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C–H Phosphonation of Pyrrolopyrimidines: Synthesis of Substituted 7- and 9-Deazapurine-8-phosphonate Derivatives

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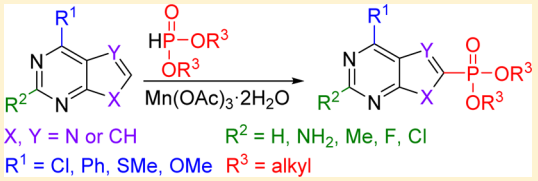
Supporting Information

ABSTRACT: The $Mn(OAc)_3$-promoted C–H phosphonation of 7-deazapurines (pyrrolo[2,3-*d*]pyrimidines) and 9-deazapurines (pyrrolo-[3,2-*d*]pyrimidines) with diethylphosphite was developed. The reactions occur regioselectively at position 8 both in 7 and 9-deazapurines, leading to new deazapurine-8-phosphonate derivatives, which can be further modified and transformed to 6-(het)aryl-deazapurine derivatives or deprotected to free phosphonic acids.



Pyrrolo[2,3-*d*]pyrimidines (7-deazapurines) and pyrrolo-[3,2-*d*]pyrimidines (9-deazapurines) are important carba-analogues of biogenic purine bases (for clarity, we will use the "purine" nomenclature and numbering throughout the paper except for the full names in the Experimental Section).[1] Derivatives bearing multiple substituents at 2, 6, 7, 8 and/or 9 positions of deazapurine heterocycles displayed diverse biological effects. For example, 7,8-diaryl-7-deazaadenine derivatives are potent inhibitors of ACK1 kinase[2] and 7-alkyl-8-arylsulfanyl-7-deazapurines are inhibitors of dihydrofolate reductase.[3] Other related compounds direct the differentiation of neuronal cells,[4] or inhibit EGFR-tyrosine kinase.[5] Therefore, development of regio- and chemoselective synthesis of highly substituted pyrrolopyrimidines is a worthwhile goal. Previous syntheses were mostly based on heterocyclizations[6] or on regio- or chemoselective cross-couplings.[7]

Alternatively, the deazapurine heterocycles can be modified by C–H activations,[8] which are typically orthogonal to the cross-couplings and nucleophilic displacement reactions and thus suitable for combinations in regio- and chemoselective synthesis of series or even libraries of derivatives bearing multiple substituents. Recently, Pd-catalyzed direct C–H arylations,[9] Ir-catalyzed C–H borylations,[10,11] Cu-mediated C–H sulfenylations[12] and Pd/Cu-catalyzed C–H aminations[13] were reported, which all proceeded at position 8 of both 7- or 9-deazapurines and on Ir-catalyzed C–H silylations,[14] which occurred preferentially on an aryl group attached at position 6. To the best of our knowledge, no C–H phosphonations of 7- or 9-deazapurines for introduction of phosphonate groups have been reported yet. Phosphonated deazapurines are attractive targets since phosphonates heterocycles in general display broad spectrum of biological activities,[15] phosphonate-analogues of nucleotides are important antivirals[16] and nucleotide analogues bearing an additional phosphonate group inhibit phosphoribosyl transferases.[17]

Number of oxidative C–H phosphonations of arenes and hetarenes based mostly on the use of Mn(III)[18,19] or Ag(I)[20] promoters have been reported. Phosphonations of purine bases and nucleosides by S_NAr-Arbuzov reaction of halopurines under microwave proceeded at position 6,[21] whereas Mn(III)-mediated phosphonation of uracil and uridine derivatives proceeded at position 5 and at position 7 of caffeine, while the same reaction did not work for adenine.[19] Here, we report on the C–H phosphonations of deazapurines.

We selected 6-phenyl-9-benzyl-7-deazapurine **1a** as a model compound for the study of its C–H phosphonations with diethylphosphite **2a** to screen the reagents and reaction conditions. After some initial experiments with Ag(I), Fe(III) and Co(III) salts which did not work or gave very low conversions, we focused on the use of $Mn(OAc)_3{\cdot}2H_2O$ (Table 1).[18,19] The reaction in AcOH using 3 equiv of $Mn(OAc)_3{\cdot}2H_2O$ at room temperature did not proceed, but when increasing the temperature to 50 or 80 °C, we obtained the desired 8-phosphonated 7-deazapurine product **3a** in 23 or 37% yields, respectively (Entries 2, 3). Increasing or decreasing of the promoter loadings had no positive effect (Entries 4, 5). Further, we tried various solvents (Entries 6–11) and we found out that the mixture of $MeCN/H_2O$ (1:1) resulted in improved 43% yield (Entry 12). Finally, further increasing of the temperature to 100 °C and using a larger excess of diethylphosphite (5 equiv) gave **3a** in 47% yield (Entry 14). We also recovered ca. 15% of the unreacted starting material and the rest was an inseparable mixture of some highly polar compounds, presumably products of oxidative degradation. Prolongation of the reaction time led to higher degree of decomposition. None of other efforts to further improve the yields was successful and therefore we used these conditions as the optimum ones for further synthesis.

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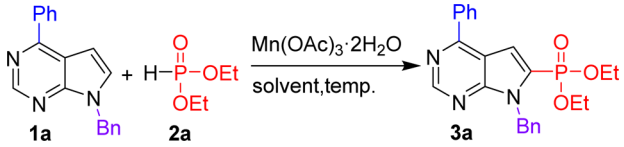
Table 1. Optimization of C−H Phosphonation Reaction of 6-Phenyl-9-benzyl-7-deazapurine 1a with Diethylphosphite



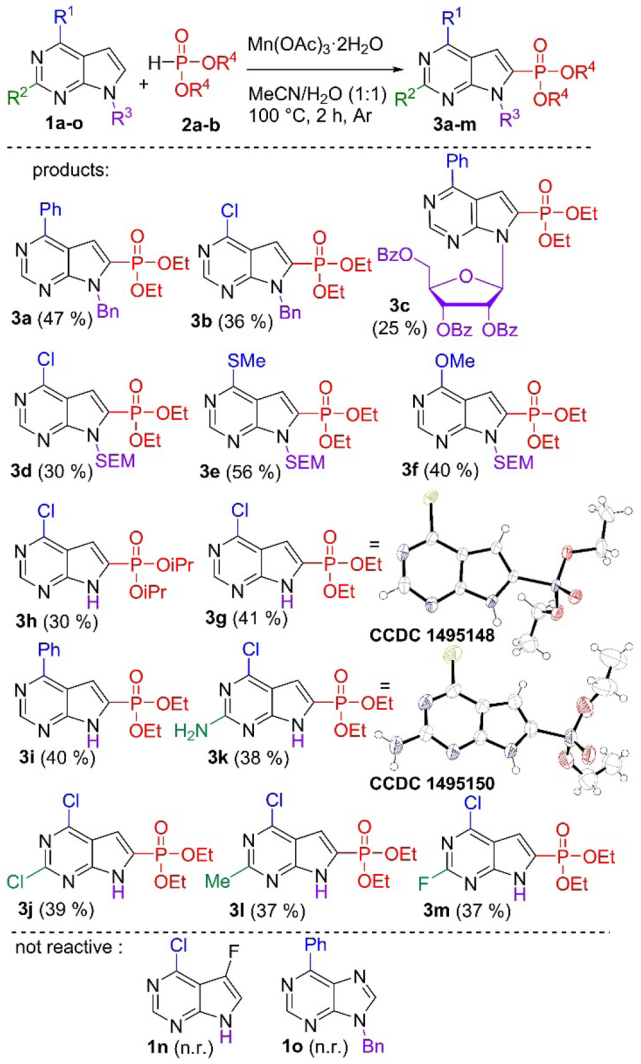
entry	solvent	*T*, °C	yield (%)
1	AcOH	20	n.r.
2	AcOH	50	23
3	AcOH	80	37
4[b]	AcOH	80	32
5[c]	AcOH	80	38
6	DMSO	80	18
7	MeCN	80	35
8	H_2O	80	34
9	AcOH/H_2O	80	36
10	NMP	80	26
11	MeCN	80	33
12	MeCN/H_2O	80	43
13	MeCN/H_2O	100	45
14[d]	**MeCN/H_2O**	**100**	**47**

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

With optimized reaction conditions in hand, our next step was to study the scope and limitation of the method. A series of diverse substituted 7-deazapurines was tested in preparative C−H phosphonation reactions (Scheme 1). The reactions of 6-chloro- and 6-substituted-7-benzyl and 7-(2-trimethylsilyl)-ethoxymethyl)-protected deazapurines **1a,b**, **1d−f** proceeded smoothly to give desired products **3a,b**, **3d−f** in acceptable 36−56% yields. Moreover, the C−H phosphonation of benzoyl-protected nucleoside **1c** resulted in 25% yield of the desired phosphono-nucleoside **3c**. Another useful substrate is 6-chloro-7-deazapurine base **1g** which is suitable for further functional group transformations at positions 6 and 9. In this case, the C−H phosphonation proceeded smoothly to give the desired 9-unsubstituted 6-chloro-8-phosphono-7-deazapurine **3g** in acceptable 41% yield. It also shows that no 9-substitution or protection is needed for the C−H phosphonations. In addition, we tried the reaction of **1g** with more bulky diisopropyl phosphite **2b** to afford the desired product **3h** in somewhat lower 30% yield. Then, we decided to explore preparative C−H phosphonations of different 2- and/or 6-substituted-7-deazapurine bases. In all cases, we obtained desired products **3i−m** in good 37−40% yields. On the other hand, attempted C−H phosphonations of 7-fluoro-7-deazapurine **1n** and 6-phenylpurine base **1o** did not proceed. The structures of compounds **3g** and **3k** were confirmed by X-ray crystallography.

The C−H phosphonation protocol was then tested on 9-deazapurines (Scheme 2). The reactions of 7-benzyl-6-chloro- and -6-phenyl-9-deazapurines **4a,b** proceeded well to give the 8-phosphonated 9-deazapurine products **5a** and **5b** in 30 and 31% yield, respectively. The C−H phosphonation of 7-unsubstituted 6-chloro- and −6-phenyl-9-deazapurine **4c,d** also proceeded to afford the corresponding phosphonated 9-deazapurine bases **5c** and **5d** in 37 or 36% yield, respectively. The structure of compound **5c** was also confirmed by X-ray crystallography.

Scheme 1. Preparative C−H Phosphonations of 7-Deazapurines



To test the synthetic utility of 6-chloro-7-deazapurine phosphonate intermediate **3g**, we performed a series of aqueous-phase Suzuki−Miyaura cross-coupling reactions with different (het)aryl boronic acids (Scheme 3).[22] All of these reactions proceeded smoothly to give a series of 6-substituted-7-deazapurine phosphonate bases **6a−g** in good 60−75% yields.

Our last goal was to develop the method for phosphodiester bond cleavage in order to obtain interesting free phosphonic acid derivatives. The deprotection was performed in two steps by reaction with bromo(trimethyl)silane in acetonitrile[23] with further aqueous workup to hydrolyze the silyl-esters (Scheme 4). We used this protocol for five different 6-chloro- or 6-substituted 7-deazapurine phosphonates either substituted at position 9 with Bn (**3a**) or SEM groups (**3d,e**) or 9-unsubstituted 7-deazapurine phoshphonates **3g,i**. The reactions proceeded in all cases to give the free phosphonic acids in acceptable yields 55−85% (which were slightly reduced by difficult isolation of the products). Interestingly, during the phosphodiester cleavage of phosphonate **3e**, the concomitant cleavage of the (2-trimethylsilyl)ethoxymethyl protecting group was observed due to strong acidic conditions. The deprotection of 6-chloro-7-deazapurine-8-phosphonate **3g** with TMSBr led

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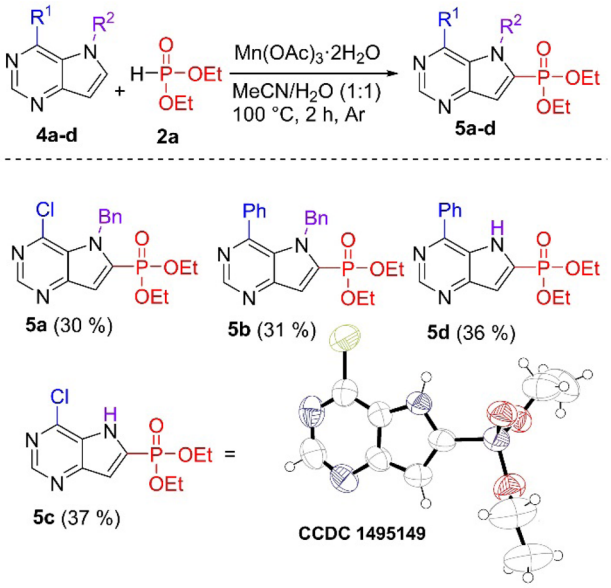
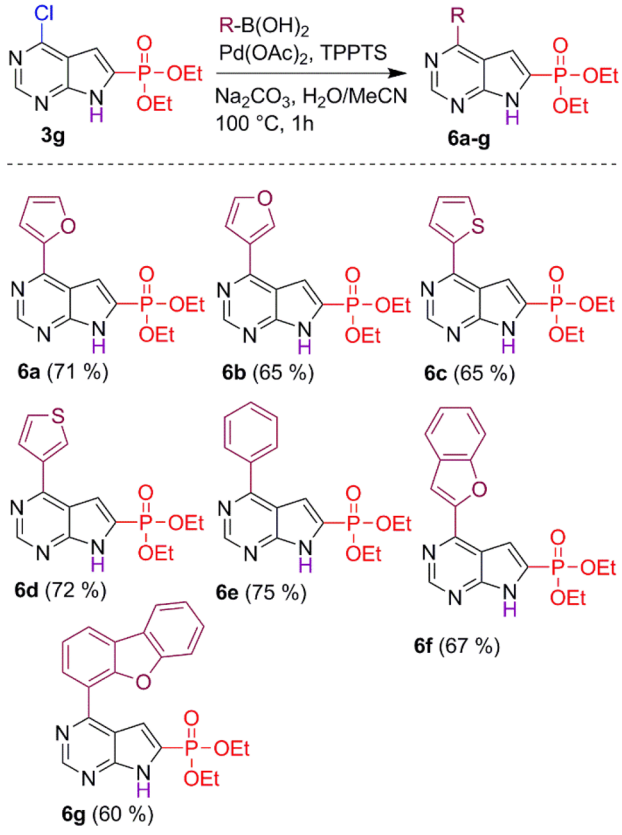
Scheme 2. Preparative C−H Phosphonations of 9-Deazapurines

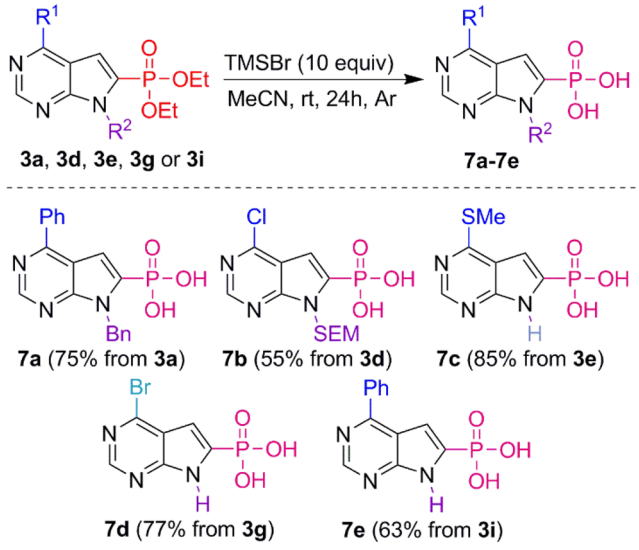


Scheme 3. Synthesis of 6-Aryl-7-deazapurine Phosphonates



to concomitant displacement of chlorine by bromine (by the action of HBr formed during the reaction) to give 6-bromo-7-deazapurine-8-phosphonic acid **7d**. Despite the rather difficult isolation of the free phosphonic acids, the sequence of C−H phosphonation followed by TMSBr treatment and hydrolysis can be used for efficient synthesis of deazapurine-8-phosphonic acids.

Scheme 4. Synthesis of 7-Deazapurine-8-phosphonic Acids



In conclusion, we have developed methodology for Manganese(III) acetate promoted direct C−H phosphonation of deazapurine nucleobases with dialkylphosphites. Reactions proceed selectively at position 8 of 7- and 9-deazapurines to give novel interesting deazapurine phosphonates. The method showed wide scope of substrates bearing different substituents. The resulting phosphonates were further modified by aqueous-phase Suzuki−Miyaura cross-coupling reactions. Protocol for phosphodiester cleavage method was also developed and several deazapurine phosphonic acids were synthesized. These methods clearly have a potential in synthesis of libraries of deazapurine derivatives for biological activity screening.

EXPERIMENTAL SECTION

General Methods. Compounds **1g**, **1k**, **1l**, **4c** and dialkylphosphites were purchased from commercial suppliers and used without any further purification. Compounds **1a**,[10,12] **1b**,[10,12] **1i**,[10,12] **4d**,[10,12] **1c**,[24] **1m**,[24] **1d**,[25] **1e**,[11] **1f**,[11] **1l**,[26] **1n**[27] and **1o**[28] were prepared according to reported procedures. Dry solvents were used as received from supplier. All reactions were carried out under argon atmosphere. All compounds were fully characterized by NMR and spectra were recorded with a 500 MHz (500.0 MHz for ^{1}H and 125.7 MHz for ^{13}C) spectrometer. ^{1}H and ^{13}C resonances were assigned based on H,C-HSQC and H,C-HMBC spectra. The samples were measured in [D_6]DMSO or [D_2]D_2O and chemical shifts (in ppm, δ-scale) are referenced to solvent signal in DMSO [δ (^{1}H) = 2.50 ppm, δ (^{13}C) = 39.7 ppm] or to dioxane as external standard in D_2O [δ (^{1}H) = 3.75 ppm, δ (^{13}C) = 67.19 ppm]. Coupling constants (J) are given in Hz. High-performance flash chromatography (HPFC) was performed on KP-Sil columns. Mass spectra were measured using electrospray (ESI) or electron impact (EI) ionization and using linear ion trap-orbitrap analyzer for HRMS. FTIR spectra were measured using the KBr method. Wavenumbers are given in cm^{-1}. Melting points were determined on a Kofler block and are uncorrected. X-ray diffraction experiment of single crystals was carried out by monochromatized Cu Kα radiation (λ = 1.54180 Å) at 180 K or employing Mo Kα radiation (λ = 0.71073 Å) at 293 K.

C−H Phosphonation of Deazapurines. General Procedure A. A suspension of deazapurine **1a−o** or **4a−d** (0.5 mmol), Mn(OAc)$_3$·2H_2O (1.5 mmol, 3 equiv) and dialkylphosphite (2.5 mmol, 0.34 mL, 5 equiv) in a mixture of acetonitrile−water (1:1, 2 mL) was stirred at 100 °C for 2 h. After cooling to room temperature, mixed with water and extracted with ethyl acetate (3 × 20 mL). Combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash

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column chromatography on silica gel using hexanes/ethyl acetate to give the pure product.

Diethyl (7-benzyl-4-phenyl-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate ***(3a)***. Deazapurine **1a** (143 mg, 0.5 mmol) and diethylphosphite **2a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **3a** according to General Procedure A. Deazapurine phosphonate **3a** was obtained as yellowish oil (100 mg, 47%) after chromatography (70 to 80% of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) 1.09 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 3.89−4.06 (m, 4H, CH_3CH_2O); 5.75 (s, 2H, CH_2−Ph); 7.11 (m, 2H, H-*o*-Bn); 7.24 (m, 1H, H-*p*-Bn); 7.29 (m, 2H, H-*m*-Bn); 7.50 (d, 1H, $J_{5,P}$ = 5.3 Hz, H-5); 7.59−7.67 (m, 3H, H-*m*,*p*-Ph); 8.21 (m, 2H, H-*o*-Ph); 9.04 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.0 (d, $J_{C,P}$ = 6.4 Hz, CH_3CH_2O); 46.9 (CH_2−Ph); 63.0 (d, $J_{C,P}$ = 5.6 Hz, CH_3CH_2O); 112.2 (d, $J_{C,P}$ = 15.9 Hz, CH-5); 113.6 (d, $J_{C,P}$ = 14.1 Hz, C-4a); 126.8 (CH-*o*-Bn); 127.5 (CH-*p*-Bn); 128.6 (CH-*m*-Bn); 129.1 (d, $J_{C,P}$ = 213.6 Hz, C-6); 129.1 (CH-*o*-Ph); 129.3 (CH-*m*-Ph); 131.1 (CH-*p*-Ph); 137.0 (C-*i*-Ph); 137.5 (C-*i*-Bn); 153.8 (d, $J_{C,P}$ = 13.7 Hz, C-7a); 153.9 (CH-2); 158.9 (C-4). IR(KBr) 3476, 2977, 1553, 1462, 1260, 1018, 770, 695, 564. HRMS (ESI) calculated for $C_{23}H_{24}O_3N_3P$ [M] 421.1559, found 421.1555.

Diethyl (7-benzyl-4-chloro-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate ***(3b)***. Deazapurine **1b** (122 mg, 0.5 mmol) and diethylphosphite **2a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **3b** according to General Procedure A. Deazapurine phosphonate **3b** was obtained as a yellowish oil (69 mg, 36%) after chromatography (50 to 60% of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) 1.09 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 3.90−4.06 (m, 4H, CH_3CH_2O); 5.72 (s, 2H, CH_2−Ph); 7.09 (m, 2H, H-*o*-Bn); 7.21−7.31 (m, 4H, H-*m*,*p*-Bn, H-5); 8.81 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.0 (d, $J_{C,P}$ = 6.4 Hz, CH_3CH_2O); 47.4 (CH_2−Ph); 63.2 (d, $J_{C,P}$ = 5.6 Hz, CH_3CH_2O); 110.5 (d, $J_{C,P}$ = 15.7 Hz, CH-5); 115.7 (d, $J_{C,P}$ = 15.0 Hz, C-4a); 126.8 (CH-*o*-Bn); 127.6 (CH-*p*-Bn); 128.6 (CH-*m*-Bn); 130.0 (d, $J_{C,P}$ = 213.1 Hz, C-6); 137.0 (C-*i*-Bn); 153.1 (d, $J_{C,P}$ = 13.9 Hz, C-7a); 153.3 (CH-2); 153.4 (d, $J_{C,P}$ = 1.3 Hz, C-4). IR(KBr) 3494, 2980, 1586, 1544, 1452, 1254, 1180, 1018, 776, 558. HRMS (ESI) calculated for $C_{17}H_{19}O_3N_3ClNaP$ [M + Na] 402.0751, found 402.0744.

Diethyl (4-phenyl-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl)phosphonate ***(3c)***. Deazapurine **1c** (192 mg, 0.3 mmol) and diethylphosphite **2a** (307 mg, 0.21 mL, 1.5 mmol) were used as starting compounds for the preparation of **3c** according to General Procedure A. Deazapurine phosphonate **3c** was obtained as a brownish oil (59 mg, 25%) after chromatography (50 to 60% of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) 1.14 and 1.19 (2 × t, 2 × 3H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.00−4.18 (m, 2 × 2H, CH_3CH_2O); 4.67 (bdd, 1H, J_{gem} = 11.8 Hz, $J_{5'a,4'}$ = 4.4 Hz, H-5′a); 4.86 (bdd, 1H, J_{gem} = 11.8 Hz, $J_{5'b,4'}$ = 3.2 Hz, H-5′b); 4.88 (m, 1H, H-4′); 6.38 (t, 1H, $J_{3',2'} = J_{3',4'}$ = 6.4 Hz, H-3′); 6.69 (d, 1H, $J_{1',2'}$ = 4.5 Hz, H-1′); 6.89 (dd, 1H, $J_{2',3'}$ = 6.4 Hz, $J_{2',1'}$ = 4.5 Hz, H-2′); 7.40−7.55 (m, 7H, H-5, H-*m*-Bz); 7.61−7.69 (m, 6H, H-*m*,*p*-Ph, H-*p*-Bz); 7.87, 7.94, and 8.00 (3 × m, 3 × 2H, H-*o*-Bz); 8.15 (m, 2H, H-*o*-Ph); 8.87 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.1 and 16.2 (2 × d, $J_{C,P}$ = 6.2 Hz, CH_3CH_2O); 63.2 (CH_2−5′); 63.5 (d, $J_{C,P}$ = 5.3 Hz, CH_3CH_2O); 70.6 (CH-3′); 72.7 (CH-2′); 79.0 (CH-4′); 88.7 (CH-1′); 114.0 (d, $J_{C,P}$ = 15.1 Hz, CH-5); 114.9 (d, $J_{C,P}$ = 14.5 Hz, C-4a); 128.5 and 128.8 (C-*i*-Bz); 129.0, 129.0, and 129.1 (CH-*m*-Bz); 129.2 (CH-*o*-Ph); 129.4 (d, $J_{C,P}$ = 210.8 Hz, C-6); 129.4 (CH-*m*-Ph); 129.4 (C-*i*-Bz); 129.5, 129.5, and 129.6 (CH-*o*-Bz); 131.3 (CH-*p*-Ph); 133.8, 134.2, and 134.3 (CH-*p*-Bz); 136.7 (C-*i*-Ph); 153.6 (CH-2); 153.8 (d, $J_{C,P}$ = 12.2 Hz, C-7a); 159.6 (C-4); 164.8, 165.0, and 165.6 (CO). IR(KBr) 3064, 2928, 2851, 1727, 1564, 1267, 1121, 1025, 972, 711, 559. HRMS (ESI) calculated for $C_{42}H_{38}N_3O_{10}PNa$ [M + Na] 798.2188, found 798.2187.

Diethyl (4-chloro-7-[2-(trimethylsilyl)ethoxymethyl]-7H-pyrrolo-[2,3-d]pyrimidin-6-yl)phosphonate ***(3d)***. Deazapurine **1d** (383 mg, 1.35 mmol) and diethylphosphite **2a** (932 mg, 0.93 mL, 6.75 mmol) were used as starting compounds for the preparation of **3d** according to General Procedure A. Deazapurine phosphonate **3d** was obtained as a brownish oil (170 mg, 30%) after chromatography (20 to 30% of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) −0.09 (s, 9H, CH_3Si); 0.84 (m, 2H, OCH_2CH_2Si); 1.28 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 3.55 (m, 2H, OCH_2CH_2Si); 4.08−4.19 (m, 4H, CH_3CH_2O); 5.81 (s, 2H, NCH_2O); 7.26 (d, 1H, $J_{5,P}$ = 5.2 Hz, H-5); 8.84 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6) −1.3 (CH_3Si); 16.3 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2O); 17.4 (OCH_2CH_2Si); 63.3 (d, $J_{C,P}$ = 5.6 Hz, CH_3CH_2O); 66.2 (OCH_2CH_2Si); 71.2 (NCH_2O); 111.3 (d, $J_{C,P}$ = 15.2 Hz, CH-5); 115.8 (d, $J_{C,P}$ = 15.0 Hz, C-4a); 130.0 (d, $J_{C,P}$ = 212.2 Hz, C-6); 153.4 (C-4); 153.4 (CH-2); 153.6 (d, $J_{C,P}$ = 13.9 Hz, C-7a). IR(KBr) 2983, 2951, 2900, 1584, 1541, 1356, 1250, 1085, 1028, 835, 781, 562. HRMS (ESI) calculated for $C_{16}H_{27}N_3O_4ClSiPNa$ [M + Na] 442.1089, found 442.1090.

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

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

Diethyl (4-chloro-7H-pyrrolo[2,3-d]pyrimidin-6-yl)phosphonate ***(3g)***. Deazapurine **1g** (77 mg, 0.5 mmol) and diethylphosphite **2a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **3g** according to General Procedure A. Deazapurine phosphonate **3g** was obtained as a white solid (60 mg, 41%) after chromatography (70 to 80% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 131−132 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.06−4.18 (m, 4H, CH_3CH_2O); 7.11 (d, 1H, $J_{5,P}$ = 4.9 Hz, H-5); 8.72 (s, 1H, H-2); 13.34 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.3 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 63.0 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 108.9 (d, $J_{C,P}$ = 17.0 Hz, CH-5); 116.2 (d, $J_{C,P}$ = 15.2 Hz, C-4a); 128.7 (d, $J_{C,P}$ = 215.5 Hz, C-6); 152.9 (C-2); 153.0 (d, $J_{C,P}$ = 1.4 Hz, C-4); 153.6 (d, $J_{C,P}$ = 15.2 Hz, C-7a). IR(KBr) 3055, 2986, 2929, 1589, 1452, 1233, 1036, 967, 851, 570. HRMS (ESI) calculated for $C_{10}H_{14}O_3N_3ClP$ [M + H] 290.0456, found 290.0455. Anal. Calcd for $C_{10}H_{13}O_3N_3ClP$: C, 41.47; H, 4.52; N, 14.51. Found: C, 41.79; H, 4.62; N, 14.53.

Diisopropyl (4-chloro-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate ***(3h)***. Deazapurine **1h** (307 mg, 2.0 mmol) and diisopropylphosphite **2b** (1662 mg, 1.7 mL, 10.0 mmol) were used

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as starting compounds for the preparation of **3h** according to General Procedure A. Deazapurine phosphonate **3h** was obtained as a white solid (190 mg, 30%) after chromatography (70 to 80% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 137−138 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.22 and 1.30 (2 × t, 2 × 6H, $J_{CH3,CH}$ = 6.2 Hz, CH_3-*i*Pr); 4.65 (dsept, 2H, $J_{CH,P}$ = 7.8 Hz, $J_{CH,CH3}$ = 6.2 Hz, CH-*i*Pr); 7.05 (d, 1H, $J_{5,P}$ = 4.9 Hz, H-5); 8.72 (s, 1H, H-2); 13.32 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 23.7 and 24.0 (2 × d, $J_{C,P}$ = 4.9 and 4.0 Hz, CH_3-*i*Pr); 71.9 (d, $J_{C,P}$ = 5.4 Hz, CH-*i*Pr); 108.5 (d, $J_{C,P}$ = 16.9 Hz, CH-5); 116.1 (d, $J_{C,P}$ = 15.1 Hz, C-4a); 130.1 (d, $J_{C,P}$ = 215.9 Hz, C-6); 152.8 (CH-2); 152.9 (C-4); 153.6 (d, $J_{C,P}$ = 15.2 Hz, C-7a). IR(KBr) 3059, 2982, 2936, 1592, 1555, 1230, 1095, 1003, 850, 771, 566. HRMS (ESI) calculated for $C_{12}H_{17}N_3O_3ClPNa$ [M + Na] 340.0588, found 340.0589. Anal. Calcd for $C_{12}H_{17}O_3N_3ClP$·0.1MeOH·0.05H_2O: C, 45.16; H, 5.48; N, 13.06. Found: C, 45.11; H, 5.24; N, 12.81.

*Diethyl (4-phenyl-7H-pyrrolo[2,3-d]pyrimidin-6-yl)phosphonate (**3i**).* Deazapurine **1i** (98 mg, 0.5 mmol) and diethylphosphite **2a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **3i** according to General Procedure A. Deazapurine phosphonate **3i** was obtained as a white solid (67 mg, 40%) after chromatography (70 to 80% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 156−157 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.06−4.19 (m, 4H, CH_3CH_2O); 7.37 (d, 1H, $J_{5,P}$ = 5.1 Hz, H-5); 7.56−7.65 (m, 3H, H-*m*,*p*-Ph); 8.19 (m, 2H, H-*o*-Ph); 8.97 (s, 1H, H-2); 13.02 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.3 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 62.8 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 110.5 (d, $J_{C,P}$ = 17.0 Hz, CH-5); 114.0 (d, $J_{C,P}$ = 14.3 Hz, C-4a); 127.8 (d, $J_{C,P}$ = 215.7 Hz, C-6); 129.0 (CH-*o*-Ph); 129.2 (CH-*m*-Ph); 130.8 (CH-*p*-Ph); 137.4 (C-*i*-Ph); 153.5 (CH-2); 154.4 (d, $J_{C,P}$ = 15.0 Hz, C-7a); 158.4 (d, $J_{C,P}$ = 1.3 Hz, C-4). IR(KBr) 3072, 2986, 2812, 1553, 1428, 1254, 1018, 976, 767, 701, 555. HRMS (ESI) calculated for $C_{16}H_{18}O_3N_3NaP$ [M + Na] 354.0977, found 354.0978. Anal. Calcd for $C_{16}H_{18}O_3N_3P$·0.1 MeOH: C, 57.81; H, 5.54; N, 12.55. Found: C, 58.06; H, 5.42; N, 12.15.

*Diethyl (2,4-dichloro-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate (**3j**).* Deazapurine **1j** (564 mg, 3 mmol) and diethylphosphite **2a** (2072 mg, 1.92 mL, 15.0 mmol) were used as starting compounds for the preparation of **3j** according to General Procedure A. Deazapurine phosphonate **3j** was obtained as a brownish solid (379 mg, 39%) after chromatography (70 to 80% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 190−191 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.07−4.17 (m, 4H, CH_3CH_2O); 7.17 (dd, 1H, $J_{5,P}$ = 5.0 Hz, $J_{5,NH}$ = 2.0 Hz, H-5); 13.51 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.3 (d, $J_{C,P}$ = 6.3 Hz, CH_3CH_2O); 63.2 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 109.3 (d, $J_{C,P}$ = 16.8 Hz, CH-5); 115.6 (d, $J_{C,P}$ = 15.3 Hz, C-4a); 129.6 (d, $J_{C,P}$ = 215.0 Hz, C-6); 152.8 and 153.6 (C-2,4); 154.8 (d, $J_{C,P}$ = 15.2 Hz, C-7a). IR(KBr) 2984, 2939, 2806, 1558, 1374, 1235, 1043, 1016, 973, 873, 555. HRMS (ESI) calculated for [M + H] $C_{10}H_{13}N_3O_3Cl_2P$: 324.0067, found 324.0066. Anal. Calcd for $C_{10}H_{12}O_3N_3Cl_2P$·0.05MeOH·0.55H_2O: C, 35.94; H, 3.66; N, 12.17. Found: C, 35.97; H, 3.99; N, 12.52.

*Diethyl (2-amino-4-chloro-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate (**3k**).* Deazapurine **1k** (337 mg, 2 mmol) and diethylphosphite **2a** (1381 mg, 1.37 mL, 10.0 mmol) were used as starting compounds for the preparation of **3k** according to General Procedure A. Deazapurine phosphonate **3k** was obtained as a yellowish solid (231 mg, 38%) after chromatography (70 to 80% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 227−228 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.24 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 3.99−4.10 (m, 4H, CH_3CH_2O); 6.78 (dd, 1H, $J_{5,P}$ = 5.1 Hz, $J_{5,NH}$ = 2.0 Hz, H-5); 6.91 (s, 2H, NH_2); 12.77 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.4 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 62.5 (d, $J_{C,P}$ = 5.3 Hz, CH_3CH_2O); 108.3 (d, $J_{C,P}$ = 15.6 Hz, C-4a); 110.2 (d, $J_{C,P}$ = 17.1 Hz, CH-5); 122.6 (d, $J_{C,P}$ = 220.7 Hz, C-6); 153.3 (C-4); 156.5 (d, $J_{C,P}$ = 15.1 Hz, C-7a); 160.9 (C-2). IR(KBr) 3222, 3091, 2981, 1624, 1557, 1230, 1054, 1028, 960, 791, 562. HRMS (ESI) calculated for $C_{10}H_{14}N_4O_3ClPNa$ [M + Na] 327.0385, found 327.0384. Anal. Calcd for $C_{10}H_{14}O_3N_4ClP$: C, 39.42; H, 4.63; N, 18.39. Found: C, 39.45; H, 4.43; N, 18.28.

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

*Diethyl (4-chloro-2-fluoro-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate (**3m**).* Deazapurine **1m** (343 mg, 2 mmol) and diethylphosphite **2a** (1381 mg, 1.37 mL, 10.0 mmol) were used as starting compounds for the preparation of **3m** according to General Procedure A. Deazapurine phosphonate **3m** was obtained as a white solid (227 mg, 37%) after chromatography (70 to 80% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 144−145 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.06−4.17 (m, 4H, CH_3CH_2O); 7.17 (dd, 1H, $J_{5,P}$ = 5.0 Hz, $J_{5,NH}$ = 2.0 Hz, H-5); 13.48 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.4 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 63.1(d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 109.7 (d, $J_{C,P}$ = 16.9 Hz, CH-5); 115.3 (dd, $J_{C,P}$ = 15.5 Hz, $J_{C,F}$ = 4.2 Hz, C-4a); 129.3 (dd, $J_{C,P}$ = 216.2 Hz, $J_{C,F}$ = 3.4 Hz, C-6); 154.6 (d, $J_{C,F}$ = 18.1 Hz, C-4); 155.0 (dd, $J_{C,F}$ = 17.0 Hz, $J_{C,P}$ = 15.5 Hz, C-7a); 158.0 (d, $J_{C,P}$ = 212.6 Hz, C-2). IR(KBr) 2984, 2942, 2795, 1576, 1410, 1234, 1125, 1016, 974, 920, 561. HRMS (ESI) calculated for [M + H] $C_{10}H_{13}N_3O_3ClFP$: 308.0360, found 308.0361. Anal. Calcd for $C_{10}H_{12}O_3N_3ClFP$·0.15MeOH: C, 38.93; H, 3.81; N, 13.19. Found: C, 39.02; H, 4.00; N, 13.45.

*Diethyl (5-benzyl-4-chloro-5H-pyrrolo[3,2-d]pyrimidin-6-yl)-phosphonate (**5a**).* Deazapurine **4a** (122 mg, 0.5 mmol) and diethylphosphite **2a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **5a** according to General Procedure A. Deazapurine phosphonate **5a** was obtained as a brownish oil (57 mg, 30%) after chromatography (50 to 60% of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) 1.10 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 3.95−4.10 (m, 4H, CH_3CH_2O); 6.02 (s, 2H, CH_2−Ph); 6.85 (m, 2H, H-*o*-Bn); 7.24 (m, 1H, H-*p*-Bn); 7.29 (m, 2H, H-*m*-Bn); 7.41 (d, 1H, $J_{7,P}$ = 4.5 Hz, H-7); 8.80 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.0 (d, $J_{C,P}$ = 6.5 Hz, CH_3CH_2O); 50.3 (CH_2−Ph); 63.5 (d, $J_{C,P}$ = 5.7 Hz, CH_3CH_2O); 113.0 (d, $J_{C,P}$ = 16.1 Hz, CH-7); 125.3 (CH-*o*-Bn); 126.7 (d, $J_{C,P}$ = 11.8 Hz, C-4a); 127.4 (CH-*p*-Bn); 128.7 (CH-*m*-Bn); 136.9 (d, $J_{C,P}$ = 209.1 Hz, C-6); 136.4 (C-*i*-Bn); 143.6 (d, $J_{C,P}$ = 2.0 Hz, C-4); 150.0 (d, $J_{C,P}$ = 17.6 Hz, C-7a); 150.5 (C-2). IR(KBr) 2983, 2929, 2848, 1718, 1619, 1455, 1377, 1248, 1015, 734, 564. HRMS (ESI) calculated for $C_{17}H_{19}N_3O_3ClNaP$ [M + Na] 402.0750, found 402.0744.

*Diethyl (5-benzyl-4-phenyl-5H-pyrrolo[3,2-d]pyrimidin-6-yl)-phosphonate (**5b**).* Deazapurine **4b** (143 mg, 0.5 mmol) and diethylphosphite **2a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **5b** according to General Procedure A. Deazapurine phosphonate **5b** was obtained as a brownish oil (65 mg, 31%) after chromatography (50 to 60% of EtOAc in hexanes). ^{1}H NMR (500 MHz, DMSO-d_6) 1.15 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.00−4.13 (m, 4H, CH_3CH_2O); 5.46 (s, 2H, CH_2−Ph); 6.17 (m, 2H, H-*o*-Bn); 7.01 (m, 2H, H-*m*-Bn); 7.07 (m, 1H, H-*p*-Bn); 7.28 (m, 2H, H-*o*-Ph); 7.35 (m, 2H, H-*m*-Ph); 7.42 (d, 1H, $J_{7,P}$ = 4.6 Hz, H-7); 7.48 (m, 1H, H-*p*-Ph); 9.01 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.1 (d, $J_{C,P}$ = 6.3 Hz, CH_3CH_2O); 50.6 (CH_2−Ph); 63.4 (d, $J_{C,P}$ = 5.8 Hz, CH_3CH_2O); 112.9 (d, $J_{C,P}$ =

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16.1 Hz, CH-7); 125.0 (CH-*o*-Bn); 127.0 (CH-*p*-Bn); 127.8 (d, $J_{C,P}$ = 10.9 Hz, C-4a); 128.0 (CH-*o*-Ph); 128.2 (CH-*m*-Bn); 129.0 (CH-*m*-Ph); 129.5 (CH-*p*-Ph); 136.2 (d, $J_{C,P}$ = 209.9 Hz, C-6); 136.7 (C-*i*-Ph); 137.3 (C-*i*-Bn); 149.6 (d, $J_{C,P}$ = 17.4 Hz, C-7a); 150.9 (CH-2); 153.0 (d, $J_{C,P}$ = 1.9 Hz, C-4). IR(KBr) 3494, 2983, 2923, 1559, 1353, 1248, 1015, 976, 695, 555. HRMS (ESI) calculated for $C_{23}H_{25}O_3N_3P$ [M + H] 422.1631, found 422.1628.

Diethyl (4-chloro-5H-pyrrolo[3,2-d]pyrimidin-6-yl)phosphonate ***(5c)***. Deazapurine **4c** (115 mg, 0.75 mmol) and diethylphosphite **2a** (518 mg, 0.51 mL, 3.75 mmol) were used as starting compounds for the preparation of **5c** according to General Procedure A. Deazapurine phosphonate **5c** was obtained as a brownish solid (80 mg, 37%) after chromatography (70 to 80% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp > 200 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6) 1.28 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 4.09–4.21 (m, 4H, CH_3CH_2O); 7.22 (d, 1H, $J_{7,P}$ = 4.2 Hz, H-7); 8.75 (s, 1H, H-2); 13.25 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.3 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2O); 63.2 (d, $J_{C,P}$ = 5.5 Hz, CH_3CH_2O); 111.3 (d, $J_{C,P}$ = 17.6 Hz, CH-7); 127.2 (d, $J_{C,P}$ = 13.2 Hz, C-4a); 134.7 (d, $J_{C,P}$ = 211.9 Hz, C-6); 144.1 (d, $J_{C,P}$ = 1.9 Hz, C-4); 149.5 (d, $J_{C,P}$ = 17.6 Hz, C-7a); 150.2 (CH-2). IR(KBr) 3494, 3052, 2995, 1604, 1473, 1233, 1027, 967, 824, 567. HRMS (ESI) calculated for $C_{10}H_{14}O_3N_3ClP$ [M + H] 290.0457, found 290.0455. Anal. Calcd for $C_{10}H_{13}O_3N_3ClP$: C, 41.47; H, 4.52; N, 14.51. Found: C, 41.74; H, 4.74; N, 14.13.

Diethyl (4-phenyl-5H-pyrrolo[3,2-d]pyrimidin-6-yl)phosphonate ***(5d)***. Deazapurine **4d** (98 mg, 0.5 mmol) and diethylphosphite **2a** (345 mg, 0.34 mL, 2.5 mmol) were used as starting compounds for the preparation of **5d** according to General Procedure A. Deazapurine phosphonate **5d** was obtained as a yellowish solid (60 mg, 36%) after chromatography (70 to 80% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 149–150 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.28 (2 × t, 2 × 3H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.10–4.19 (m, 4H, CH_3CH_2O); 7.21 (d, 1H, $J_{7,P}$ = 4.3 Hz, H-7); 7.56–7.66 (m, 3H, H-*m*,*p*-Ph); 8.06 (m, 2H, H-*o*-Ph); 9.01 (s, 1H, H-2); 12.64 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.4 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 63.0 (d, $J_{C,P}$ = 5.5 Hz, CH_3CH_2O); 111.4 (d, $J_{C,P}$ = 17.2 Hz, CH-7); 126.8 (d, $J_{C,P}$ = 12.0 Hz, C-4a); 128.9 (CH-*m*-Ph); 129.4 (CH-*o*-Ph); 130.6 (CH-*p*-Ph); 134.0 (d, $J_{C,P}$ = 212.1 Hz, C-6); 135.7 (C-*i*-Ph); 149.7 (d, $J_{C,P}$ = 17.2 Hz, C-7a); 150.6 (d, $J_{C,P}$ = 1.7 Hz, CH-2); 151.2 (CH-2). IR(KBr) 3144, 3060, 2980, 1550, 1413, 1236, 1024, 800, 701, 537. HRMS (ESI) calculated for $C_{16}H_{18}O_3N_3NaP$ [M + Na] 354.0977, found 354.0978. Anal. Calcd for $C_{16}H_{18}O_3N_3P$: C, 58.00; H, 5.48; N, 12.68. Found: C, 57.70; H, 5.31; N, 12.51.

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

Diethyl (4-(furan-2-yl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate ***(6a)***. Substituted deazapurine phosphonate **6a** was prepared according to General Procedure B by using **3g** (217 mg, 0.75 mmol) and furan-2-boronic acid (168 mg, 1.5 mmol) as starting compounds. Product **6a** was obtained as a yellowish solid (171 mg, 71%) after chromatography (80 to 90% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 141–142 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.27 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 4.06–4.17 (m, 4H, CH_3CH_2O); 6.80 (dd, 1H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 7.47 (dd, 1H, $J_{5,P}$ = 5.0 Hz, $J_{5,NH}$ = 1.4 Hz, H-5); 7.53 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 8.12 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 8.83 (s,1H, H-2); 12.94 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.4 (d, $J_{C,P}$ = 6.6 Hz, CH_3CH_2O); 62.8 (d, $J_{C,P}$ = 5.7 Hz, CH_3CH_2O); 111.0 (d, $J_{C,P}$ = 17.2 Hz, CH-5); 111.1 (d, $J_{C,P}$ = 15.2 Hz, C-4a); 113.0 (CH-4-furyl); 114.1 (CH-3-furyl); 127.7 (d, $J_{C,P}$ = 216.0 Hz, C-6); 147.2 (CH-5-furyl); 148.3 (C-4); 152.5 (C-2-furyl); 153.5 (CH-2); 154.5 (d, $J_{C,P}$ = 15.0 Hz, C-7a). IR(KBr) 3106, 2977, 2814, 1588, 1553, 1257, 1017, 956, 848, 773, 569. HRMS (ESI) calculated for $C_{14}H_{16}O_4N_3PNa$ [M + Na] 344.0772, found 344.0770. Anal. Calcd for $C_{14}H_{16}O_4N_3P{\cdot}0.2H_2O$: C, 51.76; H, 5.09; N, 12.93. Found: C, 51.99; H, 4.95; N, 12.57.

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

Diethyl (4-(thiophen-2-yl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate ***(6c)***. Substituted deazapurine phosphonate **6c** was prepared according to General Procedure B by using **3g** (145 mg, 0.5 mmol) and thiophen-2-boronic acid (128 mg, 1.0 mmol) as starting compounds. Product **6c** was obtained as a yellowish solid (110 mg, 65%) after chromatography (80 to 90% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 156–157 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.28 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.08–4.18 (m, 4H, CH_3CH_2O); 7.31 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.8 Hz, H-4-thienyl); 7.55 (d, 1H, $J_{5,P}$ = 5.1 Hz, H-5); 7.90 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.1 Hz, H-5-thienyl); 8.28 (dd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 8.82 (s, 1H, H-2); 13.01 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.4 (d, $J_{C,P}$ = 6.2 Hz, CH_3CH_2O); 62.9 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 110.1 (d, $J_{C,P}$ = 17.0 Hz, CH-5); 111.6 (d, $J_{C,P}$ = 14.5 Hz, C-4a); 127.9 (d, $J_{C,P}$ = 216.0 Hz, C-6); 129.5 (CH-4-thienyl); 130.8 (CH-3-thienyl); 131.6 (CH-5-thienyl); 142.2 (C-2-thienyl); 152.2 (d, $J_{C,P}$ = 1.4 Hz, C-4); 153.3 (CH-2); 154.4 (d, $J_{C,P}$ = 15.0 Hz, C-7a). IR(KBr) 3067, 2982, 2813, 1561, 1440, 1254, 1016, 968, 832, 703, 559. HRMS (ESI) calculated for $C_{14}H_{16}O_3N_3SPNa$ [M + Na] 360.0542, found 360.0543. Anal. Calcd for $C_{14}H_{16}O_3N_3SP$: C, 49.85; H, 4.78; N, 12.46. Found: C, 49.72; H, 4.54; N, 12.20.

Diethyl (4-(thiophen-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate ***(6d)***. Substituted deazapurine phosphonate **6d** was prepared according to General Procedure B by using **3g** (217 mg, 0.75 mmol) and thiophen-3-boronic acid (192 mg, 1.5 mmol) as starting compounds. Product **6d** was obtained as a brownish solid (182 mg, 72%) after chromatography (80 to 90% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 158–159 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.28 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.08–4.18 (m, 4H, CH_3CH_2O); 7.51 (dd, 1H, $J_{5,P}$ = 5.1 Hz, $J_{5,NH}$ = 1.8 Hz, H-5); 7.75 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 7.96 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 8.65 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 8.88 (s, 1H, H-2); 12.95 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.4 (d, $J_{C,P}$ = 6.0 Hz, CH_3CH_2O); 62.8 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 110.4 (d, $J_{C,P}$ = 17.1 Hz, CH-5); 113.1 (d, $J_{C,P}$ = 14.3 Hz, C-4a); 127.5 (CH-5-thienyl); 127.6 (d, $J_{C,P}$ = 216.0 Hz, C-6); 127.7 (CH-4-thienyl); 129.7 (CH-2-thienyl); 139.7 (C-3-thienyl); 153.4 (CH-2); 153.6 (d, $J_{C,P}$ = 1.4 Hz, C-4); 154.4 (d, $J_{C,P}$ = 14.9 Hz, C-7a). IR(KBr) 3106, 2977, 2814, 1588, 1553, 1257, 1017, 956, 848, 773, 569. HRMS (ESI) calculated for $C_{14}H_{16}O_3N_3SPNa$ [M + Na] 360.0544, found 360.0542. Anal. Calcd for $C_{14}H_{16}O_3N_3SP{\cdot}0.15H_2O$: C, 49.45; H, 4.83; N, 12.36. Found: C, 49.73; H, 4.63; N, 11.97.

Diethyl (4-phenyl-7H-pyrrolo[2,3-d]pyrimidin-6-yl)phosphonate ***(6e)***. Substituted deazapurine phosphonate **6e** was prepared according

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

Diethyl (4-(benzofuran-2-yl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate ***(6f)***. Substituted deazapurine phosphonate **6f** was prepared according to General Procedure B by using **3g** (174 mg, 0.6 mmol) and benzofuran-2-boronic acid (194 mg, 1.2 mmol) as starting compounds. Product **6f** was obtained as a yellowish solid (149 mg, 67%) after chromatography (80 to 90% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp > 200 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6) 1.30 (t, 6H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3CH_2O); 4.10−4.20 (m, 4H, CH_3CH_2O); 7.37 (ddd, 1H, $J_{5,4}$ = 7.8 Hz, $J_{5,6}$ = 7.2 Hz, $J_{5,7}$ = 1.0 Hz, H-5-benzofuryl); 7.50 (ddd, 1H, $J_{6,7}$ = 8.3 Hz, $J_{6,5}$ = 7.2 Hz, $J_{6,4}$ = 1.3 Hz, H-6-benzofuryl); 7.66 (dd, 1H, $J_{5,P}$ = 5.0 Hz, $J_{5,NH}$ = 2.0 Hz, H-5); 7.83 (ddd, 1H, $J_{4,5}$ = 7.8 Hz, $J_{4,6}$ = 1.3 Hz, $J_{4,7}$ = 0.8 Hz, H-4-benzofuryl); 7.87 (dq, 1H, $J_{7,6}$ = 8.3 Hz, $J_{7,5}$ = $J_{7,4}$ = $J_{7,3}$ = 0.8 Hz, H-7-benzofuryl); 8.01 (d, 1H, $J_{3,7}$ = 1.0 Hz, H-3-benzofuryl); 8.95 (s,1H, H-2); 13.07 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.4 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 62.9 (d, $J_{C,P}$ = 5.3 Hz, CH_3CH_2O); 109.9 (CH-3-benzofuryl); 111.1 (d, $J_{C,P}$ = 17.2 Hz, CH-5); 112.2 (CH-7-benzofuryl); 112.3 (d, $J_{C,P}$ = 15.2 Hz, C-4a); 122.8 (CH-4-benzofuryl); 124.1 (CH-5-benzofuryl); 127.0 (CH-6-benzofuryl); 128.9 (C-3a-benzofuryl); 128.5 (d, $J_{C,P}$ = 215.6 Hz, C-6); 148.3 (C-4); 153.5 (CH-2); 154.0 (C-2-benzofuryl); 154.7 (d, $J_{C,P}$ = 15.2 Hz, C-7a); 155.7 (C-7a-benzofuryl). IR(KBr) 3059, 2985, 2811, 1583, 1337, 1249, 1052, 1022, 973, 856, 750, 550. HRMS (ESI) calculated for $C_{18}H_{18}O_4N_3PNa$ [M + Na] 394.0927, found 394.0928. Anal. Calcd for $C_{18}H_{18}O_4N_3P$·0.45H_2O: C, 56.98; H, 5.02; N, 11.07. Found: C, 57.32; H, 4.77; N, 10.75.

Diethyl (4-(dibenzofuran-4-yl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phosphonate ***(6g)***. Substituted deazapurine phosphonate **6g** was prepared according to General Procedure B by using **3g** (174 mg, 0.6 mmol) and dibenzofuran-4-boronic acid (255 mg, 1.2 mmol) as starting compounds. Product **6g** was obtained as a yellowish solid (152 mg, 60%) after chromatography (80 to 90% of EtOAc in hexanes), which was crystallized from MeOH-H_2O. mp 199−200 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 1.26 (t, 6H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3CH_2O); 4.07−4.18 (m, 4H, CH_3CH_2O); 7.15 (bd, 1H, $J_{5,P}$ = 5.0 Hz, H-5); 7.48 (bt, 1H, $J_{8,7}$ = $J_{8,9}$ = 7.5 Hz, H-8-$C_{12}H_7O$); 7.58 (dt, 1H, $J_{7,6}$ = $J_{7,8}$ = 7.7 Hz, H-7-$C_{12}H_7O$); 7.64 (t, 1H, $J_{2,1}$ = $J_{2,3}$ = 7.7 Hz, H-2-$C_{12}H_7O$); 7.68 (dm, 1H, $J_{6,7}$ = 8.2 Hz, H-6-$C_{12}H_7O$); 8.04 (dd, 1H, $J_{3,2}$ = 7.6 Hz, $J_{3,1}$ = 1.4 Hz, H-3-$C_{12}H_7O$); 8.27 (ddd, 1H, $J_{9,8}$ = 7.7 Hz, $J_{9,7}$ = 1.4 Hz, $J_{9,6}$ = 0.7 Hz, H-9-$C_{12}H_7O$); 8.39 (dd, 1H, $J_{1,2}$ = 7.7 Hz, $J_{1,3}$ = 1.4 Hz, H-1-$C_{12}H_7O$); 9.09 (s, 1H, H-2); 13.08 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 16.3 (d, $J_{C,P}$ = 6.1 Hz, CH_3CH_2O); 62.9 (d, $J_{C,P}$ = 5.4 Hz, CH_3CH_2O); 111.0 (d, $J_{C,P}$ = 16.7 Hz, CH-5); 111.8 (CH-6-$C_{12}H_7O$); 115.7 (d, $J_{C,P}$ = 14.5 Hz, C-4a); 121.6 (CH-9-$C_{12}H_7O$); 122.3 (C-4-$C_{12}H_7O$); 123.4 (CH-1-$C_{12}H_7O$); 123.4 (C-9a-$C_{12}H_7O$); 123.7 and 123.7 (CH-2,8-$C_{12}H_7O$); 125.0 (C-9b-$C_{12}H_7O$); 127.5 (d, $J_{C,P}$ = 215.6 Hz, C-6); 128.3 (CH-7-$C_{12}H_7O$); 128.8 (CH-3-$C_{12}H_7O$); 152.9 (C-4a-$C_{12}H_7O$); 153.6 (CH-2); 154.0 (d, $J_{C,P}$ = 15.0 Hz, C-7a); 155.6 (C-5a-$C_{12}H_7O$); 155.8 (C-4). IR(KBr) 3082, 2984, 2815, 1587, 1564, 1253, 1188, 1019, 962, 850, 758, 528. HRMS (ESI) calculated for $C_{22}H_{20}O_4N_3PNa$ [M + Na] 444.1084, found 444.1083. Anal. Calcd for $C_{22}H_{20}O_4N_3P$: C, 62.71; H, 4.78; N, 9.97. Found: C, 62.66; H, 4.78; N, 9.64.

Synthesis of 7-Deazapurine-8-phosphonic Acids. General Procedure C. TMSBr (8.25 mmol, 1.09 mL) was added dropwise to the mixture of 7-deazapurine phosphonate **3a**, **3d**, **3e**, **3g** or **3i** (0.825 mmol) in MeCN (5 mL), and the reaction mixture was stirred for 24h at room temperature. After concentration in vacuo and codistillation with MeCN, crude reaction mixture was treated with water, sonicated, and formed precipitate was filtered off. Purification was done by reverse phase flash column chromatography (C-18, eluting water/MeOH gradient from 5 to 10%).

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

(4-Chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-d]-pyrimidin-6-yl)phosphonic acid ***(7b)***. Deazapurine phosphonic acid **7b** was prepared according to General Procedure C with addition of 2,6-lutidine (429 mg, 0.47 mL, 4.0 mmol) to phosphonate **3d** (170 mg, 0.4 mmol) and TMSBr (612 mg, 0.52 mL, 4.0 mmol). Product **7b** was obtained as a yellowish solid (80 mg, 55%), which was purified by reverse phase flash column chromatography and crystallized from MeOH-H_2O. mp > 200 °C (dec). ^{1}H NMR (500 MHz, D_2O) −0.20 (s, 9H, CH_3Si); 0.79 (m, 2H, OCH_2CH_2Si); 3.61 (m, 2H, OCH_2CH_2Si); 5.79 (s, 2H, NCH_2O); 6.97 (d, 1H, $J_{5,P}$ = 4.8 Hz, H-5); 8.31 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, D_2O) −2.0 (CH_3Si); 17.9 (OCH_2CH_2Si); 67.6 (OCH_2CH_2Si); 73.1 (NCH_2O); 108.1 (d, $J_{C,P}$ = 13.9 Hz, CH-5); 117.9 (d, $J_{C,P}$ = 13.4 Hz, C-4a); 140.5 (d, $J_{C,P}$ = 191.0 Hz, C-6); 151.6 (CH-2); 153.4 (C-4); 153.6 (d, $J_{C,P}$ = 11.5 Hz, C-7a). IR(KBr) 3056, 2954, 2893, 1586, 1456, 1251, 1075, 837, 778, 567. HRMS (ESI) calculated for $C_{12}H_{18}O_4N_3ClPSi$ [M − H] 362.0498, found 362.0499.

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

(4-Bromo-7H-pyrrolo[2,3-d]pyrimidin-6-yl)phosphonic acid ***(7d)***. Deazapurine phosphonic acid **7d** was prepared according to General Procedure C from phosphonate **3g** (723 mg, 2.5 mmol) and TMSBr (3827 mg, 3.3 mL, 25.0 mmol). Product **7d** was obtained as a white solid (532 mg, 77%), which was purified by reverse phase flash column chromatography and crystallized from MeOH-H_2O. mp 228−229 °C. ^{1}H NMR (500 MHz, D_2O) 6.72 (d, 1H, $J_{5,P}$ = 4.5 Hz, H-5); 8.29 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, D_2O) 105.7 (d, $J_{C,P}$ = 14.1 Hz, CH-5); 121.2 (d, $J_{C,P}$ = 13.2 Hz, C-4a); 140.9 (d, $J_{C,P}$ = 186.0 Hz, C-6); 143.9 (C-4); 150.3 (CH-2); 150.8 (d, $J_{C,P}$ = 12.0 Hz, C-7a). IR(KBr) 3075, 2949, 2818, 1565, 1444, 1344, 1150, 1022, 967, 845, 776, 560.

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HRMS (ESI) calculated for $C_6H_4O_3N_3PBr$ [M − H] 275.9174, found 275.9179.

(4-Phenyl-7H-pyrrolo[2,3-d]pyrimidin-6-yl)phosphonic acid (7e). Deazapurine phosphonic acid **7e** was prepared according to General Procedure C from phosphonate **3i** (133 mg, 0.4 mmol) and TMSBr (612 mg, 0.52 mL, 4.0 mmol). Product **7e** was obtained as a yellowish solid (70 mg, 63%), which was purified by reverse phase flash column chromatography and crystallized from MeOH-H_2O. mp > 200 °C (dec). ^{1}H NMR (500 MHz, DMSO-d_6) 7.13 (bd, 1H, $J_{5,P}$ = 3.5 Hz, H-5); 7.57 (m, 1H, H-*p*-Ph); 7.61 (m, 2H, H-*m*-Ph); 8.14 (m, 2H, H-*o*-Ph); 8.89 (s, 1H, H-2); 12.80 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6) 106.9 (d, $J_{C,P}$ = 16.5 Hz, CH-5); 114.1 (d, $J_{C,P}$ = 12.8 Hz, C-4a); 128.8 (CH-*o*-Ph); 129.2 (CH-*m*-Ph); 130.6 (CH-*p*-Ph); 134.6 (d, $J_{C,P}$ = 203.9 Hz, C-6); 137.7 (C-*i*-Ph); 152.5 (CH-2); 154.1 (d, $J_{C,P}$ = 13.4 Hz, C-7a); 157.3 (C-4). IR(KBr) 3047, 2783, 1595, 1415, 1165, 1066, 956, 765, 605, 557. HRMS (ESI) calculated for $C_{12}H_9O_3N_3P$ [M − H] 274.0383, found 274.0387.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01970.

Copies of ^{1}H, ^{13}C NMR spectra (PDF)
Crystallographic data (CIF)
Crystallographic data (CIF)
Crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

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