A FACILE SYNTHESIS OF 9-DEAZA ANALOGUE OF OLOMOUCINE

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Heating of 6-(benzylamino)-2-chloro-9-deazapurine (**3**) with ethanolamine afforded 6-(benzylamino)-2-[(2-hydroxyethyl)amino]-9-deazapurine (**8**). Its treatment with formaldehyde in alkaline solution, after protection of the OH group with DMTr, led to hydroxymethylation at position 9. Conversion of the hydroxymethyl group to methyl was performed by catalytic hydrogenation under simultaneous deprotection, which resulted in the formation of the 9-deaza analogue **1** of olomoucine. Compound **1** does not exhibit any significant *in vitro* cell growth inhibition of CCRF-CEM, HeLa and L-1210 cell lines. Cytostatic activity was found in 6-(benzylamino)-9-deazapurine (**2**) and its 2-chloro derivative **3** in CCRF-CEM cells with IC_{50} 13.3 and 15.8 μM, respectively.

Keywords: Pyrrolo[3,2-*d*]pyrimidines; 9-Deazapurine; 2*a*,3,4,5-Tetrahydro-2*a*,5,6,8-tetraazaacenaphthylene; CDK inhibitors; Purines; Cytokinins; Antitumor activity; Cytostatics.

Cytokinins are plant growth hormones with a wide range of physiological functions. Their crucial role consists in promotion of cell division. They are also involved in cell growth, retardation and senescence. Natural cytokinins are 6-(alkylamino)purines. Some of their synthetic analogues, *e.g.* purvalanol A and B, roscovitine, bohemine or olomoucine (Chart 1), are potent inhibitors of cyclin-dependent kinases (CDKs), which play a principal role in regulation of the cell cycle[1–8]. Myoseverin, a structurally similar microtubule-binding substance, and some of its analogues are very potent regulators of cell growth, although they do not inhibit cyclin-dependent kinases[9,10]. These modes of action possess a great therapeutic potential in various proliferative and neurodegenerative disorders. Herein, we describe the synthesis of the 9-deaza analogue **1** of olomoucine, which we performed in an

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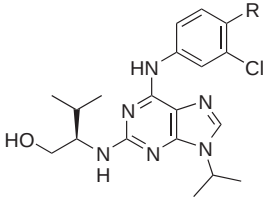
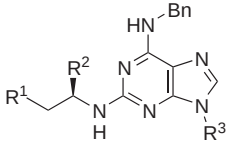
attempt to find, whether the structural modification could possibly increase the antitumor activity. Such a modification of cytokinin skeleton was described already in the literature in case of 6-(benzylamino)-9-deazapurine (**2**) and its 2-chloro derivative **3** and these compounds were tested for cytokinin activity in tobacco callus bioassay[11]. However, no assays of cytostatic activity were performed.



Purvalanol A, R = H
Purvalanol B, R = COOH



Roscovitine, R^1 = OH, R^2 = Me, R^3 = i-Pr
Bohemine, R^1 = CH_2OH, R^2 = H, R^3 = i-Pr
Olomoucine, R^1 = OH, R^2 = H, R^3 = Me

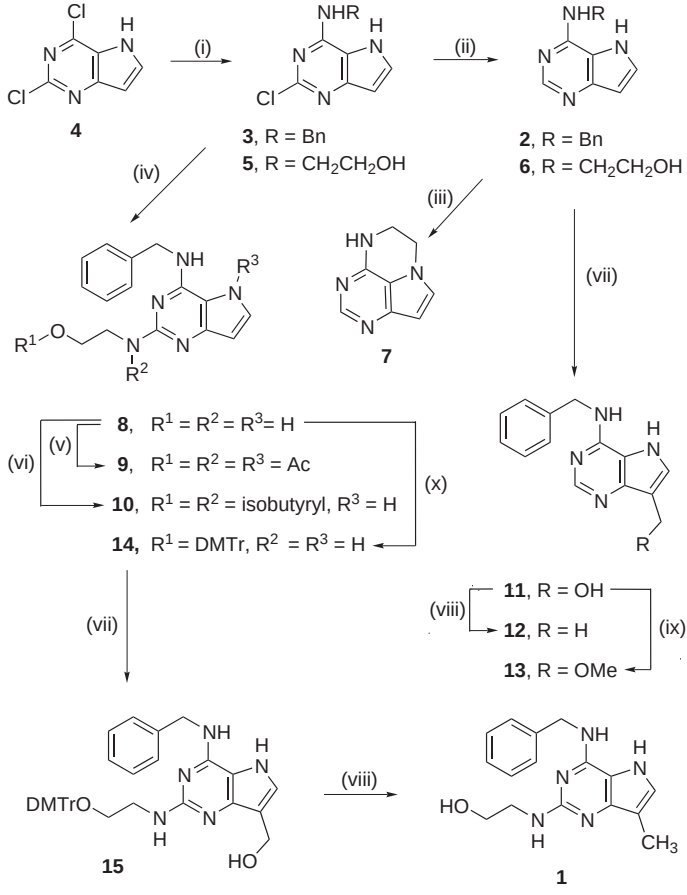
CHART 1

RESULTS AND DISCUSSION

The synthesis starts from 4-(benzylamino)-2-chloro-5*H*-pyrrolo[3,2-*d*]pyrimidine (6-(benzylamino)-2-chloro-9-deazapurine) (**3**) which was obtained[11] by nucleophilic replacement of chlorine in position 4 of 2,4-dichloro-5*H*-pyrrolo[3,2-*d*]pyrimidine (**4**; refs[12–14]) in the reaction with benzylamine (Scheme 1). The position of the benzylamino substituent in the starting compound **3** could not be proved even from the proton-coupled ^{13}C NMR spectra because of the absence of the ^3J(C-4a,NH-4) long-range coupling constant. Similarly, the interaction did not manifest itself in the 4-(2-hydroxyethyl)amino derivative **5** (ref.[13]). Nevertheless, reductive removal of the remaining chlorine atom in **3** and **5** provided compounds **2** (ref.[11]) and **6** (ref.[15]), which exhibit long-range coupling constants ^3J(C-4a,NH-4) = 2.5 and 2.4 Hz, and ^3J(C-4,H-2) = 10.7 and 11.7 Hz, respectively. The interactions confirm the position of the substitution unambiguously (Fig. 1). Additionally, the ultimate structural proof was obtained by cyclization of the (2-hydroxyethyl)amino derivative **6** to the tricyclic compound **7** under Mitsunobu reaction conditions.

Synthesis of the 9-deaza analogue **1** of olomoucine requires replacement of the remaining chlorine atom in the benzyl derivative **3** by the (2-hydroxyethyl)amino group. The reactivity of the chlorine atom in comparison with the dichloro derivative **4** decreased because of the presence of an electron-donating benzylamino group. An effective formation of the

disubstituted derivative **8** requires heating of compound **3** in ethanolamine. For the purpose of characterization of the polar compound **8** as well as for an assessment of the relative reactivity of its NH groups towards acylation, triacetate **9** and diisobutyrate **10** were prepared. The placement of the methyl group at position 7 (position 9 according to purine numbering) was attempted by hydroxymethylation with aqueous formaldehyde in alkaline solution followed by reductive removal of the benzyl-type hydroxy group[16]. In a model experiment with compound **2**, the optimum reaction



(i) RNH_2, EtOH, reflux; (ii) H_2/Pd, EtOH; (iii) diisopropyl azodicarboxylate, Ph_3P, CH_3CN; (iv) ethanolamine, 150 °C; (v) Ac_2O, reflux; (vi) isobutyryl chloride, pyridine; (vii) HCHO, K_2CO_3, dioxane–H_2O; (viii) H_2/Pd, dioxane–H_2O; (ix) MeOH, HCl, reflux; (x) DMTrCl, Bu_3N, DMSO

SCHEME 1

conditions consisted in a treatment with formaldehyde and potassium carbonate in boiling aqueous dioxane. The 7-(hydroxymethyl) derivative **11** was obtained in almost 70% yield. Deoxygenation of the benzyl-type hydroxy group performed by catalytic hydrogenation gave the 7-methyl derivative **12**. The hydroxymethyl group of compound **11** reacts easily under acid conditions with methanol under the formation of the 7-(methoxymethyl) derivative **13**. On the contrary, treatment of compound **8** with formaldehyde and potassium carbonate led to a mixture of products, which is caused probably by the presence of the unprotected primary hydroxy group. Its protection with 4,4′-dimethoxytrityl afforded compound **14**, which was successfully hydroxymethylated in position 7 to give compound **15**. Reductive removal of the benzyl-type of hydroxy group by catalytic hydrogenation causes a simultaneous deprotection under the formation of the target 9-deaza analogue **1** of olomoucine.

In vitro inhibition of cell growth with compounds **1**–**3**, **5**–**8** and **11**–**13** was evaluated in the following cell cultures: human T-lymphoblastoids CCRF-CEM cell line (ATCC CCL 119), human cervix carcinoma HeLa S3 cells (ATCC CCL 2.2) and mouse leukemia L1210 cells (ATCC CCL 219). None of the mentioned compounds showed any considerable activity (inhibition of the cell growth at c = 10 μM must be higher than 50%) in these assays except for 6-(benzylamino)-9-deazapurine (**2**) and its 2-chloro derivative **3**, which exhibited a significant activity against T-lymphoblastoids CCRF-CEM cells with IC_{50} values 13.33 and 15.80 μM, respectively. Since the described IC_{50} value on CEM cells for olomoucine itself is 62 μM (ref.[8]), it can be stated that the abstraction of nitrogen in position 9 and of the substituents in positions 2 and 9 increases slightly its antitumor activity. The results correlate with the cytostatic activity of 7,N^2,N^4-tribenzyl-5*H*-pyrrolo[3,2-*d*]pyrimidine-2,4-diamine showing the IC_{50} value 1.9 μM on the same cell line, which we described recently[17]. Although there has been

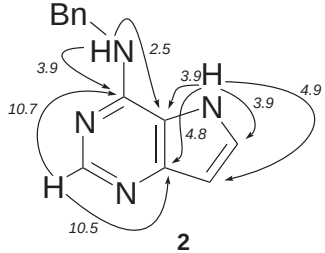


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FIG. 1
Long-range J(C,H) coupling constants derived from the proton-coupled ^{13}C NMR spectrum

so far no information about the mechanism of action, these initial results suggest that the pyrrolo[3,2-*d*]pyrimidine system could be an attractive substitute for purine in the design of antitumor compounds related to cytokinins.

EXPERIMENTAL

General

Melting points were determined on a Kofler block and are uncorrected. Analytical TLC was performed on silica gel pre-coated aluminium plates with fluorescent indicator (Merck 5554, 60 F_{254}). Spots were visualized with UV light (254 nm) or by spraying with ninhydrin (1% solution in ethanol) and a short heating to 300–400 °C. Column chromatography was carried out on silica gel (Sigma S-0507, 40–63 μm). Mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer using the EI (electron energy 70 eV) or FAB (ionisation with Xe, accelerating voltage 8 kV, thioglycerol–glycerol 3:1 mixture or bis(2-hydroxyethyl) disulfide were used as matrix). ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125.7 MHz on a Varian Unity 500 instrument in DMSO-d_6 (referenced to the solvent signal δ 2.50 and 39.70 ppm, respectively). For most of the compounds, in addition to the APT, proton-coupled ^{13}C NMR spectra were measured. Chemical shifts are in ppm and coupling constants (*J*) in Hz. UV spectra were taken on a Beckman DU-65 spectrophotometer in methanol solution. IR spectra (ν, cm^{-1}) were obtained on an FT IR Bruker Equinox IFS 55 spectrometer in chloroform or KBr pellets. Elemental analyses were carried out on a Perkin Elmer CHN Analyser 2400, Series II Sys (Perkin Elmer, Norwolk (CT), U.S.A.).

Benzyl(2-chloro-5*H*-pyrrolo[3,2-*d*]pyrimidin-4-yl)amine[11] (**3**)

A solution of compound **4** (7.0 g, 37 mmol) and benzylamine (16 ml, 150 mmol) in ethanol (400 ml) was refluxed for 4 h and then the solvent was evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:99) followed by crystallization (petroleum ether–ethyl acetate, 1:1) afforded compound **3** (8.2 g, 86%) as white crystals, m.p. 262–264 °C. MS (EI), *m/z* (rel. int.): 258 (79, M), 223 (8, M – Cl), 153 (13, M – BnNH + H), 149 (35), 118 (29), 106 (100, BnNH), 91 (68, Bn). HRMS (EI), *m/z*: 258.0690 (M); for $C_{13}H_{11}ClN_4$ calculated: 258.0672. ^{1}H NMR (500 MHz, DMSO-d_6): 11.04 (br s, 1 H, NH-5); 7.86 (t, 1 H, J(NH,CH_2) = 5.4, NH); 7.54 (t, 1 H, J(6,7) = J(6,NH) = 2.9, H-6); 7.41 (d, 2 H, J = 7.0, Ph); 7.37 (t, 2 H, J = 7.8, Ph); 7.29 (t, 1 H, J = 7.2, Ph); 6.34 (dd, 1 H, J(7,6) = 2.9, J(7,NH) = 2.1, H-7); 4.69 (d, 2 H, J(CH_2,NH) = 5.5, N-CH_2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 151.13 (d, ^4J(C-2,NH) = 2.0, C-2); 150.45 (q, ^3J(C-4,CH_2) = ^2J(C-4,NH) = 3.9, C-4); 148.44 (ddd, ^3J(C-7a,H-6) = 8.8, ^3J(C-7a,NH) = 6.8, ^2J(C-7a,H-7) = 2.9, C-7a); 138.93 (m, Ph); 129.18 (ddd, ^1J = 186.5, ^2J(C-6,H-7) = 8.8, ^2J(C-6,NH) = 3.9, C-6); 128.69 (dd, 2 C, ^1J = 160.2, ^2J = 6.8, Ph); 127.99 (dm, 2 C, ^1J = 157.2, Ph); 127.40 (dt, ^1J = 161.1, ^2J = 6.8, Ph); 112.595 (m, C-4a); 101.34 (ddd, ^1J = 174.8, ^2J(C-7,H-6) = 8.8, ^3J(C-7,NH) = 4.8, C-7); 43.76 (br t, ^1J = 138.7, N-CH_2Ph). IR (KBr): 3335, 3244, 3179, 1629, 1543, 1526, 1440, 1410, 1349. UV (MeOH): 293 (8.72), 284 (12.72), 236 (19.20). For $C_{13}H_{11}ClN_4$ (258.7) calculated: 60.35% C, 4.29% H, 13.70% Cl, 21.66% N; found: 59.89% C, 4.14% H, 13.99% Cl, 21.39% N.

2-[(2-Chloro-5*H*-pyrrolo[3,2-*d*]pyrimidin-4-yl)amino]ethan-1-ol[13] (**5**)

A solution of compound **4** (3 g, 16 mmol) and ethanolamine (2.5 ml, 41.4 mmol) in ethanol (250 ml) was refluxed for 4 h and the resulting solvent was evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:9) followed by crystallization (methanol–ethyl acetate, 1:3) afforded compound **5** (2.7 g, 79%) as white crystals, m.p. 234-235 °C. MS (EI), *m/z* (rel. int.): 212 (31, M), 193 (28), 181 (61, M – CH_2OH), 168 (100, M – CH_3CHO), 152 (37, M – $NHCH_2CH_2OH$), 145 (44, M – Cl – CH_3OH), 133 (29, M – Cl – CH_3CHO), 118 (38, M – Cl – NH_2CH_2CHO). HRMS (EI), *m/z*: 212.0534 (M); for $C_8H_9ClN_4O$ calculated: 212.0465. ^{1}H NMR (500 MHz, DMSO-d_6): 11.17 (br s, 1 H, NH-5); 7.57 (br t, 1 H, J(NH,CH_2) = 5.5, NH); 7.51 (t, 1 H, J(6,7) = J(6,NH) = 2.9, H-6); 6.30 (dd, 1 H, J(7,6) = 3.0, J(7,NH) = 2.1, H-7); 4.92 (br s, 1 H, OH); 3.61 (t, 2 H, J(CH_2,CH_2) = 5.5, OCH_2); 3.53 (q, 2 H, J(CH_2,CH_2) = J(CH_2,NH) = 5.5, NCH_2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 151.17 (d, ^4J(C-2,NH) = 2.0, C-2); 150.81 (q, ^3J(C-4,CH_2) = ^2J(C-4,NH) = 3.9, C-4); 148.18 (ddd, ^3J(C-7a,H-6) = 8.8, ^3J(C-7a,NH) = 6.8, ^2J(C-7a,H-7) = 2.9, C-7a); 128.875 (ddd, ^1J = 186.5, ^2J(C-6,H-7) = 8.8, ^2J(C-6,NH) = 3.9, C-6); 112.79 (ddd, ^3J(C-4a,H-6) = 6.8, ^3J(C-4a,H-7) = 5.9, ^2J(C-4a,NH) = 3.9, C-4a); 101.27 (ddd, ^1J = 174.8, ^2J(C-7,H-6) = 8.8, ^3J(C-7,NH) = 4.8, C-7); 59.80 (tt, ^1J = 141.6, ^2J = 3.9, OCH_2); 42.90 (br t, ^1J = 137.7, NCH_2). IR (KBr): 3308, 3259, 3173, 2745, 1652, 1638, 1559, 1539, 1495, 1348. UV (MeOH): 283 (11.82), 276 (11.10), 235 (19.12). For $C_8H_9ClN_4O$ (212.6) calculated: 45.19% C, 4.27% H, 16.67% Cl, 26.35% N; found: 44.95% C, 4.38% H, 17.03% Cl, 26.58% N.

Benzyl(5*H*-pyrrolo[3,2-*d*]pyrimidin-4-yl)amine[11] (**2**) Hydrochloride

Compound **3** (940 g, 3.6 mmol) in ethanol (250 ml) was hydrogenated under slight overpressure in the presence of Pd/C catalyst (10 wt.%, 100 mg) overnight. The catalyst was filtered off through a Celite pad and the filtrate evaporated. Chromatography on a silica gel column (methanol–chloroform, 3:97) followed by crystallization (ethyl acetate–methanol, 6:1) afforded hydrochloride of compound **2** (910 mg, 96%) as white crystals, m.p. 155–157 °C. MS (EI), *m/z* (rel. int.): 224 (100, M), 147 (7), 129 (8), 119 (33, M – BnNH + H), 111 (8), 106 (86, BnNH), 97 (11), 91 (41, Bn). HRMS (EI), *m/z*: 224.1065 (M); for $C_{13}H_{12}N_4$ calculated: 224.1062. ^{1}H NMR (500 MHz, DMSO-d_6): 12.99 (br s, 1 H, NH-5); 10.33 (t, 1 H, J(NH,CH_2) = 6.1, NH); 8.61 (s, 1 H, H-2); 7.87 (t, 1 H, J(6,7) = (6, NH) = 3.0, H-6); 7.41 (m, 2 H, Ph); 7.34 (m, 2 H, Ph); 7.27 (m, 1 H, Ph); 6.55 (dd, 1 H, J(7,6) = 3.1, J(7,NH) = 2.0, H-7); 4.87 (d, 1 H, J(CH_2,NH) = 6.1, N-CH_2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 150.96 (dq, ^3J(C-4,H-2) = 10.7, ^3J(C-4,CH_2) = ^2J(C-4,NH) = 3.9, C-4); 145.39 (d, ^1J = 209.0, C-2); 138.01 (m, Ph); 133.52 (dddd, ^3J(C-7a,H-2) = 10.5, ^3J(C-7a,H-6) = 7.8, ^3J(C-7a,NH) = 4.8, ^2J(C-7a,H-7) = 2.9, C-7a); 131.405 (ddd, ^1J = 190.4, ^2J(C-6,H-7) = 7.8, ^2J(C-6,NH) = 3.9, C-6); 128.69 (dd, 2 C, ^1J = 161.1, ^2J = 7.8, Ph); 127.70 (dm, 2 C, ^1J = 158.2, Ph); 127.48 (dt, ^1J = 161.1, ^2J = 7.8, Ph); 113.29 (dddd, ^3J(C-4a,H-6) = 7.8, ^3J(C-4a,H-7) = 5.9, J(C-4a,NH) = 3.9 and 2.5, C-4a); 96.81 (ddd, ^1J = 181.6, ^2J(C-7,H-6) = 8.8, ^3J(C-7,NH) = 4.9, C-7); 43.865 (tt, ^1J = 139.7, ^3J = 3.9, N-CH_2Ph). IR ($CHCl_3$): 3243, 3185, 3111, 2985, 1652, 1592, 1513, 1489, 1406, 1357. UV (MeOH): 285 (21.64), 232 (13.56). For $C_{13}H_{13}ClN_4$ (260.7) calculated: 59.89% C, 5.03% H, 13.60% Cl, 21.49% N; found: 59.34% C, 5.02% H, 13.64% Cl, 21.29% N.

2-[(5*H*-Pyrrolo[3,2-*d*]pyrimidin-4-yl)amino]ethan-1-ol[15] (**6**) Hydrochloride

Compound **5** (2.1 g, 9.7 mmol) in ethanol (400 ml) was hydrogenated under slight overpressure in the presence of Pd/C catalyst (10 wt.%, 200 mg) overnight. The catalyst was filtered off through a Celite pad and the filtrate evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:19) followed by crystallization (ethyl acetate–methanol, 4:1) afforded hydrochloride of **6** (1.8 g, 86%) as white crystals, m.p. 242–244 °C. MS (EI), *m/z* (rel. int.): 178 (27, M), 159 (17), 147 (53, M – CH_2OH), 134 (100, M – CH_3CHO), 118 (67, M – $NHCH_2CH_2OH$), 107 (14). HRMS (EI), *m/z*: 178.0845 (M); for $C_8H_{10}N_4O$ calculated: 178.0855. ^{1}H NMR (500 MHz, DMSO-d_6): 12.74 (s, 1 H, NH-5); 9.67 (t, 1 H, J(NH,CH_2) = 5.5, NH); 8.61 (s, 1 H, H-2); 7.81 (t, 1 H, J(6,7) = J(6,NH) = 3.0, H-6); 6.51 (dd, 1 H, J(7,6) = 3.0, J(7,NH) = 2.0, H-7); 4.80 (br s, 1 H, OH); 3.69–3.62 (m, 4 H, OCH_2 + NCH_2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 151.19 (dq, ^3J(C-4,H-2) = 11.7, ^3J(C-4,CH_2) = ^2J(C-4,NH) = 2.9, C-4); 145.20 (d, ^1J = 209.0, C-2); 133.26 (dddd, ^3J(C-7a,H-2) = 9.8, ^3J(C-7a,H-6) = 6.8, ^3J(C-7a,NH) = 4.8, ^2J(C-7a,H-7) = 2.9, C-7a); 131.13 (ddd, ^1J = 190.4, ^2J(C-6,H-7) = 8.8, ^2J(C-6,NH) = 3.9, C-6); 113.28 (dddd, ^3J(C-4a,H-6) = 7.8, ^3J(C-4a,H-7) = 5.9, J(C-4a,NH) = 3.9 and 2.4, C-4a); 96.80 (ddd, ^1J = 180.7, ^2J(C-7,H-6) = 8.8, ^3J(C-7,NH) = 5.9, C-7); 59.40 (tt, ^1J = 141.6, ^2J = 3.9, OCH_2); 43.62 (br t, ^1J = 140.6, NCH_2). IR (KBr): 3332, 3227, 3180, 3098, 3024, 1650, 1587, 1569, 1509, 1482, 1396, 1353, 1331, 1075, 1064, 1054. UV (MeOH): 282 (17.32), 233 (11.16). For $C_8H_{11}ClN_4O$ (214.7) calculated: 44.76% C, 5.17% H, 16.52% Cl, 26.10% N; found: 44.85% C, 5.10% H, 16.43% Cl, 7.28% N.

2*a*,3,4,5-Tetrahydro-2*a*,5,6,8-tetraazaacenaphthylene (**7**) Hydrochloride

A solution of diisopropyl azodicarboxylate (700 mg, 3.4 mmol) in acetonitrile (10 ml) was added dropwise within 5 min to a suspension of hydrochloride of compound **6** (300 mg, 1.4 mmol) and triphenylphosphine (900 mg, 3.4 mmol) in acetonitrile (50 ml). The reaction mixture was stirred overnight, excess water was added and the volatiles were evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:25) followed by crystallization (ethyl acetate) afforded hydrochloride of **7** (190 mg, 69%) as white crystals, m.p. 227–229 °C. MS (EI), *m/z* (rel. int.): 160 (94, M), 159 (100, M – H), 133 (12), 118 (19), 106 (24), 36 (39). MS (FAB), *m/z* (rel. int.): 161 (100, M + H). HRMS (FAB), *m/z*: 161.0897 (M + H); for $C_8H_9N_4$ calculated: 161.0827. ^{1}H NMR (500 MHz, DMSO-d_6): 12.70 (br, 1 H, NH); 10.35 (br, 1 H, NH); 8.52 (s, 1 H, H-2); 7.93 (d, 1 H, J(6,7) = 2.9, H-6); 6.23 (d, 1 H, J(7,6) = 2.9, H-7); 4.69 (t, 2 H, J = 9.8, CH_2); 4.10 (t, 2 H, J = 9.8, CH_2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 146.55 (m, C-4); 146.51 (ddd, ^3J(C-7a,H-2) = 11.7, ^3J(C-7a,H-6) = 9.8, ^2J(C-7a,H-7) = 2.9, C-7a); 140.49 (d, ^1J = 213.9, C-2); 133.99 (dd, ^1J = 189.5, ^2J(C-6,H-7) = 8.8, C-6); 108.35 (t, ^3J(C-4a,H-6) = ^3J(C-4a,H-7) = 6.8, C-4a); 104.10 (dd, ^1J = 177.7, ^2J(C-7,H-6) = 7.8, C-7); 48.14 (br t, ^1J = 151.4, N-CH_2); 44.16 (tt, ^1J = 149.4, ^2J = 2.9, N-CH_2). IR (KBr): 3134, 3113, 3067, 3034, 3000, 1691, 1677, 1631, 1552, 1508, 1442, 1392, 1354. UV (MeOH): 276 (8.68), 240 (22.36). For $C_8H_9ClN_4$ (196.6) calculated: 48.86% C, 4.61% H, 18.03% Cl, 28.49% N; found: 48.34% C, 4.72% H, 18.03% Cl, 27.76% N.

2-[(4-Benzylamino-5*H*-pyrrolo[3,2-*d*]pyrimidin-2-yl)amino]ethan-1-ol (**8**)

A mixture of compound **3** (1.8 g, 6.8 mmol) and ethanolamine (22 ml, 520 mmol) was heated at 150 °C for 4 h. The reaction mixture was diluted with ethyl acetate, washed with brine, dried over anhydrous magnesium sulfate and evaporated. Chromatography on a silica

gel column (methanol–chloroform, 1:9) afforded compound **8** (1.5 g, 77%) as a colorless oil. MS (EI), *m/z* (rel. int.): 283 (14, M), 265 (11, M – H_2O), 252 (52, M – CH_2OH), 239 (37, M – CH_2CH_2OH), 160 (9, M – BnNH – OH), 148 (7), 134 (17), 118 (6), 106 (24, BnNH), 91 (100, Bn). HRMS (EI), *m/z*: 283.1421; for $C_{15}H_{17}N_5O$ calculated: 283.1433. ^{1}H NMR (500 MHz, DMSO-d_6): 10.55 (br s, 1 H, NH-5); 7.39 (d, 2 H, *J* = 7.5, Ph); 7.35 (t, 1 H, *J*(NH,CH_2) = 5.5, NH-4); 7.34 (t, 2 H, *J* = 7.5, Ph); 7.26 (t, 1 H, *J* = 7.5, Ph); 7.23 (d, 1 H, *J*(6,7) = 2.9, H-6); 6.02 (d, 1 H, *J*(7,6) = 2.9, H-7); 5.82 (t, 1 H, *J*(NH,CH_2) = 5.6, NH-2); 4.80 (br, 1 H, OH); 4.67 (d, 2 H, *J*(CH_2,NH) = 5.5, N-CH_2Ph); 3.52 (t, 2 H, *J*(CH_2,CH_2) = 5.8, CH_2O); 3.31 (q, 2 H, *J*(CH_2,CH_2) = *J*(CH_2,NH) = 5.7, NC**H**$_2$$CH_2O$). ^{13}C NMR (125.7 MHz, DMSO-d_6): 157.98 (t, ^{3}*J*(C-2,CH_2) = 3.9, C-2); 150.09 (td, ^{3}*J*(C-4,CH_2) = 3.9, ^{2}*J*(C-4,NH) = 2.9, C-4); 147.76 (dd, ^{3}*J*(C-7a,H-6) = 7.8, ^{2}*J*(C-7a,H-7) = 2.9, C-7a); 140.09 (m, Ph); 128.57 (dd, 2 C, ^{1}*J* = 160.2, ^{2}*J* = 7.8, Ph); 127.84 (dm, 2 C, ^{1}*J* = 157.2, Ph); 127.095 (dt, ^{1}*J* = 161.1, ^{2}*J* = 7.8, Ph); 126.69 (dd, ^{1}*J* = 183.6, ^{2}*J*(C-6,H-7) = 8.8, C-6); 109.56 (t, ^{3}*J*(C-4a,H-6) = ^{3}*J*(C-4a,H-7) = 6.8, C-4a); 99.60 (dd, ^{1}*J* = 172.9, ^{2}*J*(C-7,H-6) = 8.8, C-7); 61.33 (br t, ^{1}*J* = 139.65, OCH_2); 44.42 (br t, ^{1}*J* = 134.8, NCH_2CH_2); 43.24 (tt, ^{1}*J* = 138.7, ^{3}*J* = 4.9, CH_2Ph). Compound **8** was further characterized as acetate (salt) and hydrochloride.

2-[(4-Benzylamino-5H-pyrrolo[3,2-d]pyrimidin-2-yl)amino]ethan-1-ol acetate. Acetic acid (1 ml) was added to the solution of compound **8** (280 mg, 1 mmol) in methanol (15 ml). The solvent was evaporated and the residue crystallized (methanol–chloroform, 1:25) to afford acetate of compound **8** (330 mg, 97%) as white crystals, m.p. 170–173 °C. IR (KBr): 3326, 3254, 3228, 3167, 1664, 1619, 1595, 1542, 1529, 1394, 1319. For $C_{17}H_{21}N_5O_3$ (343.4) calculated: 59.46% C, 6.16% H, 20.40% N; found: 59.25% C, 6.26% H, 20.28% N.

2-[(4-Benzylamino-5H-pyrrolo[3,2-d]pyrimidin-2-yl)amino]ethan-1-ol hydrochloride. Methanolic hydrogen chloride (1 M, 1 ml) was added to a solution of compound **8** (280 mg, 1 mmol) in methanol (15 ml). The solvent was evaporated and the residue crystallized (methanol–chloroform, 1:25) to afford hydrochloride of compound **8** (310 mg, 97%) as white crystals, m.p. 204–206 °C. UV (MeOH): 292 (14.98), 235 (24.18). For $C_{15}H_{18}ClN_5O$ (319.8) calculated: 56.34% C, 5.67% H, 11.09% Cl, 21.90% N; found: 56.13% C, 5.75% H, 11.26% Cl, 21.64% N.

2-{*N*-[5-Acetyl-4-(benzylamino)-5*H*-pyrrolo[3,2-*d*]pyrimidin-2-yl]acetamido}ethyl Acetate (**9**)

Acetate of compound **8** (2 g, 5.8 mmol) in an acetic anhydride–acetic acid mixture (1:1, 20 ml) was refluxed for 2 h. Methanol (20 ml) was added and the reaction mixture was evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:99) and crystallization (ethyl acetate–petroleum ether, 1:2) afforded compound **9** (1.9 g, 80%) as white crystals, m.p. 155–157 °C. MS (EI), *m/z* (rel. int.): 409 (100, M), 366 (36, M – Ac), 350 (6, M – AcO), 324 (30, M – 2 Ac + H), 308 (63, M – Ac – AcO + H), 294 (48), 279 (20), 264 (84, M – 2 Ac – AcO), 252 (41). HRMS (EI), *m/z*: 409.1763 (M); for $C_{21}H_{23}N_5O_4$ calculated: 409.1750. ^{1}H NMR (500 MHz, DMSO-d_6): 8.95 (t, 1 H, *J*(NH,CH_2) = 5.6, NH); 8.12 (d, 1 H, *J*(6,7) = 3.8, H-6); 7.33 (m, 4 H, Ph); 7.24 (m, 1 H, Ph); 6.68 (d, 1 H, *J*(7,6) = 3.8, H-7); 4.69 (d, 2 H, *J*(CH_2,NH) = 5.6, CH_2Ph); 4.08 (m, 4 H, OCH_2 + NC**H**$_2$$CH_2O$); 2.695 (s, 3 H, Ac); 2.15 (s, 3 H, Ac); 1.80 (s, 3 H, Ac). ^{13}C NMR (125.7 MHz, DMSO-d_6): 171.64 (q, ^{2}*J*(CO,CH_3) = 6.8, CO); 171.11 (qt, ^{2}*J*(CO,CH_3) = 6.8, ^{3}*J*(CO,CH_2) = 2.9, CO); 170.22 (qt, ^{2}*J*(CO,CH_3) = 6.8, ^{3}*J*(CO,CH_2) = 2.9, CO); 156.61 (m, C-2); 153.89 (dd, ^{3}*J*(C-7a,H-6) = 9.8, ^{2}*J*(C-7a,H-7) = 2.9, C-7a); 150.69 (br q, ^{3}*J*(C-4,CH_2) = ^{2}*J*(C-4,NH) = 2,9, C-4); 139.13 (m, Ph); 133.13 (dd, ^{1}*J* = 192.4, ^{2}*J*(C-6,H-7) = 8.8, C-6); 128.65 (dd, 2 C, ^{1}*J* = 160.2, ^{2}*J* = 7.8, Ph); 127.22 (dm, 2 C, ^{1}*J* =

161.1, Ph); 127.115 (dt, ^1J = 160.2, ^2J = 6.8, Ph); 111.18 (dt, ^3J(C-4a,H-6) = ^3J(C-4a,H-7) = 4.9, ^2J(C-4a,NH) = 2.0, C-4a); 108.81 (dd, ^1J = 178.7, ^2J(C-7,H-6) = 6.8, C-7); 61.87 (tt, ^1J = 149.4, ^2J = 3.9, OCH_2); 44.25 (tt, ^1J = 141.6, ^3J = 3.9, CH_2Ph); 44.16 (tm, ^1J = 138.7, NCH_2CH_2O); 24.87 (q, ^1J = 129.9, CH_3); 24.02 (q, ^1J = 130.9, CH_3); 20.68 (q, ^1J = 128.9, CH_3). For $C_{21}H_{23}N_5O_4$ (423.5) calculated: 61.60% C, 5.66% H, 17.10% N; found: 61.29% C, 5.71% H, 16.92% N.

2-{*N*-[4-(Benzylamino)-5*H*-pyrrolo[3,2-*d*]pyrimidin-2-yl-2-isopropanamido}ethyl 2-Methylpropanoate (**10**)

Isobutyryl chloride (1 ml, 10 mmol) was added to a solution of acetate of compound **8** (345 mg, 1 mmol) in pyridine (15 ml) at 0 °C and the reaction mixture was kept at room temperature overnight. Methanol (10 ml) was added, the reaction mixture was taken into ethyl acetate, washed with saturated aqueous sodium hydrogencarbonate and brine, dried over anhydrous magnesium sulfate and evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:99) followed by crystallization (ethyl acetate–petroleum ether, 1:2) afforded compound **10** (230 mg, 54%) as white crystals, m.p. 142–148 °C. MS (EI), *m/z* (rel. int.): 423 (5, M), 352 (6, M – $COCH(CH_3)_2$), 335 (22, M – $(CH_3)_2CHCOOH$), 264 (23, M – $COCH(CH_3)_2$ – $(CH_3)_2CHCOOH$), 252 (9), 160 (22), 132 (8), 106 (5), 91 (30, Bn), 73 (21), 43 (100, i-Pr). HRMS (EI), *m/z*: 423.2314 (M); for $C_{23}H_{29}N_5O_3$ calculated: 423.2270. ^{1}H NMR (500 MHz, DMSO-d_6): 10.98 (br s, 1 H, NH-5); 7.74 (t, 1 H, J(NH,CH_2) = 5.5, NH); 7.53 (t, 1 H, J(6,7) = J(6,NH) = 2.7, H-6); 7.35 (m, 4 H, Ph); 7.25 (m, 1 H, Ph); 6.355 (dd, 1 H, J(7,6) = 2.7, J(7,NH) = 1.6, H-7); 4.70 (d, 2 H, J(CH_2,NH) = 5.5, CH_2Ph); 4.13 (t, 2 H, J(CH_2,CH_2) = 5.7, OCH_2); 4.02 (t, 2 H, J(CH_2,CH_2) = 5.7, NCH_2CH_2O); 3.00 (sept, 1 H, J(CH,CH_3) = 6.7, $CH(CH_3)_2$); 2.27 (sept, 1 H, J(CH,CH_3) = 6.9, $CH(CH_3)_2$); 0.90 (d, 12 H, J(CH_3,CH) = 6.8, CH_3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 177.48 (m, CO); 171.915 (m, CO); 153.74 (m, C-2); 149.93 (q, ^3J(C-4,CH_2) = ^2J(C-4,NH) = 3.9, C-4); 147.76 (ddd, ^3J(C-7a,H-6) = 8.8, ^3J(C-7a,NH) = 5.8, ^2J(C-7a,H-7) = 2.9, C-7a); 139.50 (m, Ph); 128.785 (ddd, ^1J = 186.5, ^2J(C-6,H-7) = 8.8, ^2J(C-6,NH) = 3.9, C-6); 128.55 (dd, 2 C, ^1J = 160.2, ^2J = 6.8, Ph); 127.57 dtt, 2 C, ^1J = 158.2, ^2J = 6.8, ^3J = 3.9, Ph); 127.13 (dt, ^1J = 160.2, ^2J = 6.8, Ph); 111.925 (ddd, ^3J(C-4a,H-6) = 6.9, ^3J(C-4a,H-7) = 5.9, ^2J(C-4a,NH) = 3.9, C-4a); 101.68 (ddd, ^1J = 173.8, ^2J(C-7,H-6) = 7.8, ^3J(C-7,NH) = 4.8, C-7); 62.21 (tt, ^1J = 149.6, ^2J = 3.9, OCH_2); 45,12 (tt, ^1J = 140.6, ^2J = 3.9, NCH_2CH_2O); 43.50 (tt, ^1J = 138.7, ^3J = 3.9, CH_2Ph); 33.255 (d pent, ^1J = 130.0, ^2J = 3.9, $CH(CH_3)_2$); 31.965 (d pent, ^1J = 131.8, ^2J = 3.9, $CH(CH_3)_2$); 19.83 (q pent, ^1J = 127.0, ^2J = 4.9, CH_3); 18.62 (q pent, ^1J = 127.9, ^2J = 4.9, CH_3). For $C_{23}H_{29}N_5O_3$ (423.5) calculated: 65.23% C, 6.90% H, 16.54% N; found: 65.20% C, 6.96% H, 16.12% N.

[4-(Benzylamino)-5*H*-pyrrolo[3,2-*d*]pyrimidin-7-yl]methanol (**11**)

Aqueous formaldehyde (37%, 5 ml, 66 mmol) was added to hydrochloride of compound **2** (690 mg, 2.7 mmol) and potassium carbonate (1.4 g, 10 mmol) in a dioxane–water mixture (4:1, 50 ml) and the solution was refluxed for 1 h. The solvent was evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:20) followed by crystallization (ethyl acetate–petroleum ether, 1:1) afforded compound **11** (450 mg, 67%) as white crystals, m.p. 194–197 °C. MS (EI), *m/z* (rel. int.): 254 (12, M), 236 (21, M – H_2O), 149 (100, M – BnNH + H), 132 (26), 117 (32, M – BnNH – CH_2OH), 106 (70, BnNH), 91 (53, Bn). MS (FAB), *m/z* (rel. int.): 255 (54, M + H), 215 (10), 201(24), 181 (11), 149 (8), 110 (22), 91 (100, Bn). ^{1}H NMR

(500 MHz, DMSO-d_6): 10.97 (br s, 1 H, NH-5); 8.23 (s, 1 H, H-2); 7.72 (t, 1 H, J(NH,CH_2) = 5.6, NH); 7.46 (s, 1 H, H-6); 7.26 (d, 2 H, J = 8.2, Ph); 7.21 (t, 2 H, J = 7.3, Ph); 7.13 (t, 1 H, J = 6.8, Ph); 4.90 (br, 1 H, OH); 4.75 (d, 2 H, J(CH_2,NH) = 5.6, CH_2Ph); 4.62 (s, 2 H, OCH_2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 149.53 (d, ^1J = 197.3, C-2); 149.51 (dq, ^3J(C-4,H-2) = 10.8, ^3J(C-4,CH_2) = ^2J(C-4,NH) = 3.9, C-4); 143.50 (m, C-7a); 139.725 (m, Ph); 128.60 (dd, 2 C, ^1J = 160.2, ^2J = 7.8, Ph); 127.37 (dm, 2 C, ^1J = 158.2, Ph); 127.16 (dt, ^1J = 160.2, ^2J = 6.8, Ph); 126.44 (dt, ^1J = 185.55, ^3J(C-6,CH_2) = 4.9, C-6); 116.28 (br dt, ^2J(C-7,H-6) = 6.8, ^2J(C-7,CH_2) = 7.9, C-7); 113.92 (d, ^3J(C-4a,H-6) = 6.8, C-4a); 54.09 (td, ^1J = 140.6, ^3J(CH_2,H-6) = 1.9, OCH_2); 43.45 (tt, ^1J = 138.7, ^3J = 3.9, CH_2Ph). IR (KBr): 3281, 3247, 3194, 1653, 1632, 1566, 1535, 1495, 1455, 1420, 1334, 1042. UV (MeOH): 282 (13.52), 238 (20.26). For $C_{14}H_{14}N_4O$ (254.3) calculated: 66.13% C, 5.55% H, 23.03% N; found: 65.89% C, 5.46% H, 23.11% N.

Benzyl(7-methyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-4-yl)amine (**12**) Hydrochloride

A solution of compound **11** (280 mg, 1.1 mmol) in a dioxane–water mixture (10:1, 50 ml) was acidified with hydrochloric acid and the mixture was hydrogenated over Pd/C (5%, 50 mg) at slight overpressure overnight. The catalyst was filtered off and the filtrate was evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:20) followed by crystallization (ethyl acetate–petroleum ether, 1:2) afforded hydrochloride of compound **12** (235 mg, 78%) as white crystals, m.p. 222–225 °C. MS (EI), *m/z* (rel. int.): 238 (99, M), 220 (6), 161 (7, M – Ph), 147 (10, M – Bn), 133 (41, M – BnNH + H), 106 (100, BnNH), 91 (54, Bn). ^{1}H NMR (500 MHz, DMSO-d_6): 14.76 (br, 1 H, NH); 12.71 (br s, 1 H, NH); 10.25 (t, 1 H, J(NH,CH_2) = 6.0, NH); 8.60 (s, 1 H, H-2); 7.64 (br d, 1 H, J(6,NH) = 2.7, H-6); 7.39 (d, 2 H, J = 7.2, Ph); 7.33 (t, 2 H, J = 7.2, Ph); 7.26 (t, 1 H, J = 7.2, Ph); 4.86 (d, 2 H, J(CH_2,NH) = 6.0, CH_2Ph); 2.25 (s, 3 H, CH_3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 150.82 (dq, ^3J(C-4,H-2) = 10.7, ^3J(C-4, CH_2) = ^2J(C-4,NH) = 3.9, C-4); 144.97 (br d, ^1J = 208.0, C-2); 138.06 (m, Ph); 132.69 (m, C-7a); 129.59 (br dpent, ^1J = 188.5, ^3J(C-6,CH_3) = 5.9, ^3J(C-6,NH) = 3.9, C-6); 128.66 (dd, 2 C, ^1J = 160.2, ^2J = 7.8, Ph); 127.66 (dm, 2 C, ^1J = 158.2, Ph); 127.425 (dt, ^1J = 160.2, ^2J = 7.8, Ph); 113.21 (ddd, ^3J(C-4a,H-6) = 8.8, J(C-4a,NH) = 3.9 and 1.9, C-4a); 106.08 (pentd, ^2J(C-7,H-6) = ^2J(C-7,CH_3) = 6.8, ^3J(C-7,NH) = 3.9, C-7); 43.82 (tt, ^1J = 139.7, ^3J = 3.9, CH_2Ph); 8.70 (q, ^1J = 127.9, CH_3). IR (KBr): 3249, 3185, 3155, 2812, 2789, 1653, 1596, 1516, 1472, 1360. UV (MeOH): 285 (17.25), 241 (13.78). For $C_{14}H_{15}ClN_4$ (274.7) calculated: 61.20% C, 5.50% H, 12.90% Cl, 20.39% N; found: 60.98% C, 5.53% H, 12.98% Cl, 20.43% N.

Benzyl[7-(methoxymethyl)-5*H*-pyrrolo[3,2-*d*]pyrimidin-4-yl]amine (**13**)

Methanolic hydrogen chloride (1 M, 1 ml) was added to a solution of compound **11** (250 mg, 1 mmol) in methanol (20 ml) and the mixture was refluxed for 1 h. The reaction mixture was neutralized with methanolic ammonia (1 M) and evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:20) followed by crystallization (ethyl acetate–petroleum ether, 2:1) afforded compound **13** (250 mg, 92%) as white crystals, m.p. 147–149 °C. MS (FAB), *m/z* (rel. int.): 269 (67, M + H), 237 (17), 147 (18, M – Bn – OMe + H), 102 (69), 91 (100). ^{1}H NMR (500 MHz, DMSO-d_6): 13.10 (br s, 1 H, NH-5); 10.46 (t, 1 H, J(NH,CH_2) = 5.8, NH); 8.62 (s, 1 H, H-2); 7.89 (d, 1 H, J(6,NH) = 2.1, H-6); 7.36 (d, 2 H, J = 7.2, Ph); 7.31 (t, 2 H, J = 7.2, Ph); 7.24 (t, 1 H, J = 7.2, Ph); 4.87 (d, 2 H, J(CH_2,NH) = 5.8, CH_2Ph); 4.54 (s, 2 H, CH_2O); 3.26 (s, 3 H, OCH_3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 151.04 (m, C-4); 145.56 (d, ^1J = 209.0, C-2); 137.94 (m, Ph); 132.34 (m, C-7a); 130.91 (br dq, ^1J = 189.5, ^2J(C-6,NH) =

^3J(C-6,CH_2) = 4.9, C-6); 128.68 (dd, 2 C, ^1J = 160.2, ^2J = 7.8, Ph); 127.66 (dm, 2 C, ^1J = 158.2, Ph); 127.48 (dt, ^1J = 161.1, Ph); 113.45 (br dd, ^3J(C-4a,H-6) = 8.8, ^2J(C-4a, NH) = 3.0, C-4a); 108.355 (m, C-7); 63.53 (tq, ^1J = 143.6, ^3J(OCH_2,OCH_3) = 4.9, OCH_2); 57.11 (qt, ^1J = 140.6, ^3J(OCH_3,OCH_2) = 3.9, OCH_3), 43.83 (tt, ^1J = 140.6, ^3J(CH_2Ph,Ph) = 3.9, CH_2Ph). IR ($CHCl_3$): 3251, 3194, 3112, 2970, 1653, 1597, 1509, 1472, 1407, 1357. For $C_{15}H_{16}N_4O$ (268.3) calculated: 67.15% C, 6.01% H, 20.88% N; found: 66.97% C, 5.84% H, 20.65% N.

N^4-Benzyl-*N*^{2}-{2-[(4,4′-dimethoxytrityl)oxy]ethyl}-5*H*-pyrrolo[3,2-*d*]pyrimidine-2,4-diamine (**14**)

Tributylamine (7.2 ml, 30 mmol) and 4,4′-dimethoxytrityl chloride (3 g, 4.4 mmol) were added to acetate of compound **8** (1.4 g, 4 mmol) in dimethyl sulfoxide (20 ml) and the reaction mixture was stirred for 3 h. Methanol (10 ml) was added, the reaction mixture was taken into ethyl acetate, washed with saturated aqueous sodium hydrogencarbonate and brine, dried over anhydrous magnesium sulfate and evaporated. Chromatography on a silica gel column (methanol–triethylamine–chloroform, 2:8:90) afforded compound **14** (2.1 g, 89%) as a colorless oil. MS (FAB), *m/z*: 586 (M + H). ^{1}H NMR (500 MHz, DMSO-d_6): 12.35 (br s, 1 H, NH); 10.50 (br, 1 H, NH); 9.80 (br s, 1 H, NH); 7.50 (t, 1 H, *J*(6,7) = *J*(6,NH) = 2.8, H-6); 7.36–7.14 (m, 14 H, Ph); 6.77 (m, 4 H, Ph); 6.22 (br t, 1 H, *J*(7,6) = *J*(7,NH) = 3.0, H-7); 4.64 (d, 2 H, *J*(CH_2,NH) = 5.5, CH_2Ph); 3.67 (s, 6 H, OCH_3); 3.55 (br q, 2 H, *J*(CH_2,CH_2) = *J*(CH_2,NH) = 5.5, NC**H**$_2$$CH_2$O); 3.08 (t, 2 H, *J*($CH_2$,$CH_2$) = 5.1, CH_2O). ^{13}C NMR (125.7 MHz, DMSO-d_6): 158.13 (2 C, Ph); 152.25 (C-2); 151.25 (C-4); 145.07 (Ph); 138.52 (Ph); 135.77 (2 C, Ph); 134.47 (C-7a); 129.83 (4 C, Ph); 128.50 (4 C, Ph); 127.83 (4 C, Ph); 127.59 (Ph); 127.21 (Ph); 126.71 (C-6); 113.14 (4 C, Ph); 108.43 (C-4a); 95.54 (C-7); 85.53 (**C**Ph(Ph-OCH_3)$_2$); 61.70 (OCH_2); 55.13 (2 C, OCH_3); 43.53 (NCH_2); 41.34 (NCH_2). For $C_{36}H_{37}N_5O_3$ (587.7) calculated: 73.82% C, 6.02% H, 11.96% N; found: 73.59% C, 5.94% H, 11.77% N.

{4-Benzylamino-2-[2-(4,4′-dimethoxytrityloxy)ethylamino]-5*H*-pyrrolo[3,2-*d*]-pyrimidin-7-yl}methanol (**15**)

Aqueous formaldehyde (37%, 8 ml) was added to compound **14** (1.8 g, 3.1 mmol) and potassium carbonate (2.5 g, 18 mmol) in a dioxane–water mixture (4:1, 30 ml) and the solution was refluxed for 1 h. The reaction mixture was taken into ethyl acetate, washed with brine, dried over anhydrous magnesium sulfate and evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:20) afforded compound **15** (1.3 g, 67%) as colorless thick oil. MS (FAB), *m/z* (rel. int.): 616 (M + H). ^{1}H NMR (500 MHz, DMSO-d_6): 10.45 (br s, 1 H, NH-5); 7.45 (br, 1 H, NH); 7.40–7.15 (m, 15 H, Ph + H-6); 6.80 (m, 4 H, Ph); 6.10 (br s, 1 H, NH); 4.61 (d, 2 H, *J*(CH_2,NH) = 5.6, CH_2Ph); 4.60 (br, 1 H, OH); 4.50 (s, 2 H, C**H**$_2$OH); 3.69 (s, 6 H, OCH_3); 3.50 (q, 2 H, *J*(CH_2,CH_2) = *J*(CH_2,NH) = 6.3, NC**H**$_2$$CH_2$O); 3.03 (t, 2 H, *J*($CH_2$,$CH_2$) = 6.3, OC**H**$_2$$CH_2$N). ^{13}C NMR (125.7 MHz, DMSO-d_6): 158.08 (m, 2 C, Ph); 157.225 (m, C-2); 149.97 (q, ^3J(C-4,CH_2) = ^2J(C-4,NH) = 3.9, C-4); 145.45 (t, 2 C, ^2J = 6.8, Ph); 140.11 (dt, ^3J(C-7a,H-6) = 9.8, ^3J(C-7a,CH_2) = 4.9, C-7a); 136.17 (t, 2 C, ^2J = 6.8, Ph); 129.81 (m, 4 C, Ph); 128.45 (m, 2 C, Ph); 127.88 (m, 2 C, Ph); 127.82 (m, 2 C, Ph); 127.705 (m, 2 C, Ph); 126.96 (m, Ph); 126.63 (m, Ph); 125.34 (dd, ^1J = 180.7, ^3J(C-6,CH_2) = 2.9, C-6); 114.29 (dt, ^2J(C-7,H-6) = 6.8, ^2J(C-7,CH_2) = 4.9, C-7); 113.18 (dd, 4 C, ^1J = 160.2, ^2J = 4.9, Ph); 109.51 (d, ^3J(C-4a,H-6) = 6.8, C-4a); 85.26 (s, OC-Ph_3); 62.86 (br t, ^1J = 142.6, CH_2OH);

55.10 (q, 2 C, ^1J = 144.5, OCH_3); 54.45 (t, ^1J = 140.6, OCH_2CH_2N); 43.20 (br t, ^1J = 138.7, CH_2Ph); 41.55 (br t, ^1J = 136.7, NCH_2CH_2O). For $C_{37}H_{37}N_5O_4$ (615.7) calculated: 72.17% C, 6.06% H, 11.37% N; found: 72.34% C, 5.91% H, 11.09% N.

2-{[4-(Benzylamino)-7-methyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-2-yl]amino}ethan-1-ol (**1**) Hydrochloride

A solution of compound **15** (610 mg, 1 mmol) in a dioxane–water mixture (7:1, 50 ml) was acidified with hydrochloric acid and the reaction mixture was hydrogenated at slight overpressure in the presence of Pd/C catalyst (10 wt.%, 50 mg) overnight. The catalyst was filtered off through a Celite pad and the filtrate was evaporated. Chromatography on a silica gel column (methanol–chloroform, 1:12) followed by crystallization (ethyl acetate–ethanol, 3:1) afforded the title hydrochloride **1** (235 mg, 71%) as white crystals, m.p. 250–252 °C. MS (EI), *m/z* (rel. int.): 297 (20, M), 278 (7), 266 (49, M – CH_2OH), 253 (26, M – CH_2CH_2OH), 174 (10), 162 (6), 148 (15), 130 (6), 120 (10), 106 (16, BnNH), 91 (100, Bn). ^{1}H NMR (500 MHz, DMSO-d_6): 12.44 (br, 1 H, NH); 11.90 (s, 1 H, NH); 9.68 (t, 1 H, J(NH,CH_2) = 5.8, NH); 7.39 (d, 2 H, J = 7.4, Ph); 7.32 (t, 2 H, J = 7.5, Ph); 7.27 (br d, 1 H, J(6,7) = 2.9, H-6); 7.24 (t, 1 H, J = 7.2, Ph); 4.91 (br, 1 H, OH); 4.72 (d, 2 H, J(CH_2,NH) = 5.8, CH_2Ph); 3.52 (t, 2 H, J(CH_2,CH_2) = 5.5, $NC\mathbf{H}_2CH_2O$); 3.45 (dt, 2 H, J(CH_2,OH) = 5.7, J(CH_2,CH_2) = 5.5, $OC\mathbf{H}_2CH_2N$); 2.10 (s, 3 H, CH_3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 152.27 (m, C-2); 151.25 (q, ^3J(C-4,CH_2) = ^2J(C-4,NH) = 3.9, C-4); 138.64 (m, Ph); 133.21 (m, C-7a); 128.61 (dd, 2 C, ^1J = 160.2, ^2J = 6.8, Ph); 127.91 (dm, 2 C, ^1J = 158.2, Ph); 127.34 (dt, ^1J = 163.1, ^2J = 7.8, Ph); 127.29 (dq, ^1J = 180.0, ^3J(C-6,CH_3) = 4.9, C-6); 108.27 (dt, ^3J(C-4a,H-6) = 7.8, J(C-4a,NH) = 2.9, C-4a); 104.14 (pent, ^2J(C-7,H-6) = ^2J(C-7,CH_3) = 6.8, C-7); 59.60 (t, ^1J = 141.6, OCH_2CH_2N); 43.77 (t, 2 C, ^1J = 138.7, NCH_2CH_2O); 8.54 (q, ^1J = 127.0, CH_3). IR (KBr): 3361, 3269, 3215, 1659, 1649, 1616, 1593, 1573, 1543, 1474, 1390, 1355, 1059. UV (MeOH): 294 (15.96), 237 (23.80). For $C_{16}H_{20}ClN_5O$ (333.8) calculated: 57.57% C, 6.04% H, 10.62% Cl, 20.98% N; found: 57.72% C, 6.02% H, 10.89% Cl, 20.77% N.

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