Starting from **10** (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 h. Purification was performed by HPFC (EtOAc/hexane, 0–20%) to give **20h** (1.21 g, 78%) as a yellowish solid, m.p. 109 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.03 (s, 9 H, CH_3Si), 0.93–0.97 (m, 2 H, OCH_2CH_2Si), 2.73 (s, 3 H, CH_3S), 3.70–3.73 (m, 2 H, OCH_2CH_2Si), 5.61 (s, 2 H, NCH_2O), 6.58 (s, 1 H, H-5), 6.75 (ddd, $J_{6',5'}$ = 8.0, $J_{6',2'}$ = 2.4 Hz, $J_{6',4'}$ = 1.0 Hz, 1 H, H-6′), 7.07–7.08 (m, 1 H, H-2′), 7.13 (ddd, $J_{4',5'}$ = 7.6, $J_{4',2'}$ = 1.7 Hz, $J_{4',6'}$ = 0.9 Hz, 1 H, H-4′), 7.25 (t, $J_{5',4'}$ = $J_{5',6'}$ = 7.8 Hz, 1 H, H-5′), 8.70 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 11.9 (CH_3S), 18.0 (OCH_2CH_2Si), 66.7 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3324, 2950, 1610, 1553, 1538, 1479, 1464, 1437, 1353, 1251, 1171, 1060, 851, 833, 785 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{19}H_{27}ON_4SSi$ 387.1669; found 387.1670.

Oxidation to Sulfones; General Procedure: A 4-MeS-pyrrolo[2,3-*d*]-pyrimidine **20a**–**h** and **23l** (2 mmol, 1 equiv.) was dissolved in CH_2Cl_2 (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 room temp. 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 with CH_2Cl_2 (2 × 25 mL). The combined organic layers were dried with sodium sulfate, solvents were evaporated, and the residue was purified by flash chromatography (HPFC; $CHCl_3$/MeOH, 20:1).

6-(4-Methoxyphenyl)-4-(methylsulfonyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (23a): Starting from pyrrolo[2,3-*d*]pyrimidine **20a** (803 mg, 2 mmol) and *m*-CPBA (900 mg, 4 mmol), the reaction was performed according to the General Procedure to give **23a** (668 mg, 77%) as a white solid, m.p. 147 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.01 (s, 9 H, CH_3Si), 0.98–1.01 (m, 2 H, OCH_2CH_2Si), 3.36 (s, 3 H, CH_3SO_2), 3.74–3.78 (m, 2 H, OCH_2CH_2Si), 3.89 (s, 3 H, CH_3O), 5.67 (s, 2 H, NCH_2O), 7.03–

7.05 (m, 2 H, H-*m*-Ph), 7.14 (s, 1 H, H-5), 7.77–7.78 (m, 2 H, H-*o*-Ph), 8.95 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 18.0 (OCH_2CH_2Si), 40.1 (CH_3SO_2), 55.4 (CH_3O), 67.2 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3132, 3010, 2953, 2929, 2899, 1473, 1413, 1344, 1302, 1245, 1174, 1138, 1123, 1066, 1015, 869, 845, 782, 755, 761, 537 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (23b): Starting from pyrrolo[2,3-*d*]pyrimidine **20b** (745 mg, 2 mmol) and *m*-CPBA (900 mg, 4 mmol), the reaction was performed according to the General Procedure to give **23b** (528 mg, 65%) as a white solid, m.p. 109 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.17 (s, 9 H, CH_3Si), 0.78–0.80 (m, 2 H, OCH_2CH_2Si), 3.37 (s, 3 H, CH_3SO_2), 3.44–3.47 (m, 2 H, OCH_2CH_2Si), 6.34 (s, 2 H, NCH_2O), 7.37 (ddd, $J_{5,4}$ = 7.5, $J_{5,6}$ = 4.8 Hz, $J_{5,3}$ = 1.2 Hz, 1 H, H-5-py), 7.48 (s, 1 H, H-5), 7.85 (btd, $J_{4,5}$ = $J_{4,3}$ = 7.7, $J_{4,6}$ = 1.8 Hz, 1 H, H-4-py), 7.91 (dt, $J_{3,4}$ = 7.9, $J_{3,5}$ = $J_{3,6}$ = 1.1 Hz, 1 H, H-3-py), 8.75 (ddd, $J_{6,5}$ = 4.8 Hz, $J_{6,4}$ = 1.8 Hz, $J_{6,3}$ = 0.9 Hz, 1 H, H-6-py), 9.01 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.6 (CH_3Si), 17.7 (OCH_2CH_2Si), 40.0 (CH_3SO_2), 66.7 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 2950, 2899, 1476, 1347, 1323, 1302, 1248, 1135, 1063, 1051, 863, 791, 767, 528 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (23c): Starting from pyrrolo[2,3-*d*]pyrimidine **20c** (755 mg, 2 mmol) and *m*-CPBA (900 mg, 4 mmol), the reaction was performed according to the General Procedure to give **23c** (717 mg, 89%) as a yellow solid, m.p. 107 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.03 (s, 9 H, CH_3Si), 0.98–1.01 (m, 2 H, OCH_2CH_2Si), 3.37 (s, 3 H, CH_3SO_2), 3.70–3.73 (m, 2 H, OCH_2CH_2Si), 5.82 (s, 2 H, NCH_2O), 7.20 (dd, $J_{4,5}$ = 5.1, $J_{4,3}$ = 3.7 Hz, 1 H, H-4-thienyl), 7.27 (s, 1 H, H-5), 7.53 (dd, $J_{5,4}$ = 5.1, $J_{5,3}$ = 1.2 Hz, 1 H, H-5-thienyl), 7.77 (dd, $J_{3,4}$ = 3.7, $J_{3,5}$ = 1.2 Hz, 1 H, H-3-thienyl), 8.95 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 17.9 (OCH_2CH_2Si), 40.1 (CH_3SO_2), 67.0 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3004, 2959, 2929, 2893, 1544, 1485, 1413, 1353, 1302, 1248, 1138, 1123, 1069, 863, 839, 779, 764, 534 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (23d): Starting from pyrrolo[2,3-*d*]pyrimidine **20d** (723 mg, 2 mmol) and *m*-CPBA (900 mg, 4 mmol), the reaction was performed according to the General Procedure to give **23d** (600 mg, 76%) as a yellow solid, m.p. 146 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.06 (s, 9 H, CH_3Si), 0.93–0.96 (m, 2 H, OCH_2CH_2Si), 3.36 (s, 3 H, CH_3SO_2), 3.62–3.65 (m, 2 H, OCH_2CH_2Si), 5.91 (s, 2 H, NCH_2O), 6.60 (dd, $J_{4,3}$ = 3.5, $J_{4,5}$ = 1.8 Hz, 1 H, H-4-furyl), 7.16 (dd, $J_{3,4}$ = 3.5, $J_{3,5}$ = 0.7 Hz, 1 H, H-3-furyl), 7.39 (s, 1 H, H-5), 7.64 (dd, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.7 Hz, 1 H, H-5-furyl), 8.93 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.7 (OCH_2CH_2Si), 40.1 (CH_3SO_2), 66.8 (OCH_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) ppm. HRMS (ESI): *m*/*z* calcd. 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 (23e): Starting from pyrrolo[2,3-*d*]pyrimidine **20e** (755 mg, 2 mmol) and *m*-CPBA (900 mg, 4 mmol), the reaction was performed according to the General Procedure to give **23e** (507 mg, 62%) as a yellow solid, m.p. 178 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.02 (s, 9 H, CH_3Si), 0.99–1.03 (m, 2 H, OCH_2CH_2Si), 3.37 (s, 3 H, CH_3SO_2), 3.74–3.77 (m, 2 H, OCH_2CH_2Si), 5.78 (s, 2 H, NCH_2O), 7.24 (s, 1 H, H-5), 7.49 (dd, $J_{5,4}$ = 5.0, $J_{5,2}$ = 2.9 Hz, 1 H, H-5-thienyl), 7.57 (dd, $J_{4,5}$ = 5.0, $J_{4,2}$ = 1.3 Hz, 1 H, H-4-thienyl), 8.07 (dd, $J_{2,5}$ = 2.9, $J_{2,4}$ = 1.3 Hz, 1 H, H-2-thienyl), 8.95 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 18.0 (OCH_2CH_2Si), 40.1 (CH_3SO_2), 67.1 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3102, 3007, 2953, 2929, 2896, 1583, 1550, 1467, 1350, 1311, 1251, 1135, 1126, 1072, 863, 833, 776, 534 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (23f): Starting from pyrrolo[2,3-*d*]pyrimidine **20f** (633 mg, 1.75 mmol) and *m*-CPBA (784 mg, 3.5 mmol), the reaction was performed according to the General Procedure to give **23f** (430 mg, 62%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.03 (s, 9 H, CH_3Si), 0.96–0.99 (m, 2 H, OCH_2CH_2Si), 3.36 (s, 3 H, CH_3SO_2), 3.67–3.70 (m, 2 H, OCH_2CH_2Si), 5.78 (s, 2 H, NCH_2O), 6.88 (dd, $J_{4,5}$ = 1.9, $J_{4,2}$ = 0.9 Hz, 1 H, H-4-furyl), 7.19 (s, 1 H, H-5), 7.57 (bt, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, 1 H, H-5-furyl), 8.15 (dd, $J_{2,5}$ = 1.5, $J_{2,4}$ = 0.9 Hz, 1 H, H-2-thienyl), 8.93 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 17.9 (OCH_2CH_2Si), 40.0 (CH_3SO_2), 66.9 (OCH_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) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{23}N_3O_4SiS$ 393.1179; found 393.1177.

6-(2,4-Dimethoxypyrimidin-5-yl)-4-(methylsulfonyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (23g): Starting from pyrrolo[2,3-*d*]pyrimidine **20g** (650 mg, 1.5 mmol) and *m*-CPBA (672 mg, 3 mmol), the reaction was performed according to the General Procedure to give **23g** (598 mg, 86%) as a white solid, m.p. 122 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.08 (s, 9 H, CH_3Si), 0.82–0.85 (m, 2 H, OCH_2CH_2Si), 3.37 (s, 3 H, CH_3SO_2), 3.48–3.51 (m, 2 H, OCH_2CH_2Si), 4.03 (s, 3 H, CH_3O-4′), 4.09 (s, 3 H, CH_3O-2′), 5.63 (s, 2 H, NCH_2O), 7.19 (s, 1 H, H-5), 8.50 (s, 1 H, H-6′), 8.98 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.8 (OCH_2CH_2Si), 40.0 (CH_3SO_2), 54.5 (CH_3O-4′), 55.3 (CH_3O-2′), 67.0 (OCH_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′) ppm. IR (KBr): $\tilde{\nu}$ = 3031, 3007, 2953, 2923, 2890, 1601, 1550, 1470, 1401, 1380, 1344, 1320, 1248, 1081, 866, 839, 776, 761, 531 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (23l): Starting from pyrrolo[2,3-*d*]pyrimidine **20l** (218 mg, 0.6 mmol) and *m*-CPBA (207 mg, 1.2 mmol), the reaction was performed according to the General Procedure to give **23l** (168 mg, 71%) as a white solid, m.p. 145 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.04 (s, 9 H, CH_3Si),

0.92–0.95 (m, 2 H, OCH_2CH_2Si), 3.38 (s, 3 H, CH_3SO_2), 3.58–3.62 (m, 2 H, OCH_2CH_2Si), 5.86 (s, 2 H, NCH_2O), 7.61 (q, $J_{5,F}$ = 1.1 Hz, 1 H, CH-5), 9.11 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.7 (OCH_2CH_2Si), 39.8 (CH_3SO_2), 67.4 (OCH_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) ppm. ^{19}F NMR (470.3 MHz, $CDCl_3$): δ = –56.86 (s, 1 F, F-2) ppm. IR (KBr): $\tilde{\nu}$ = 2956, 2926, 2893, 1547, 1431, 1371, 1344, 1320, 1233, 1180, 1159, 1138, 1093, 863, 836, 528 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{14}H_{20}O_3N_3F_3NaSSi$ 418.0839; found 418.0838.

Amination of Sulfones to 7-Deazaadenines; General Procedure: A 4-methylsulfonyl-7*H*-pyrrolo[2,3-*d*]pyrimidine **23a**–**g** and **23l** (1 mmol) were dissolved in 1,4-dioxane (5 mL) and aq. ammonia (25% w/w, 5 mL) was added. The reaction mixture was stirred at 50 °C overnight, the solvents were evaporated, and the residue was purified by flash chromatography (HPFC; EtOAc/MeOH, 20:1).

6-(4-Methoxyphenyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine (24a): Starting from pyrrolo[2,3-*d*]pyrimidine **23a** (434 mg, 1 mmol), the reaction was performed according to the General Procedure to give **24a** (308 mg, 83%) as a white solid, m.p. 142 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = –0.03 (s, 9 H, CH_3Si), 0.94–0.98 (m, 2 H, OCH_2CH_2Si), 3.70–3.74 (m, 2 H, OCH_2CH_2Si), 3.87 (s, 3 H, CH_3O), 5.19 (br. s, 2 H, NH_2), 5.54 (s, 2 H, NCH_2O), 6.38 (s, 1 H, H-5), 6.99–7.01 (m, 2 H, H-*m*-Ph), 7.65–7.67 (m, 2 H, H-*o*-Ph), 8.35 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 18.0 (OCH_2CH_2Si), 55.3 (CH_3O), 66.5 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3324, 3138, 2950, 2917, 2899, 1664, 1592, 1553, 1455, 1440, 1314, 1248, 1222, 1084, 860, 833, 749, 737 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (24b): Starting from pyrrolo[2,3-*d*]pyrimidine **23b** (404 mg, 1 mmol), the reaction was performed according to the General Procedure to give **24b** (320 mg, 94%) as a yellowish solid, m.p. 137 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = –0.15 (s, 9 H, CH_3Si), 0.82–0.85 (m, 2 H, OCH_2CH_2Si), 3.52–3.55 (m, 2 H, OCH_2CH_2Si), 5.51 (br. s, 2 H, NH_2), 6.09 (s, 2 H, NCH_2O), 6.85 (s, 1 H, H-5), 7.26 (ddd, $J_{5,4}$ = 7.4, $J_{5,6}$ = 4.8 Hz, $J_{5,3}$ = 1.2 Hz, 1 H, H-5-py), 7.76 (btd, $J_{4,5}$ = $J_{4,3}$ = 7.7, $J_{4,6}$ = 1.8 Hz, 1 H, H-4-py), 7.82 (dt, $J_{3,4}$ = 8.0, $J_{3,5}$ = $J_{3,6}$ = 1.1 Hz, 1 H, H-3-py), 8.37 (s, 1 H, H-2), 8.68 (ddd, $J_{6,5}$ = 4.8, $J_{6,4}$ = 1.8 Hz, $J_{6,3}$ = 1.0 Hz, 1 H, H-6-py) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.6 (CH_3Si), 17.7 (OCH_2CH_2Si), 66.2 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3309, 3114, 3043, 2950, 1673, 1595, 1589, 1562, 1556, 1455, 1323, 1248, 1096, 1069, 863, 839, 761 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (24c): Starting from pyrrolo[2,3-*d*]pyrimidine **23c** (410 mg, 1 mmol), the reaction was performed according to the General Procedure to give **24c** (316 mg, 91%) as a yellowish solid, m.p. 151 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = –0.04 (s, 9 H, CH_3Si), 0.94–0.98 (m, 2 H, OCH_2CH_2Si), 3.67–3.70 (m, 2 H, OCH_2CH_2Si), 5.58 (br. s, 2 H, NH_2), 5.68 (s, 2 H, NCH_2O), 6.59 (s, 1 H, H-5), 7.14 (dd, $J_{4,5}$ = 5.1, $J_{4,3}$ = 3.6 Hz, 1 H, H-4-thienyl), 7.38 (dd, $J_{5,4}$ = 5.1, $J_{5,3}$ = 1.2 Hz, 1 H, H-5-thienyl), 7.58 (dd, $J_{3,4}$ = 3.6, $J_{3,5}$ = 1.2 Hz, 1 H, H-3-thienyl), 8.33 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.9 (OCH_2CH_2Si), 66.4 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3455, 3291, 3159, 3090, 2950, 2914, 1643, 1592, 1547, 1476, 1311, 1248, 1081, 863, 854, 833, 707 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (24d): Starting from pyrrolo[2,3-*d*]pyrimidine **23d** (393 mg, 1 mmol), the reaction was performed according to the General Procedure to give **24d** (280 mg, 85%) as a yellowish solid, m.p. 153 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = –0.07 (s, 9 H, CH_3Si), 0.91–0.94 (m, 2 H, OCH_2CH_2Si), 3.61–3.64 (m, 2 H, OCH_2CH_2Si), 5.64 (br. s, 2 H, NH_2), 5.75 (s, 2 H, NCH_2O), 6.53 (dd, $J_{4,3}$ = 3.4, $J_{4,5}$ = 1.8 Hz, 1 H, H-4-furyl), 6.72 (s, 1 H, H-5), 6.92 (dd, $J_{3,4}$ = 3.4, $J_{3,5}$ = 0.8 Hz, 1 H, H-3-furyl), 7.53 (dd, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.8 Hz, 1 H, H-5-furyl), 8.31 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.8 (OCH_2CH_2Si), 66.2 (OCH_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) ppm. HRMS (ESI): *m*/*z* calcd. 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 (24e): Starting from pyrrolo[2,3-*d*]pyrimidine **23e** (410 mg, 1 mmol), the reaction was performed according to the General Procedure to give **24e** (292 mg, 84%) as a white solid, m.p. 159 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = –0.04 (s, 9 H, CH_3Si), 0.96–0.99 (m, 2 H, OCH_2CH_2Si), 3.72–3.75 (m, 2 H, OCH_2CH_2Si), 5.42 (br. s, 2 H, NH_2), 5.64 (s, 2 H, NCH_2O), 6.53 (s, 1 H, H-5), 7.42 (dd, $J_{5,4}$ = 5.0, $J_{5,2}$ = 2.9 Hz, 1 H, H-5-thienyl), 7.44 (dd, $J_{4,5}$ = 5.0, $J_{4,2}$ = 1.4 Hz, 1 H, H-4-thienyl), 7.84 (dd, $J_{2,5}$ = 2.9, $J_{2,4}$ = 1.3 Hz, 1 H, H-2-thienyl), 8.34 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 18.0 (OCH_2CH_2Si), 66.5 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3446, 3288, 3135, 3102, 2950, 2917, 2890, 1634, 1595, 1556, 1470, 1302, 1293, 1251, 1081, 860, 836 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (24f): Starting from pyrrolo[2,3-*d*]pyrimidine **23f** (394 mg, 1 mmol), the reaction was performed according to the General Procedure to give **24f** (248 mg, 71%) as a white solid. ^1H NMR (500 MHz, $CDCl_3$): δ = –0.05 (s, 9 H, CH_3Si), 0.93–0.97 (m, 2 H, OCH_2CH_2Si), 3.65–3.69 (m, 2 H, OCH_2CH_2Si), 5.57 (br. s, 2 H, NH_2), 5.63 (s, 2 H, NCH_2O), 6.51 (s, 1 H, H-5), 6.76 (dd, $J_{4,5}$ = 1.9, $J_{4,2}$ = 0.9 Hz, 1 H, H-4-furyl), 7.51 (t, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, 1 H, H-5-furyl), 7.97 (dd, $J_{2,5}$ = 1.5, $J_{2,4}$ = 0.9 Hz, 1 H, H-2-thienyl), 8.31 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.4 (CH_3Si), 17.9 (OCH_2CH_2Si), 66.3 (OCH_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) ppm. HRMS (ESI): *m*/*z* calcd. 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 (24g): Starting from pyrrolo[2,3-*d*]pyrimidine deazapurine **23g** (465 mg, 1 mmol), the reaction was performed according to the General Procedure to give **24g** (374 mg, 93%) as a white solid, m.p. 104 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = –0.10 (s, 9 H, CH_3Si), 0.80–0.83 (m, 2 H,

OCH_2CH_2Si), 3.47–3.49 (m, 2 H, OCH_2CH_2Si), 4.01 (s, 3 H, CH_3O-4′), 4.07 (s, 3 H, CH_3O-2′), 5.50 (s, 2 H, NCH_2O), 5.58 (br. s, 2 H, NH_2), 6.51 (s, 1 H, H-5), 8.35 (s, 1 H, H-2), 8.43 (s, 1 H, H-6′) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.8 (OCH_2CH_2Si), 54.4 (CH_3O-4′), 55.1 (CH_3O-2′), 66.3 (OCH_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′) ppm. IR (KBr): $\tilde{\nu}$ = 3437, 3413, 3339, 3219, 3138, 2959, 2896, 1646, 1610, 1586, 1559, 1473, 1398, 1377, 1299, 1251, 1087, 1015, 866, 833 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (24l): Starting from pyrrolo[2,3-*d*]pyrimidine deazapurine **23l** (130 mg, 0.33 mmol), the reaction was performed according to the General Procedure to give **24l** (100 mg, 90%) as a white solid, m.p. 140 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.06 (s, 9 H, CH_3Si), 0.90–0.93 (m, 2 H, OCH_2CH_2Si), 3.57–3.60 (m, 2 H, OCH_2CH_2Si), 5.71 (s, 2 H, NCH_2O), 5.80 (br. s, 2 H, NH_2), 6.96 (q, $J_{5,F}$ = 1.1 Hz, 1 H, H-5), 8.40 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.6 (CH_3Si), 17.7 (OCH_2CH_2Si), 66.8 (OCH_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) ppm. ^{19}F NMR (470.3 MHz, $CDCl_3$): δ = –56.03 (s, 1 F, F-2) ppm. IR (KBr): $\tilde{\nu}$ = 3135, 2953, 2929, 1655, 1601, 1562, 1544, 1365, 1314, 1251, 1180, 1129, 1120, 869, 836 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{13}H_{20}ON_4F_3Si$ 333.1353; found 333.1353.

Deprotection of SEM Group; General Procedure: A SEM-protected pyrrolo[2,3-*d*]pyrimidine **19a**–**h**, **19j**–**l**, **24a**–**g**, **24l**, or **27j**–**l** was dissolved in trifluoroacetic acid (2 mL) and the reaction mixture was stirred at room temp. for 30 min. The mixture was then diluted with $NaHCO_3$ (to pH 7) and EtOAc (25 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (×2). The combined organic layers were dried with sodium sulfate, and concentrated under reduced pressure to give a solid. Aq. ammonia (25% w/w, 15 mL) was added and the mixture was stirred at room temp. overnight to form white precipitate of product, which was isolated by filtration.

4-Methoxy-6-(4-methoxyphenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (21a): Starting from pyrrolo[2,3-*d*]pyrimidine **19a** (772 mg, 2 mmol), the reaction was performed according to the General Procedure to give **21a** (458 mg, 90%) as a white solid, m.p. 278 °C. ^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, CH_3O-*p*), 4.04 (s, 3 H, CH_3O-4), 6.83 (s, 1 H, H-5), 7.01–7.03 (m, 2 H, H-*m*-C_6H_4OMe), 7.85–7.87 (m, 2 H, H-*o*-C_6H_4OMe), 8.36 (s, 1 H, H-2), 12.41 (br. s, 1 H, NH) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3150, 3013, 2995, 2941, 2842, 1622, 1598, 1544, 1503, 1482, 1332, 1254, 1177, 1126, 1024, 976, 890, 827, 773 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{14}H_{14}O_2N_3$ 256.1081; found 256.1081.

4-Methoxy-6-(pyridin-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (21b): Starting from pyrrolo[2,3-*d*]pyrimidine **19b** (356 mg, 1 mmol), the reaction was performed according to the General Procedure to give **21b** (192 mg, 85%) as a white solid, m.p. >350 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 4.06 (s, 3 H, CH_3O), 7.20 (s, 1 H, H-5), 7.34 (ddd, $J_{5,4}$ = 7.5, $J_{5,6}$ = 4.8 Hz, $J_{5,3}$ = 1.1 Hz, 1 H, H-5-py), 7.89 (td, $J_{4,5}$ = $J_{4,3}$ = 7.8, $J_{4,6}$ = 1.8 Hz, 1 H, H-4-py), 8.06 (dt, $J_{3,4}$ = 8.0, $J_{3,5}$ = $J_{3,6}$ = 1.1 Hz, 1 H, H-2-furyl), 8.41 (s, 1 H, H-2), 8.64 (ddd, $J_{6,5}$ = 4.8, $J_{6,4}$ = 1.8 Hz, $J_{6,3}$ = 1.0 Hz, 1 H, H-6-py), 12.64 (v. br. s., 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]-DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3066, 3007, 2983, 2935, 2857, 2797, 1601, 1589, 1580, 1479, 1458, 1443, 1410, 1329, 1278, 1242, 1180, 1126, 979, 887, 842, 752 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (21c): Starting from pyrrolo[2,3-*d*]pyrimidine **19c** (724 mg, 2 mmol), the reaction was performed according to the General Procedure to give **21c** (416 mg, 90%) as a yellowish solid, m.p. 227 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 4.04 (s, 3 H, CH_3O), 6.68 (s, 1 H, H-5), 7.15 (dd, $J_{4,5}$ = 5.1, $J_{4,3}$ = 3.6 Hz, 1 H, H-4-thienyl), 7.58 (br. d, $J_{5,4}$ = 5.1 Hz, 1 H, H-5-thienyl), 7.62 (br. d, $J_{3,4}$ = 3.6 Hz, 1 H, H-3-thienyl), 8.38 (s, 1 H, H-2), 12.60 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3210, 3123, 3069, 2988, 2947, 2875, 2842, 1610, 1592, 1562, 1485, 1407, 1344, 1329, 1299, 1216, 1183, 1123, 973, 890, 773, 695 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (21d): Starting from pyrrolo[2,3-*d*]pyrimidine **19d** (345 mg, 1 mmol), the reaction was performed according to the General Procedure to give **21d** (172 mg, 80%) as a white solid, m.p. 243 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 4.04 (s, 3 H, CH_3O), 6.64 (dd, $J_{4,3}$ = 3.4, $J_{4,5}$ = 1.8 Hz, 1 H, H-4-furyl), 6.67 (s, 1 H, H-5), 6.99 (dd, $J_{3,4}$ = 3.4, $J_{3,5}$ = 0.8 Hz, 1 H, H-3-furyl), 7.79 (dd, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.8 Hz, 1 H, H-5-furyl), 8.38 (s, 1 H, H-2), 12.59 (v. br. s., 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (21e): Starting from pyrrolo[2,3-*d*]pyrimidine **19e** (723 mg, 1 mmol), the reaction was performed according to the General Procedure to give **21e** (414 mg, 90%) as a white solid, m.p. 232 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 4.04 (s, 3 H, CH_3O), 6.85 (s, 1 H, H-5), 7.66 (dd, $J_{5,4}$ = 5.1, $J_{5,2}$ = 2.9 Hz, 1 H, H-5-thienyl), 7.69 (dd, $J_{4,5}$ = 5.1, $J_{4,2}$ = 1.4 Hz, 1 H, H-4-thienyl), 8.00 (dd, $J_{2,5}$ = 2.9, $J_{2,4}$ = 1.4 Hz, 1 H, H-2-thienyl), 8.37 (s, 1 H, H-2), 12.47 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3216, 3126, 3081, 3066, 3016, 2983, 2944, 2863, 1610, 1592, 1562, 1479, 1341, 1323, 1180, 1126, 973, 899, 878, 770, 653 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (21f): Starting from pyrrolo[2,3-*d*]pyrimidine **19f** (691 mg, 2 mmol), the reaction was performed according to the General Procedure to give **21f** (281 mg, 65%) as a white solid, m.p. 218 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 4.04 (s, 3 H, CH_3O), 6.79 (d, $J_{5,NH}$ = 2.1 Hz, 1 H, H-5), 7.05 (dd, $J_{4,5}$ = 1.9, $J_{4,2}$ = 0.8 Hz, 1 H, H-4-furyl), 7.77 (t, $J_{5,2}$ = $J_{5,4}$ = 1.7 Hz, 1 H, H-5-furyl), 8.21 (br. dd, $J_{2,5}$ = 1.5, $J_{2,4}$ = 0.8 Hz, 1 H, H-2-furyl), 8.36 (s, 1 H, H-2), 12.37 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3216, 3174, 3141, 3129, 3001, 2944, 2899, 2860, 1604, 1586, 1491, 1338, 1332, 1159, 1129, 1072, 973, 872, 767, 650, 588 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (21h): Pyrrolo[2,3-*d*]pyrimidine **19h** (1.02 g, 2.75 mmol) was used according to the General Procedure. Crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH, 10:1) to give **21h** (147 mg, 22%) as a yellowish solid, m.p. 296 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 4.04 (s, 3 H, CH_3O), 5.15 (br. s, 2 H, NH_2), 6.57 (ddd, $J_{6',5'}$ = 7.8, $J_{6',2'}$ = 2.2 Hz, $J_{6',4'}$ = 1.2 Hz, 1 H, H-6′), 6.71 (s, 1 H, H-5), 7.02–7.06 (m, 2 H, H-2′,4′), 7.09 (t, $J_{5',4'} = J_{5',6'}$ = 7.9 Hz, 1 H, H-5′), 8.36 (s, 1 H, H-2), 12.38 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3330, 3225, 3126, 1983, 2947, 1598, 1586, 1479, 1355, 1126, 776 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{13}H_{13}ON_4$ 241.1084; found 241.1084.

6-(Uracil-5-yl)-pyrrolo[2,3-*d*]pyrimidin-4-one (22i): Pyrrolo[2,3-*d*]pyrimidine **19g** (731 mg, 1.75 mmol) was deprotected according to the General Procedure directly followed by heating to reflux in a solution of THF/dioxane/HCl (1:1:1, 9 mL) for 2 h. The reaction mixture was evaporated and ethanol (5 mL) was added. The mixture was then kept in a refrigerator overnight to furnish **22i** (416 mg, 97%) as yellowish crystals, m.p. > 350 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 7.00 (d, $J_{5,NH}$ = 2.3 Hz, 1 H, H-5), 7.83 (s, 1 H, H-2), 7.97 (d, $J_{6',NH}$ = 6.1 Hz, 1 H, H-6′), 11.31 (dd, $J_{NH,6'}$ = 6.1, $J_{NH,NH}$ = 1.8 Hz, 1 H, NH-1′), 11.39 (d, $J_{NH,NH}$ = 1.8 Hz, 1 H, NH-3′), 11.85 (v. br. s, 1 H, NH-3), 11.90 (d, $J_{NH,5}$ = 2.3 Hz, 1 H, NH-7) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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′) ppm. IR (KBr): $\tilde{\nu}$ = 3261, 3219, 3183, 3156, 3114, 3063, 2908, 1706, 1682, 1583, 1565, 1524, 1416, 1257, 1227, 1192, 914, 824, 782, 555 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (25a): Starting from pyrrolo[2,3-*d*]pyrimidine **24a** (148 mg, 0.4 mmol), the reaction was performed according to the General Procedure to give **25a** (77 mg, 80%) as a white solid, m.p. 324 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 3.79 (s, 3 H, CH_3O), 6.76 (d, $J_{5,NH}$ = 2.2 Hz, 1 H, H-5), 6.88 (br. s, 2 H, NH_2), 7.00–7.02 (m, 2 H, H-*m*-Ph), 7.69–7.71 (m, 2 H, H-*o*-Ph), 8.01 (s, 1 H, H-2), 11.87 (br. d, $J_{NH,5}$ = 2.0 Hz, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. HRMS (ESI): *m*/*z* calcd. 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 (25b): Starting from pyrrolo[2,3-*d*]pyrimidine **24b** (256 mg, 0.75 mmol), the reaction was performed according to the General Procedure to give **25b** (117 mg, 74%) as a white solid, m.p. 326 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 7.08 (br. s, 2 H, NH_2), 7.23 (br. s, 1 H, H-5), 7.25–7.28 (m, 1 H, H-5-py), 7.82–7.88 (m, 2 H, H-3,4-py), 8.07 (s, 1 H, H-2), 8.59 (dt, $J_{6,5}$ = 4.7, $J_{6,4} = J_{6,3}$ = 1.4 Hz, 1 H, H-6-py), 12.08 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3398, 3078, 2971, 2923, 2845, 2809, 1637, 1622, 1595, 1580, 1464, 1443, 1359, 1284, 758 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (25c): Starting from pyrrolo[2,3-*d*]pyrimidine **24c** (347 mg, 1 mmol), the reaction was performed according to the General Procedure to give **25c** (160 mg, 74%) as a greyish solid, m.p. 345 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.73 (s, 1 H, H-5), 6.96 (br. s, 2 H, NH_2), 7.11 (dd, $J_{4,5}$ = 5.1, $J_{4,3}$ = 3.6 Hz, 1 H, H-4-thienyl), 7.46–7.50 (m, 2 H, H-3,5-thienyl), 8.03 (s, 1 H, H-2), 12.06 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3464, 3300, 3117, 3108, 3096, 2988, 1637, 1586, 1556, 1485, 1314, 764, 698 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{10}H_9N_4S$ 217.0542; found 217.0543.

6-(Furan-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine (25d): Pyrrolo[2,3-*d*]pyrimidine **24d** (248 mg, 0.75 mmol) was deprotected according to the General Procedure. Crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH, 10:1) to give **25d** (119 mg, 79%) as a white solid, m.p. 300 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.59 (dd, $J_{4,3}$ = 3.4, $J_{4,5}$ = 1.8 Hz, 1 H, H-4-furyl), 6.76 (d, $J_{5,NH}$ = 1.9 Hz, 1 H, H-5), 6.83 (dd, $J_{3,4}$ = 3.4, $J_{3,5}$ = 0.9 Hz, 1 H, H-3-furyl), 7.00 (br. s, 2 H, NH_2), 7.72 (dd, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.9 Hz, 1 H, H-5-furyl), 8.03 (s, 1 H, H-2), 11.99 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3461, 3309, 3150, 3117, 3102, 2980, 2839, 1640, 1592, 1574, 1476, 1302, 1015, 767 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{10}H_9ON_4$ 201.0771; found 201.0771.

6-(Thiophen-3-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine (25e): Pyrrolo[2,3-*d*]pyrimidine **24e** (260 mg, 0.75 mmol) was deprotected according to the General Procedure. Crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH, 10:1) to give **25e** (117 mg, 72%) as a white solid, m.p. > 350 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.74 (d, $J_{5,NH}$ = 2.2 Hz, 1 H, H-5), 6.91 (br. s, 2 H, NH_2), 7.48 (dd, $J_{4,5}$ = 5.0, $J_{4,2}$ = 1.3 Hz, 1 H, H-4-thienyl), 7.64 (dd, $J_{5,4}$ = 5.0, $J_{5,2}$ = 2.9 Hz, 1 H, H-5-thienyl), 7.82 (dd, $J_{2,5}$ = 2.9, $J_{2,4}$ = 1.3 Hz, 1 H, H-2-thienyl), 8.02 (s, 1 H, H-2), 11.92 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3467, 3297, 3111, 3087, 3025, 2905, 1646, 1595, 1562, 1485, 1320, 791, 761 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{10}H_9N_4S$ 217.0542; found 217.0543.

6-(Furan-3-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine (25f): Pyrrolo[2,3-*d*]pyrimidine **24f** (247 mg, 0.75 mmol) was deprotected according to the General Procedure. Crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH, 10:1) to give **25f** (98 mg, 65%) as a white solid, m.p. > 350 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.63 (d, $J_{5,NH}$ = 2.1 Hz, 1 H, H-5), 6.84 (dd, $J_{4,5}$ = 1.9, $J_{4,2}$ = 0.9 Hz, 1 H, H-4-furyl), 6.88 (br. s, 2 H, NH_2), 7.75 (t, $J_{5,4} = J_{5,2}$ = 1.7 Hz, 1 H, H-5-furyl), 8.01 (s, 1 H, H-2), 8.10 (dd, $J_{2,5}$ = 1.6, $J_{2,4}$ = 0.9 Hz, 1 H, H-2-furyl), 11.81 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3458, 3297, 3168, 3117, 2893, 2929, 2860, 1643, 1592, 1577, 1482, 1335, 1320, 779,

770 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{10}H_9ON_4$ 201.0771; found 201.0771.

6-(Uracil-5-yl)-pyrrolo[2,3-*d*]pyrimidin-4-amine (25i): Pyrrolo[2,3-*d*]pyrimidine **24g** (302 mg, 0.75 mmol) was deprotected according to the General Procedure directly followed by heating to reflux in a solution of THF/dioxane/HCl (1:1:1, 9 mL) for 24 h. The reaction mixture was evaporated and ethanol (5 mL) was added. The mixture was then kept in a refrigerator overnight to furnish **25i** (141 mg, 77%) as yellowish crystals, m.p. >350 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 7.52 (d, $J_{5,NH}$ = 2.2 Hz, 1 H, H-5), 8.15 (d, $J_{6',NH}$ = 6.1 Hz, 1 H, H-6′), 8.32 (s, 1 H, H-2), 11.48 (d, $J_{NH,NH}$ = 1.8 Hz, 1 H, NH-3′), 11.51 (dd, $J_{NH,6'}$ = 6.1, $J_{NH,NH}$ = 1.8 Hz, 1 H, NH-1′), 12.81 (d, $J_{NH,5}$ = 2.2 Hz, 1 H, NH-7) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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′) ppm. IR (KBr): $\tilde{\nu}$ = 3318, 3267, 3150, 3043, 2956, 2851, 2788, 2729, 1709, 1676, 1595, 1574, 1446, 1442, 1245, 1224, 1216, 770 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{10}H_9O_2N_6$ 245.0782; found 245.0782.

4,6-Dichloro-7*H*-pyrrolo[2,3-*d*]pyrimidine (28j): Pyrrolo[2,3-*d*]pyrimidine **27j** (318 mg, 1 mmol) was deprotected according to the General Procedure. Crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH, 10:1) to give **28j** (124 mg, 66%) as a white solid, m.p. 250 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.72 (s, 1 H, H-5), 8.60 (s, 1 H, H-2), 12.48 (v. br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 97.3 (CH-5), 117.3 (C-4a), 127.6 (C-6), 149.4 (C-4), 150.9 (CH-2), 151.4 (C-7a) ppm. IR (KBr): $\tilde{\nu}$ = 3126, 3072, 2962, 2935, 2794, 2678, 2651, 1610, 1565, 1497, 1443, 1338, 1260, 1213, 988, 872, 815 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_6H_3N_3Cl_2$ 186.9704; found 186.9705.

6-Bromo-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidine (28k): Pyrrolo[2,3-*d*]pyrimidine **27k** (363 mg, 1 mmol) was deprotected according to the General Procedure. Crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH, 10:1) to give **28k** (174 mg, 75%) as a white solid, m.p. 258 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.80 (s, 1 H, H-5), 8.58 (s, 1 H, H-2), 13.43 (v. br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 101.2 (CH-5), 114.4 (C-6), 117.6 (C-4a), 149.1 (C-4), 150.8 (CH-2), 152.5 (C-7a) ppm. IR (KBr): $\tilde{\nu}$ = 3123, 3090, 3069, 3022, 2950, 2920, 2875, 2803, 1604, 1559, 1494, 1422, 1335, 1263, 1210, 988, 866, 806 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_6H_3N_3ClBr$ 230.9199; found 230.9200.

4-Chloro-6-(trifluoromethyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (28l): Pyrrolo[2,3-*d*]pyrimidine **27l** (246 mg, 0.7 mmol) was deprotected according to the General Procedure. Crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH, 10:1) to give **28l** (113 mg, 73%) as a white solid, m.p. 191 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 7.30 (q, $J_{5,F}$ = 1.3 Hz, 1 H, H-5), 8.79 (s, 1 H, H-2), 13.92 (v. br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]-DMSO): δ = 101.4 (br. q, $J_{C,F}$ = 3.7 Hz, CH-5), 115.8 (C-4a), 120.7 (br. q, $J_{C,F}$ = 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) ppm. ^{19}F NMR (470.3 MHz, [D$_6$]DMSO): δ = δ = –56.66 (s, 1 F, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3093, 3081, 2992, 2863, 2809, 2758, 2696, 1598, 1577, 1547, 1416, 1314, 1257, 1245, 1222, 1180, 1141, 979, 872 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_7H_3N_3ClF_3$ 220.9968; found 220.9969.

6-Chloro-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidine (21j): Pyrrolo[2,3-*d*]pyrimidine **19j** (471 mg, 1.5 mmol) was deprotected according to the General Procedure. Crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH, 10:1) to give **21j** (150 mg, 55%) as a white solid, m.p. 235 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 4.01 (s, 3 H, CH_3O), 6.52 (s, 1 H, H-5), 8.38 (s, 1 H, H-2), 12.89 (v.br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_7H_7ON_3Cl$ 184.0272; found 184.0272.

6-Bromo-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidine (21k): Starting from pyrrolo[2,3-*d*]pyrimidine **19k** (347 mg, 1.25 mmol), the reaction was performed according to the General Procedure to give **21k** (142 mg, 50%) as a white solid, m.p. 234 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 4.01 (s, 3 H, CH_3O), 6.60 (s, 1 H, H-5), 8.36 (s, 1 H, H-2), 12.84 (v. br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3697, 3129, 3087, 3049, 2988, 2959, 2938, 2866, 2818, 1607, 1589, 1479, 1461, 1413, 1347, 1326, 1141, 979, 896 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_7H_7ON_3{}^{79}Br$ 227.9767; found 227.9768.

4-Methoxy-6-(trifluoromethyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (21l): Pyrrolo[2,3-*d*]pyrimidine **19l** (420 mg, 1.2 mmol) was deprotected according to the General Procedure. Crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH, 10:1) to give **21l** (198 mg, 75%) as a white solid, m.p. 190 °C. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 3.44 (s, 3 H, CH_3O), 7.10 (q, $J_{5,F}$ = 1.3 Hz, 1 H, H-5), 8.54 (s, 1 H, H-2), 13.36 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. ^{19}F NMR (470.3 MHz, [D$_6$]DMSO): δ = –56.00 (s, 1 F, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_8H_7ON_3F_3$ 218.0536; found 218.0534.

6-(Trifluoromethyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine (25l): Pyrrolo[2,3-*d*]pyrimidine **24l** (100 mg, 0.3 mmol) was deprotected according to the General Procedure. Crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH, 10:1) to give **25l** (55 mg, 90%) as a white solid, m.p. >350 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 7.09 (q, $J_{5',F}$ = 1.4 Hz, 1 H, H-5), 7.32 (br. s, 2 H, NH_2), 8.14 (s, 1 H, H-2), 12.68 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. ^{19}F NMR (470.3 MHz, [D$_6$]DMSO): δ = –55.67 (s, 1 F, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3494, 3072, 2983, 2920, 2845, 2809, 2735, 2669, 1661, 1586, 1380, 1329, 1204, 1177, 1120, 1081 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_7H_6N_4F_3$ 203.0539; found 203.0538.

Deprotection of the OMe Group to give Pyrrolo[2,3-*d*]pyrimidin-4-ones; General Procedure: To a stirred mixture of a 4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidine **21a**–**f**, **21h**, or **21l** (0.50 mmol, 1 equiv.) and NaI (272 mg, 2.5 mmol, 5 equiv.) in anhydrous 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 (22a): Starting from pyrrolo[2,3-*d*]pyrimidine **21a** (128 mg, 0.5 mmol), the reaction was performed according to the General Procedure to give **22a** (103 mg, 85%) as a greyish solid, m.p. > 300 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, CH_3O), 6.79 (d, $J_{5,NH}$ = 2.4 Hz, 1 H, H-5), 6.97–6.99 (m, 2 H, H-*m*-C_6H_4OMe), 7.75–7.76

(m, 2 H, H-*o*-C_6H_4OMe), 7.84 (bd, $J_{2,NH}$ = 3.2 Hz, 1 H, H-2), 11.81 (br. s, 1 H, NH-3), 12.22 (br. d, $J_{NH,5}$ = 2.4 Hz, 1 H, NH-7) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (22b): Starting from pyrrolo[2,3-*d*]pyrimidine **21b** (113 mg, 0.5 mmol), the reaction was performed according to the General Procedure to give **22b** (75 mg, 71%) as a greyish solid, m.p. >300 °C. ^1H NMR (500.0 MHz, [D$_6$]DMSO): δ = 7.17 (s, 1 H, H-5), 7.27 (ddd, $J_{5,4}$ = 7.5, $J_{5,6}$ = 4.8 Hz, $J_{5,3}$ = 1.1 Hz, 1 H, H-5-py), 7.83 (ddd, $J_{4,3}$ = 8.0, $J_{4,5}$ = 7.5 Hz, $J_{4,6}$ = 1.8 Hz, 1 H, H-4-py), 7.89 (s, 1 H, H-2), 7.94 (dt, $J_{3,4}$ = 8.0, $J_{3,5}$ = $J_{3,6}$ = 1.1 Hz, 1 H, H-3-py), 8.58 (ddd, $J_{6,5}$ = 4.8, $J_{6,4}$ = 1.8 Hz, $J_{6,3}$ = 1.0 Hz, 1 H, H-6-py), 11.89 (br. s, 1 H, NH-3), 12.48 (br. s, 1 H, NH-7) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3111, 3043, 2956, 2908, 2854, 2830, 1667, 1595, 1568, 1529, 1467, 1443, 1428, 1257, 1210, 1156, 919, 878, 836, 752 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (22c): Starting from pyrrolo[2,3-*d*]pyrimidine **21c** (231 mg, 1 mmol), the reaction was performed according to the General Procedure to give **22c** (195 mg, 90%) as a yellowish solid, m.p. > 350 °C. ^1H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.62 (s, 1 H, H-5), 7.08–7.10 (m, 1 H, H-4-thienyl), 7.45–7.48 (m, 2 H, H-3,5-thienyl), 7.86 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3198, 3138, 3105, 3072, 3037, 2959, 2911, 2845, 1673, 1589, 1535, 1494, 1431, 1386, 1254, 1195, 919, 856, 770, 683 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (22d): Starting from pyrrolo[2,3-*d*]pyrimidine **21d** (65 mg, 0.3 mmol), the reaction was performed according to the General Procedure to give product **22d** (55 mg, 92%) as a greyish solid, m.p. > 350 °C. ^1H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.57 (dd, $J_{4,3}$ = 3.4, $J_{4,5}$ = 1.8 Hz, 1 H, H-4-furyl), 6.61 (s, 1 H, H-5), 7.79 (dd, $J_{3,4}$ = 3.4, $J_{3,5}$ = 0.8 Hz, 1 H, H-3-furyl), 7.69 (dd, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.8 Hz, 1 H, H-5-furyl), 7.84 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (22e): Starting from pyrrolo[2,3-*d*]pyrimidine **21e** (231 mg, 1 mmol), the reaction was performed according to the General Procedure to give **22e** (152 mg, 70%) as a greyish solid, m.p. > 350 °C. ^1H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.80 (s, 1 H, H-5), 7.60 (dd, $J_{4,5}$ = 5.0, $J_{4,2}$ = 1.5 Hz, 1 H, H-4-thienyl), 7.61 (dd, $J_{5,4}$ = 5.0, $J_{5,2}$ = 2.7 Hz, 1 H, H-5-thienyl), 7.84 (dd, $J_{2,5}$ = 2.7, $J_{2,4}$ = 1.5 Hz, 1 H, H-2-thienyl), 7.86 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (22f): Starting from pyrrolo[2,3-*d*]pyrimidine **21f** (215 mg, 1 mmol), the reaction was performed according to the General Procedure to give **22f** (160 mg, 80%) as a greyish solid, m.p. > 350 °C. ^1H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.69 (s, 1 H, H-5), 6.97 (dd, $J_{4,5}$ = 1.9, $J_{4,2}$ = 0.9 Hz, 1 H, H-4-furyl), 7.72 (t, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, 1 H, H-5-furyl), 7.84 (s, 1 H, H-2), 8.10 (dd, $J_{2,5}$ = 1.5, $J_{2,4}$ = 0.9 Hz, 1 H, H-2-furyl) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3105, 3037, 2965, 2848, 2806, 2717, 2663, 1679, 1562 cm^{-1}. 1601, 1559, 1425, 1389, 1242, 1213. HRMS (ESI): *m*/*z* calcd. 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 (22h): Starting from pyrrolo[2,3-*d*]pyrimidine **21h** (120 mg, 0.5 mmol), the reaction was performed according to the General Procedure to give **22h** (85 mg, 75%) as a greyish solid, m.p. > 350 °C. ^1H NMR (500.0 MHz, [D$_6$]DMSO): δ = 5.10 (br. s, 2 H, NH_2), 6.50 (ddd, $J_{6',5'}$ = 7.9, $J_{6',2'}$ = 2.2 Hz, $J_{6',4'}$ = 1.1 Hz, 1 H, H-6′), 6.67 (d, $J_{5,NH}$ = 2.2 Hz, 1 H, H-5), 6.94–6.97 (m, 2 H, H-2′,4′), 7.05 (t, $J_{5',4'}$ = $J_{5',6'}$ = 8.0 Hz, 1 H, H-5′), 7.84 (s, 1 H, H-2), 11.82 (br. s, 1 H, NH-3), 12.19 (br. s, 1 H, NH-7) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3401, 3321, 3219, 3147, 3028, 2959, 2899, 2854, 1673, 1613, 1595, 1482, 1263, 1239, 919, 773 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (22l): Starting from pyrrolo[2,3-*d*]pyrimidine **21l** (163 mg, 0.75 mmol), the reaction was performed according to the General Procedure to give **22l** (45 mg, 30%) as a greyish solid, m.p. >350 °C. ^1H NMR (500.0 MHz, [D$_6$]DMSO): δ = 6.88 (s, 1 H, H-5), 7.88 (s, 1 H, H-2), 11.76 (v. br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 103.1 (CH-5), 107.9 (C-4a), 122.2 (br. q, $J_{C,F}$ = 266.8 Hz, CF_3), 123.2 (m, C-6), 144.6 (m, CH-2), 151.6 (m, C-7a), 158.9 (C-4) ppm. ^{19}F NMR (470.3 MHz, $CDCl_3$): δ = –55.36 (s, 1 F, F-2) ppm. IR (KBr): $\tilde{\nu}$ = 3075, 2995, 2920, 2830, 1691, 1592, 1532, 1389, 1219, 1207, 1177, 1123 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_7H_4ON_3F_3Na$ 226.0199; found 226.0198.

One-Pot C–H Borylation/Substitution Sequence; General Procedures

Procedure A: Pyrrolo[2,3-*d*]pyrimidine **1**, **8**, or **9** (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 anhydrous 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 and 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 added and the mixture was heated for 4 h at 80 °C. The solution was cooled to room temperature, diluted with EtOAc (25 mL) and with a saturated aq. solution of NH_4Cl (25 mL). The aqueous solution was then ex-

tracted three times with EtOAc and the combined organic layers were dried with Na_2SO_4, filtered, and the solvents were evaporated under vacuum. The crude product was purified by flash chromatography (HPFC; hexane/EtOAc).

Procedure B: Performed as described in Procedure A, but using $CuBr_2$ (1.34 g, 6.0 mmol, 3 equiv.) instead of $CuCl_2$.

Procedure C: Pyrrolo[2,3-*d*]pyrimidine **1**, **8**, **9**, or **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 anhydrous 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, then the crude mixture was dissolved in CH_2Cl_2 (8 mL). The solution was transferred by using 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 h. The solution was then cooled to room temperature, and CH_2Cl_2 (25 mL) and a saturated solution of NH_4Cl (25 mL) were added. The aqueous solution was then extracted two times with CH_2Cl_2 and the combined organic layers were dried with Na_2SO_4, filtered, and the solvents were evaporated under vacuum. The crude product was purified by flash chromatography (HPFC; hexane/EtOAc).

Procedure D: Pyrrolo[2,3-*d*]pyrimidine **1** (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 anhydrous 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, then the residue was dissolved in acetone (10 mL) and $Cu(NO_3)_2·3H_2O$ (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 °C for 2.5 h. The solution was cooled to room temp., and EtOAc (15 mL) and a saturated solution of NH_4Cl (15 mL) were added. The aqueous solution was then extracted three times with EtOAc and the combined organic layers were dried with Na_2SO_4, filtered, and the solvents were evaporated under vacuum. The crude product was purified by flash chromatography (HPFC; hexane/EtOAc).

7-Benzyl-6-chloro-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (26j): Starting from **1** (285 mg, 1 mmol), the reaction was performed according to General Procedure A to give **26j** (146 mg, 46%) as a yellowish solid, m.p. 118 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.58 (s, 2 H, CH_2-Bn), 6.82 (s, 1 H, H-5), 7.26–7.34 (m, 5 H, H-*o*,*m*,*p*-Bn), 7.48–7.58 (m, 3 H, H-*m*,*p*-Ph), 8.06–8.08 (m, 2 H, H-*o*-Ph), 8.98 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 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) ppm. HRMS (ESI): *m*/*z* calcd. 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): Starting from **1** (285 mg, 1 mmol), the reaction was performed according to General Procedure B to give **26k** (229 mg, 63%) as a yellowish solid, m.p. 110 °C. ^{1}H NMR (499.8 MHz, $CDCl_3$): δ = 5.60 (s, 2 H, CH_2Ph), 6.98 (s, 1 H, H-5), 7.26–7.33 (m, 5 H, H-*o*,*m*,*p*-Bn), 7.51–7.58 (m, 3 H, H-*m*,*p*-Ph), 8.08–8.10 (m, 2 H, H-*o*-Ph), 8.97 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 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) ppm. HRMS (ESI): *m*/*z* calcd. 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 (26l): Starting from **1** (285 mg, 1 mmol), the reaction was performed according to General Procedure C to give **26l** (120 mg, 34%) as a white solid. ^{1}H NMR (499.8 MHz, $CDCl_3$): δ = 5.68 (s, 2 H, CH_2Ph), 7.18–7.19 (m, 2 H, H-*o*-Bn), 7.26–7.31 (m, 3 H, H-*m*,*p*-Bn), 7.30 (q, $J_{H,F}$ = 1.1 Hz, 1 H, H-5), 7.54–7.61 (m, 3 H, H-*m*,*p*-Ph), 8.10–8.12 (m, 2 H, H-*o*-Ph), 9.10 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 46.8 (CH_2Ph), 103.7 (q, $J_{C,F}$ = 4.3 Hz, CH-5), 116.9 (C-4a), 120.7 (q, $J_{C,F}$ = 269.2 Hz, CF_3), 126.9 (CH-*o*-Bn), 127.8 (CH-*p*-Bn), 128.1 (q, $J_{C,F}$ = 38.1 Hz, 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) ppm. ^{19}F{^{1}H} NMR (470.3 MHz, $CDCl_3$): δ = –55.79 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{20}H_{15}N_3F_3$ 354.1213; found 354.1214.

7-Benzyl-6-cyano-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (26m): Starting from **1** (143 mg, 0.5 mmol), the reaction was performed according to General Procedure D to give **26m** (90 mg, 58%) as a white solid, m.p. 123 °C. ^{1}H NMR (499.8 MHz, $CDCl_3$): δ = 5.65 (s, 2 H, CH_2Ph), 7.31–7.33 (m, 1 H, H-*p*-Bn), 7.35–7.36 (m, 2 H, H-*m*-Bn), 7.42–7.44 (m, 2 H, H-*o*-Bn), 7.49 (s, 1 H, H-5), 7.56–7.59 (m, 3 H, H-*m*,*p*-Ph), 8.06–8.08 (m, 2 H, H-*o*-Ph), 9.14 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 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) ppm. HRMS (ESI): *m*/*z* calcd. 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 (27j): Starting from **8** (568 mg, 2 mmol), the reaction was performed according to General Procedure A to give **27j** (350 mg, 55%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.06 (s, 9 H, CH_3Si), 0.90–0.94 (m, 2 H, OCH_2CH_2Si), 3.58–3.61 (m, 2 H, OCH_2CH_2Si), 5.70 (s, 2 H, NCH_2O), 6.62 (s, 1 H, H-5), 8.65 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.7 (OCH_2CH_2Si), 67.1 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (27k): Starting from **8** (568 mg, 2 mmol), the reaction was performed according to General Procedure B to give **27k** (403 mg, 56%) as a white solid, m.p. 49 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.06 (s, 9 H, CH_3Si), 0.90–0.94 (m, 2 H, OCH_2CH_2Si), 3.57–3.60 (m, 2 H, OCH_2CH_2Si), 5.71 (s, 2 H, NCH_2O), 6.77 (s, 1 H, H-5), 8.64 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.7 (OCH_2CH_2Si), 67.0 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (27l): Starting from **8** (568 mg, 2 mmol), the reaction was performed according to General Procedure C to give **27l** (264 mg, 38%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.06 (s, 9 H, CH_3Si), 0.91–0.94 (m, 2 H, OCH_2CH_2Si), 3.57–3.61 (m, 2 H, OCH_2CH_2Si), 5.79 (s, 2 H, NCH_2O), 7.12 (q, $J_{5,F}$ = 1.1 Hz, 1 H, H-5), 8.79 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.6 (CH_3Si), 17.7 (OCH_2CH_2Si), 67.2 (OCH_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) ppm. ^{19}F NMR (470.3 MHz, $CDCl_3$): δ = –56.61 (s, 1 F, F-2) ppm. IR (KBr): $\tilde{\nu}$ = 3950, 2929, 2899, 1592, 1553, 1544, 1446, 1431, 1413, 1371, 1353, 1248, 1189, 1147, 1096, 860, 842 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (19j): Starting from **9** (1116 mg, 4 mmol), the reaction was performed according to General Procedure A to give **19j** (590 mg, 47%) as a white solid, m.p. 80 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.07 (s, 9 H, CH_3Si), 0.90–0.93 (m, 2 H, OCH_2CH_2Si), 3.57–3.60 (m, 2 H, OCH_2CH_2Si), 4.10 (s, 3 H, CH_3O), 5.66 (s, 2 H, NCH_2O), 6.51 (s, 1 H, H-5), 8.47 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.7 (OCH_2CH_2Si), 53.8 (CH_3O), 66.6 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 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 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (19k): Starting from **9** (1116 mg, 4 mmol), the reaction was performed according to General Procedure B to give **19k** (490 mg, 34%) as a white solid, m.p. 82 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.06 (s, 9 H, CH_3Si), 0.90–0.93 (m, 2 H, OCH_2CH_2Si), 3.56–3.60 (m, 2 H, OCH_2CH_2Si), 4.11 (s, 3 H, CH_3O), 5.67 (s, 2 H, NCH_2O), 6.65 (s, 1 H, H-5), 8.45 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.5 (CH_3Si), 17.7 (OCH_2CH_2Si), 53.8 (CH_3O), 66.6 (OCH_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) ppm. IR (KBr): $\tilde{\nu}$ = 3099, 2953, 2914, 1896, 1863, 1595, 1473, 1461, 1416, 1383, 1353, 1317, 1242, 1227, 1093, 911, 842 cm^{-1}. HRMS (ESI): *m*/*z* calcd. 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 (19l): Starting from **9** (1116 mg, 4 mmol), the reaction was performed according to General Procedure C to give **19l** (472 mg, 34%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.07 (s, 9 H, CH_3Si), 0.90–0.93 (m, 2 H, OCH_2CH_2Si), 3.56–3.59 (m, 2 H, OCH_2CH_2Si), 4.14 (s, 3 H, CH_3O), 5.75 (s, 2 H, NCH_2O), 7.02 (q, $J_{5,F}$ = 1.2 Hz, 1 H, H-5), 8.58 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.6 (CH_3Si), 17.7 (OCH_2CH_2Si), 54.0 (CH_3O), 66.7 (OCH_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) ppm. ^{19}F NMR (470.3 MHz, $CDCl_3$): δ = –56.07 (s, 1 F, F-2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{14}H_{21}O_2N_3F_3Si$ 348.1350; found 348.1351.

4-(Methylsulfanyl)-6-(trifluoromethyl)-7-[2-(trimethylsilyl)ethoxymethyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (20l): Starting from **10** (1116 mg, 4 mmol), the reaction was performed according to General Procedure C to give **20l** (472 mg, 34%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.06 (s, 9 H, CH_3Si), 0.90–0.93 (m, 2 H, OCH_2CH_2Si), 2.72 (s, 3 H, CH_3S), 3.56–3.59 (m, 2 H, OCH_2CH_2Si), 5.75 (s, 2 H, NCH_2O), 7.01 (q, $J_{5,F}$ = 1.1 Hz, 1 H, H-5), 8.76 (s, 1 H, H-2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –1.6 (CH_3Si), 11.9 (CH_3S), 17.7 (OCH_2CH_2Si), 66.8 (OCH_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) ppm. ^{19}F NMR (470.3 MHz, $CDCl_3$): δ = –56.20 (s, 1 F, F-2) ppm. IR (KBr): $\tilde{\nu}$ = 2953, 2923, 2890, 1556, 1443, 1368, 1275, 1251, 1183, 1153, 1129, 1090, 860, 833 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{14}H_{21}ON_3F_3SSi$ 364.1121; found 364.1123.

4-Amino-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxamide (25m): A solution of **28l** (111 mg, 0.5 mmol) and aq. ammonia (25% w/w, 5 mL) in dioxane (5 mL) was stirred in an autoclave at 120 °C for 18 h. The solvents were then evaporated and the residue was purified by flash chromatography (HPFC; $CHCl_3$/MeOH, 5:1) to give **25m** (45 mg, 50%) as a white powder, m.p. > 350 °C. ^{1}H NMR (500.0 MHz, [D$_6$]DMSO): δ = 7.08 (s, 1 H, H-5), 7.16 (br. s, 2 H, NH_2-4), 7.35 and 7.70 (2×br. s, 2× 1 H, $CONH_2$), 8.07 (s, 1 H, H-2), 11.82 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]-DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3428, 3404, 3330, 3177, 3108, 2995, 2908, 2782, 1694, 1655, 1628, 1598, 1538, 1437, 1386, 1335 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_7H_8ON_5$ 178.0723; found 178.0721.

6-(3-Aminophenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine (25h): A mixture of pyrrolo[2,3-*d*]pyrimidin-4-one **22h** (57 mg, 0.25 mmol), benzyltriethylammonium chloride (114 g, 0.5 mmol), and *N*,*N*-dimethylaniline (35 µL, 0.275 mmol) in anhydrous MeCN (2.5 mL) was stirred at room temp., then phosphorus oxychloride (115 µL, 1.25 mmol) was added. The mixture was stirred at 100 °C for 6 h, then the solvents were evaporated under reduced pressure and the residue was diluted with water and neutralized with aqueous ammonia to pH 7. The 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. The mixture was stirred at 120 °C for 18 h, then the solvents were evaporated and the residue was purified by flash chromatography (HPFC; $CHCl_3$/MeOH, 5:1) to give **25h** (22 mg, 40%) as a brown solid, m.p. >350 °C. ^{1}H NMR (500.0 MHz, [D$_6$]-DMSO): δ = 6.53 (ddd, $J_{6',5'}$ = 8.0, $J_{6',2'}$ = 2.2 Hz, $J_{6',4'}$ = 1.0 Hz, 1 H, H-6′), 6.83 (d, $J_{5,NH}$ = 1.9 Hz, 1 H, H-5), 6.92–6.96 (m, 2 H, H-2′,4′), 7.08 (bt, $J_{5',4'}$ = $J_{5',6'}$ = 7.9 Hz, 1 H, H-5′), 7.32 (br. s, 2 H, NH_2-4), 8.09 (s, 1 H, H-2), 12.07 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]DMSO): δ = 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) ppm. IR (KBr): $\tilde{\nu}$ = 3348, 3120, 2956, 2926, 2851, 1673, 1619, 1601, 1538, 1488, 1317, 1287, 764 cm^{-1}. HRMS (ESI): *m*/*z* calcd. for $C_{12}H_{12}N_5$ 226.1087; found 226.1086.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra of the products.

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