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Efficient synthesis of 2,9-disubstituted 8-hydroxyadenine derivatives

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An efficient and general method for the synthesis of 2,9-disubstituted 8-hydroxyadenines, which are expected to have various biological activities, was realized. 5-Amino-4-cyano-2-hydroxyimidazoles (**1**) were prepared from aminomalononitrile and isocyanates as key intermediates. The condensation of **1a** with amidines, imidates, guanidine, urea and thioureas afforded 8-hydroxyadenines (**2**–**6**) possessing various substituents at the 2-position. Furthermore, selective alkylation of 2-amino- and 2-hydroxyadenines (**4** and **6**) successively proceeded to give the corresponding 2-alkylamino- and 2-alkoxyadenines (**5** and **7**), respectively. 2-Alkylthioadenines (**15**) were prepared by an analogous reaction of **1a** with benzoyl isothiocyanate and subsequent *S*-alkylation. The imidazoles **1** are most useful intermediates for the synthesis of 8-hydroxyadenine derivatives.

9-Benzyladenine derivatives substituted in positions 2 and/or 8 constitute a variety of pharmacologically active compounds for which different targets can be postulated. Because they resemble the structure of adenosine, they may compete with the neuromodulator at its specific pharmacological receptors, transport proteins, or metabolic enzymes. For example, the following have been reported: 9-benzyladenine inhibits adenylate cyclase,[1] 9-(4-bromoacetamidobenzyl)adenine inhibits adenosine deaminase,[2] 2-substituted 9-benzyladenines with anti-inflammatory activity,[3] N^6-methyl-9-(2-fluorobenzyl)-adenine has anti-convulsant activity,[4] 2-chloro-9-(2,6-difluorobenzyl)adenine inhibits *c*AMP phosphodiesterase type 2,[5] 9-(2-fluorobenzyl)-N^6-methyl-2-trifluoromethyladenine inhibits *c*AMP phosphodiesterase type 4,[6] N^6-dimethyl-9-(4-methylbenzyl)-2-trifluoromethyladenine has anti-rhinovirus activity,[7] and 9-(2-methoxybenzyl)-2-propyladenines have anti-TNF-α activity.[8] Very recently we found a relatively potent interferon-inducing activity in 9-benzyl-8-hydroxyadenines.[9] Interestingly, 8-hydroxyadenine was found as an oxidized metabolite of DNA lesions.[10] Furthermore, certain 9-substituted (mainly 9-benzyl-) 8-hydroxyadenine derivatives show antagonism to a corticotropin-releasing hormone receptor,[11] anti-rhinovirus activity,[12] and excellent binding affinity to a benzodiazepine receptor.[13] As just described, 9-benzyl- and/or 8-hydroxyadenine derivatives possess various types of biological activities depending upon their substituents on the adenine ring. 9-Substituted 8-hydroxyadenines have been mostly synthesized by hydrolysis of the corresponding 8-bromoadenines,[12–14] oxidation of adenines at the 8-position,[15] and ring closure of 4,5-diaminopyrimidine with phosgene[11] or urea.[16] However, it is quite difficult to introduce directly a variety of substituents at the 2-position of the adenine nucleus according to the previously reported synthetic methods. Accordingly, we directed our efforts to the development of a novel and widely applicable method for the synthesis of 2,9-disubstituted 8-hydroxyadenines.[17] Herein we describe an efficient method for the preparation of such 8-hydroxyadenine derivatives *via* cyclization of 5-amino-4-cyano-2-hydroxyimidazoles. In particular, our attention was focused on the synthesis of 8-hydroxyadenines possessing a benzyl group at the 9-position in expectation of the biological activities as noted above.

Results and discussion

Our first attempts to achieve the synthesis of 1-substituted 5-amino-4-cyano-2-hydroxyimidazoles (**1**) were made by the reaction of aminomalononitrile *p*-toluenesulfonate (1.0 equiv) and *i*-Pr_2NEt (0.8 equiv) with benzyl isocyanate generated from the reaction of triphosgene and benzylamine in THF. It should be noted that the reaction efficiency was highly dependent on the quantity of *i*-Pr_2NEt used. The reaction in the presence of 0.8 equiv (*vs.* aminomalononitrile *p*-toluenesulfonate) of *i*-Pr_2NEt was found to proceed smoothly. However, the use of more than 1.0 equiv of *i*-Pr_2NEt drastically decreased the yield of **1** (*ca.* 20% yield in the case of **1a**) because the excess base causes polymerization of free aminomalononitrile.[18] Reactions with various amines under similar conditions were carried out. Moderate to high yields of the corresponding products (**1b**–**i**) could be obtained for a wide array of benzylamines with triphosgene and aminomalononitrile. Both electron-donating and -withdrawing substituents on the aromatic ring of the benzylamines are tolerated in the reaction. However, the reaction with 4-aminobenzylamine was complicated, and hence the corresponding 1-(4-aminobenzyl)imidazole derivative could hardly be obtained. An efficient formation could be obtained for α-naphthylmethylamine and aniline, yielding the corresponding 1-α-naphthylmethylimidazole (**1j**) and 1-phenylimidazole (**1k**) in good yields (75% and 73%), respectively. In the case of alkylamines, such as butylamine, heptylamine, phenethylamine and 3-phenylpropylamine, the reactions gave the products (**1l**–**o**) in low yields (19%–41%). The use of larger amounts of an isocyanate and prolongation of the reaction time did not improve the yields.

The cyclization of the 1-substituted 5-amino-4-cyano-2-hydroxyimidazoles (**1a**–**o**) using formamidine hydrochloride (4.0–8.0 equiv) in refluxing 2-methoxyethanol was explored. Such cyclization was found to give the desired 9-substituted 8-hydroxyadenine products (**2a**–**o**) in good to moderate yields (42%–87%). In the case of the cyclization of 1-alkylimidazoles (**1l**–**m**), the yields were lower than those of the reaction of 1-benzylimidazole derivatives (Scheme 1).

A series of 2-substituted 9-benzyl-8-hydroxyadenine derivatives (**3**–**6**) were synthesized under similar cyclization conditions employing the representative 1-benzylimidazole (**1a**) to further explore the reaction scope (Scheme 2). By the use of acetamidine and benzamidine, the cyclization reaction gave the desired products, 2-methyl- and 2-phenyl-9-benzyl-8-hydroxyadenines (**3a** and **3h**), in 70% and 31% yields, respectively. The condensation of **1a** with imidate hydrochlorides, which were prepared from the corresponding nitriles, afforded 2-alkyl-9-benzyl-8-hydroxyadenines (**3b**–**d**). 2-Amino-9-benzyl-8-hydroxyadenine (**4**) was produced in 75% yield by the reaction of **1a** and guanidine hydrochloride under the same conditions as those of the reaction with amidines. When urea was used in

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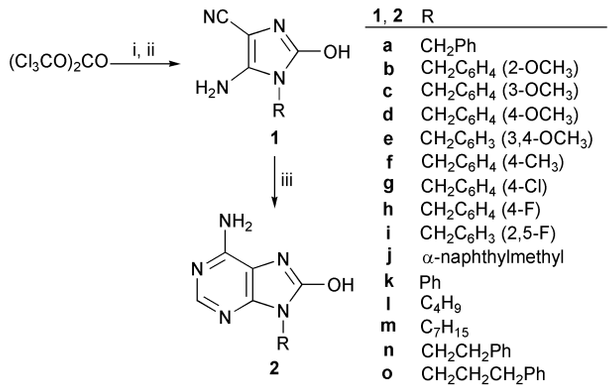
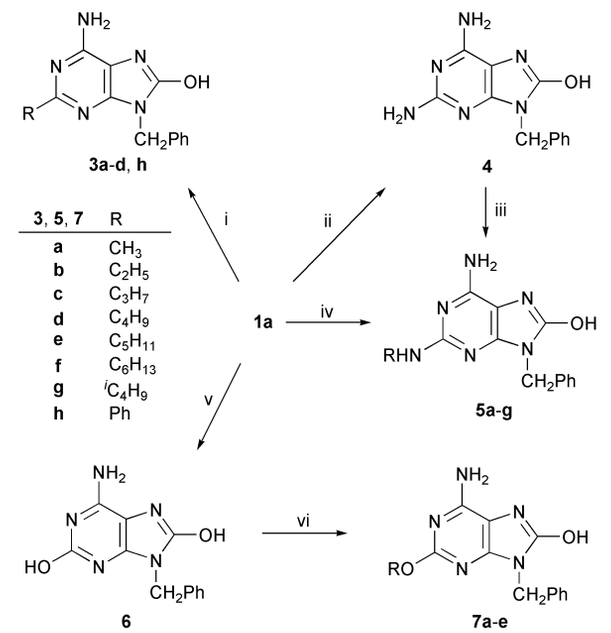


Scheme 1 *Reagents and conditions*: (i) RNH_2, *i*-Pr_2NEt, THF, −80 °C; (ii) $H_2NCH(CN)_2$, THF, rt; (iii) $HC(NH)NH_2$·HCl, $HOCH_2CH_2OCH_3$, reflux.

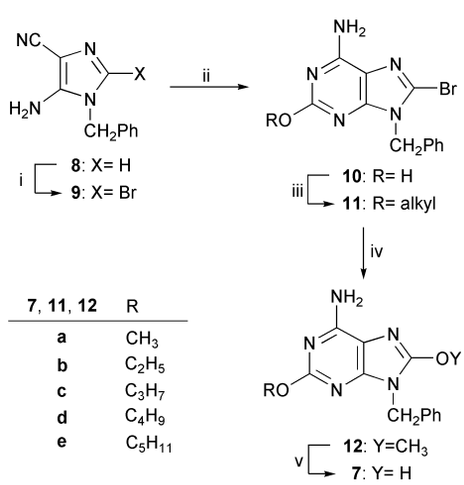


Scheme 2 *Reagents and conditions*: (i) $RC(NH)NH_2$·HCl or $RC(NH)OC_2H_5$·HCl, $NaOC_2H_5$, C_2H_5OH, reflux; (ii) $H_2NC(NH)NH_2$·HCl, $NaOC_2H_5$, C_2H_5OH, reflux; (iii) aldehyde, $NaBH_3CN$, CH_3OH, rt; (iv) $RHNCSNH_2$, neat; (v) H_2NCONH_2, neat; (vi) alkyl halide, LiH, DMF, rt.

the cyclization of **1a**, the elimination of ammonia proceeded smoothly in preference to the dehydration to give 2-hydroxyadenine (**6**) in 72% yield. On the other hand, in the case of thiourea, a 2-aminoadenine derivative (**4**) was formed with accompanying elimination of hydrogen sulfide. It should be noted that a 2-mercapto product, which might be formed by the elimination of ammonia, could not be detected in the reaction mixture. The reactions of **1a** with *N*-methyl- and *N*-ethylthioureas proceeded similarly to afford the 2-methylamino- and 2-ethylaminoadenines (**5a** and **5b**), respectively (44% and 12%).

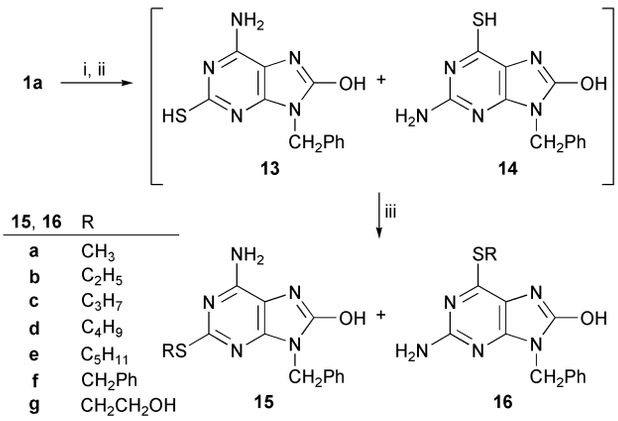
Subsequently, the alkylation of the 2-amino group of **4** and the 2-hydroxyl group of **6** was investigated in order to prepare various 2-alkylamino- and 2-alkoxyadenine derivatives. The selective alkylation of the 2-amino group of **4** was achieved by the reductive alkylation with an aldehyde using sodium cyanoborohydride ($NaBH_3CN$).[19] The reductive alkylation of **4** with acetaldehyde (34 equiv) gave 9-benzyl-2-ethylamino-8-hydroxyadenine (**5b**) in 63% yield. The structure of the product was confirmed by comparison with **5b** prepared above. It should be noted that the reductive alkylation proceeded regioselectively at the 2-amino group, although traces of multi-alkylated products were detected in the reaction mixture. The regioselectivity would be caused by the difference in basicity between the 2- and 6-amino groups.[20] The alkylation of **4** with other aliphatic aldehydes (8 equiv) smoothly afforded the corresponding 2-alkylamino-9-benzyl-8-hydroxyadenines (**5c**–**f**) in good yields (67%–94%). In the case of a bulky aldehyde, isobutyraldehyde, the reaction was slightly suppressed and the desired product (**5g**) was obtained in 53% yield together with recovery of **4** in 40% yield. On the other hand, the O^2-alkylation of **6** with alkyl halides in the presence of lithium hydride gave 2-alkoxy derivatives (**7a**–**e**) in low yields. The use of larger amounts of the reagents and a higher reaction temperature did not improve the yields of **7**, but the formation of 2-*O*, 7-*N*-dialkylated products was observed in the reaction mixture.

Therefore, we attempted to develop an efficient synthetic route to obtain the 2-alkoxy derivatives (**7**) (Scheme 3). To prevent the alkylation at the 7-*N*, we chose 9-benzyl-8-bromo-2-hydroxyadenine (**10**) as a key intermediate. The intermediate **10** was synthesized in two steps from 5-amino-1-benzyl-4-cyanoimidazole (**8**).[21] The imidazole **8** was brominated by *N*-bromosuccinimide, followed by cyclization with urea to give **10** in 77% yield (2 steps) *via* the isolation of the 2-bromoimidazole (**9**). Subsequent alkylation of **10** proceeded on the 2-hydroxyl group regioselectively to give the corresponding 2-alkoxy derivatives (**11a**–**e**) without any di-alkylated products except in the case of **11a**. Unfortunately, the hydrolysis of **11** under acidic conditions proceeded not only at the 8-bromo group but also at the 2-alkoxy group, while the hydrolysis of **11** under basic conditions hardly proceeded. Although the hydrolysis of **11** failed to give the desired 2-alkoxy-8-hydroxyadenines (**7**) directly, the hydrolysis of 8-methoxyadenines **12**, which are methanolysis products of **11**, enabled the preparation of **7**. Thus, the conversion of the 8-bromo group of **11** into a methoxy group was easily achieved by refluxing in a mixture of methanol and 1 M sodium hydroxide solution. Finally, hydrolysis of 8-methoxyadenines **12** was accomplished under acidic conditions to yield 2-alkoxy-9-benzyl-8-hydroxyadenine derivatives (**7a**–**e**) in better yields compared with the yields described in Scheme 2.



Scheme 3 *Reagents and conditions*: (i) NBS. THF, rt; (ii) urea, neat; (iii) alkyl halide, K_2CO_3, DMF, rt; (iv) 1 M NaOH aq., CH_3OH, reflux; (v) *c.* HCl, rt.

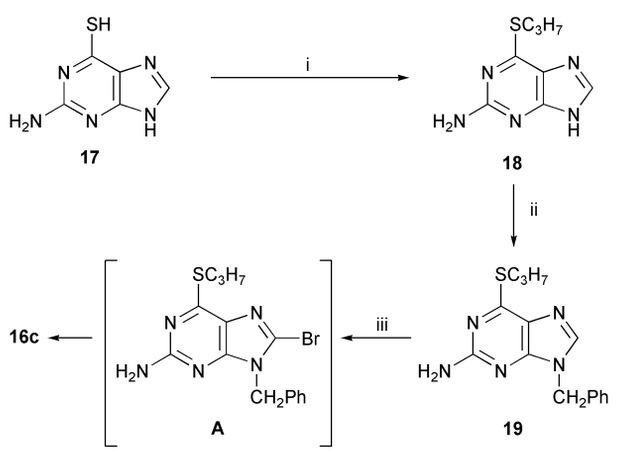
As the condensation reaction of **1a** with thiourea failed to give 9-benzyl-8-hydroxy-2-mercaptoadenine (**13**) as shown in Scheme 2, cyclization of **1a** with benzoyl isothiocyanate was examined (Scheme 4). Treatment of **1a** with benzoyl isothiocyanate followed by the cyclization in the presence of 2 M sodium hydroxide in refluxing THF gave a mixture of the desired 9-benzyl-8-hydroxy-2-mercaptoadenine (**13**) and 9-benzyl-8-hydroxythioguanine (**14**). The isolation of each product was not accomplished because of the easy formation of disulfides by air oxidation of **13** and **14** during the silica gel column chromatography. Therefore, the mixture was directly alkylated under N_2 bubbling conditions using alkyl halides in



Scheme 4 *Reagents and conditions*: (i) BzNCS, THF, rt; (ii) 2 M NaOH aq., THF, reflux; (iii) alkyl halide, K_2CO_3, DMF, rt (in the case of **15g** and **16g**, the reaction was carried out at 60 °C).

the presence of potassium carbonate to result in the isolation of the corresponding 2-alkylthio derivatives (**15a**–**g**) as well as the 6-alkylthio derivatives (**16a**–**g**) without the formation of any disulfides (**15** : **16** = 3 : 1 ~ 2 : 1).

The structures of the by-products **16** were determined by an alternative synthesis. The 6-propylthiopurine (**16c**) was representatively synthesized from thioguanine (**17**) as outlined in Scheme 5. Thus, the propylation of the thiol group of **17** afforded the 6-propylthiopurine (**18**), which was subsequently benzylated at the 9-position to provide 9-benzyl-6-propylthioguanine (**19**). Subsequent bromination of **19** in acetic acid gave the corresponding product (**16c**) without isolation of an 8-bromo intermediate (**A**).

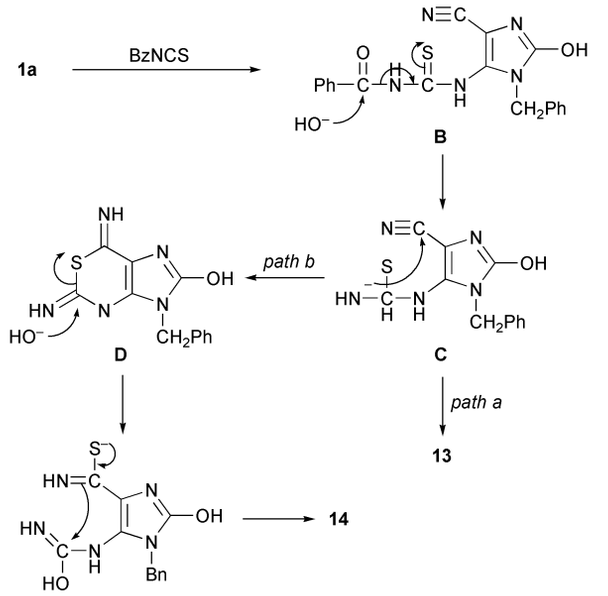


Scheme 5 *Reagents and conditions*: (i) C_3H_7I, K_2CO_3, DMF, rt; (ii) $PhCH_2Br$, K_2CO_3, DMF, rt.; (iii) Br_2, AcOH, 70 °C.

Considering the foregoing results, we propose a plausible reaction pathway for the formation of **13** and **14** as depicted in Scheme 6. The addition of benzoyl isothiocyanate to the 5-amino group of **1a** gives an *N*-benzoylthiourea intermediate (**B**). Under basic conditions, the benzoyl group of **B** is saponified to give a thiourea intermediate (**C**). When the terminal amino group of **C** cyclizes with the cyano group (path a), the desired 2-mercapto derivative (**13**) is formed. On the other hand, attack of the generated thiorate anion of **C** on the cyano group gives a 1,3-thiazine intermediate **D** (path b) and subsequent Dimroth-type rearrangement of **D** would give the 6-mercapto derivative **14**.

Conclusion

We have developed a novel and efficient synthetic method for 8-hydroxyadenines (**2**–**7** and **15**) *via* 5-amino-4-cyano-2-hydroxyimidazole derivatives (**1**) as key intermediates.



Scheme 6

Furthermore, an alternative synthetic route to obtain 2-alkoxy-8-hydroxyadenines (**7**) efficiently *via* 5-amino-2-bromo-4-cyanoimidazole (**9**) was established. These methods allowed us to introduce various types of substituents directly at the 2- and 9-positions of the 8-hydroxyadenine nucleus using relatively nontoxic and inexpensive reagents under mild conditions. Biological activities of 2,9-disubstituted 8-hydroxyadenines prepared here have been partially studied, and the detailed results will be reported elsewhere.

Experimental

Melting points were determined on a Yanagimoto melting-point apparatus and are uncorrected. UV absorption spectra were recorded on a Shimadzu 260 spectrophotometer. IR spectra were measured using a Perkin Elmer 1640 FT-IR spectrometer (KBr). ^{1}H NMR spectra were recorded on a JEOL GX-270 (270 MHz) or JEOL JNM EX-400 (400 MHz) spectrometer using DMSO-d_6 as a solvent. Chemical shifts are given in ppm (δ), coupling constants (J) are given in Hz, and splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; *, deuterium exchangeable. ^{13}C NMR spectra were recorded on a JEOL JNM EX-400 (100 MHz) spectrometer using DMSO-d_6 as a solvent. Chemical shifts are given in ppm (δ) relative to internal solvent signals. Mass spectra were recorded on a JMS-SX 102A spectrometer. Elemental analyses were performed on a Yanagimoto MT-3 instrument, and the results (C, H, N) were within ±0.3% of the theoretical values. Thin-layer chromatographic (TLC) analyses were carried out on 0.25 mm Silica Gel 60 F_{254} plates (Art 5715, Merck). The silica gel used for column chromatography was Silica Gel 60 (230–400 mesh, Merck).

Typical procedure for the synthesis of 1-substituted 5-amino-4-cyano-2-hydroxyimidazole derivatives 1a–o

To a solution of triphosgene (6.58 mmol) in dry THF (20 mL) was added a solution of a primary amine (19.74 mmol) and *N*,*N*-diisopropylethylamine (31.59 mmol) in dry THF (40 mL) dropwise at −80 °C. To the mixture was added a solution of aminomalononitrile *p*-toluenesulfonate (19.74 mmol) and *N*,*N*-diisopropylethylamine (15.79 mmol) in dry THF (20 mL) dropwise at room temperature. The mixture was stirred at room temperature for 24 h. THF was removed under reduced pressure, and the residue was partitioned between AcOEt (200 mL) and water (100 mL). The organic layer was washed with brine (100 mL) and extracted with 1 M NaOH solution (2 × 100 mL).

The combined 1 M NaOH solution layer was neutralized with 10% $NaHSO_4$ solution and extracted with AcOEt (200 mL). The organic layer was washed with brine (100 mL) and dried over $MgSO_4$. The solvent was evaporated off, and the residue was triturated with Et_2O (20 mL) and then filtered to give **1**.

5-Amino-1-benzyl-4-cyano-2-hydroxyimidazole 1a. Yield 85%; mp 216–218 °C (recrystallized from AcOEt) (Found: C, 61.61; H, 4.82; N, 25.95. Calc. for $C_{11}H_{10}N_4O$: C, 61.67; H, 4.71; N, 26.15%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 269.0 (ε/dm^3 mol^{-1} cm^{-1} 13 800); ν_{max}/cm^{-1} 3456, 2202, 1720, 1652, 1494, 737; δ_H 4.75 (2 H, s, 1-CH_2), 6.48 (2 H, s*, 5-NH_2), 7.20–7.36 (5 H, m, 1-Ph), 9.89 (1 H, s*, 2-OH); δ_C 42.1, 67.4, 115.3, 127.0, 127.3, 128.4, 136.8, 144.8, 149.8; *m*/*z* (EI) 214 (M$^+$, 33%), 91 (100).

5-Amino-4-cyano-2-hydroxy-1-(2-methoxybenzyl)imidazole 1b. Yield 41%; mp 230–232 °C (recrystallized from EtOH) (Found: C, 58.99; H, 5.01; N, 22.90. Calc. for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95; N, 22.94%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 269.4 (ε/dm^3 mol^{-1} cm^{-1} 14 600); ν_{max}/cm^{-1} 3456, 2194, 1680, 1634, 1494, 1249, 760, 632; δ_H 3.82 (3 H, s, 1-CH_3), 4.70 (2 H, s, 1-CH_2), 6.37 (2 H, s*, 5-NH_2), 6.70 (1 H, d, *J* 7.7, 1-Ar), 6.89 (1 H, t, *J* 7.7, 1-Ar), 7.01 (1 H, d, *J* 7.7, 1-Ar), 7.25 (1 H, t, *J* 7.7, 1-Ar), 9.90 (1 H, s*, 2-OH); δ_C 38.0, 55.3, 67.4, 110.6, 115.3, 120.3, 124.3, 125.8, 128.3, 145.1, 149.6, 156.2; *m*/*z* (EI) 244 (M$^+$, 26%), 121 (100), 91 (75).

5-Amino-4-cyano-2-hydroxy-1-(3-methoxybenzyl)imidazole 1c. Yield 54%; mp 222–224 °C (washed with AcOEt) (Found: C, 58.97; H, 4.97; N, 22.84. Calc. for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95; N, 22.94%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 268.2 (ε/dm^3 mol^{-1} cm^{-1} 15 400); ν_{max}/cm^{-1} 3429, 3322, 3228, 2200, 1706, 1651, 1606, 1495, 1348, 1258, 1050, 767; δ_H 3.71 (3 H, s, 1-CH_3), 4.72 (2 H, s, 1-CH_2), 6.47 (2 H, s*, 5-NH_2), 6.77–6.84 (3 H, m, 1-Ar), 7.23 (1 H, t, *J* 7.8, 1-Ar), 9.89 (1 H, s*, 2-OH); δ_C 42.1, 55.0, 67.4, 112.4, 113.1, 115.3, 119.1, 129.5, 138.3, 144.7, 149.8, 159.2; *m*/*z* (EI) 244 (M$^+$, 38%), 121 (100), 91 (17).

5-Amino-4-cyano-2-hydroxy-1-(4-methoxybenzyl)imidazole 1d. Yield 41%; mp 214–216 °C (washed with AcOEt) (Found: C, 58.64; H, 4.96; N, 22.77. Calc. for $C_{12}H_{12}N_4O_2$·1/10 H_2O: C, 58.58; H, 5.00; N, 22.77%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 268.4 (ε/dm^3 mol^{-1} cm^{-1} 14 500); ν_{max}/cm^{-1} 3425, 3327, 3222, 2201, 1716, 1657, 1513, 1249, 1178, 1026; δ_H 3.71 (3 H, s, 1-CH_3), 4.67 (2 H, s, 1-CH_2), 6.47 (2 H, s*, 5-NH_2), 6.87 and 7.20 (each 2 H, each d, *J* 8.3, 1-Ar), 9.85 (1 H, s*, 2-OH); δ_C 41.6, 55.0, 67.3, 113.8, 115.3, 128.7, 128.8, 144.7, 149.8, 158.6; *m*/*z* (EI) 244 (M$^+$, 10%), 121 (100) [Found: HRMS (EI) *m*/*z* 244.0954. Calc. for $C_{12}H_{12}N_4O_2$: (M$^+$) 244.0960].

5-Amino-4-cyano-1-(3,4-dimethoxybenzyl)-2-hydroxyimidazole 1e. Yield 58%; mp 189–190 °C (washed with AcOEt) (Found: C, 56.75; H, 5.11; N, 20.30. Calc. for $C_{13}H_{14}N_4O_3$: C, 56.93; H, 5.14; N, 20.43%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 269.8 (ε/dm^3 mol^{-1} cm^{-1} 13 900); ν_{max}/cm^{-1} 3381, 3208, 2198, 1721, 1654, 1517, 1259, 1144, 1026; δ_H 3.70 and 3.71 (each 3 H, each s, 1-CH_3), 4.66 (2 H, s, 1-CH_2), 6.45 (2 H, s*, 5-NH_2), 6.76 (1 H, dd, *J* 2.0 and 8.1, 1-Ar), 6.88 (1 H, d, *J* 8.1, 1-Ar), 6.96 (1 H, d, *J* 2.0, 1-Ar), 9.85 (1 H, s*, 2-OH); δ_C 41.9, 55.4, 55.5, 67.3, 111.6, 111.8, 115.3, 119.5, 129.2, 144.7, 148.2, 148.5, 149.8; *m*/*z* (EI) 274 (M$^+$, 14%), 151 (100).

5-Amino-4-cyano-2-hydroxy-1-(4-methylbenzyl)imidazole 1f. Yield 58%; mp 208–210 °C (washed with AcOEt) (Found: C, 62.99; H, 5.27; N, 24.33. Calc. for $C_{12}H_{12}N_4O$: C, 63.15; H, 5.30; N, 24.55%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 266.8 (ε/dm^3 mol^{-1} cm^{-1} 12 700); ν_{max}/cm^{-1} 3423, 3202, 2213, 1691, 1655, 1492, 1345, 762; δ_H 2.25 (3 H, s, 1-CH_3), 4.70 (2 H, s, 1-CH_2), 6.46 (2 H, s*, 5-NH_2), 7.11–7.12 (4 H, m, 1-Ar), 9.86 (1 H, br s*, 2-OH); δ_C 20.6, 41.9, 67.3, 115.3, 127.1, 128.9, 133.8, 136.4, 144.8, 149.8; *m*/*z* (EI) 228 (M$^+$, 27%), 105 (100).

5-Amino-1-(4-chlorobenzyl)-4-cyano-2-hydroxyimidazole 1g. Yield 50%; mp 198–199 °C (washed with AcOEt) (Found: C, 53.14; H, 3.72; N, 22.42. Calc. for $C_{11}H_9ClN_4O$: C, 53.13; H, 3.65; N, 22.53%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 266.6 (ε/dm^3 mol^{-1} cm^{-1} 13 100); ν_{max}/cm^{-1} 3330, 3217, 2197, 1713, 1650, 1495, 1412, 1346, 1095; δ_H 4.74 (2 H, s, 1-CH_2), 6.51 (2 H, s*, 5-NH_2), 7.25 and 7.39 (each 2 H, each d, *J* 8.5, 1-Ar), 9.92 (1 H, s*, 2-OH); δ_C 41.5, 67.5, 115.2, 128.4, 129.0, 132.0, 135.8, 144.6, 149.7; *m*/*z* (EI) 250 (M$^+$ + 2, 9%), 248 (M$^+$, 29), 127 (31), 125 (100) [Found: HRMS (EI) *m*/*z* 248.0460. Calc. for $C_{11}H_9ClN_4O$: (M$^+$) 248.0465].

5-Amino-4-cyano-1-(4-fluorobenzyl)-2-hydroxyimidazole 1h. Yield 54%; mp 213–215 °C (washed with AcOEt) (Found: C, 56.67; H, 3.85; N, 24.04. Calc. for $C_{11}H_9FN_4O$: C, 56.89; H, 3.91; N, 24.13%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 264.8 (ε/dm^3 mol^{-1} cm^{-1} 13 500); ν_{max}/cm^{-1} 3325, 3187, 2200, 1706, 1653, 1511, 1345, 1231, 777; δ_H 4.73 (2 H, s, 1-CH_2), 6.50 (2 H, s*, 5-NH_2), 7.15 (2 H, t, *J* 8.8, 1-Ar), 7.29 (2 H, dd, *J* 5.6 and 8.8, 1-Ar), 9.90 (1 H, s*, 2-OH); δ_C 41.5, 67.4, 115.1, 115.2, 115.3, 129.2, 129.3, 133.0, 144.6, 149.7, 160.2, 162.6; *m*/*z* (EI) 232 (M$^+$, 29%), 109 (100) [Found: HRMS (EI) *m*/*z* 232.0753. Calc. for $C_{11}H_9FN_4O$: (M$^+$) 232.0760].

5-Amino-4-cyano-1-(2,5-difluorobenzyl)-2-hydroxyimidazole 1i. Yield 92%; mp 223–225 °C (washed with AcOEt) (Found: C, 52.03; H, 3.40; N, 21.79. Calc. for $C_{11}H_8F_2N_4O$·1/4 H_2O: C, 51.87; H, 3.36; N, 22.00%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 267.6 (ε/dm^3 mol^{-1} cm^{-1} 13 000); ν_{max}/cm^{-1} 3336, 3228, 2204, 1709, 1656, 1499, 1347, 1196, 742; δ_H 4.81 (2 H, s, 1-CH_2), 6.50 (2 H, s*, 5-NH_2), 6.73–6.77 (1 H, m, 1-Ar), 7.15–7.20 (1 H, m, 1-Ar), 7.24–7.30 (1 H, m, 1-Ar), 9.99 (1 H, br s*, 2-OH); δ_C 36.9, 68.0, 114.2, 114.3, 114.50, 114.54, 115.1, 115.4, 115.5, 115.6, 115.7, 116.8, 116.9, 117.0, 117.1, 125.6, 125.7, 125.8, 125.9, 144.6, 149.5, 154.6, 156.9, 157.0, 159.3; *m*/*z* (EI) 250 (M$^+$, 47%), 127 (100) [Found: HRMS (EI) *m*/*z* 250.0658. Calc. for $C_{11}H_8F_2N_4O$: (M$^+$) 250.0666].

5-Amino-4-cyano-2-hydroxy-1-(α-naphthylmethyl)imidazole 1j. Yield 75%; mp 242–244 °C; λ_{max}(EtOH–H_2O = 1 : 9)/nm 268.8 (ε/dm^3 mol^{-1} cm^{-1} 16 200); δ_H 5.26 (2 H, s, 1-CH_2), 6.48 (2 H, s*, 5-NH_2), 6.90 (1 H, d, *J* 7.7, 1-Ar), 7.45 (1 H, t, *J* 7.7, 1-Ar), 7.56–7.61 (2 H, m, 1-Ar), 7.84 (1 H, d, *J* 7.7, 1-Ar), 7.97 (1 H, d, *J* 7.3, 1-Ar), 8.15 (1 H, d, *J* 8.8, 1-Ar), 9.97 (1 H, br s*, 2-OH); *m*/*z* (EI) 264 (M$^+$, 20%), 141 (100), 115 (21) [Found: HRMS (EI) *m*/*z* 264.0980. Calc. for $C_{15}H_{12}N_4O$: (M$^+$) 264.1011].

5-Amino-4-cyano-2-hydroxy-1-phenylimidazole 1k. Yield 73%; mp 222–223 °C (washed with AcOEt) (Found: C, 57.38; H, 4.32; N, 26.78. Calc. for $C_{10}H_8N_4O$·1/2 H_2O: C, 57.41; H, 4.34; N, 26.78%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 263.6 (ε/dm^3 mol^{-1} cm^{-1} 13 200); ν_{max}/cm^{-1} 3432, 3299, 3159, 2198, 1707, 1642, 1498, 1294, 1108, 763; δ_H 6.13 (2 H, s*, 5-NH_2), 7.31 (2 H, d, *J* 7.8, 1-Ph), 7.41–7.51 (3 H, m, 1-Ph), 10.04 (1 H, s*, 2-OH); δ_C 68.3, 115.1, 127.9, 128.4, 129.3, 132.3, 144.2, 149.2; *m*/*z* (EI) 200 (M$^+$, 100%), 171 (48), 119 (41), 77 (34) [Found: HRMS (EI) *m*/*z* 200.0695. Calc. for $C_{10}H_8N_4O$: (M$^+$) 200.0698].

5-Amino-1-butyl-4-cyano-2-hydroxyimidazole 1l. Yield 22%; mp 140–142 °C (washed with AcOEt) (Found: C, 52.79; H, 6.64; N, 30.63. Calc. for $C_8H_{12}N_4O$·1/10 H_2O: C, 52.79; H, 6.76; N, 30.78%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 263.8 (ε/dm^3 mol^{-1} cm^{-1} 14 000); ν_{max}/cm^{-1} 3210, 2195, 1706, 1649, 1500; δ_H 0.86 (3 H, t, *J* 7.6, 1-CH_3), 1.18–1.27 (2 H, m, 1-CH_2), 1.41–1.48 (2 H, m, 1-CH_2), 3.48 (2 H, t, *J* 7.3, 1-CH_2), 6.39 (2 H, s*, 5-NH_2), 9.71 (1 H, s*, 2-OH); δ_C 13.6, 19.2, 30.0, 67.0, 115.5,

144.9, 149.7; *m/z* (EI) 180 (M^+, 50%), 124 (100) [Found: HRMS (EI) *m/z* 180.0999. Calc. for $C_8H_{12}N_4O$: (M^+) 180.1011].

5-Amino-4-cyano-1-heptyl-2-hydroxyimidazole 1m. Yield 19%; mp 147–149 °C (Found: C, 59.44; H, 8.19; N, 24.94. Calc. for $C_{11}H_{18}N_4O$: C, 59.44; H, 8.16; N, 25.20%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 261.6 (ε/dm^3 mol^{-1} cm^{-1} 5200), 298.6 (3600); ν_{max}/cm^{-1} 3331, 2928, 2203, 1702, 1646, 1497, 1346; δ_H 0.84 (3 H, t, *J* 6.8, 1-CH_3), 1.16–1.28 (8 H, m, 1-CH_2), 1.42–1.50 (2 H, m, 1-CH_2), 3.47 (2 H, t, *J* 7.3, 1-CH_2), 6.39 (2 H, s*, 5-NH_2), 9.67 (1 H, br s*, 2-OH); δ_C 13.9, 22.0, 25.9, 27.9, 28.3, 31.2, 67.0, 115.6, 144.9, 149.7; *m/z* (EI) 222 (M^+, 48%), 124 (100) [Found: HRMS (EI) *m/z* 222.1486. Calc. for $C_{11}H_{18}N_4O$: (M^+) 222.1481].

5-Amino-4-cyano-2-hydroxy-1-phenethylimidazole 1n. Yield 41%; mp 194–196 °C (recrystallized from EtOH) (Found: C, 62.80; H, 5.30; N, 23.62. Calc. for $C_{12}H_{12}N_4O$·1/6 EtOH: C, 62.79; H, 5.55; N, 23.75%); λ_{max}(EtOH)/nm 268.2 (ε/dm^3 mol^{-1} cm^{-1} 10 200); ν_{max}/cm^{-1} 3428, 2195, 1704, 1647, 1497; δ_H 2.79 (2 H, t, *J* 7.8, 1-CH_2), 3.72 (2 H, t, *J* 7.8, 1-CH_2), 6.45 (2 H, s*, 5-NH_2), 7.18–7.30 (5 H, m, 1-Ph), 9.77 (1 H, s*, 2-OH); δ_C 33.7, 40.4, 67.3, 115.5, 126.4, 128.3, 128.8, 138.0, 144.8, 149.6; *m/z* (EI) 228 (M^+, 32%), 124 (25), 104 (100), 91 (48) [Found: HRMS (EI) *m/z* 228.1016. Calc. for $C_{12}H_{12}N_4O$: (M^+) 228.1011].

5-Amino-4-cyano-2-hydroxy-1-(3-phenylpropyl)imidazole 1o. Yield 40%; mp 191–193 °C (recrystallized from EtOH–hexane) (Found: C, 63.89; H, 5.82; N, 22.61. Calc. for $C_{13}H_{14}N_4O$·1/6 H_2O: C, 63.66; H, 5.89; N, 22.84%); λ_{max}(EtOH)/nm 268.2 (ε/dm^3 mol^{-1} cm^{-1} 11 000); ν_{max}/cm^{-1} 3420, 2204, 1657; δ_H 1.73–1.81 (2 H, m, 1-CH_2), 2.54 (2 H, t, *J* 8.1, 1-CH_2), 3.55 (2 H, t, *J* 7.3, 1-CH_2), 6.45 (2 H, s*, 5-NH_2), 7.16–7.28 (5 H, m, 1-Ph), 9.76 (1 H, s*, 2-OH); δ_C 29.8, 32.1, 67.2, 115.5, 125.8, 128.1, 128.3, 141.3, 144.9, 149.7; *m/z* (EI) 242 (M^+, 100%), 118 (60), 91 (83) [Found: HRMS (EI) *m/z* 242.1158. Calc. for $C_{13}H_{14}N_4O$: (M^+) 242.1168].

Typical procedure for the synthesis of 9-substituted 8-hydroxyadenine derivatives 2a–o

A mixture of **1** (2.34 mmol) and formamidine hydrochloride (9.34 mmol) in 2-methoxyethanol (10 mL) was refluxed for 24 h. If any **1** remained in the reaction mixture, additional formamidine hydrochloride (9.34 mmol) was added to the reaction mixture and it was refluxed for another 24 h. The solvent was evaporated and the residue was triturated with water and then filtered to give **2**.

9-Benzyl-8-hydroxyadenine 2a. Yield 80%; mp 278–280 °C (recrystallized from EtOH) (lit.,[16] 270 °C) (Found: C, 59.56; H, 4.54; N, 28.84. Calc. for $C_{12}H_{11}N_5O$: C, 59.74; H, 4.60; N, 29.03%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 270.2 (ε/dm^3 mol^{-1} cm^{-1} 11 900); ν_{max}/cm^{-1} 3402, 3193, 1705, 1653, 1499, 1408, 1373; δ_H 4.91 (2 H, s, 9-CH_2), 6.43 (2 H, s*, 6-NH_2), 7.24–7.30 (5 H, m, 9-Ph), 8.01 (1 H, s, 2-H), 10.23 (1 H, s*, 8-OH); δ_C 42.4, 103.3, 127.3, 127.4, 128.5, 137.1, 146.6, 147.3, 151.1, 152.0; *m/z* (EI) 241 (M^+, 100%), 212 (22), 136 (18), 91 (61).

8-Hydroxy-9-(2-methoxybenzyl)adenine 2b. Yield 81%; mp >300 °C (recrystallized from EtOH) (Found: C, 57.23; H, 4.98; N, 25.02. Calc. for $C_{13}H_{13}N_5O_2$·1/6 EtOH: C, 57.41; H, 5.06; N, 25.11%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 271.2 (ε/dm^3 mol^{-1} cm^{-1} 12 500); ν_{max}/cm^{-1} 3424, 1705, 1651, 1246; δ_H 3.83 (3 H, s, 9-CH_3), 4.88 (2 H, s, 9-CH_2), 6.44 (2 H, s*, 6-NH_2), 6.71 (1 H, d, *J* 7.7, 9-Ar), 6.82 (1 H, t, *J* 7.7, 9-Ar), 7.01 (1 H, d, *J* 7.7, 9-Ar), 7.23 (1 H, t, *J* 7.7, 9-Ar), 7.96 (1 H, s, 2-H), 10.25 (1 H, s*, 8-OH); δ_C 37.5, 55.6, 103.4, 110.6, 120.2, 124.4, 126.1, 128.3, 146.6, 147.6, 151.1, 152.1, 156.3; *m/z* (EI) 271 (M^+, 35%), 240 (100), 121 (62), 91 (61) [Found: HRMS (EI) *m/z* 271.1076. Calc. for $C_{13}H_{13}N_5O_2$: (M^+) 271.1069].

8-Hydroxy-9-(3-methoxybenzyl)adenine 2c. Yield 74%; mp 274–276 °C (recrystallized from EtOH) (Found: C, 57.24; H, 5.00; N, 24.99. Calc. for $C_{13}H_{13}N_5O_2$·1/5 EtOH: C, 57.38; H, 5.10; N, 24.97%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 271.4 (ε/dm^3 mol^{-1} cm^{-1} 12 300); ν_{max}/cm^{-1} 3408, 1719, 1654; δ_H 3.70 (3 H, s, 9-CH_3), 4.88 (2 H, s, 9-CH_2), 6.43 (2 H, s*, 6-NH_2), 6.81–6.85 (3 H, m, 9-Ar), 7.21 (1 H, t, *J* 7.8, 9-Ar), 8.01 (1 H, s, 2-H), 10.22 (1 H, s*, 8-OH); δ_C 42.3, 55.0, 103.3, 112.5, 113.3, 119.4, 129.6, 138.6, 146.6, 147.3, 151.1, 152.0, 159.3; *m/z* (EI) 271 (M^+, 100%), 242 (35), 136 (44), 121 (68) [Found: HRMS (EI) *m/z* 271.1074. Calc. for $C_{13}H_{13}N_5O_2$: (M^+) 271.1069].

8-Hydroxy-9-(4-methoxybenzyl)adenine 2d. Yield 83%; mp 274–276 °C (recrystallized from EtOH) (Found: C, 57.47; H, 4.98; N, 25.11. Calc. for $C_{13}H_{13}N_5O_2$·1/7 EtOH: C, 57.43; H, 5.03; N, 25.20%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 271.0 (ε/dm^3 mol^{-1} cm^{-1} 12 700); ν_{max}/cm^{-1} 3388, 1703, 1615, 1512, 1250; δ_H 3.69 (3 H, s, 9-CH_3), 4.83 (2 H, s, 9-CH_2), 6.41 (2 H, s*, 6-NH_2), 6.86 and 7.24 (each 2 H, each d, *J* 8.5, 9-Ar), 8.01 (1 H, s, 2-H), 10.19 (1 H, s*, 8-OH); δ_C 41.9, 55.0, 103.2, 113.8, 128.9, 129.1, 146.6, 147.3, 151.0, 151.9, 158.6; *m/z* (EI) 271 (M^+, 48%), 121 (100) [Found: HRMS (EI) *m/z* 271.1063. Calc. for $C_{13}H_{13}N_5O_2$: (M^+) 271.1069].

9-(3,4-Dimethoxybenzyl)-8-hydroxyadenine 2e. Yield 65%; mp 262–265 °C (recrystallized from EtOH) (Found: C, 54.34; H, 4.98; N, 22.55. Calc. for $C_{14}H_{15}N_5O_3$·1/2 H_2O: C, 54.19; H, 5.20; N, 22.57%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 272.6 (ε/dm^3 mol^{-1} cm^{-1} 12 000); ν_{max}/cm^{-1} 3411, 1717, 1651, 1517; δ_H 3.69 (6 H, s, 9-CH_3), 4.83 (2 H, s, 9-CH_2), 6.45 (2 H, s*, 6-NH_2), 6.78 (1 H, dd, *J* 2.0 and 8.1, 9-Ar), 6.86 (1 H, d, *J* 8.1, 9-Ar), 6.99 (1 H, d, *J* 2.0, 9-Ar), 8.02 (1 H, s, 2-H), 10.22 (1 H, s*, 8-OH); δ_C 42.2, 55.3, 55.6, 103.3, 111.6, 111.7, 119.7, 129.6, 146.6, 147.3, 148.2, 148.6, 150.9, 152.0; *m/z* (EI) 301 (M^+, 48%), 151 (100) [Found: HRMS (EI) *m/z* 301.1187. Calc. for $C_{14}H_{15}N_5O_3$: (M^+) 301.1175].

8-Hydroxy-9-(4-methylbenzyl)adenine 2f. Yield 86%; mp 299–301 °C (recrystallized from EtOH) (Found: C, 61.05; H, 5.23; N, 26.93. Calc. for $C_{13}H_{13}N_5O$·1/9 EtOH: C, 60.99; H, 5.29; N, 26.89%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 270.8 (ε/dm^3 mol^{-1} cm^{-1} 12 600); ν_{max}/cm^{-1} 3391, 1705, 1654; δ_H 2.24 (3 H, s, 9-CH_3), 4.86 (2 H, s, 9-CH_2), 6.42 (2 H, s*, 6-NH_2), 7.10 and 7.18 (each 2 H, each d, *J* 7.8, 9-Ar), 8.01 (1 H, s, 2-H), 10.21 (1 H, s*, 8-OH); δ_C 20.6, 42.2, 103.3, 127.4, 129.0, 134.1, 136.5, 146.6, 147.3, 151.1, 152.0; *m/z* (EI) 255 (M^+, 82%), 226 (26), 105 (100) [Found: HRMS (EI) *m/z* 255.1118. Calc. for $C_{13}H_{13}N_5O$: (M^+) 255.1120].

9-(4-Chlorobenzyl)-8-hydroxyadenine 2g. Yield 72%; mp 293–295 °C (recrystallized from EtOH) (Found: C, 52.17; H, 3.69; N, 25.41. Calc. for $C_{12}H_{10}ClN_5O$: C, 52.28; H, 3.66; N, 25.40%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 270.4 (ε/dm^3 mol^{-1} cm^{-1} 13 100); ν_{max}/cm^{-1} 3401, 1658, 1496, 1406; δ_H 4.90 (2 H, s, 9-CH_2), 6.44 (2 H, s*, 6-NH_2), 7.30 and 7.37 (each 2 H, each d, *J* 8.5, 9-Ar), 8.01 (1 H, s, 2-H), 10.25 (1 H, br s*, 8-OH); δ_C 41.7, 103.3, 128.5, 129.3, 132.0, 136.1, 146.7, 147.2, 151.1, 151.9; *m/z* (EI) 277 (M^+ + 2, 29%), 275 (M^+, 85), 246 (25), 136 (22), 127 (32), 125 (100) [Found: HRMS (EI) *m/z* 275.0580. Calc. for $C_{12}H_{10}ClN_5O$: (M^+) 275.0574].

9-(4-Fluorobenzyl)-8-hydroxyadenine 2h. Yield 77%; mp 270–272 °C (recrystallized from EtOH) (Found: C, 54.97; H, 3.87; N, 26.38. Calc. for $C_{12}H_{10}FN_5O$·1/5 H_2O: C, 54.84; H, 3.99; N, 26.64%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 270.0 (ε/dm^3 mol^{-1} cm^{-1} 8000); ν_{max}/cm^{-1} 3400, 1706, 1654, 1510; δ_H 4.89 (2 H, s, 9-CH_2), 6.45 (2 H, s*, 6-NH_2), 7.13 (2 H, t, *J* 8.8, 9-Ar), 7.34 (2 H, dd,

J 5.4 and 8.8, 9-Ar), 8.01 (1 H, s, 2-H), 10.26 (1 H, s*, 8-OH); δ_C 41.7, 103.3, 115.2, 115.4, 129.6, 133.3, 146.7, 147.2, 151.06, 151.11, 151.9, 160.2, 162.7; *m/z* (EI) 259 (M^+, 51%), 109 (100) [Found: HRMS (EI) *m/z* 259.0875. Calc. for $C_{12}H_{10}FN_5O$: (M^+) 259.0869].

9-(2,5-Difluorobenzyl)-8-hydroxyadenine 2i. Yield 74%; mp 242–245 °C (recrystallized from EtOH) (Found: C, 51.09; H, 3.20; N, 24.64. Calc. for $C_{12}H_9F_2N_5O{\cdot}1/3\ H_2O$: C, 50.89; H, 3.44; N, 24.73%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 270.0 (ε/dm^3 mol^{-1} cm^{-1} 13 200); ν_{max}/cm^{-1} 3428, 1716, 1652, 1494; δ_H 4.96 (2 H, s, 9-CH_2), 6.46 (2 H, s*, 6-NH_2), 6.99–7.04 (1 H, m, 9-Ar), 7.13–7.20 (1 H, m, 9-Ar), 7.23–7.29 (1 H, m, 9-Ar), 8.01 (1 H, s, 2-H), 10.28 (1 H, s*, 8-OH); δ_C 36.2, 103.5, 115.5, 115.7, 115.78, 115.81, 115.9, 116.0, 116.8, 116.9, 117.0, 117.1, 125.60, 125.64, 125.79, 125.82, 146.7, 147.1, 151.1, 151.8, 154.6, 156.8, 157.0, 159.2; *m/z* (EI) 277 (M^+, 100%), 150 (33), 127 (63) [Found: HRMS (EI) *m/z* 277.0765. Calc. for $C_{12}H_9F_2N_5O$: (M^+) 277.0775].

8-Hydroxy-9-(α-naphthylmethyl)adenine 2j. Yield 87%; mp 294–296 °C (recrystallized from EtOH) (Found: C, 65.58; H, 4.80; N, 23.07. Calc. for $C_{16}H_{13}N_5O{\cdot}1/5$ EtOH: C, 65.55; H, 4.76; N, 23.30%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 270.8 (ε/dm^3 mol^{-1} cm^{-1} 17 400); δ_H 5.39 (2 H, s, 9-CH_2), 6.50 (2 H, s*, 6-NH_2), 7.21 (1 H, d, *J* 7.6, 9-Ar), 7.41 (1 H, t, *J* 7.6, 9-Ar), 7.53–7.61 (2 H, m, 9-Ar), 7.84 (1 H, d, *J* 7.6, 9-Ar), 7.95 (1 H, d, *J* 8.3, 9-Ar), 8.00 (1 H, s, 2-H), 8.36 (1 H, d, *J* 7.8, 9-Ar), 10.35 (1 H, s*, 8-OH); δ_C 40.6, 103.5, 123.3, 125.0, 125.3, 125.9, 126.4, 127.8, 128.5, 130.4, 132.0, 133.2, 146.8, 147.6, 151.1, 152.1; *m/z* (EI) 291 (M^+, 63%), 141 (100), 115 (18) [Found: HRMS (EI) *m/z* 291.1125. Calc. for $C_{16}H_{13}N_5O$: (M^+) 291.1120].

8-Hydroxy-9-phenyladenine 2k. Yield 74%; mp >300 °C (recrystallized from EtOH) (Found: C, 56.77; H, 4.44; N, 28.57. Calc. for $C_{11}H_9N_5O{\cdot}1/3$ EtOH·1/6 H_2O: C, 57.06; H, 4.65; N, 28.52%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 270.8 (ε/dm^3 mol^{-1} cm^{-1} 11 400); ν_{max}/cm^{-1} 3451, 1709, 1645, 1499; δ_H 6.55 (2 H, s*, 6-NH_2), 7.38 (1 H, t, *J* 7.7, 9-Ph), 7.50 (2 H, t, *J* 7.7, 9-Ph), 7.60 (2 H, d, *J* 7.7, 9-Ph), 8.01 (1 H, s, 2-H), 10.47 (1 H, s*, 8-OH); δ_C 103.5, 125.9, 127.2, 128.7, 133.4, 147.0, 150.98, 151.04, 161.0; *m/z* (EI) 227 (M^+, 100%), 226 (65) [Found: HRMS (EI) *m/z* 227.0797. Calc. for $C_{11}H_9N_5O$: (M^+) 227.0807].

9-Butyl-8-hydroxyadenine 2l. Yield 42%; mp 222–224 °C (recrystallized from EtOH) (Found: C, 52.01; H, 6.26; N, 33.59. Calc. for $C_9H_{13}N_5O$: C, 52.16; H, 6.32; N, 33.79%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 270.8 (ε/dm^3 mol^{-1} cm^{-1} 13 800); ν_{max}/cm^{-1} 3416, 1704, 1655; δ_H 0.87 (3 H, t, *J* 7.3, 9-CH_3), 1.20–1.30 (2 H, m, 9-CH_2), 1.59–1.66 (2 H, m, 9-CH_2), 3.71 (2 H, t, *J* 7.1, 9-CH_2), 6.37 (2 H, s*, 6-NH_2), 8.00 (1 H, s, 2-H), 10.10 (1 H, s*, 8-OH); δ_C 13.5, 19.3, 30.0, 103.1, 146.5, 147.6, 151.0, 152.0; *m/z* (EI) 207 (M^+, 62%), 191 (36), 165 (60), 151 (100), 136 (48) [Found: HRMS (EI) *m/z* 207.1113. Calc. for $C_9H_{13}N_5O$: (M^+) 207.1120].

9-Heptyl-8-hydroxyadenine 2m. Yield 47%; mp 193–195 °C (recrystallized from EtOH) (Found: C, 57.03; H, 7.59; N, 27.28. Calc. for $C_{12}H_{19}N_5O{\cdot}1/4\ H_2O$: C, 56.79; H, 7.74; N, 27.59%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 271.0 (ε/dm^3 mol^{-1} cm^{-1} 12 500); ν_{max}/cm^{-1} 3396, 2926, 1702, 1614, 1407; δ_H 0.83 (3 H, t, *J* 6.6, 9-CH_3), 1.18–1.26 (8 H, m, 9-CH_2), 1.62–1.68 (2 H, m, 9-CH_2), 3.70 (2 H, t, *J* 7.3, 9-CH_2), 6.40 (2 H, s*, 6-NH_2), 8.01 (1 H, s, 2-H), 10.12 (1 H, s*, 8-OH); δ_C 13.9, 22.0, 26.0, 27.9, 28.2, 31.1, 103.1, 146.5, 147.6, 150.9, 152.0; *m/z* (EI) 249 (M^+, 82%), 233 (39), 206 (32), 165 (46), 151 (100) [Found: HRMS (EI) *m/z* 249.1596. Calc. for $C_{12}H_{19}N_5O$: (M^+) 249.1590].

8-Hydroxy-9-phenethyladenine 2n. Yield 82%; mp 241–243 °C (recrystallized from EtOH) (Found: C, 60.86; H, 5.18; N, 26.83. Calc. for $C_{13}H_{13}N_5O{\cdot}1/6$ EtOH: C, 60.90; H, 5.37; N, 26.63%); λ_{max}(EtOH–H_2O = 1 : 9)/nm 270.6 (ε/dm^3 mol^{-1} cm^{-1} 11 900); ν_{max}/cm^{-1} 3399, 1705, 1655, 1408, 1371; δ_H 3.00 (2 H, t, *J* 7.3, 9-CH_2), 3.95 (2 H, t, *J* 7.3, 9-CH_2), 6.38 (2 H, s*, 6-NH_2), 7.15–7.26 (5 H, m, 9-Ph), 8.01 (1 H, s, 2-H), 10.10 (1 H, s*, 8-OH); δ_C 33.5, 40.3, 103.1, 126.3, 128.3, 128.5, 138.2, 146.4, 147.4, 150.9, 151.8; *m/z* (EI) 255 (M^+, 19%), 151 (100) [Found: HRMS (EI) *m/z* 255.1114. Calc. for $C_{13}H_{13}N_5O$: (M^+) 255.1120].

8-Hydroxy-9-(3-phenylpropyl)adenine 2o. Yield 75%; mp 243–245 °C (recrystallized from EtOH) (Found: C, 61.76; H, 5.75; N, 24.73. Calc. for $C_{14}H_{15}N_5O{\cdot}1/3$ EtOH: C, 61.88; H, 6.02; N, 24.60%); λ_{max}(EtOH)/nm 270.4 (ε/dm^3 mol^{-1} cm^{-1} 11 200); ν_{max}/cm^{-1} 3457, 3144, 1703, 1371; δ_H 1.91–1.98 (2 H, m, 9-CH_2), 2.58 (2 H, t, *J* 7.6, 9-CH_2), 3.75 (2 H, t, *J* 7.1, 9-CH_2), 6.39 (2 H, s*, 6-NH_2), 7.15–7.25 (5 H, m, 9-Ph), 8.01 (1 H, s, 2-H), 10.15 (1 H, br s*, 8-OH); δ_C 29.6, 32.3, 38.9, 103.2, 125.8, 128.2, 128.3, 141.2, 146.5, 147.5, 150.9, 152.0; *m/z* (EI) 269 (M^+, 56%), 165 (100), 136 (53), 91 (27) [Found: HRMS (EI) *m/z* 269.1280. Calc. for $C_{14}H_{15}N_5O$: (M^+) 269.1277].

Typical procedure for the synthesis of 3a and 3h

To a solution of Na (37.37 mmol) in dry ethanol (40 mL) was added the amidine hydrochloride (46.71 mmol) and the mixture was stirred at room temperature for 5 min. The resulting precipitate was filtered off and a mixture of the filtrate and **1a** (4.67 mmol) was refluxed for 48 h. The solvent was removed under reduced pressure and the residue was partitioned between AcOEt (50 mL) and water (50 mL). The organic layer was washed with brine (50 mL) and dried over $MgSO_4$. After filtration, the solvent was evaporated off and the solidified residue was chromatographed on silica gel.

9-Benzyl-8-hydroxy-2-methyladenine 3a. Yield 70%; mp >300 °C (washed with hot MeOH) (Found: C, 60.96; H, 5.14; N, 27.26. Calc. for $C_{13}H_{13}N_5O$: C, 61.17; H, 5.13; N, 27.43%); λ_{max}(EtOH)/nm 272.6 (ε/dm^3 mol^{-1} cm^{-1} 11 900); ν_{max}/cm^{-1} 3411, 3107, 1698, 1611, 1412, 703; δ_H 2.31 (3 H, s, 2-CH_3), 4.89 (2 H, s, 9-CH_2), 6.35 (2 H, s*, 6-NH_2), 7.24–7.31 (5 H, m, 9-Ph), 10.10 (1 H, s*, 8-OH); δ_C 25.2, 42.2, 101.0, 127.15, 127.23, 128.4, 137.2, 146.5, 148.0, 152.1, 159.5; *m/z* (EI) 255 (M^+, 100%), 226 (32), 164 (36), 150 (35), 91 (88).

9-Benzyl-8-hydroxy-2-phenyladenine 3h. Yield 31%; mp >300 °C (washed with hot MeOH) (Found: C, 66.62; H, 4.66; N, 21.56. Calc. for $C_{18}H_{15}N_5O{\cdot}1/3\ H_2O$: C, 66.86; H, 4.88; N, 21.66%); λ_{max}(EtOH)/nm 285.4 (ε/dm^3 mol^{-1} cm^{-1} 15 400) and 291.6 (15 000); ν_{max}/cm^{-1} 3358, 1708, 1653, 1606, 1400, 700; δ_H 5.00 (2 H, s, 9-CH_2), 6.49 (2 H, s*, 6-NH_2), 7.23–7.45 (8 H, m, 2-Ph and 9-Ph), 8.26 (2 H, d, *J* 6.4, 2-Ph), 10.28 (1 H, s*, 8-OH); δ_C 42.9, 102.4, 127.5, 127.9, 128.0, 128.7, 128.9, 130.0, 137.5, 138.2, 147.0, 148.6, 152.7, 156.8; *m/z* (EI) 317 (M^+, 100%), 226 (43), 91 (24).

Typical procedure for the synthesis of 3b–d

To a solution of Na (5.61 mmol) in dry ethanol (10 mL) was added imidate hydrochloride (5.61 mmol) and the mixture was stirred at room temperature for 5 min. To the mixture was added **2a** (0.47 mmol) in dry ethanol (5 mL) and the mixture was refluxed for 48 h. The solvent was removed under reduced pressure, and the residue was partitioned between AcOEt (50 mL) and water (50 mL). The organic layer was washed with brine (30 mL) and dried over $MgSO_4$. After filtration, the solvent was evaporated off and the solidified residue was chromatographed on silica gel.

9-Benzyl-2-ethyl-8-hydroxyadenine 3b. Yield 37%; mp >300 °C (washed with MeOH) (Found: C, 62.25; H, 5.56; N, 25.82. Calc. for $C_{14}H_{15}N_5O$: C, 62.44; H, 5.61; N, 26.01%);

λ_{max}(EtOH)/nm 272.6 (ε/dm^3 mol^{-1} cm^{-1} 11 700); ν_{max}/cm^{-1} 3416, 3096, 1698, 1610, 1407, 698; δ_H 1.17 (3 H, t, *J* 7.6, 2-CH_3), 2.58 (2 H, q, *J* 7.6, 2-CH_2), 4.89 (2 H, s, 9-CH_2), 6.34 (2 H, s*, 6-NH_2), 7.23–7.33 (5 H, m, 9-Ph), 10.09 (1 H, s*, 8-OH); δ_C 12.9, 31.5, 42.3, 101.2, 127.3, 127.4, 128.4, 137.2, 146.6, 148.0, 152.1, 163.8; *m*/*z* (EI) 269 (M^+, 100%), 240 (34), 178 (32), 164 (30), 91 (72) [Found: HRMS (EI) *m*/*z* 269.1284. Calc. for $C_{14}H_{15}N_5O$: (M^+) 269.1277].

9-Benzyl-8-hydroxy-2-propyladenine 3c. Yield 41%; mp >300 °C (washed with MeOH) (Found: C, 63.39; H, 6.08; N, 24.52. Calc. for $C_{15}H_{17}N_5O$: C, 63.59; H, 6.05; N, 24.72%); λ_{max}(EtOH)/nm 272.4 (ε/dm^3 mol^{-1} cm^{-1} 12 100); ν_{max}/cm^{-1} 3425, 3136, 1702, 1653, 1404, 699; δ_H 0.86 (3 H, t, *J* 7.3, 2-CH_3), 1.62–1.71 (2 H, m, 2-CH_2), 2.53 (2 H, t, *J* 7.6, 2-CH_2), 4.89 (2 H, s, 9-CH_2), 6.33 (2 H, s*, 6-NH_2), 7.24–7.32 (5 H, m, 9-Ph), 10.09 (1 H, s*, 8-OH); δ_C 13.7, 21.5, 40.3, 42.3, 101.2, 127.3, 127.4, 128.4, 137.2, 146.6, 147.9, 152.1, 162.8; *m*/*z* (EI) 283 (M^+, 67%), 268 (40), 255 (100), 91 (63) [Found: HRMS (EI) *m*/*z* 283.1439. Calc. for $C_{15}H_{17}N_5O$: (M^+) 283.1433].

9-Benzyl-2-butyl-8-hydroxyadenine 3d. Yield 32%; mp 283–285 °C (recrystallized from MeOH) (Found: C, 64.08; H, 6.39; N, 23.29. Calc. for $C_{16}H_{19}N_5O{\cdot}1/6\ H_2O$: C, 63.98; H, 6.49; N, 23.32%); λ_{max}(EtOH)/nm 272.6 (ε/dm^3 mol^{-1} cm^{-1} 12 200); ν_{max}/cm^{-1} 3428, 1701, 1653, 1406, 699; δ_H 0.86 (3 H, t, *J* 7.3, 2-CH_3), 1.23–1.32 (2 H, m, 2-CH_2), 1.59–1.67 (2 H, m, 2-CH_2), 2.56 (2 H, t, *J* 7.3, 2-CH_2), 4.89 (2 H, s, 9-CH_2), 6.32 (2 H, s*, 6-NH_2), 7.24–7.31 (5 H, m, 9-Ph), 10.08 (1 H, s*, 8-OH); δ_C 13.8, 21.7, 30.4, 38.0, 42.3, 101.1, 127.3, 127.4, 128.4, 137.2, 146.6, 147.9, 152.1, 162.9; *m*/*z* (EI) 297 (M^+, 19%), 268 (16), 255 (100), 164 (14), 91 (30) [Found: HRMS (EI) *m*/*z* 297.1594. Calc. for $C_{16}H_{19}N_5O$: (M^+) 297.1590].

Preparation of 2-amino-9-benzyl-8-hydroxyadenine 4

Compound **4** was prepared by the reaction of **1a** with guanidine hydrochloride according to the synthetic method for the preparation of **3a** and **3h**. Yield 75%; mp 279–281 °C (recrystallized from EtOH) (Found: C, 56.03; H, 4.78; N, 32.59. Calc. for $C_{12}H_{12}N_6O$: C, 56.24; H, 4.72; N, 32.79%); λ_{max}(EtOH)/nm 248.2 (ε/dm^3 mol^{-1} cm^{-1} 8400) and 291.6 (11 000); ν_{max}/cm^{-1} 3380, 3176, 1703, 1655, 1614, 1432; δ_H 4.80 (2 H, s, 9-CH_2), 5.72 and 6.00 (each 2 H, each s*, 2-NH_2 and 6-NH_2), 7.22–7.32 (5 H, m, 9-Ph), 9.66 (1 H, s*, 8-OH); δ_C 42.0, 95.6, 127.0, 127.1, 128.4, 137.5, 147.5, 149.4, 152.1, 159.2; *m*/*z* (EI) 256 (M^+, 100%), 165 (73), 91 (36) [Found: HRMS (EI) *m*/*z* 256.1065. Calc. for $C_{12}H_{12}N_6O$: (M^+) 256.1073].

Typical procedure for the synthesis of 5a, b

A mixture of **1a** (0.70 mmol) and thiourea (7.00 mmol) was heated at 180 °C (at 120 °C in the case of **5b**) for 1–3 h. The residue was triturated with water (20 mL) and the resulting precipitate was filtered. The obtained solid was chromatographed on silica gel.

9-Benzyl-8-hydroxy-2-methylaminoadenine 5a. Yield 44%; mp 251–253 °C (Found: C, 56.12; H, 5.18; N, 29.82. Calc. for $C_{13}H_{14}N_6O{\cdot}1/2\ H_2O$: C, 55.91; H, 5.41; N, 30.09%); λ_{max}(EtOH)/nm 249.0 (ε/dm^3 mol^{-1} cm^{-1} 10 000) and 296.2 (9600); ν_{max}/cm^{-1} 3425, 3337, 1707, 1624, 1476, 1387; δ_H 2.69 (3 H, d, *J* 4.6, 2-CH_3), 4.80 (2 H, s, 9-CH_2), 6.03 (2 H, s*, 6-NH_2), 6.15 (1 H, br q*, *J* 4.6, 2-NH), 7.23–7.32 (5 H, m, 9-Ph), 9.64 (1 H, br s*, 8-OH); δ_C 28.2, 42.0, 95.4, 127.1, 127.3, 128.3, 137.5, 147.4, 149.3, 152.1, 159.0; *m*/*z* (EI) 270 (M^+, 100%), 179 (68), 91 (29) [Found: HRMS (EI) *m*/*z* 270.1236. Calc. for $C_{13}H_{14}N_6O$: (M^+) 270.1229].

9-Benzyl-2-ethylamino-8-hydroxyadenine 5b. Yield 12%; mp 280–282 °C (recrystallized from EtOH) (Found: C, 59.17; H, 5.75; N, 29.14. Calc. for $C_{14}H_{16}N_6O{\cdot}1/15\ H_2O$: C, 58.89; H, 5.70; N, 29.43%); λ_{max}(EtOH)/nm 250.2 (ε/dm^3 mol^{-1} cm^{-1} 10 700) and 296.2 (9700); ν_{max}/cm^{-1} 3443, 1698, 1623, 1468; δ_H 1.04 (3 H, t, *J* 6.8, 2-CH_3), 3.15–3.21 (2 H, m, 2-CH_2), 4.79 (2 H, s, 9-CH_2), 6.00 (2 H, s*, 6-NH_2), 6.17 (1 H, t*, *J* 6.5, 2-NH), 7.23–7.32 (5 H, m, 9-Ph), 9.62 (1 H, s*, 8-OH); δ_C 14.9, 35.6, 42.0, 95.4, 127.1, 127.3, 128.3, 137.5, 147.4, 149.3, 152.1, 158.3; *m*/*z* (EI) 284 (M^+, 100%), 269 (35), 193 (44), 91 (41) [Found: HRMS (EI) *m*/*z* 284.1392. Calc. for $C_{14}H_{16}N_6O$: (M^+) 284.1386].

Typical procedure for the synthesis of 5b–g

To a suspension of **4** (0.98 mmol) and $NaBH_3CN$ (5.85 mmol) in methanol (30 mL) was added an aldehyde (7.81 mmol) (in the case of **5b**, 33.17 mmol of acetaldehyde was used), and the mixture was stirred for 2 days. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel.

9-Benzyl-2-ethylamino-8-hydroxyadenine 5b. Yield 63%; Product **5b** was identified with a standard sample synthesized from **1a**.

9-Benzyl-8-hydroxy-2-propylaminoadenine 5c. Yield 74%; mp 270–272 °C (recrystallized from EtOH) (Found: C, 60.33; H, 6.09; N, 28.04. Calc. for $C_{15}H_{18}N_6O$: C, 60.39; H, 6.08; N, 28.17%); λ_{max}(EtOH)/nm 250.6 (ε/dm^3 mol^{-1} cm^{-1} 10 600) and 297.2 (9700); ν_{max}/cm^{-1} 3442, 1698, 1623, 1468; δ_H 0.84 (3 H, t, *J* 7.6, 2-CH_3), 1.41–1.50 (2 H, m, 2-CH_2), 3.11 (2 H, q, *J* 6.7, 2-CH_2), 4.79 (2 H, s, 9-CH_2), 5.98 (2 H, s*, 6-NH_2), 6.20 (1 H, t*, *J* 6.7, 2-NH), 7.23–7.30 (5 H, m, 9-Ph), 9.61 (1 H, s*, 8-OH); δ_C 11.5, 22.4, 42.1, 42.9, 95.3, 127.1, 127.4, 128.3, 137.5, 147.3, 149.3, 152.1, 158.5; *m*/*z* (EI) 298 (M^+, 100%), 269 (87), 256 (18), 207 (19), 91 (53) [Found: HRMS (EI) *m*/*z* 298.1538. Calc. for $C_{15}H_{18}N_6O$: (M^+) 298.1542].

9-Benzyl-2-butylamino-8-hydroxyadenine 5d. Yield 67%; mp 262–264 °C (recrystallized from EtOH) (Found: C, 61.58; H, 6.42; N, 26.91. Calc. for $C_{16}H_{20}N_6O$: C, 61.52; H, 6.45; N, 26.90%); λ_{max}(EtOH)/nm 250.2 (ε/dm^3 mol^{-1} cm^{-1} 9800) and 297.2 (8900); ν_{max}/cm^{-1} 3442, 3332, 1699, 1623, 1468; δ_H 0.85 (3 H, t, *J* 7.3, 2-CH_3), 1.23–1.32 (2 H, m, 2-CH_2), 1.40–1.47 (2 H, m, 2-CH_2), 3.15 (2 H, q, *J* 6.7, 2-CH_2), 4.79 (2 H, s, 9-CH_2), 5.98 (2 H, s*, 6-NH_2), 6.17 (1 H, t*, *J* 6.7, 2-NH), 7.23–7.29 (5 H, m, 9-Ph), 9.61 (1 H, s*, 8-OH); δ_C 13.8, 19.7, 31.4, 40.6, 42.1, 95.3, 127.1, 127.4, 128.3, 137.5, 147.3, 149.3, 152.1, 158.5; *m*/*z* (EI) 312 (M^+, 100%), 283 (18), 269 (76), 256 (22), 91 (86) [Found: HRMS (EI) *m*/*z* 312.1696. Calc. for $C_{16}H_{20}N_6O$: (M^+) 312.1699].

9-Benzyl-8-hydroxy-2-pentylaminoadenine 5e. Yield 87%; mp 265–267 °C (recrystallized from EtOH) (Found: C, 62.52; H, 6.81; N, 25.80. Calc. for $C_{17}H_{22}N_6O$: C, 62.56; H, 6.79; N, 25.75%); λ_{max}(EtOH)/nm 250.6 (ε/dm^3 mol^{-1} cm^{-1} 9400) and 297.4 (8400); ν_{max}/cm^{-1} 3443, 3330, 1700, 1622, 1532, 1467; δ_H 0.84 (3 H, t, *J* 7.1, 2-CH_3), 1.21–1.29 (4 H, m, 2-CH_2), 1.41–1.48 (2 H, m, 2-CH_2), 3.14 (2 H, q, *J* 6.8, 2-CH_2), 4.79 (2 H, s, 9-CH_2), 5.97 (2 H, s*, 6-NH_2), 6.17 (1 H, t*, *J* 6.8, 2-NH), 7.23–7.29 (5 H, m, 9-Ph), 9.60 (1 H, s*, 8-OH); δ_C 13.9, 21.9, 28.7, 28.9, 40.9, 42.0, 95.3, 127.1, 127.4, 128.3, 137.5, 147.3, 149.3, 152.0, 158.4; *m*/*z* (EI) 326 (M^+, 100%), 283 (16), 269 (81), 256 (24), 91 (62) [Found: HRMS (EI) *m*/*z* 326.1863. Calc. for $C_{17}H_{22}N_6O$: (M^+) 326.1855].

9-Benzyl-2-hexylamino-8-hydroxyadenine 5f. Yield 94%; mp 260–261 °C (recrystallized from EtOH) (Found: C, 63.32; H, 7.22; N, 24.60. Calc. for $C_{18}H_{24}N_6O$: C, 63.51; H, 7.11; N, 24.69%); λ_{max}(EtOH)/nm 251.0 (ε/dm^3 mol^{-1} cm^{-1} 11 300) and 296.8 (10 100); ν_{max}/cm^{-1} 3445, 3331, 1699, 1621, 1531, 1467; δ_H 0.84 (3 H, t, *J* 6.8, 2-CH_3), 1.21–1.29 (6 H, m, 2-CH_2), 1.41–

1.48 (2 H, m, 2-CH_2), 3.14 (2 H, q, *J* 6.3, 2-CH_2), 4.79 (2 H, s, 9-CH_2), 5.96 (2 H, s*, 6-NH_2), 6.16 (1 H, t*, *J* 6.3, 2-NH), 7.23–7.31 (5 H, m, 9-Ph), 9.60 (1 H, s*, 8-OH); δ_C 13.9, 22.1, 26.2, 29.2, 31.1, 41.0, 42.1, 95.3, 127.1, 127.4, 128.3, 137.5, 147.3, 149.3, 152.1, 158.4; *m*/*z* (EI) 340 (M^+, 100%), 269 (75), 91 (43) [Found: HRMS (EI) *m*/*z* 340.2020. Calc. for $C_{18}H_{24}N_6O$: (M^+) 340.2012].

9-Benzyl-8-hydroxy-2-isobutylaminoadenine 5g. Yield 53%; mp 266–267 °C (recrystallized from EtOH) (Found: C, 61.41; H, 6.47; N, 26.92. Calc. for $C_{16}H_{20}N_6O$: C, 61.52; H, 6.45; N, 26.90%); λ_{max}(EtOH)/nm 250.4 (ε/dm^3 mol^{-1} cm^{-1} 11 700) and 297.2 (10 400); ν_{max}/cm^{-1} 3431, 3337, 1695, 1621, 1467; δ_H 0.84 (6 H, d, *J* 6.4, 2-CH_3), 1.74–1.84 (1 H, m, 2-CH), 2.98 (2 H, t, *J* 6.4, 2-CH_2), 4.79 (2 H, s, 9-CH_2), 5.96 (2 H, s*, 6-NH_2), 6.22 (1 H, t*, *J* 6.4, 2-NH), 7.21–7.31 (5 H, m, 9-Ph), 9.61 (1 H, s*, 8-OH); δ_C 20.3, 27.7, 42.1, 48.8, 95.3, 127.1, 127.4, 128.3, 137.5, 147.3, 149.3, 152.1, 158.6; *m*/*z* (EI) 312 (M^+, 66%), 269 (100), 256 (20), 91 (49) [Found: HRMS (EI) *m*/*z* 312.1696. Calc. for $C_{16}H_{20}N_6O$: (M^+) 312.1699].

Preparation of 9-benzyl-2,8-dihydroxyadenine 6

A mixture of **1a** (2.00 g, 9.34 mmol) and urea (5.61 g, 93.42 mmol) was heated at 180 °C for 2 h. The residue was triturated with water (30 mL) and the resulting precipitate was filtered to give **6** (1.73 g, 72%). Mp >300 °C (washed with hot MeOH) (Found: C, 54.62; H, 4.46; N, 26.96. Calc. for $C_{12}H_{11}N_5O_2 \cdot 3/10\ H_2O$: C, 54.88; H, 4.45; N, 26.66%); ν_{max}/cm^{-1} 3356, 1685, 1621, 1460, 1360, 701; δ_H 4.76 (2 H, s, 9-CH_2), 6.36 (2 H, s*, 6-NH_2), 7.22–7.34 (5 H, m, 9-Ph), 9.64 and 10.45 (each 1 H, each br s*, 2-OH and 8-OH); *m*/*z* (EI) 257 (M^+, 62%), 166 (29), 91 (100) [Found: HRMS (EI) *m*/*z* 257.0929. Calc. for $C_{12}H_{11}N_5O_2$: (M^+) 257.0913].

Typical procedure for the synthesis of 2-alkoxy-9-benzyl-8-hydroxyadenine derivatives 7a–e

A mixture of **6** (0.78 mmol) and LiH (1.56 mmol) in dry DMF (7 mL) was stirred at room temperature for 1 h. To the mixture was added an alkyl halide (1.56 mmol) and the mixture was stirred at room temperature for 2 days. The solvent was removed under reduced pressure, and the residue was triturated with water (10 mL). The resulting suspension was neutralized with 10% $NaHSO_4$ solution and extracted with AcOEt (20 mL). The organic layer was washed with brine (10 mL) and dried over $MgSO_4$. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel.

9-Benzyl-8-hydroxy-2-methoxyadenine 7a. Yield 6%; mp >300 °C (recrystallized from MeOH–AcOEt) (Found: C, 57.57; H, 4.74; N, 25.83. Calc. for $C_{13}H_{13}N_5O_2$: C, 57.56; H, 4.83; N, 25.82%); λ_{max}(EtOH)/nm 242.0 (ε/dm^3 mol^{-1} cm^{-1} 5900) and 280.4 (12 200); ν_{max}/cm^{-1} 3416, 1705, 1467, 1361, 702; δ_H 3.74 (3 H, s, 2-CH_3), 4.84 (2 H, s, 9-CH_2), 6.47 (2 H, s*, 6-NH_2), 7.25–7.31 (5 H, m, 9-Ph), 9.96 (1 H, s*, 8-OH); δ_C 42.4, 53.8, 98.3, 127.3, 127.5, 128.4, 137.1, 147.7, 149.2, 152.2, 160.4; *m*/*z* (EI) 271 (M^+, 100%), 180 (58), 91 (39) [Found: HRMS (EI) *m*/*z* 271.1058. Calc. for $C_{13}H_{13}N_5O_2$: (M^+) 271.1069].

9-Benzyl-2-ethoxy-8-hydroxyadenine 7b. Yield 11%; mp >300 °C (recrystallized from MeOH–AcOEt) (Found: C, 59.09; H, 5.28; N, 24.60. Calc. for $C_{14}H_{15}N_5O_2$: C, 58.94; H, 5.30; N, 24.55%); λ_{max}(EtOH)/nm 244.0 (ε/dm^3 mol^{-1} cm^{-1} 6600) and 280.6 (14 000); ν_{max}/cm^{-1} 3434, 3162, 1702, 1631, 1422, 1377, 1343, 709; δ_H 1.23 (3 H, t, *J* 7.0, 2-CH_3), 4.18 (2 H, q, *J* 7.0, 2-CH_2), 4.84 (2 H, s, 9-CH_2), 6.42 (2 H, s*, 6-NH_2), 7.24–7.33 (5 H, m, 9-Ph), 9.93 (1 H, s*, 8-OH); δ_C 14.4, 42.3, 61.8, 98.2, 127.3, 127.4, 128.4, 137.1, 147.7, 149.2, 152.2, 159.9; *m*/*z* (EI) 285 (M^+, 100%), 194 (23), 166 (35), 91 (60) [Found: HRMS (EI) *m*/*z* 285.1232. Calc. for $C_{14}H_{15}N_5O_2$: (M^+) 285.1226].

9-Benzyl-8-hydroxy-2-propoxyadenine 7c. Yield 12%; mp >300 °C (recrystallized from MeOH–AcOEt) (Found: C, 60.10; H, 5.71; N, 23.37. Calc. for $C_{15}H_{17}N_5O_2$: C, 60.19; H, 5.72; N, 23.40%); λ_{max}(EtOH)/nm 241.2 (ε/dm^3 mol^{-1} cm^{-1} 5800) and 281.0 (11 000); ν_{max}/cm^{-1} 3422, 3175, 1702, 1637, 1356, 700; δ_H 0.91 (3 H, t, *J* 7.3, 2-CH_3), 1.60–1.69 (2 H, m, 2-CH_2), 4.08 (2 H, t, *J* 6.6, 2-CH_2), 4.84 (2 H, s, 9-CH_2), 6.42 (2 H, s*, 6-NH_2), 7.24–7.33 (5 H, m, 9-Ph), 9.93 (1 H, s*, 8-OH); δ_C 10.4, 21.8, 42.3, 67.6, 98.2, 127.3, 127.4, 128.4, 137.1, 147.7, 149.2, 152.2, 160.1; *m*/*z* (EI) 299 (M^+, 100%), 257 (40), 166 (46), 91 (95) [Found: HRMS (EI) *m*/*z* 299.1377. Calc. for $C_{15}H_{17}N_5O_2$: (M^+) 299.1382].

9-Benzyl-2-butoxy-8-hydroxyadenine 7d. Yield 13%; mp >300 °C (recrystallized from MeOH–AcOEt) (Found: C, 61.45; H, 6.11; N, 22.31. Calc. for $C_{16}H_{19}N_5O_2$: C, 61.33; H, 6.11; N, 22.35%); λ_{max}(EtOH)/nm 243.4 (ε/dm^3 mol^{-1} cm^{-1} 6900) and 280.8 (14 200); ν_{max}/cm^{-1} 3422, 3170, 1702, 1635, 1357, 701; δ_H 0.89 (3 H, t, *J* 7.3, 2-CH_3), 1.31–1.40 (2 H, m, 2-CH_2), 1.57–1.64 (2 H, m, 2-CH_2), 4.13 (2 H, t, *J* 6.6, 2-CH_2), 4.84 (2 H, s, 9-CH_2), 6.43 (2 H, s*, 6-NH_2), 7.23–7.33 (5 H, m, 9-Ph), 9.94 (1 H, s*, 8-OH); δ_C 13.6, 18.7, 30.5, 42.3, 65.8, 98.2, 127.3, 127.4, 128.4, 137.1, 147.7, 149.2, 152.2, 160.0; *m*/*z* (EI) 313 (M^+, 100%), 257 (46), 166 (40), 91 (75) [Found: HRMS (EI) *m*/*z* 313.1546. Calc. for $C_{16}H_{19}N_5O_2$: (M^+) 313.1539].

9-Benzyl-8-hydroxy-2-pentoxyadenine 7e. Yield 10%; mp >300 °C (Found: C, 62.36; H, 6.52; N, 21.28. Calc. for $C_{17}H_{21}N_5O_2$: C, 62.37; H, 6.47; N, 21.39%); λ_{max}(EtOH)/nm 244.2 (ε/dm^3 mol^{-1} cm^{-1} 6600) and 280.8 (13 900); ν_{max}/cm^{-1} 3422, 3171, 1703, 1636, 1356, 701; δ_H 0.86 (3 H, t, *J* 7.1, 2-CH_3), 1.27–1.34 (4 H, m, 2-CH_2), 1.59–1.66 (2 H, m, 2-CH_2), 4.12 (2 H, t, *J* 6.8, 2-CH_2), 4.84 (2 H, s, 9-CH_2), 6.42 (2 H, s*, 6-NH_2), 7.24–7.33 (5 H, m, 9-Ph), 9.94 (1 H, s*, 8-OH); δ_C 13.8, 21.8, 27.6, 28.1, 42.3, 66.1, 98.2, 127.3, 127.4, 128.4, 137.1, 147.7, 149.2, 152.2, 160.0; *m*/*z* (EI) 327 (M^+, 90%), 257 (60), 166 (34), 91 (100) [Found: HRMS (EI) *m*/*z* 327.1690. Calc. for $C_{17}H_{21}N_5O_2$: (M^+) 327.1695].

Preparation of 5-amino-1-benzyl-2-bromo-4-cyanoimidazole 9

To a solution of **8**[21] (250 mg, 1.26 mmol) in dry THF (5 mL) was added *N*-bromosuccinimide (247 mg, 1.39 mmol) in dry THF (4 mL), and the reaction mixture was stirred at room temperature for 10 min. After evaporation, the resulting solid was partitioned between AcOEt (10 mL) and saturated $NaHCO_3$ solution (10 mL). The organic layer was washed with brine (10 mL) and dried over $MgSO_4$. After filtration, the solvent was evaporated off, and the solidified product was chromatographed on silica gel ($CHCl_3$–MeOH = 40 : 1) to give **9** (307 mg, 88%). Mp 193–194 °C (recrystallized from benzene) (Found: C, 47.87; H, 3.26; N, 20.21. Calc. for $C_{11}H_9BrN_4$: C, 47.68; H, 3.27; N, 20.22%); λ_{max}(EtOH)/nm 248.2 (ε/dm^3 mol^{-1} cm^{-1} 13 700); ν_{max}/cm^{-1} 3336, 3183, 2221, 1649, 1594, 1491, 1180, 723; δ_H 5.10 (2 H, s, 1-CH_2), 6.68 (2 H, s*, 5-NH_2), 7.10 (2 H, d, *J* 7.3, 1-Ph), 7.29 (1 H, t, *J* 7.3, 1-Ph), 7.36 (2 H, t, *J* 7.3, 1-Ph); δ_C 46.6, 90.8, 113.0, 116.2, 126.4, 127.6, 128.7, 135.3, 149.6; *m*/*z* (EI) 278 (M^+ + 2, 10%), 276 (M^+, 11), 91 (100) [Found: HRMS (EI) *m*/*z* 276.0004. Calc. for $C_{11}H_9BrN_4$: (M^+) 276.0011].

Preparation of 9-benzyl-8-bromo-2-hydroxyadenine 10

A mixture of **9** (0.70 g, 2.53 mmol) and urea (1.52 g, 25.26 mmol) was heated at 160 °C for 12 h. Additional urea (1.52 g, 25.26 mmol) was added to the reaction mixture and it was heated at 160 °C for another 12 h. The residue was triturated with water (20 mL) and the resulting precipitate was filtered to give **10** (708 mg, 88%). Mp >300 °C (washed with hot MeOH); δ_H 5.12 (2 H, s, 9-CH_2), 7.20–7.36 (5 H, m, 9-Ph), 7.67 (2 H, br s*, 6-NH_2), 10.62 (1 H, br s*, 2-OH); *m*/*z* (FAB, Gly) 322

(M^+ + 3, 5%), 320 (M^+ + 1, 5) [Found: HRMS (FAB) *m/z* 320.0142. Calc. for $C_{12}H_{11}BrN_5O$: (M^+ + H) 320.0147].

Typical procedure for the synthesis of 2-alkoxy-9-benzyl-8-bromoadenine derivatives 11a–e

A mixture of **10** (0.78 mmol) and K_2CO_3 (2.34 mmol) in dry DMF (5 mL) was stirred at room temperature for 1 h and an alkyl halide (2.34 mmol) was added to the mixture. The resulting mixture was stirred at room temperature for 3 days. The solvent was removed under reduced pressure and the residue was triturated with water (10 mL). The suspension was neutralized with 10% $NaHSO_4$ solution and extracted with AcOEt (20 mL). The organic layer was washed with brine (10 mL) and dried over $MgSO_4$. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel.

9-Benzyl-8-bromo-2-methoxyadenine 11a. Yield 23%; mp 211–212 °C (washed with hexane); λ_{max}(EtOH)/nm 271.6 (ε/dm^3 mol^{-1} cm^{-1} 14 200); ν_{max}/cm^{-1} 3424, 3175, 1652, 1598, 1480, 1353; δ_H 3.81 (3 H, s, 2-CH_3), 5.25 (2 H, s, 9-CH_2), 7.24–7.36 (5 H, m, 9-Ph), 7.45 (2 H, br s*, 6-NH_2); δ_C 46.4, 54.0, 115.4, 123.7, 127.2, 127.8, 128.7, 136.0, 152.4, 155.7, 161.9; *m/z* (EI) 335 (M^+ + 2, 35%), 333 (M^+, 34), 254 (50), 91 (100) [Found: HRMS (EI) *m/z* 333.0236. Calc. for $C_{13}H_{12}BrN_5O$: (M^+) 333.0225].

9-Benzyl-8-bromo-2-ethoxyadenine 11b. Yield 45%; mp 161–162 °C (washed with hexane) (Found: C, 48.38; H, 4.02; N, 20.13. Calc. for $C_{14}H_{14}BrN_5O$: C, 48.29; H, 4.05; N, 20.11%); λ_{max}(EtOH)/nm 272.0 (ε/dm^3 mol^{-1} cm^{-1} 15 200); ν_{max}/cm^{-1} 3322, 3180, 1649, 1593, 1465, 1406, 1333, 1261, 1173, 1034, 736; δ_H 1.26 (3 H, t, *J* 6.9, 2-CH_3), 4.24 (2 H, q, *J* 6.9, 2-CH_2), 5.23 (2 H, s, 9-CH_2), 7.22–7.36 (5 H, m, 9-Ph), 7.41 (2 H, br s*, 6-NH_2); δ_C 14.5, 46.4, 62.0, 115.3, 123.6, 127.2, 127.7, 128.7, 136.0, 152.4, 155.7, 161.4; *m/z* (EI) 349 (M^+ + 2, 39%), 347 (M^+, 40), 334 (18), 332 (18), 240 (18), 91 (100) [Found: HRMS (EI) *m/z* 347.0392. Calc. for $C_{14}H_{14}BrN_5O$: (M^+) 347.0382].

9-Benzyl-8-bromo-2-propoxyadenine 11c. Yield 67%; mp 145–146 °C (washed with hexane) (Found: C, 49.76; H, 4.42; N, 19.25. Calc. for $C_{15}H_{16}BrN_5O$: C, 49.74; H, 4.45; N, 19.33%); λ_{max}(EtOH)/nm 272.2 (ε/dm^3 mol^{-1} cm^{-1} 15 000); ν_{max}/cm^{-1} 3468, 3175, 1641, 1599, 1475, 1406, 1333, 1179; δ_H 0.93 (3 H, t, *J* 7.6, 2-CH_3), 1.62–1.71 (2 H, m, 2-CH_2), 4.15 (2 H, t, *J* 6.8, 2-CH_2), 5.24 (2 H, s, 9-CH_2), 7.22–7.36 (5 H, m, 9-Ph), 7.42 (2 H, br s*, 6-NH_2); δ_C 10.4, 21.8, 46.3, 67.8, 115.3, 123.6, 127.2, 127.7, 128.7, 136.0, 152.4, 155.7, 161.6; *m/z* (EI) 363 (M^+ + 2, 15%), 361 (M^+, 15), 321 (11), 319 (11), 240 (13), 91 (100) [Found: HRMS (EI) *m/z* 361.0547. Calc. for $C_{15}H_{16}BrN_5O$: (M^+) 361.0538].

9-Benzyl-8-bromo-2-butoxyadenine 11d. Yield 74%; mp 141–142 °C (washed with hexane) (Found: C, 50.95; H, 4.81; N, 18.56. Calc. for $C_{16}H_{18}BrN_5O$: C, 51.08; H, 4.82; N, 18.61%); λ_{max}(EtOH)/nm 272.2 (ε/dm^3 mol^{-1} cm^{-1} 14 900); ν_{max}/cm^{-1} 3487, 3115, 1640, 1594, 1342, 1181, 731; δ_H 0.89 (3 H, t, *J* 7.3, 2-CH_3), 1.33–1.42 (2 H, m, 2-CH_2), 1.60–1.67 (2 H, m, 2-CH_2), 4.20 (2 H, t, *J* 6.4, 2-CH_2), 5.24 (2 H, s, 9-CH_2), 7.22–7.35 (5 H, m, 9-Ph), 7.39 (2 H, br s*, 6-NH_2); δ_C 13.6, 18.7, 30.6, 46.4, 66.0, 115.3, 123.6, 127.2, 127.7, 128.7, 136.0, 152.4, 155.7, 161.6; *m/z* (EI) 377 (M^+ + 2, 39%), 375 (M^+, 39), 321 (30), 319 (34), 240 (23), 91 (100) [Found: HRMS (EI) *m/z* 375.0687. Calc. for $C_{16}H_{18}BrN_5O$: (M^+) 375.0695].

9-Benzyl-8-bromo-2-pentoxyadenine 11e. Yield 68%; mp 120–121 °C (washed with hexane) (Found: C, 52.21; H, 5.13; N, 17.91. Calc. for $C_{17}H_{20}BrN_5O$: C, 52.32; H, 5.17; N, 17.94%); λ_{max}(EtOH)/nm 272.2 (ε/dm^3 mol^{-1} cm^{-1} 15 100); ν_{max}/cm^{-1} 3314, 3173, 2955, 1653, 1596, 1474, 1406, 1338, 1178; δ_H 0.86 (3 H, t, *J* 7.1, 2-CH_3), 1.26–1.38 (4 H, m, 2-CH_2), 1.62–1.69 (2 H, m, 2-CH_2), 4.19 (2 H, t, *J* 6.8, 2-CH_2), 5.24 (2 H, s, 9-CH_2), 7.22–7.36 (5 H, m, 9-Ph), 7.42 (2 H, br s*, 6-NH_2); δ_C 13.8, 21.8, 27.7, 28.1, 46.3, 66.2, 115.3, 123.6, 127.1, 127.7, 128.7, 136.0, 152.4, 155.7, 161.5; *m/z* (EI) 391 (M^+ + 2, 21%), 389 (M^+, 21), 321 (27), 319 (28), 240 (19), 91 (100) [Found: HRMS (EI) *m/z* 389.0859. Calc. for $C_{17}H_{20}BrN_5O$: (M^+) 389.0851].

Typical procedure for the synthesis of 2-alkoxy-9-benzyl-8-methoxyadenine derivatives 12a–e

A solution of **11** (0.28 mmol) in methanol (2 mL) and 1 M NaOH solution (2 mL) was refluxed for 8 h. After evaporation, the residue was triturated with water (5 mL) and the mixture was neutralized with 10% $NaHSO_4$ solution. The mixture was extracted with AcOEt (10 mL) and the organic layer was washed with brine (5 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure, and the product was chromatographed on silica gel.

9-Benzyl-2,8-dimethoxyadenine 12a. Yield 82%; mp 208–209 °C (washed with hexane); λ_{max}(EtOH)/nm 248.2 (ε/dm^3 mol^{-1} cm^{-1} 8900) and 270.2 (11 500); ν_{max}/cm^{-1} 3352, 3187, 1651, 1604, 1563, 1477, 1355, 1253, 1008; δ_H 3.77 and 4.03 (each 3 H, each s, 2-CH_3 and 8-CH_3), 5.03 (2 H, s, 9-CH_2), 6.87 (2 H, s*, 6-NH_2), 7.23–7.34 (5 H, m, 9-Ph); δ_C 43.8, 53.7, 56.8, 110.0, 127.2, 127.5, 128.6, 136.7, 150.9, 153.5, 154.6, 160.5; *m/z* (EI) 285 (M^+, 100%), 270 (18), 194 (23), 91 (53) [Found: HRMS (EI) *m/z* 285.1233. Calc. for $C_{14}H_{15}N_5O_2$: (M^+) 285.1226].

9-Benzyl-2-ethoxy-8-methoxyadenine 12b. Yield 78%; mp 169–170 °C (washed with hexane) (Found: C, 60.29; H, 5.64; N, 23.36. Calc. for $C_{15}H_{17}N_5O_2$: C, 60.19; H, 5.72; N, 23.40%); λ_{max}(EtOH)/nm 248.2 (ε/dm^3 mol^{-1} cm^{-1} 9000) and 270.4 (11 500); ν_{max}/cm^{-1} 3478, 3121, 1643, 1613, 1567, 1470, 1405, 1337, 1263, 1029, 998; δ_H 1.25 (3 H, t, *J* 6.9, 2-CH_3), 4.03 (3 H, s, 8-CH_3), 4.21 (2 H, q, *J* 6.9, 2-CH_2), 5.02 (2 H, s, 9-CH_2), 6.81 (2 H, s*, 6-NH_2), 7.22–7.34 (5 H, m, 9-Ph); δ_C 14.6, 43.7, 56.8, 61.7, 109.9, 127.2, 127.5, 128.6, 136.8, 151.0, 153.4, 154.6, 160.0; *m/z* (EI) 299 (M^+, 100%), 284 (33), 180 (15), 91 (77) [Found: HRMS (EI) *m/z* 299.1374. Calc. for $C_{15}H_{17}N_5O_2$: (M^+) 299.1382].

9-Benzyl-8-methoxy-2-propoxyadenine 12c. Yield 81%; mp 140–141 °C (washed with hexane) (Found: C, 61.35; H, 6.15; N, 22.26. Calc. for $C_{16}H_{19}N_5O_2$: C, 61.33; H, 6.11; N, 22.35%); λ_{max}(EtOH)/nm 248.6 (ε/dm^3 mol^{-1} cm^{-1} 9200) and 270.8 (11 600); ν_{max}/cm^{-1} 3478, 3152, 1646, 1607, 1566, 1404, 1354, 1256, 1007; δ_H 0.93 (3 H, t, *J* 7.3, 2-CH_3), 1.61–1.70 (2 H, m, 2-CH_2), 4.02 (3 H, s, 8-CH_3), 4.11 (2 H, t, *J* 6.8, 2-CH_2), 5.03 (2 H, s, 9-CH_2), 6.82 (2 H, s*, 6-NH_2), 7.22–7.34 (5 H, m, 9-Ph); δ_C 10.4, 21.9, 43.7, 56.8, 67.5, 109.9, 127.2, 127.5, 128.6, 136.7, 150.9, 153.4, 154.5, 160.2; *m/z* (EI) 313 (M^+, 100%), 284 (19), 271 (43), 180 (16), 91 (67) [Found: HRMS (EI) *m/z* 313.1549. Calc. for $C_{16}H_{19}N_5O_2$: (M^+) 313.1539].

9-Benzyl-2-butoxy-8-methoxyadenine 12d. Yield 71%; mp 149–150 °C (washed with hexane) (Found: C, 62.34; H, 6.54; N, 21.41. Calc. for $C_{17}H_{21}N_5O_2$: C, 62.37; H, 6.47; N, 21.39%); λ_{max}(EtOH)/nm 248.8 (ε/dm^3 mol^{-1} cm^{-1} 8800) and 270.8 (11 200); ν_{max}/cm^{-1} 3326, 3128, 1655, 1607, 1474, 1403, 1345, 999; δ_H 0.90 (3 H, t, *J* 7.3, 2-CH_3), 1.33–1.42 (2 H, m, 2-CH_2), 1.59–1.66 (2 H, m, 2-CH_2), 4.03 (3 H, s, 8-CH_3), 4.16 (2 H, t, *J* 6.6, 2-CH_2), 5.03 (2 H, s, 9-CH_2), 6.82 (2 H, s*, 6-NH_2), 7.22–7.34 (5 H, m, 9-Ph); δ_C 13.7, 18.7, 30.6, 43.7, 56.8, 65.6, 109.9, 127.2, 127.5, 128.6, 136.7, 150.9, 153.4, 154.5, 160.2; *m/z* (EI) 327 (M^+, 100%), 284 (15), 271 (58), 180 (19), 91 (90) [Found: HRMS (EI) *m/z* 327.1704. Calc. for $C_{17}H_{21}N_5O_2$: (M^+) 327.1695].

9-Benzyl-8-methoxy-2-pentoxyadenine 12e. Yield 76%; mp 147–148 °C (washed with hexane) (Found: C, 63.09; H, 6.81; N, 20.44. Calc. for $C_{18}H_{23}N_5O_2$: C, 63.32; H, 6.79; N, 20.51%); λ_{max}(EtOH)/nm 248.8 (ε/dm^3 mol^{-1} cm^{-1} 9000) and 271.0 (11 400); ν_{max}/cm^{-1} 3333, 3190, 1661, 1606, 1566, 1402, 1342, 996; δ_H 0.87 (3 H, t, *J* 7.1, 2-CH$_3$), 1.27–1.38 (4 H, m, 2-CH$_2$), 1.61–1.68 (2 H, m, 2-CH$_2$), 4.02 (3 H, s, 8-CH$_3$), 4.15 (2 H, t, *J* 6.6, 2-CH$_2$), 5.02 (2 H, s, 9-CH$_2$), 6.82 (2 H, s*, 6-NH$_2$), 7.21–7.34 (5 H, m, 9-Ph); δ_C 13.9, 21.9, 27.7, 28.2, 43.7, 56.8, 65.9, 109.9, 127.2, 127.5, 128.6, 136.7, 150.9, 153.4, 154.5, 160.2; *m*/*z* (EI) 341 (M$^+$, 79%), 271 (70), 180 (18), 91 (100) [Found: HRMS (EI) *m*/*z* 341.1843. Calc. for $C_{18}H_{23}N_5O_2$: (M$^+$) 341.1852].

Typical procedure for the synthesis of 2-alkoxy-9-benzyl-8-hydroxyadenine derivatives 7a–e

A solution of **12** (0.24 mmol) in *c.* HCl was stirred at room temperature for 4 h. After evaporation, the residue was chromatographed on silica gel to give **7**, which was identified by comparison with a standard sample synthesized from **6**. Yield: **7a** (74%); **7b** (81%); **7c** (82%); **7d** (87%); **7e** (84%).

Typical procedure for the synthesis of 2-alkylthio-9-benzyl-8-hydroxyadenines 15a–g and 6-alkylthio-2-amino-9-benzyl-8-hydroxypurines 16a–g

To a solution of **1a** (4.67 mmol) in dry THF (40 mL) was added dropwise benzoyl isothiocyanate (10.28 mmol). The mixture was stirred at room temperature for 48 h. After evaporation, the residue was triturated with ether (10 mL) and the resulting precipitate was filtered. The obtained solid product was dissolved in THF (120 mL) and 2 M NaOH solution (12 mL) and the mixture was refluxed for 48 h. After the removal of THF under reduced pressure, the aqueous solution was acidified to pH 3 with 10% $NaHSO_4$ solution and the resulting precipitate was filtered. A mixture of the obtained solid product and potassium carbonate (4.67 mmol) in dry DMF (30 mL) was stirred under N_2 bubbling at room temperature for 1 h. To the mixture was added an alkyl halide (4.67 mmol) and the mixture was stirred at room temperature (except for the preparation **15g** and **16g** where the reaction was carried out at 60 °C) for 6 h. After evaporation, the residue was triturated with water (10 mL) and the resulting suspension was neutralized with 10% $NaHSO_4$ solution. The resulting precipitate was filtered and the crude product was chromatographed on silica gel.

9-Benzyl-8-hydroxy-2-methylthioadenine 15a. Yield 43%; mp >300 °C (washed with MeOH) (Found: C, 54.17; H, 4.70; N, 24.15. Calc. for $C_{13}H_{13}N_5OS$: C, 54.34; H, 4.56; N, 24.37%); λ_{max}(EtOH)/nm 266.0 (ε/dm^3 mol^{-1} cm^{-1} 13 100) and 283.0 (13 400); ν_{max}/cm^{-1} 3143, 1705, 1652, 1603, 1374, 696; δ_H 2.41 (3 H, s, 2-CH$_3$), 4.87 (2 H, s, 9-CH$_2$), 6.50 (2 H, s*, 6-NH$_2$), 7.26–7.32 (5 H, m, 9-Ph), 10.08 (1 H, s*, 8-OH); δ_C 13.5, 42.5, 100.2, 127.4, 127.6, 128.5, 137.0, 146.7, 148.0, 151.8, 161.9; *m*/*z* (EI) 287 (M$^+$, 100%), 196 (50), 91 (35) [Found: HRMS (EI) *m*/*z* 287.0845. Calc. for $C_{13}H_{13}N_5OS$: (M$^+$) 287.0841].

2-Amino-9-benzyl-8-hydroxy-6-methylthiopurine 16a. Yield 13%; mp >300 °C (washed with MeOH); λ_{max}(EtOH)/nm 318.2 (ε/dm^3 mol^{-1} cm^{-1} 11 600); ν_{max}/cm^{-1} 3328, 1710, 1608, 1447, 1160, 716; δ_H 2.47 (3 H, s, 6-CH$_3$), 4.83 (2 H, s, 9-CH$_2$), 6.23 (2 H, s*, 2-NH$_2$), 7.20–7.30 (5 H, m, 9-Ph), 10.92 (1 H, s*, 8-OH); δ_C 11.0, 42.1, 109.9, 127.0, 127.2, 128.5, 136.9, 145.1, 149.2, 152.8, 158.7; *m*/*z* (EI) 287 (M$^+$, 100%), 196 (35), 91 (30) [Found: HRMS (EI) *m*/*z* 287.0838. Calc. for $C_{13}H_{13}N_5OS$: (M$^+$) 287.0841].

9-Benzyl-2-ethylthio-8-hydroxyadenine 15b. Yield 38%; mp 297–299 °C (recrystallized from MeOH) (Found: C, 55.65; H, 4.94; N, 23.08. Calc. for $C_{14}H_{15}N_5OS$: C, 55.80; H, 5.02; N, 23.24%); λ_{max}(EtOH)/nm 266.0 (ε/dm^3 mol^{-1} cm^{-1} 11 900) and 283.4 (12 100); ν_{max}/cm^{-1} 3343, 1707, 1652, 1602, 1372, 698; δ_H 1.24 (3 H, t, *J* 7.1, 2-CH$_3$), 2.99 (2 H, q, *J* 7.1, 2-CH$_2$), 4.86 (2 H, s, 9-CH$_2$), 6.51 (2 H, s*, 6-NH$_2$), 7.25–7.31 (5 H, m, 9-Ph), 10.09 (1 H, s*, 8-OH); δ_C 14.8, 24.3, 42.5, 100.2, 127.4, 127.6, 128.4, 137.0, 146.8, 148.0, 151.8, 161.4; *m*/*z* (EI) 301 (M$^+$, 100%), 268 (32), 210 (31), 91 (69) [Found: HRMS (EI) *m*/*z* 301.0987. Calc. for $C_{14}H_{15}N_5OS$: (M$^+$) 301.0997].

2-Amino-9-benzyl-6-ethylthio-8-hydroxypurine 16b. Yield 21%; mp 268–270 °C (washed with MeOH) (Found: C, 55.76; H, 4.99; N, 23.09. Calc. for $C_{14}H_{15}N_5OS$: C, 55.80; H, 5.02; N, 23.24%); λ_{max}(EtOH)/nm 319.2 (ε/dm^3 mol^{-1} cm^{-1} 12 200); ν_{max}/cm^{-1} 3331, 1711, 1604, 1447, 1260, 1157, 711; δ_H 1.27 (3 H, t, *J* 7.3, 6-CH$_3$), 3.17 (2 H, q, *J* 7.3, 6-CH$_2$), 4.85 (2 H, s, 9-CH$_2$), 6.25 (2 H, s*, 2-NH$_2$), 7.23–7.33 (5 H, m, 9-Ph), 10.93 (1 H, s*, 8-OH); δ_C 15.2, 22.3, 42.1, 109.9, 127.0, 127.3, 128.5, 136.9, 144.6, 149.3, 152.8, 158.7; *m*/*z* (EI) 301 (M$^+$, 100%), 268 (38), 210 (26), 91 (35) [Found: HRMS (EI) *m*/*z* 301.0992. Calc. for $C_{14}H_{15}N_5OS$: (M$^+$) 301.0997].

9-Benzyl-8-hydroxy-2-propylthioadenine 15c. Yield 39%; mp 297–299 °C (recrystallized from MeOH) (Found: C, 57.12; H, 5.42; N, 22.13. Calc. for $C_{15}H_{17}N_5OS$: C, 57.12; H, 5.43; N, 22.21%); λ_{max}(EtOH)/nm 266.4 (ε/dm^3 mol^{-1} cm^{-1} 12 600) and 283.2 (12 800); ν_{max}/cm^{-1} 3423, 1705, 1651, 1372, 695; δ_H 0.93 (3 H, t, *J* 7.3, 2-CH$_3$), 1.56–1.65 (2 H, m, 2-CH$_2$), 2.97 (2 H, t, *J* 7.1, 2-CH$_2$), 4.86 (2 H, s, 9-CH$_2$), 6.47 (2 H, s*, 6-NH$_2$), 7.25–7.33 (5 H, m, 9-Ph), 10.07 (1 H, s*, 8-OH); δ_C 13.3, 22.6, 32.0, 42.5, 100.2, 127.4, 127.5, 128.4, 137.1, 146.8, 148.0, 151.8, 161.5; *m*/*z* (EI) 315 (M$^+$, 100%), 273 (70), 91 (70) [Found: HRMS (EI) *m*/*z* 315.1163. Calc. for $C_{15}H_{17}N_5OS$: (M$^+$) 315.1154].

2-Amino-9-benzyl-8-hydroxy-6-propylthiopurine 16c. Yield 13%; mp 267–268 °C (Found: C, 57.01; H, 5.41; N, 22.07. Calc. for $C_{15}H_{17}N_5OS$: C, 57.12; H, 5.43; N, 22.21%); λ_{max}(EtOH)/nm 319.2 (ε/dm^3 mol^{-1} cm^{-1} 14 600); ν_{max}/cm^{-1} 3452, 1710, 1606, 1448, 1157, 711; δ_H 0.96 (3 H, t, *J* 7.3, 6-CH$_3$), 1.61–1.66 (2 H, m, 6-CH$_2$), 3.17 (2 H, t, *J* 7.1, 6-CH$_2$), 4.85 (2 H, s, 9-CH$_2$), 6.23 (2 H, s*, 2-NH$_2$), 7.21–7.32 (5 H, m, 9-Ph), 10.91 (1 H, s*, 8-OH); δ_C 13.1, 22.7, 29.7, 42.1, 109.9, 127.0, 127.2, 128.5, 136.9, 144.7, 149.3, 152.8, 158.6; *m*/*z* (EI) 315 (M$^+$, 100%), 273 (72), 91 (61) [Found: HRMS (EI) *m*/*z* 315.1145. Calc. for $C_{15}H_{17}N_5OS$: (M$^+$) 315.1154].

9-Benzyl-2-butylthio-8-hydroxyadenine 15d. Yield 41%; mp 297–299 °C (washed with MeOH) (Found: C, 58.39; H, 5.86; N, 21.15. Calc. for $C_{16}H_{19}N_5OS$: C, 58.34; H, 5.81; N, 21.26%); λ_{max}(EtOH)/nm 267.0 (ε/dm^3 mol^{-1} cm^{-1} 13 700) and 283.6 (14 000); ν_{max}/cm^{-1} 3422, 3143, 1703, 1654, 1607, 1378, 693; δ_H 0.85 (3 H, t, *J* 7.3, 2-CH$_3$), 1.31–1.40 (2 H, m, 2-CH$_2$), 1.53–1.61 (2 H, m, 2-CH$_2$), 3.00 (2 H, t, *J* 7.1, 2-CH$_2$), 4.87 (2 H, s, 9-CH$_2$), 6.48 (2 H, s*, 6-NH$_2$), 7.25–7.31 (5 H, m, 9-Ph), 10.09 (1 H, s*, 8-OH); δ_C 13.5, 21.4, 29.7, 31.4, 42.4, 100.2, 127.4, 127.5, 128.4, 137.0, 146.8, 147.9, 151.8, 161.5; *m*/*z* (EI) 329 (M$^+$, 100%), 300 (41), 287 (97), 273 (34), 91 (94) [Found: HRMS (EI) *m*/*z* 329.1305. Calc. for $C_{16}H_{19}N_5OS$: (M$^+$) 329.1310].

2-Amino-9-benzyl-6-butylthio-8-hydroxypurine 16d. Yield 12%; mp 253–254 °C (recrystallized from MeOH) (Found: C, 57.25; H, 5.69; N, 20.77. Calc. for $C_{16}H_{19}N_5OS{\cdot}1/3\ H_2O$: C, 57.29; H, 5.91; N, 20.88%); λ_{max}(EtOH)/nm 318.8 (ε/dm^3 mol^{-1} cm^{-1} 14 200); ν_{max}/cm^{-1} 3325, 1711, 1607, 1448, 1158, 713; δ_H 0.89 (3 H, t, *J* 7.3, 6-CH$_3$), 1.34–1.43 (2 H, m, 6-CH$_2$), 1.56–1.63 (2 H, m, 6-CH$_2$), 3.19 (2 H, t, *J* 7.3, 6-CH$_2$), 4.84 (2 H, s, 9-CH$_2$), 6.24 (2 H, s*, 2-NH$_2$), 7.23–7.33 (5 H, m, 9-Ph), 10.92 (1 H, s*, 8-OH); δ_C 13.5, 21.3, 27.5, 31.4, 42.1, 109.9, 127.0, 127.3, 128.5, 136.9, 144.7, 149.3, 152.8, 158.6; *m*/*z* (EI) 329

(M^+, 100%), 287 (46), 273 (82), 91 (96) [Found: HRMS (EI) *m/z* 329.1317. Calc. for $C_{16}H_{19}N_5OS$: (M^+) 329.1310].

9-Benzyl-8-hydroxy-2-pentylthioadenine 15e. Yield 34%; mp 286–288 °C (washed with MeOH) (Found: C, 59.30; H, 6.20; N, 20.22. Calc. for $C_{17}H_{21}N_5OS$: C, 59.45; H, 6.16; N, 20.39%); λ_{max}(EtOH)/nm 267.6 (ε/dm^3 mol^{-1} cm^{-1} 13 700) and 283.8 (13 900); ν_{max}/cm^{-1} 3416, 3141, 1704, 1653, 1606, 1379, 692; δ_H 0.83 (3 H, t, *J* 6.8, 2-CH$_3$), 1.22–1.35 (4 H, m, 2-CH$_2$), 1.56–1.62 (2 H, m, 2-CH$_2$), 2.99 (2 H, t, *J* 7.1, 2-CH$_2$), 4.87 (2 H, s, 9-CH$_2$), 6.48 (2 H, s*, 6-NH$_2$), 7.27–7.31 (5 H, m, 9-Ph), 10.07 (1 H, s*, 8-OH); δ_C 13.9, 21.7, 29.1, 30.0, 30.5, 42.5, 100.3, 127.4, 127.5, 128.4, 137.1, 146.8, 148.0, 151.8, 161.6; *m/z* (EI) 343 (M^+, 100%), 300 (33), 287 (75), 273 (40), 91 (91) [Found: HRMS (EI) *m/z* 343.1475. Calc. for $C_{17}H_{21}N_5OS$: (M^+) 343.1467].

2-Amino-9-benzyl-8-hydroxy-6-pentylthiopurine 16e. Yield 20%; mp 248–250 °C (washed with Et$_2$O) (Found: C, 58.55; H, 6.11; N, 19.98. Calc. for $C_{17}H_{21}N_5OS{\cdot}1/3\ H_2O$: C, 58.43; H, 6.25; N, 20.04%); λ_{max}(EtOH)/nm 318.8 (ε/dm^3 mol^{-1} cm^{-1} 14 400); ν_{max}/cm^{-1} 3332, 1709, 1606, 1447, 1159, 714; δ_H 0.86 (3 H, t, *J* 7.1, 6-CH$_3$), 1.25–1.39 (4 H, m, 6-CH$_2$), 1.58–1.65 (2 H, m, 6-CH$_2$), 3.18 (2 H, t, *J* 7.1, 6-CH$_2$), 4.85 (2 H, s, 9-CH$_2$), 6.23 (2 H, s*, 2-NH$_2$), 7.23–7.33 (5 H, m, 9-Ph), 10.92 (1 H, s*, 8-OH); δ_C 13.8, 21.6, 27.8, 29.0, 30.3, 42.1, 109.9, 127.0, 127.3, 128.5, 136.9, 144.7, 149.3, 152.8, 158.6; *m/z* (EI) 343 (M^+, 100%), 287 (36), 273 (82), 91 (75) [Found: HRMS (EI) *m/z* 343.1462. Calc. for $C_{17}H_{21}N_5OS$: (M^+) 343.1467].

9-Benzyl-2-benzylthio-8-hydroxyadenine 15f. Yield 40%; mp 294–296 °C (washed with MeOH) (Found: C, 62.65; H, 4.75; N, 18.97. Calc. for $C_{19}H_{17}N_5OS$: C, 62.79; H, 4.71; N, 19.27%); λ_{max}(EtOH)/nm 269.0 (ε/dm^3 mol^{-1} cm^{-1} 14 300) and 283.6 (15 100); ν_{max}/cm^{-1} 3417, 3141, 1705, 1652, 1604, 1376, 696; δ_H 4.28 (2 H, s, 2-CH$_2$), 4.91 (2 H, s, 9-CH$_2$), 6.55 (2 H, s*, 6-NH$_2$), 7.18–7.35 (10 H, m, 2-Ph and 9-Ph), 10.12 (1 H, s*, 8-OH); δ_C 34.0, 42.4, 100.4, 126.7, 127.3, 128.2, 128.5, 128.8, 137.0, 138.9, 146.8, 147.9, 151.8, 160.9; *m/z* (EI) 363 (M^+, 100%), 330 (51), 91 (72) [Found: HRMS (EI) *m/z* 363.1151. Calc. for $C_{19}H_{17}N_5OS$: (M^+) 363.1154].

2-Amino-9-benzyl-6-benzylthio-8-hydroxypurine 16f. Yield 19%; mp 263–264 °C (washed with MeOH) (Found: C, 62.21; H, 4.68; N, 18.90. Calc. for $C_{19}H_{17}N_5OS{\cdot}1/5\ H_2O$: C, 62.18; H, 4.78; N, 19.08%); λ_{max}(EtOH)/nm 320.8 (ε/dm^3 mol^{-1} cm^{-1} 13 400); ν_{max}/cm^{-1} 3321, 1706, 1606, 1447, 1156, 711; δ_H 4.47 (2 H, s, 6-CH$_2$), 4.85 (2 H, s, 9-CH$_2$), 6.35 (2 H, s*, 2-NH$_2$), 7.20–7.43 (10 H, m, 6-Ph and 9-Ph), 10.93 (1 H, s*, 8-OH); δ_C 31.4, 42.2, 109.6, 127.0, 127.2, 128.3, 128.5, 129.1, 136.8, 138.4, 143.9, 149.6, 152.8, 158.5; *m/z* (EI) 363 (M^+, 100%), 330 (22), 272 (19), 91 (60) [Found: HRMS (EI) *m/z* 363.1164. Calc. for $C_{19}H_{17}N_5OS$: (M^+) 363.1154].

9-Benzyl-2-(2-hydroxyethylthio)-8-hydroxyadenine 15g. Yield 21%; mp 262–263 °C (recrystallized from EtOH) (Found: C, 52.28; H, 4.77; N, 21.76. Calc. for $C_{14}H_{15}N_5O_2S{\cdot}1/4\ H_2O$: C, 52.24; H, 4.85; N, 21.76%); λ_{max}(EtOH–H_2O = 1/9)/nm 282.4 (ε/dm^3 mol^{-1} cm^{-1} 13 100); ν_{max}/cm^{-1} 3419, 1705, 1651, 1602, 1500, 1368, 698; δ_H 3.11 (2 H, t, *J* 6.3, 2-CH$_2$), 3.58 (2 H, q, *J* 6.3, 2-CH$_2$), 4.85 (1 H, t*, *J* 6.3, 2-OH), 4.86 (2 H, s, 9-CH$_2$), 6.50 (2 H, s*, 6-NH$_2$), 7.25–7.32 (5 H, m, 9-Ph), 10.09 (1 H, s*, 8-OH); δ_C 32.9, 42.5, 60.3, 100.3, 127.5, 127.7, 128.5, 137.1, 146.8, 148.0, 151.7, 161.3; *m/z* (EI) 317 (M^+, 81%), 299 (30), 273 (78), 91 (100) [Found: HRMS (EI) *m/z* 317.0939. Calc. for $C_{14}H_{15}N_5O_2S$: (M^+) 317.0946].

2-Amino-9-benzyl-8-hydroxy-6-(2-hydroxyethylthio)purine 16g. Yield 17%; mp 233–235 °C; λ_{max}(EtOH–H_2O = 1/9)/nm 319.6 (ε/dm^3 mol^{-1} cm^{-1} 12 200); ν_{max}/cm^{-1} 3448, 1711, 1604, 1446, 1156, 704; δ_H 3.28 (2 H, t, *J* 5.8, 6-CH$_2$), 3.60 (2 H, q, *J* 5.8, 6-CH$_2$), 4.85 (2 H, s, 9-CH$_2$), 4.95 (1 H, t*, *J* 5.8, 6-OH), 6.24 (2 H, s*, 2-NH$_2$), 7.22–7.33 (5 H, m, 9-Ph), 10.95 (1 H, br s*, 8-OH); δ_C 30.6, 42.1, 60.3, 109.9, 127.0, 127.3, 128.5, 136.9, 144.5, 149.3, 152.8, 158.6; *m/z* (EI) 317 (M^+, 100%), 286 (29), 273 (97), 183 (20), 91 (87) [Found: HRMS (EI) *m/z* 317.0937. Calc. for $C_{14}H_{15}N_5O_2S$: (M^+) 317.0946].

Preparation of 2-amino-6-propylthiopurine 18

A mixture of thioguanine (**17**, 700 mg, 4.19 mmol) and K_2CO_3 (579 mg, 4.19 mmol) in dry DMF (30 mL) was stirred at room temperature for 30 min. To the mixture was added 1-iodopropane (0.41 mL, 4.19 mmol) and the mixture was stirred at room temperature for 2 h. The solvent was removed under reduced pressure, and the residue was triturated with water (20 mL). The resulting suspension was neutralized with 10% $NaHSO_4$ solution and extracted with AcOEt (50 mL). The organic layer was washed with brine (30 mL) and dried over $MgSO_4$. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel ($CHCl_3$–MeOH = 30 : 1) to give **18** (812 mg, 93%). Mp 197–198 °C (washed with Et$_2$O) (lit.,[22] 189–190 °C) (Found: C, 46.10; H, 5.36; N, 33.11. Calc. for $C_8H_{11}N_5S{\cdot}1/30\ Et_2O$: C, 46.14; H, 5.40; N, 33.08%); λ_{max}(EtOH)/nm 242.2 (ε/dm^3 mol^{-1} cm^{-1} 15 400) and 310.2 (11 800); ν_{max}/cm^{-1} 3487, 3295, 3181, 2971, 2818, 1614, 1560, 1498, 1357, 1256, 916; δ_H 0.98 (3 H, t, *J* 7.3, 6-CH$_3$), 1.62–1.71 (2 H, m, 6-CH$_2$), 3.23 (2 H, t, *J* 7.1, 6-CH$_2$), 6.28 (2 H, s*, 2-NH$_2$), 7.87 (1 H, s, 8-H), 12.47 (1 H, br s*, 9-H); δ_C 13.2, 22.7, 29.3, 123.9, 138.6, 151.6, 158.9, 159.6; *m/z* (EI) 209 (M^+, 100%), 194 (40), 181 (47), 167 (55) [Found: HRMS (EI) *m/z* 209.0731. Calc. for $C_8H_{11}N_5S$: (M^+) 209.0735].

Preparation of 2-amino-9-benzyl-6-propylthiopurine 19

A mixture of **18** (500 mg, 2.39 mmol) and K_2CO_3 (330 mg, 2.39 mmol) in dry DMF (20 mL) was stirred at room temperature for 30 min. To the mixture was added benzyl bromide (0.28 mL, 2.39 mmol) and the mixture was stirred at room temperature for 4 h. The solvent was removed under reduced pressure, and the residue was triturated with water (20 mL). The resulting suspension was neutralized with 10% $NaHSO_4$ solution and extracted with AcOEt (50 mL). The organic layer was washed with brine (30 mL) and dried over $MgSO_4$. After filtration, the solvent was evaporated and the residue was chromatographed on silica gel ($CHCl_3$) to give **19** (447 mg, 63%). Mp 137–138 °C (washed with Et$_2$O) (Found: C, 60.12; H, 5.75; N, 23.32. Calc. for $C_{15}H_{17}N_5S$: C, 60.17; H, 5.72; N, 23.39%); λ_{max}(EtOH)/nm 246.0 (ε/dm^3 mol^{-1} cm^{-1} 15 100) and 310.6 (13 400); ν_{max}/cm^{-1} 3483, 3312, 3195, 1622, 1575, 1456, 1404, 1232, 1180, 922, 730; δ_H 0.98 (3 H, t, *J* 7.3, 6-CH$_3$), 1.63–1.72 (2 H, m, 6-CH$_2$), 3.24 (2 H, t, *J* 7.1, 6-CH$_2$), 5.24 (2 H, s, 9-CH$_2$), 6.47 (2 H, s*, 2-NH$_2$), 7.21–7.34 (5 H, m, 9-Ph), 8.01 (1 H, s, 8-H); δ_C 13.2, 22.7, 29.3, 45.6, 124.0, 127.1, 127.6, 128.6, 137.1, 140.6, 150.9, 159.6; *m/z* (EI) 299 (M^+, 100%), 271 (20), 257 (24), 208 (22), 91 (80) [Found: HRMS (EI) *m/z* 299.1196. Calc. for $C_{15}H_{17}N_5S$: (M^+) 299.1205].

Preparation of 2-amino-9-benzyl-8-hydroxy-6-propylthiopurine 16c (from 19)

To a solution of **18** (200 mg, 0.67 mmol) in acetic acid (10 mL) was added bromine-saturated water (1 mL) and the mixture was heated at 70 °C for 2 h. After evaporation, the residue was partitioned between AcOEt (30 mL) and water (30 mL). The organic layer was washed with brine (20 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the residue was chromatographed on silica gel ($CHCl_3$) to give **16c** (36 mg, 17%), which was identified by comparison with a standard sample synthesized from **1a**.

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