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Preparation of novel 3,7-, 7,9- and 1,7-disubstituted guanines

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Abstract—Treatment of guanosine with arylmethyl halides in *N*,*N*-dimethylacetamide results in a series of 3,7-bis(arylmethyl) guanines and 7,9-bis(arylmethyl)guaninium halides. The same reaction on 7-arylmethyl guanines yields 3,7- and 7,9- differently disubstituted guanines. When 7-arylmethyl guanines are reacted with (hetero)arylmethyl halides in the presence of sodium hydride in *N*,*N*-dimethylformamide, 3,7- and 1,7-disubstituted guanines are obtained. All of these compounds, but one, are new and the preparation of 3,7-bis(substituted) guanines from guanosine as well as of 3,7- and 1,7-di(hetero)arylmethyl guanines from 7-substituted guanine is unprecedented.

1. Introduction

Despite the abundance of work produced on purines, very few examples of dialkylated guanines, moreover restricted to methyl or benzyl analogs, are known in the literature. For instance, 7-(aryl)methyl-3-methyl guanines were prepared from 7-methyl guanine[1] or from 3-methyl guanines[2–4] but direct transformation of guanosine, as well as of 7-arylmethyl guanines, into 3,7-diarylmethyl guanines is hitherto not described. Guanines dialkylated at positions 7,9 have been obtained from guanine by alkylation at neutral pH[5,6] and 7,9-diarylalkyl-N^2-acetylguaninium bromides were prepared from N^2-acetyl-7-benzyl guanine,[7,8] while from guanosine only one example of 7,9-bis arylmethylation has been reported to yield 7,9-bis(4-nitrobenzyl) guaninium bromide.[9] Dialkylations at positions 1,7 occur on O^6-methyl guanine,[2,10] on 1-benzyl-2′-deoxy guanosine[11] as well as on N^2-acetyl-8-bromo guanine[12] but no examples of alkylation at position 1 of 7-arylmethyl guanines are known.

In this paper, we report a series of guanines where identical or different (hetero)arylmethyl appendages are attached at various positions of the purine nucleus. In particular, the synthesis and characterization of 3,7-, 7,9- and 1,7-(hetero)-arylmethylated guanines will be presented.

2. Results and discussion

Interested in disubstituted guanines and with the intention to prepare 7-(2-naphthylmethyl)guanine, we reacted guanosine and 2-naphthylmethyl bromide (molar ratio 1:1) in *N*,*N*-dimethylacetamide (DMA) at 90°C, according to a procedure reported to give 7-(4-nitrobenzyl)guanine in 22% yield.[9] Surprisingly, along with the expected 7-(2-naphthylmethyl)guanine **50** (yield 31%), two other compounds were isolated after flash chromatographic partition: 2-amino-3,7-bis(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one **1** (6%) and 2-amino-7,9-bis(2-naphthylmethyl)-6-oxo-6,9-dihydro-1*H*-purin-7-ium bromide **2** (19%), an interesting result despite the modest yields since formation of 7,9-bis(4-nitrobenzyl)guaninium bromide is expected to occur only in the presence of excess arylmethylbromide,[9] and especially because to our knowledge formation of 3,7-isomers from guanosine is unreported.

The structures of compounds **1**, **2** and **50** were studied by NMR and MS spectroscopy and the substituents' position was determined through $^{1}H-^{13}C$ heteronuclear long range correlations detected in gHMBC experiments (Fig. 1). MS and ^{1}H NMR data were in agreement in assigning a mono-substituted structure to compound **50** (m/z=291 $[M+H]^+$) and two regioisomeric di-substituted structures to compounds **1** (m/z=432 $[M+H]^+$ and **2** (m/z=432 $[M-Br]^+$). The naphthylmethyl groups' position was then unambiguously attributed through gHMBC correlations of CH_2-10 and CH_2-10′ protons with guanine carbons, i.e. H10/C5, H10/C8 in the case of 7-substituents (**1**, **2** and **50**), H10′/C2, H10′/C4 in the case of 3-substituents (**1**) and H10′/C4, H10′/C8 for 9-substituents (**2**). Assignment of ^{13}C NMR signals of the guanine skeleton was possible with the help of literature data for guanine derivatives.[13] As a matter of fact, only the hydrogen bearing carbon C8 was

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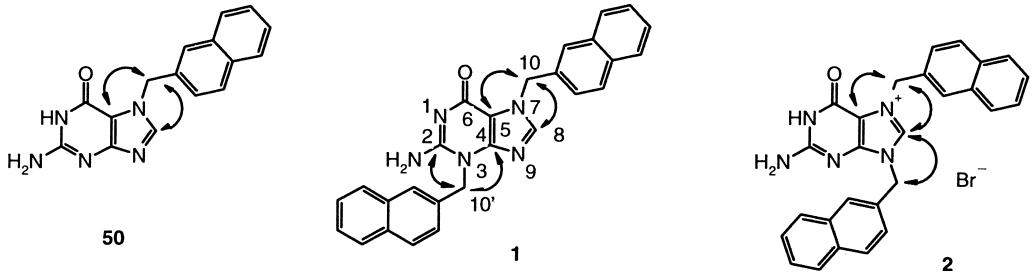
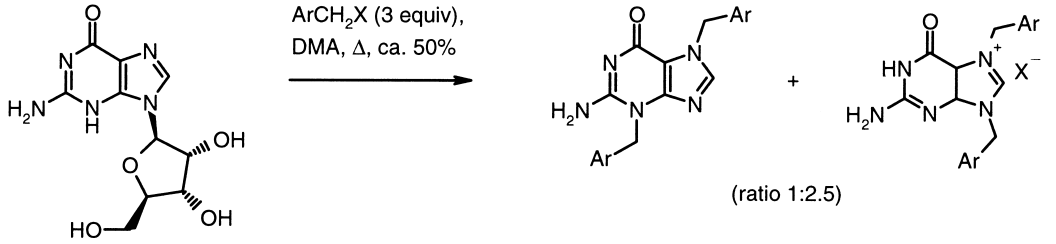


Figure 1. Most important $^{1}H-^{13}C$ long range correlations for the assigment of naphthylmethyl substituents position in compound **50**, **1** and **2**.



Scheme 1.

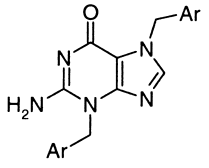
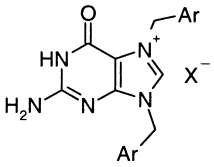
directly attributed in the gHSQC experiments whereas C4 and C5 could be identified but not distinguished by means of H8/C5 and H8/C4 gHMBC responses. Therefore, the C4 and C5 signals—whose correlations are fundamental to differentiate 9- from 7-substituents—were assigned with the help of the aforementioned literature data (C4~151 ppm; C5~116 ppm). C2 (~154 ppm) and C6 (~157 ppm) were attributed similarly to distinguish 3- from 1- substituents. The downfield shift of H8 signals (9.34 ppm) observed in compound **2** with respect to **50** and **1** (~8.1 ppm) is explained by the presence of a positive charge on the guanine ring.

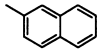
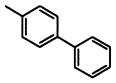
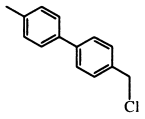
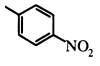
This result prompted us to study the reaction in more detail. So, the reaction was repeated using a 1:3 molar ratio of nucleoside/halide and the reaction course was monitored by HPLC. Concomitantly with the immediate formation of 7-(2-naphthylmethyl)guanosine, the coexistence of 7-(2-naphthylmethyl)guanine, 3,7-bis and 7,9-bis(substituted)-guanines was detected a few minutes after time zero. Then, 7-(2-naphthylmethyl)guanosine disappeared quickly, 7-(2-naphthylmethyl)guanine faded slowly, 3,7-bis(2-naphthylmethyl)guanine reached a steady maximum concentration after about 1 h, while the 7,9-bis(2-naphthylmethyl)guanine concentration increased constantly during the reaction period. After 8 h, 7-arylalkyl guanine, 3,7-bis and 7,9-bis regioisomers accounted respectively for about 2, 20 and 60% of the reaction mixture. After work-up and flash chromatography the two isomers were isolated with yields of 15 and 41%, respectively. In general, for the cases presented here, periods of time ranging typically from 6 to 8 h at 90°C with (hetero)arylmethyl bromides and at 120°C with (hetero)arylmethyl chlorides are required. In this way, 3,7- and 7,9-disubstituted guanines, in a ratio of about 1:2.5, were obtained as pure compounds after flash chromatography in about 50% yield (Scheme 1).

This procedure leads to the one step preparation from guanosine of the bis-substituted guanines presented in Table 1.

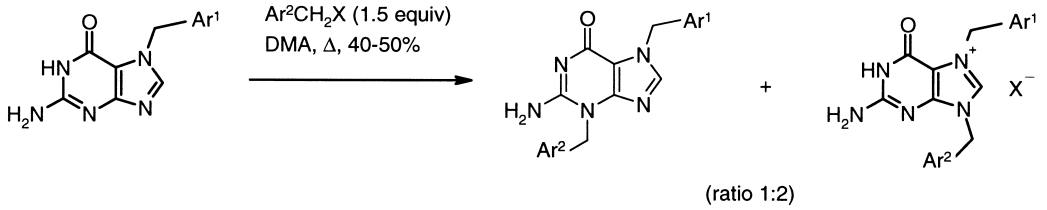
Access limited only to equally decorated guanines represented a restriction to our need. For this reason we started from 7-arylmethyl guanines and performed on them a

Table 1. 3,7-Bis and 7,9-bis substituted guanines

Compound #	Yield (%)	Ar	Compound #	Yield (%)
1	15		**2**	41
3	14		**4**	35
5[a]	16		**6**[a]	36
7	15		**8**	34
9	13		**10**	38[b]
11	15		**12**	40

[a] From arylmethyl chloride.
[b] Lit.[9]: 37%.



Scheme 2.

Table 2. 3,7- and 7,9-Disubstituted guanines

Compound #	Yield (%)	Ar^1	Ar^2	Compound #	Yield (%)
1	13			**2**	35
13[a]	14			**14**[a]	31
15	13			**16**	28

[a] From arylmethyl chloride.

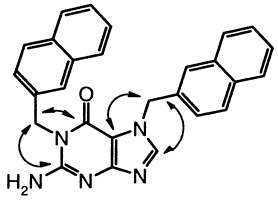


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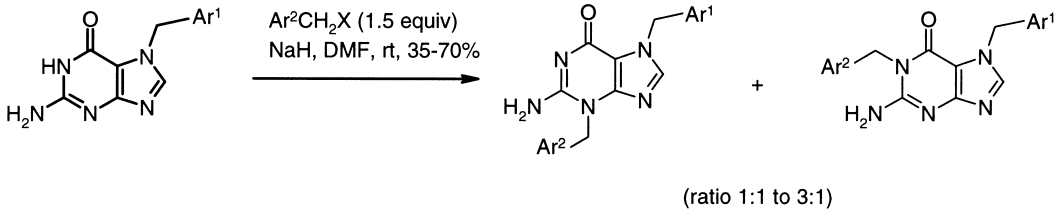
Figure 2. Most important $^{1}H-^{13}C$ long range correlations for the assigment of naphthylmethyl substituents position in compound **17**.

second alkylation with different halides. The desired 7-arylmethyl guanines were conveniently prepared from guanosine by the procedure described for 7-benzyl guanine.[14] So 7-(2-naphthylmethyl), 7-(4-phenyl)benzyl and 7-(4-methoxycarbonyl)benzyl guanines (**50**–**52**, respectively) were obtained in good yield from guanosine and the proper bromides at room temperature in dimethylsulfoxide (DMSO). When 7-arylmethyl guanines were reacted in DMA with different halides (Scheme 2), again mixtures of 3,7- and 7,9-disubstituted guanines, in a ratio of ca. 1:2, were isolated after flash chromatography in 40–50% yield, together with some starting 7-arylmethyl guanine (ca. 5–10%). The compounds prepared are shown in Table 2.

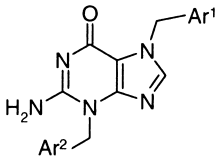
With the aim to improve the synthesis of 3,7 disubstituted guanines a different protocol was applied to the second alkylation reaction. This method, modelled after a literature procedure[15] for the preparation of 3-methyl-7-benzyl guanine from 3-methyl guanine, had been previously utilized in our labs for preparing 3-methyl-7-arylmethyl guanines (compounds **53** and **54**).

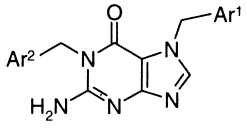
When such methodology was applied to 7- instead of 3-substituted guanines, relying upon the reaction of 7-arylmethyl guanines with (hetero)arylmethyl halides in the presence of NaH in DMF at room temperature, mixtures of the two isomers, originating from alkylation of N^1 and N^3, were obtained. In particular, when 7-(2-naphthylmethyl)guanine was reacted with 2-naphthylmethyl bromide, 2-amino-3,7-bis(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (**1**) and 2-amino-1,7-bis(2-naphthyl-

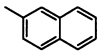
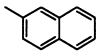
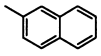
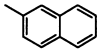
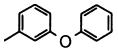
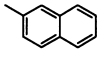
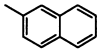
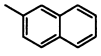
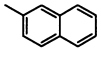
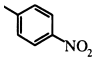
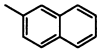
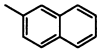
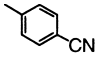
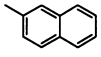
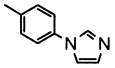
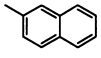
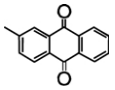
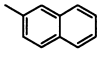
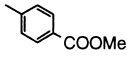
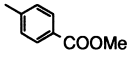
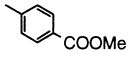
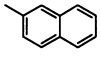
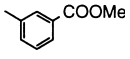
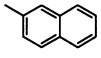
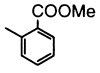
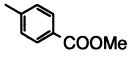
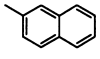
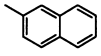
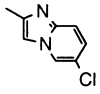


Scheme 3.

Table 3. 3,7- and 1,7-Disubstituted guanines





Compound #	Yield (%)	Ar^1	Ar^2	Compound #	Yield (%)
1	40			**17**	21
18[a]	26			**19**[a]	15
20	33			**21**	20
22	31			**23**	25
24	29			**25**	22
26	33			**27**	12
28	37			**29**	33
30	28			**31**	29
32	30			**33**	25
34	27			**35**	18
36	36			**37**	14
38	32			**39**	32
40	21			**41**	14
42	26			**43**	22
44	34			**45**	26
46	12			**47**	16
48	32			**49**	36

[a] From arylmethyl chloride.

methyl)-1,7-dihydro-6*H*-purin-6-one (**17**) were isolated as the main products in 60% yield, in a ratio of 2:1, together with about 5% unreacted 7-(2-naphthylmethyl)guanine.

The regiochemistry of compound **17** was determined similarly to compounds **1**, **2** and **50** on the basis of H10/C5-H10/C8 gHMBC correlations for the 7-substituent and H10′/C2-H10′/C6 for the 1-substituent (Fig. 2).

If this approach meets only in part with the need to improve the yields of 3,7-disubstituted guanines nevertheless it represents an unprecedented two step preparation from guanosine of structurally interesting and otherwise not easily accessible compounds (Scheme 3).

The reaction performed with different halides always produced the expected mixture in moderate yield, with

ratios between about 3:1 and 1:1 in favor of the 3,7-isomer (Table 3).

3. Conclusion

In conclusion we have shown that application of simple and known alkylation reactions to guanosine provides novel disubstituted guanines and, in particular, that from 7-arylmethyl guanine different procedures can direct the reaction toward the formation of different regioisomers. In this way, series of previously unreported 3,7-, 7,9- and 1,7-disubstituted guanines have been prepared in low to moderate yields straight through one or two steps from guanosine.

4. Experimental

4.1. General

All experiments dealing with moisture-sensitive compounds were conducted under dry argon. Starting materials, unless otherwise specified, were commercially available, of the best grade, and used without further purification. Elemental analyses were performed in the Analytical Department on Carlo Erba EA1108 or EA1110 instruments and C, H and N values were within ±0.4% of theoretical values. NMR spectra were recorded in DMSO-d_6 on a Varian Mercury spectrometer equipped with a 5 mm inverse detection probe operating at 400 MHz (^{1}H) and 100 MHz (^{13}C). Chemical shifts were referenced to the residual solvent signal (DMSO-d_5, 2.49 ppm for ^{1}H NMR and 39.5 ppm for ^{13}C NMR) and J values are given in Hz. IR spectra were recorded with a Perkin–Elmer FT-IR Spectrum 1000 spectrophotometer. Mass spectra were recorded on a Finnigan MAT LCQ ion trap instrument, equipped with an electrospray (ESI) ion source. Positive and negative ions spectra were acquired in separate chromatographic runs. HPLC conditions: column X-Terra RP-18 3.5 μM, 4.6×50 mm^2, mobile phase: (A) 5 mM ammonium acetate (pH 5) 95%/acetonitrile 5%; (B) acetonitrile 95%/water 5%. Gradient from 10% (B) to 90% (B) in 8 min, flow 1 mL/min, detector UV 215–400 nM (254 nM). Column chromatographic separations were carried out on 40/60 μm silica gel (Merck). Thin-layer chromatography was performed on Merck silica gel 60 plates coated with 250 μM layer with fluorescent indicator. Components were visualized by UV light (λ=254 nm) and iodine vapors. Where not otherwise noted, compounds have been prepared from (hetero)arylmethyl bromides.

Some of the (hetero)arylmethyl halides have been prepared following methodologies reported in the literature. Namely, 4-(bromomethyl)-1,1′-biphenyl, 5-(bromomethyl)-1,3-benzodioxole and 1-(bromomethyl)-3-phenoxybenzene were prepared from the corresponding commercial alcohols with carbon tetrabromide/triphenylphosphine[16] in dichloromethane. Intermediate 1-[4-(bromomethyl)phenyl]-1*H*-imidazole was prepared by reaction of 48% HBr on [4-(1*H*-imidazol-1-yl)phenyl]methanol, that was obtained by reduction of ethyl 4-(1*H*-imidazol-1-yl)benzoate with $LiAlH_4$, in turn achieved from ethyl 4-fluorobenzoate and imidazole.[17] Methyl 2-(bromomethyl)benzoate[18] was synthesized by radical bromination of methyl(2-methyl) benzoate with NBS/benzoyl peroxide in *n*-heptane. Finally 6-chloro-2-(chloromethyl)imidazo[1,2-*a*]pyridine was obtained from the condensation of 5-chloro-2-pyridinylamine with 1,3-dichloroacetone.[19]

4.1.1. 2-Amino-3,7-bis(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (1) and 2-amino-7,9-bis(2-naphthylmethyl)-6-oxo-6,9-dihydro-1*H*-purin-7-ium bromide (2). A mixture of guanosine (0.71 g, 2.5 mmol) and 2-naphthylmethyl bromide (1.66 g, 7.5 mmol) in DMA (25 mL) was stirred at 90°C for 8 h. After solvent evaporation the crude reaction product was fractionated by flash chromatography (eluant: dichloromethane/methanol 10:1) to yield **1** (0.16 g, 0.37 mmol, 15%) white solid, mp 255°C. IR (film, cm^{-1}): 3052; 1680; 1670; 1540; 1500; 1450; 815; 780; 750. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.47 (2H, s), 5.69 (2H, s), 6.98 (2H, br. s), 7.37 (1H, dd, J=1.8, 8.5 Hz), 7.44–7.50 (4H, m), 7.53 (1H, dd, J=1.7, 8.5 Hz), 7.68 (1H, s), 7.79–7.88 (7H, m), 8.1 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 46.8 (1C), 49.2 (1C), 110.7 (1C), 125–127 (8C), 128–129 (6C), 132–135 (6C), 140.5 (1C), 148.4 (1C), 153.9 (1C), 162.1 (1C); MS m/z 432 [M+H]$^+$; Anal. calcd for $C_{27}H_{21}N_5O$: C, 75.16; H, 4.91; N, 16.23. Found: C, 74.95; H, 5.16; N, 15.88, and **2** (0.44 g, 1.02 mmol, 41%) white solid, mp 209–210°C. IR (film, cm^{-1}): 1700; 1645; 1575; 1560; 1505; 800; 780.^{1}H NMR (400 MHz, DMSO-d_6): δ 5.56 (2H, s), 5.81 (2H, s), 6.97 (2H, br. s), 7.50–7.60 (6H, m), 7.85–7.95 (8H, m), 9.34 (1H, s), 11.65 (1H, br. s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 48.1 (1C), 51.6 (1C), 107.6 (1C), 125–129 (14C), 132–133 (6C), 136.6 (1C), 150.7 (1C), 158.7 (1C), 160 (1C); MS m/z 432 [M−Br]$^+$; Anal. calcd $C_{27}H_{22}N_5OBr$: C, 63.29; H, 4.33; N, 13.67. Found: C, 63.41; H, 4.51; N, 13.36.

With the same procedure the following compounds were prepared.

4.1.2. 2-Amino-3,7-bis(1,1′-biphenyl-4-ylmethyl)-3,7-dihydro-6*H*-purin-6-one (3). Yield: 14%, white solid, mp >300°C.^{1}H NMR (400 MHz, DMSO-d_6): δ 5.35 (2H, s), 5.55 (2H, s), 7.09 (2H, br. s), 7.3–7.5 (10H, m), 7.58–7.67 (8H, m), 8.12 (1H, s); MS m/z 484 [M+H]$^+$; Anal. calcd for $C_{31}H_{25}N_5O$: C, 77.00; H, 5.21; N, 14.48. Found: C, 76.76; H, 5.43; N, 14.06.

4.1.3. 2-Amino-7,9-bis[(1,1′-biphenyl)-4-ylmethyl]-6-oxo-6,9-dihydro-1*H*-purin-7-ium bromide (4). Yield: 35%, white solid, mp 205–206°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.4 (2H, s), 5.64 (2H, s), 7.2 (2H, br. s), 7.34–7.58 (10H, m), 7.64 (4H, m), 7.69 (4H, m), 9,51 (1H, s), 11.7 (1H, bs); MS m/z 484 [M−Br]$^+$; Anal. calcd for $C_{31}H_{26}N_5OBr$: C, 65.96; H, 4.64; N, 12.41. Found: C, 65.63; H, 4.90; N, 12.15.

4.1.4. 2-Amino-3,7-bis{[4′-(chloromethyl)[1,1′-biphenyl]-4-yl]methyl}-3,7-dihydro-6*H*-purin-6-one (5). Yield 16%, white solid, mp>290°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.77 (2H, s), 4.78 (2H, s), 5.35 (2H, s), 5.54 (2H, s), 7.01 (2H, br. s), 7.45–7.5 (8H, m), 7.60–7.65 (8H, m), 8.09 (1H, s); MS m/z 580 [M+H]$^+$; Anal. calcd for $C_{33}H_{27}Cl_2N_5O$: C, 68.28; H, 4.69; N, 12.06. Found: C, 68.30; H, 4.92; N, 11.71.

4.1.5. 2-Amino-7,9-bis{[4′-(chloromethyl)[1,1′-biphenyl]-4-yl]methyl}-6-oxo-6,9-dihydro-1*H*-purin-7-ium bromide (6). Yield: 36%, white solid, mp 213–216°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.64 (2H, s), 4.65 (2H, s), 5.25 (2H, s), 5.65 (2H, s), 7.09 (2H, br. s), 7.30–7.50 (8H, m), 7.60–7.70 (8H, m), 9.41 (1H, s), 11.8 (1H, br. s); MS *m/z* 580 $[M-Br]^+$; Anal. calcd for $C_{33}H_{28}Cl_2N_5OBr$: C, 59.83; H, 4.41; N, 10.57. Found: C, 60.05; H, 4.61; N, 10.33.

4.1.6. 2-Amino-3,7-bis(3,4-dichlorobenzyl)-3,7-dihydro-6*H*-purin-6-one (7). Yield 15%, white solid, mp 262–264°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.27 (2H, s), 5.47 (2H, s), 7.02 (2H, br. s), 7.14 (1H, dd, *J*=8.2, 2 Hz), 7.36 (1H, dd, *J*=8.2, 2 Hz), 7.52 (1H, d, *J*=2 Hz), 7.57 (1H, d, *J*=8.2 Hz), 7.59 (1H, d, *J*=8.2 Hz), 7.67 (1H, d, *J*=2 Hz), 8.09 (1H, s); MS *m/z* 468 $[M+H]^+$; Anal. calcd for $C_{19}H_{13}Cl_4N_5O$: C, 48.64; H, 2.79; N, 14.93. Found: C, 48.16; H, 2.81; N, 14.87.

4.1.7. 2-Amino-7,9-bis(3,4-dichlorobenzyl)-6-oxo-6,9-dihydro-1*H*-purin-7-ium bromide (8). Yield: 34%; white solid, mp 209–210°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.32 (2H, s), 5.57 (2H, s), 7.09 (2H, br. s), 7.39 (1H, dd, *J*=8.3, 2.1 Hz), 7.44 (1H, dd, *J*=8.3, 2.1 Hz), 7.67 (2H, d, *J*=8.3 Hz), 7.7 (1H, d, *J*=2.1 Hz), 7.75 (1H, d, *J*=2.1 Hz), 9.29 (1H, s), 11.65 (1H, br. s); MS *m/z* 468 $[M-Br]^+$; Anal. calcd for $C_{19}H_{14}Cl_4N_5OBr$: C, 41.49; H, 2.57; N, 12.73. Found: C, 41.73; H, 2.66; N, 13.04.

4.1.8. 2-Amino-3,7-bis(4-nitrobenzyl)-3,7-dihydro-6*H*-purin-6-one (9). Yield 13%, white solid, mp 271–272°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.44 (2H, s), 5.64 (2H, s), 7.09 (2H, br. s), 7.44 (2H, d, *J*=8.8 Hz), 7.56 (2H, d, *J*=8.8 Hz), 8.10 (1H, s), 8.18–8.22 (4H, m); MS *m/z* 422 $[M+H]^+$; Anal. calcd for $C_{19}H_{15}N_7O_5$: C, 54.16; H, 3.59; N, 23.27. Found: C, 54.17; H, 3.70; N, 22.79.

4.1.9. 2-Amino-7,9-bis(4-nitrobenzyl)-6-oxo-6,9-dihydro-1*H*-purin-7-ium bromide (10). Yield: 38%, white solid, mp 204–206°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.32 (2H, s), 5.68 (2H, s), 7.15 (2H, bs), 7.35–7.7 (4H, m), 8.2–8.4 (4H, m), 9.2 (1H, s), 11.76 (1H, br. s); MS *m/z* 422 $[M-Br]^+$; Anal. calcd for $C_{19}H_{16}N_7O_5Br$: C, 45.43; H, 3.21; N, 19.52. Found: C, 45.52; H, 3.51; N, 19.11.

4.1.10. 2-Amino-3,7-dibenzyl-3,7-dihydro-6*H*-purin-6-one (11). Yield 15%, white solid, mp 256–258°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.29 (2H, s), 5.49 (2H, s), 6.93 (2H, br. s), 7.19–7.38 (10H, m), 8.02 (1H, s); MS *m/z* 332 $[M+H]^+$; Anal. calcd for $C_{19}H_{17}N_5O$: C, 68.87; H, 5.17; N, 21.13. Found: C, 68.91; H, 5.31; N, 20.76.

4.1.11. 2-Amino-7,9-dibenzyl-6-oxo-6,9-dihydro-1*H*-purin-7-ium bromide (12). Yield: 40%, white solid, mp 212°C (dec.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.32 (2H, s), 5.61 (2H, s), 6.95 (2H, br. s), 7.19–7.46 (10H, m), 9.31 (1H, s), 11.69 (1H, br. s); MS *m/z* 332 $[M-Br]^+$; Anal. calcd for $C_{19}H_{18}N_5OBr$: C, 55.35; H, 4.40; N, 16.99. Found: C, 55.70; H, 4.61; N, 16.55.

4.1.12. 2-Amino-3-(1,1′-biphenyl)-4-ylmethyl-7-(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (13) and 2-amino-9-[(1,1′-biphenyl)-4-ylmethyl]-7-(2-naphthylmethyl)-6-oxo-6,9-dihydro-1*H*-purin-7-ium bromide (14). A suspension of 2-amino-7-(2-naphthylmethyl)-1,7-dihydro-6*H*-purin-6-one hydrochloride (0.500 g, 1.52 mmol) and 4-(chloromethyl)-1,1′-biphenyl (0.46 g, 2.3 mmol) in DMA (40 mL) was warmed under stirring at 90°C for 5 h. The solvent was evaporated under reduced pressure and the crude reaction product was fractionated by flash chromatography (eluant: dichloromethane/methanol 10:1) to yield **13** (0.09 g, 0.197 mmol, yield: 14%), whitish solid, mp 262–265°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.35 (2H, s), 5.68 (2H, s), 6.98 (2H, br. s), 7.35–7.6 (12H, m), 7.84–7.89 (4H, m), 8.11 (1H, s); MS *m/z* 458 $[M+H]^+$; Anal. calcd for $C_{29}H_{23}N_5O$: C, 76.13; H, 5.07; N, 15.31. Found: C, 75.95; H, 5.26; N, 14.93 and **14** (0.215 g, 0.47 mmol, yield: 31%), white solid, mp 233–235°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.38 (2H, s), 5.78 (2H, s), 7.25 (2H, br. s), 7.3–7.8 (16H, m), 9.35 (1H, s), 11.73 (1H, br.s); MS *m/z* 458 $[M-Br]^+$; Anal. calcd for $C_{29}H_{24}N_5OBr$: C, 64.69; H, 4.49; N, 13.01. Found: C, 64.77; H, 4.65; N, 12.76.

With this procedure the following compounds were prepared.

4.1.13. 2-Amino-3,7-bis(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (1). Yield 13%.

4.1.14. 2-Amino-7,9-bis(2-naphthylmethyl)-6-oxo-6,9-dihydro-1*H*-purin-7-ium bromide (2). Yield: 35%.

4.1.15. 2-Amino-3-(2-naphthylmethyl)-7-[(1,1′-biphenyl)-4-ylmethyl]-3,7-dihydro-6*H*-purin-6-one (15). Yield 13%, white solid, mp 289–290°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.47 (2H, s), 5.55 (2H, s), 6.99 (2H, br. s), 7.3–7.49 (8H, m), 7.61 (4H, m), 7.69 (1H, s), 7.8–7.87 (3H, m), 8.08 (1H, s); MS *m/z* 458 $[M+H]^+$; Anal. calcd for $C_{29}H_{23}N_5O$: C, 76.13; H, 5.07; N, 15.31. Found: C, 75.71; H, 5.18; N, 14.87.

4.1.16. 2-Amino-7-([1,1′-biphenyl]-4-ylmethyl)-9-(2-naphthylmethyl)-6-oxo-6,9-dihydro-1*H*-purin-7-ium bromide (16). Yield: 28%, whitish solid, mp 245–250°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.52 (2H, s), 5.64 (2H, s), 7.22 (2H, br. s), 7.36 (1H, t, *J*=7.3 Hz), 7.45 (2H, t, *J*=7.3 Hz), 7.53 (5H, m), 7.64 (2H, d, *J*=7.3 Hz), 7.68 (2H, d, *J*=8.6 Hz), 7.88–7.97 (4H, m), 9.48 (1H, s), 11.63 (1H, br. s); MS *m/z* 458 $[M-Br]^+$; Anal. calcd for $C_{29}H_{24}N_5OBr$: C, 64.69; H, 4.49; N, 13.01. Found: C, 64.62; H, 4.56; N, 13.09.

4.1.17. 2-Amino-3,7-bis(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (1) and 2-amino-1,7-bis(2-naphthylmethyl)-1,7-dihydro-6*H*-purin-6-one (17). To a suspension of 7-(2-naphthylmethyl) guanine hydrochloride (0.165 g, 0.5 mmol) in anhydrous DMF (4 mL), 60% NaH (0.050 g, 1.2 mmol) was added and the mixture was stirred at room temperature for 3 h. A solution of 2-naphthylmethyl bromide (0.165 g, 0.75 mmol) in anhydrous DMF (1 mL) was added dropwise and the reaction mixture was stirred for 3 h at room temperature. After solvent evaporation the crude reaction product was fractionated by flash chromatography (eluant dichloromethane/methanol 20:1) to yield **1** (0.086 g, 0.2 mmol, 40%) and **17** (0.045 g, 0.105 mmol, 21%), white solid, mp 260°C; IR (film, cm^{-1}): 3047;

1700; 1650; 1570; 1520; 1440; 1380; 775; 750. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.38 (2H, s), 5.66 (2H, s), 6.74 (2H, br. s), 7.36 (1H, dd, J=8.5, 1.7 Hz), 7.46–7.53 (5H, m), 7.62 (1H, s), 7.75–7.90 (7H, m), 8.23 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 43.4 (1C), 49.4 (1C), 107.2 (1C), 124–128 (14C), 132–135 (6C), 144.1 (1C), 153.1 (1C), 154.4 (1C), 158.2 (1C); MS m/z 432 $[M+H]^+$; Anal. calcd for $C_{27}H_{21}N_5O$: C, 75.16; H, 4.91; N, 16.23. Found: C, 74.85; H, 4.98; N, 15.94.

With this procedure and starting from the convenient 7-arylmethylguanine hydrochlorides and (hetero)arylmethyl halides the following compounds were prepared.

4.1.18. 2-Amino-3-(3,4-dichlorobenzyl)-7-(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (18). Yield 26%, whitish solid, mp 235–238°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.28 (2H, s), 5.67 (2H, s), 7.0 (2H, br. s), 7.14 (1H, dd, J=8.3, 2.2 Hz), 7.47–7.57 (5H, m), 7.82–7.90 (4H, m), 8.11 (1H, s); MS m/z 450 $[M+H]^+$; Anal. calcd for $C_{23}H_{17}Cl_2N_5O$: C, 61.35; H, 3.81; N, 15.55. Found: C, 61.24; H, 3.88; N, 15.32.

4.1.19. 2-Amino-1-(3,4-dichlorobenzyl)-7-(2-naphthylmethyl)-1,7-dihydro-6*H*-purin-6-one (19). Yield: 15%, white solid, mp 212–213°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.21 (2H, s), 5.6 (2H, s), 6.87 (2H, br. s), 7.3–7.9 (10H, m), 8.24 (1H, s); MS m/z 450 $[M+H]^+$; Anal. calcd for $C_{23}H_{17}Cl_2N_5O$: C, 61.35; H, 3.81; N, 15.55. Found: C, 61.38; H, 4.11; N, 15.12.

4.1.20. 2-Amino-7-(2-naphthylmethyl)-3-(3-phenoxybenzyl)-3,7-dihydro-6*H*-purin-6-one (20). Yield: 33%, white solid, mp 220–226°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.34 (2H, s), 5.69 (2H, s), 6.87 (1H, dd, J=7.8, 1.7 Hz), 6.95–7.0 (4H, m), 7.12 (1H, t, J=7.7 Hz), 7.3–7.4 (3H, m), 7.41 (2H, br. s), 7.50–7.55 (3H, m), 7.85–7.9 (4H, m), 8.21 (1H, s); MS m/z 474 $[M+H]^+$; Anal. calcd for $C_{29}H_{23}N_5O_2$: C, 73.56; H, 4.90; N, 14.79. Found: C, 73.35; H, 5.04; N, 14.59.

4.1.21. 2-Amino-7-(2-naphthylmethyl)-1-(3-phenoxybenzyl)-1,7-dihydro-6*H*-purin-6-one (21). Yield: 20%, whitish solid, mp 218–222°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.25 (2H, s), 5.61 (2H, s), 6.8–7.8 (18H, m), 8.29 (1H, s); MS m/z 474 $[M+H]^+$; Anal. calcd for $C_{29}H_{23}N_5O_2$: C, 73.56; H, 4.90; N, 14.79. Found: C, 73.20; H, 4.94; N, 14.72.

4.1.22. 2-Amino-7-(2-naphthylmethyl)-3-(2-quinolinylmethyl)-3,7-dihydro-6*H*-purin-6-one (22). Yield: 31%, white solid, mp 285–286°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.59 (2H, s), 5.7 (2H, s), 6.99 (2H, br. s), 7.37 (1H, d, J=8.5 Hz), 7.5–7.75 (5H, m), 7.85–7.97 (6H, m), 8.06 (1H, s), 8.35 (1H, d, J=8.5 Hz); MS m/z 433 $[M+H]^+$; Anal. calcd for $C_{26}H_{20}N_6O$: C, 72.21; H, 4.66; N, 19.43. Found: C, 71.80; H, 4.73; N, 19.4.

4.1.23. 2-Amino-7-(2-naphthylmethyl)-1-(2-quinolinylmethyl)-1,7-dihydro-6*H*-purin-6-one (23). Yield: 25%, white solid, mp 265–269°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.46 (2H, s), 5.63 (2H, s), 6.77 (2H, br. s), 7.39 (1H, d, J=8.5 Hz), 7.46–7.51 (3H, m), 7.59 (1H, t, J=7 Hz), 7.73 (1H, t, J=7 Hz), 7.75 (1H, s), 7.8–7.97 (5H, m), 8.22 (1H, s), 8.35 (1H, d, J=8.5 Hz); MS m/z 433 $[M+H]^+$; Anal. calcd for $C_{26}H_{20}N_6O$: C, 72.21; H, 4.66; N, 19.43. Found: C, 71.84; H, 4.71; N, 19.15.

4.1.24. 2-Amino-3-(2,1,3-benzoxadiazol-5-ylmethyl)-7-(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (24). Yield: 29%, white solid, mp>300°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.44 (2H, s), 5.71 (2H, s), 7.07 (2H, br. s), 7.5–7.6 (4H, m), 7.69 (1H, s), 7.85–7.9 (4H, m), 8.06 (1H, d, J=9.4 Hz), 8.14 (1H, s); MS m/z 424 $[M+H]^+$; Anal. calcd for $C_{23}H_{17}N_7O_2$: C, 65.24; H, 4.05; N, 23.15. Found: C, 65.31; H, 4.24; N, 22.76.

4.1.25. 2-Amino-1-(2,1,3-benzoxadiazol-5-ylmethyl)-7-(2-naphthylmethyl)-1,7-dihydro-6*H*-purin-6-one (25). Yield: 22%, whitish solid, mp 284–286°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.33 (2H, s), 5.64 (2H, s), 6.82 (2H, br. s), 7.44–7.51 (4H, m), 7.62 (1H, s), 7.79 (1H, s), 7.89–7.90 (3H, m), 8.01 (1H, d, J=9.3 Hz), 8.24 (1H, s); MS m/z 424 $[M+H]^+$; Anal. calcd for $C_{23}H_{17}N_7O_2$: C, 65.24; H, 4.05; N, 23.15. Found: C, 64.89; H, 4.14; N, 22.75.

4.1.26. 2-Amino-3-(1,3-benzodioxol-5-ylmethyl)-7-(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (26). Yield: 33%, whitish solid, mp>280°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.21 (2H, s), 5.69 (2H, s), 5.97 (2H, s), 6.77 (1H, dd, J=7.9, 1.3 Hz), 6.84 (1H, d, J=7.9 Hz), 6.87 (1H, d, J=1.3 Hz), -6.95 (2H, br. s), 7.52 (2H, m), 7.54 (1H, dd, J=8.5, 1.5 Hz), 7.85–7.9 (4H, m), 8.13 (1H, s); MS m/z 426 $[M+H]^+$; Anal. calcd for $C_{24}H_{19}N_5O_3$: C, 67.76; H, 4.50; N, 16.46. Found: C, 67.41; H, 4.58; N, 16.21.

4.1.27. 2-Amino-1-(1,3-benzodioxol-5-ylmethyl)-7-(2-naphthylmethyl)-1,7-dihydro-6*H*-purin-6-one (27). Yield: 12%, white solid, mp 258–263°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.19 (2H, s), 5.61 (2H, s), 5.94 (2H, s), 6.75 (1H, dd, J=7.7, 1.2 Hz), 6.85 (1H, d, J=7.7 Hz), 6.89 (2H, br. s), 6.93 (1H, d, J=1.2 Hz), 7.5–7.9 (7H, m), 8.22 (1H, s); MS m/z 426 $[M+H]^+$; Anal. calcd for $C_{24}H_{19}N_5O_3$: C, 67.76; H, 4.50; N, 16.46. Found: C, 67.61; H, 4.72; N, 16.01.

4.1.28. 2-Amino-7-(2-naphthylmethyl)-3-(4-nitrobenzyl)-3,7-dihydro-6*H*-purin-6-one (28). Yield: 37%, whitish solid, mp 268–269°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.46 (2H, s), 5.70 (2H, s), 7.05 (2H, br. s), 7.46 (2H, d, J=8.8 Hz), 7.5–7.6 (3H, m), 7.87–7.91 (4H, m), 8.12 (1H, s), 8.20 (2H, d, J=8.8 Hz); MS m/z 427 $[M+H]^+$; Anal. calcd for $C_{23}H_{18}N_6O_3$: C, 64.78; H, 4.25; N, 19.71. Found: C, 64.91; H, 4.51; N, 19.41.

4.1.29. 2-Amino-7-(2-naphthylmethyl)-1-(4-nitrobenzyl)-1,7-dihydro-6*H*-purin-6-one (29). Yield: 33%, white solid, mp>285°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.34 (2H, s), 5.63 (2H, s), 6.8 (2H, br. s), 7.4 (2H, d, J=8.7 Hz), 7.47 (1H, dd, J=8.5, 1.7 Hz), 7.51 (2H, m), 7.77 (1H, s), 7.85–7.9 (3H, m), 8.16 (2H, d, J=8.7 Hz), 8.24 (1H, s); MS m/z 427 $[M+H]^+$; Anal. calcd for $C_{23}H_{18}N_6O_3$: C, 64.78; H, 4.25; N, 19.71. Found: C, 64.44; H, 4.35; N, 19.36.

4.1.30. 2-Amino-3-(3,4-difluorobenzyl)-7-(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (30). Yield: 28%, white solid, mp 236–237°C; ^{1}H NMR (400 MHz,

DMSO-d_6): δ 5.27 (2H, s), 5.67 (2H, s), 7.0–7.05 (3H, m), 7.3–7.55 (5H, m), 7.83–7.87 (4H, m), 8.12 (1H, s); MS *m/z* 418 $[M+H]^+$; Anal. calcd for $C_{23}H_{17}F_2N_5O$: C, 66.18; H, 4.11; N, 16.78. Found: C, 66.04; H, 4.42; N, 16.36.

4.1.31. 2-Amino-1-(3,4-difluorobenzyl)-7-(2-naphthylmethyl)-1,7-dihydro-6*H*-purin-6-one (31). Yield: 29%, white solid, mp 219–220°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.16 (2H, s), 5.61 (2H, s), 6.73 (2H, br. s), 6.97–7.36 (3H, m), 7.44–7.51 (3H, m), 7.76 (1H, s), 7.80–7.88 (3H, m), 8.19 (1H, s); MS *m/z* 418 $[M+H]^+$; Anal. calcd for $C_{23}H_{17}F_2N_5O$: C, 66.18; H, 4.11; N, 16.78. Found: C, 65.75; H, 4.22; N, 16.43.

4.1.32. 4-{[2-Amino-7-(2-naphthylmethyl)-6-oxo-6,7-dihydro-3*H*-purin-3-yl]methyl}benzonitrile (32). Yield: 30%, whitish solid, mp 276–278°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.38 (2H, s), 5.67 (2H, s), 7.00 (2H, br. s), 7.36 (2H, d, *J*=8.4 Hz), 7.48–7.55 (3H, m), 7.78 (2H, d, *J*=8.4 Hz), 7.84–7.89 (4H, m), 8.09 (1H, s); MS *m/z* 407 $[M+H]^+$; Anal. calcd for $C_{24}H_{18}N_6O$: C, 70.92; H, 4.46; N, 20.68. Found: C, 70.66; H, 4.71; N, 20.24.

4.1.33. 4-{[2-Amino-7-(2-naphthylmethyl)-6-oxo-6,7-dihydro-1*H*-purin-1-yl]methyl}benzonitrile (33). Yield: 25%, whitish solid, mp 245–246°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.27 (2H, s), 5.60 (2H, s), 6.74 (2H, br. s), 7.31 (2H, d, *J*=8.3 Hz), 7.43–7.50 (3H, m), 7.7–7.75 (3H, m), 7.80–7.88 (3H, m), 8.20 (1H, s); MS *m/z* 407 $[M+H]^+$; Anal. calcd for $C_{24}H_{18}N_6O$: C, 70.92; H, 4.46; N, 20.68. Found: C, 70.69; H, 4.53; N, 20.38.

4.1.34. 2-Amino-3-[4-(1*H*-imidazol-1-yl)benzyl]-7-(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (34). Yield: 27%, white solid, mp>280°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.37 (2H, s), 5.68 (2H, s), 7.00 (2H, br. s), 7.06 (1H, s), 7.35 (2H, d, *J*=8.5 Hz), 7.45–7.65 (6H, m), 7.83–7.90 (4H, m), 8.11 (1H, s), 8.15 (1H, m); MS *m/z* 448 $[M+H]^+$; Anal. calcd for $C_{26}H_{21}N_7O$: C, 69.78; H, 4.73; N, 21.91. Found: C, 69.77; H, 4.89; N, 21.47.

4.1.35. 2-Amino-1-[4-(1*H*-imidazol-1-yl)benzyl]-7-(2-naphthylmethyl)-1,7-dihydro-6*H*-purin-6-one (35). Yield: 18%, brownish solid, mp 251–255°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.28 (2H, s), 5.61 (2H, s), 6.83 (2H, br. s), 7.02 (1H, s), 7.3–7.6 (8H, m), 7.75–7.83 (4H, m), 8.22 (1H, s), 8.18 (1H, m); MS *m/z* 448 $[M+H]^+$; Anal. calcd for $C_{26}H_{21}N_7O$: C, 69.78; H, 4.73; N, 21.91. Found: C, 69.57; H, 4.79; N, 21.61.

4.1.36. 2-{[2-Amino-7-(2-naphthylmethyl)-6-oxo-6,7-dihydro-3*H*-purin-3-yl]methyl}anthra-9,10-quinone (36). Yield: 36%, whitish solid, mp 250°C (dec.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.52 (2H, s), 5.69 (2H, s), 7.09 (2H, br. s), 7.40–7.50 (3H, m), 7.70–7.90 (7H, m), 8.04 (1H, d, *J*=1.7 Hz), 8.12 (1H, s), 8.15–8.20 (3H, m); MS *m/z* 512 $[M+H]^+$; Anal. calcd for $C_{31}H_{21}N_5O_3$: C, 72.79; H, 4.14; N, 13.69. Found: C, 72.74; H, 4.29; N, 13.51.

4.1.37. 2-{[2-Amino-7-(2-naphthylmethyl)-6-oxo-6,7-dihydro-1*H*-purin-1-yl]methyl}anthra-9,10-quinone (37). Yield: 14%, whitish solid, mp 216–219°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.43 (2H, s), 5.62 (2H, s), 6.81 (2H, br. s), 7.35–7.45 (3H, m), 7.65–7.87 (7H, m), 7.99–8.20 (5H, m); MS *m/z* 512 $[M+H]^+$; Anal. calcd for $C_{31}H_{21}N_5O_3$: C, 72.79; H, 4.14; N, 13.69. Found: C, 72.54; H, 4.34; N, 13.36.

4.1.38. Methyl 4-{[2-amino-7-(2-naphthylmethyl)-6-oxo-6,7-dihydro-3*H*-purin-3-yl]methyl}benzoate (38). Yield: 32%, white solid, mp>280°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.81 (3H, s), 5.38 (2H, s), 5.67 (2H, s), 6.97 (2H, br. s), 7.31 (2H, d, *J*=8.4 Hz), 7.48–7.54 (3H, m), 7.83–7.90 (6H, m), 8.08 (1H, s); MS *m/z* 440 $[M+H]^+$; Anal. calcd for $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.08; H, 4.89; N, 15.65.

4.1.39. Methyl 4-{[2-amino-7-(2-naphthylmethyl)-6-oxo-6,7-dihydro-1*H*-purin-1-yl]methyl}benzoate (39). Yield: 32%, white solid, mp 202–206°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.82 (3H, s), 5.26 (2H, s), 5.60 (2H, s), 6.72 (2H, br. s), 7.25 (2H, d, *J*=8.2 Hz), 7.43–7.49 (3H, m), 7.74 (1H, s). 7.80–7.87 (5H, m), 8.19 (1H, s); MS *m/z* 440 $[M+H]^+$; Anal. calcd for $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.10; H, 5.11; N, 15.33.

4.1.40. Methyl 4-({2-amino-3-[4-(methoxycarbonyl)benzyl]-6-oxo-3,6-dihydro-7*H*-purin-7-yl}methyl) benzoate (40). Yield: 21%, white solid, mp 247–248°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.81 (3H, s), 3.82 (3H, s), 5.38 (2H, s), 5.58 (2H, s), 6.99 (2H, br. s), 7.31 (2H, d, *J*=8.5 Hz), 7.44 (2H, d, *J*=8.5 Hz), 7.89–7.92 (4H, m), 8.05 (1H, s); MS *m/z* 448 $[M+H]^+$; Anal. calcd for $C_{23}H_{21}N_5O_5$: C, 61.74; H, 4.73; N, 15.65. Found: C, 61.37; H, 4.87; N, 15.18.

4.1.41. Methyl 4-({2-amino-7-[4-(methoxycarbonyl)benzyl]-6-oxo-6,7-dihydro-1*H*-purin-1-yl}methyl) benzoate (41). Yield: 14%, whitish solid, mp 212–214°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.85 (3H, s), 3.87 (3H, s), 5.31 (2H, s), 5.50 (2H, s), 6.75 (2H, br. s), 7.3–7.9 (8H, m), 8.22 (1H, s); MS *m/z* 448 $[M+H]^+$; Anal. calcd for $C_{23}H_{21}N_5O_5$: C, 61.74; H, 4.73; N, 15.65. Found: C, 61.57; H, 5.08; N, 15.27.

4.1.42. Methyl 3-{[2-amino-7-(2-naphthylmethyl)-6-oxo-6,7-dihydro-3*H*-purin-3-yl] methyl}benzoate (42). Yield: 26%, whitish solid, mp 240–241°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.79 (3H, s), 5.37 (2H, s), 5.67 (2H, s), 7.00 (2H, br. s), 7.45–7.5 (5H, m), 7.81–7.88 (6H, m), 8.10 (1H, s); MS *m/z* 440 $[M+H]^+$; Anal. calcd for $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.29; H, 4.86; N, 15.85.

4.1.43. Methyl 3-{[2-amino-7-(2-naphthylmethyl)-6-oxo-6,7-dihydro-1*H*-purin-1-yl]methyl}benzoate (43). Yield: 22%, whitish solid, mp 210°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.80 (3H, s), 5.23 (2H, s), 5.61 (2H, s), 6.74 (2H, s), 7.41–7.49 (5H, m), 7.75–7.87 (6H, m), 8.19 (1H, s); MS *m/z* 440 $[M+H]^+$; Anal. calcd for $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 67.83; H, 4.92; N, 15.59.

4.1.44. Methyl 2-{[2-amino-7-(2-naphthylmethyl)-6-oxo-6,7-dihydro-3*H*-purin-3-yl] methyl}benzoate (44). Yield: 34%, white solid, mp 259–260°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.88 (3H, s), 5.61 (2H, s), 5.68 (2H, s), 5.69 (1H, dd, *J*=7.7, 1.2 Hz), 6.93 (2H, br. s), 7.38–7.56 (5H, m),

7.85–7.90 (4H, m), 7.97 (1H, dd, J=7.7, 1.4 Hz), 8.03 (1H, s); MS m/z 440 $[M+H]^+$; Anal. calcd for $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.35; H, 5.19; N, 15.54.

4.1.45. Methyl 2-{[2-amino-7-(2-naphthylmethyl)-6-oxo-6,7-dihydro-1*H*-purin-1-yl]methyl}benzoate (45). Yield: 26%, white solid, mp 227–228°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.86 (3H, s), 5.48 (2H, s), 5.59 (2H, s), 6.5–6.7 (3H, m), 7.35–7.5 (5H, m), 7.73 (1H, s), 7.81–7.87 (3H, m), 7.94 (1H, dd, J=7.7, 1.3 Hz), 8.19 (1H, s); MS m/z 440 $[M+H]^+$; Anal. calcd for $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.05; H, 4.87; N, 15.79.

4.1.46. Methyl 4-{[2-amino-3-(2-naphthylmethyl)-6-oxo-3,6-dihydro-7*H*-purin-7-yl]methyl}benzoate (46). Yield: 12%, white solid, mp 276–277°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.82 (3H, s), 5.47 (2H, s), 5.60 (2H, s), 7.00 (2H, br. s), 7.38–7.5 (5H, m), 7.68 (1H, s), 7.80–7.92 (5H, m), 8.06 (1H, s); MS m/z 440 $[M+H]^+$; Anal. calcd for $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.06; H, 5.00; N, 15.52.

4.1.47. Methyl 4-{[2-amino-1-(2-naphthylmethyl)-6-oxo-1,6-dihydro-7*H*-purin-7-yl]methyl}benzoate (47). Yield: 16%, whitish solid, mp 245–248°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.82 (3H, s), 5.33 (2H, s), 5.54 (2H, s), 6.73 (2H, br. s), 7.31 (1H, dd, J=8.3, 2.1 Hz), 7.37 (2H, d, J=8.5 Hz), 7.42–7.47 (2H, m), 7.59 (1H, s), 7.75–7.85 (3H, m), 7.90 (2H, d, J=8.5 Hz), 8.16 (1H, s); MS m/z 440 $[M+H]^+$; Anal. calcd for $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.14; H, 4.94; N, 15.52.

4.1.48. 2-Amino-3-[(6-chloroimidazo[1,2-*a*]pyridin-2-yl)-methyl]-7-(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (48). Yield: 32%, white solid, mp 278–281°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.37 (2H, s), 5.69 (2H, s), 7.01 (2H, br. s), 7.32 (1H, dd, J=9.5, 2.3 Hz), 7.45–7.50 (3H, m), 7.60–7.90 (6H, m), 8.09 (1H, s), 8.73 (1H, dd, J=2.3, 0.7 Hz); MS m/z 456 $[M+H]^+$; Anal. calcd for $C_{24}H_{18}ClN_7O$: C, 63.23; H, 3.98; N, 21.51. Found: C, 62.98; H, 4.21; N, 20.93.

4.1.49. 2-Amino-1-[(6-chloroimidazo[1,2-*a*]pyridin-2-yl)-methyl]-7-(2-naphthylmethyl)-1,7-dihydro-6*H*-purin-6-one (49). Yield: 36%, white solid, mp 260–261°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.28 (2H, s), 5.64 (2H, s), 6.86 (2H, br. s), 7.29 (1H, dd, J=9.6, 2.2 Hz), 7.47–7.52 (3H, m), 7.57 (1H, dd, J=9.6, 0.9 Hz), 7.77 (1H, s), 7.82 (1H, s), 7.84–7.90 (3H, m), 8.19 (1H, s), 8.77 (1H, dd, J=2.2, 0.9 Hz); MS m/z 456 $[M+H]^+$; Anal. calcd for $C_{24}H_{18}ClN_7O$: C, 63.23; H, 3.98; N, 21.51. Found: C, 62.82; H, 4.14; N, 20.87.

4.1.50. 2-Amino-7-(2-naphthylmethyl)-1,7-dihydro-6*H*-purin-6-one hydrochloride (50). To a solution of guanosine (0.57 g, 2 mmol) in anhydrous DMSO (3 mL) 2-naphthylmethyl bromide (1.01 g, 4.5 mmol) was added and the reaction mixture was stirred at rt for 8 h. Aqueous 37% hydrochloric acid (1.5 mL) was added and the clear solution stirred for 30 min at rt. The mixture was poured into methanol (10 mL) and stirred until a white precipitate formed. The solid was filtered, washed with methanol and dried to yield title compound (0.59 g, 1.81 mmol, 90% yield), white solid, mp 282–284°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.69 (2H, s), 7.42 (3H, br. s), 7.50–7.55 (3H, m), 7.87–7.93 (4H, m), 8.94 (1H, s), 11.64 (1H, br. s) ^{13}C NMR (100 MHz, DMSO-d_6): δ 50.8 (1C), 107.8 (1C), 126–129 (7C), 133–134 (3C), 140.7 (1C), 151.2 (1C), 153.6 (1C), 154.6 (1C); MS m/z 291 $[M+H]^+$; Anal. calcd $C_{16}H_{14}N_5OCl$: C, 58.63; H, 4.31; N, 21.37. Found: C, 58.53; H, 4.42; N, 20.86.

4.1.51. 2-Amino-7-[(4-phenyl)benzyl]-1,7-dihydro-6*H*-purin-6-one hydrochloride (51). From guanosine and 4-(bromomethyl)-1,1′-biphenyl, 85% yield, white solid, mp>290°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.53 (2H, s), 7.40 (3H, br. s), 7.34 (1H, t, J=7.3 Hz), 7.42–7.47 (3H, m), 7.61–7.65 (4H, m), 8.77 (1H, s), 11.71 (1H, br. s); MS m/z 318 $[M+H]^+$; Anal. calcd $C_{18}H_{16}N_5OCl$: C, 61.11; H, 4.56; N, 19.79. Found: C, 60.73; H, 4.65; N 19.55.

4.1.52. Methyl 4-[(2-amino-6-oxo-1,6-dihydro-7*H*-purin-7-yl)methyl]benzoate hydrochloride (52). From guanosine and methyl 4-(bromomethyl) benzoate, 92% yield. White solid, mp>290°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.82 (3H, s), 5.56 (2H, s), 7.35 (3H, br. s), 7.43 (2H, d, J=8.1 Hz), 7.92 (2H, d, J=8.1 Hz), 8.7 (1H, s), 11.62 (1H, br. s); MS m/z 300 $[M+H]^+$; Anal. calcd $C_{14}H_{14}N_5O_3Cl$: C, 50.08; H, 4.20; N, 20.86. Found: C, 50.12; H, 4.25; N, 20.68.

4.1.53. 2-Amino-3-methyl-7-(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (53). To a suspension of 3-methyl guanine (0.1 g, 0.5 mmol) in anhydrous DMF (2 mL), 60% NaH (0.024 g, 0.6 mmol) was added and the mixture was stirred at room temperature for 2 h. A solution of 2-naphthylmethyl bromide (0.13 g, 0.56 mmol) in anhydrous DMF (1 mL) was added and the reaction mixture was stirred for 3 h at room temperature. After solvent evaporation the crude reaction product was purified by flash chromatography (eluant: dichloromethane/methanol 20:1) to yield 2-amino-3-methyl-7-(2-naphthylmethyl)-3,7-dihydro-6*H*-purin-6-one (52% yield), white solid, mp 263–266°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.49 (3H, s), 5.66 (2H, s), 6.85 (2H, s), 7.45–7.50, (3H, m), 7.80–7.90, (4H, m), 8.08 (1H, s); MS m/z 306 $[M+H]^+$; Anal. calcd for $C_{17}H_{15}N_5O$: C, 66.87; H, 4.95; N, 22.94. Found: C, 66.31; H, 5.13; N, 21.88.

4.1.54. 2-Amino-7-([1,1′-biphenyl]-4-ylmethyl)-3-methyl-3,7-dihydro-6*H*-purin-6-one (54). This has been prepared analogously to **53**, in 48% yield, white solid, mp 283–285°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.49 (3H, s), 5.52 (2H, s), 6.85 (2H, s), 7.33 (1H, t, J=7.4 Hz), 7.40–7.47 (4H, m), 7.57–7.61 (4H, m), 8.06 (1H, s); MS m/z 332 $[M+H]^+$; Anal. calcd for $C_{17}H_{15}N_5O$: C, 68.87; H, 5.17; N, 21.13. Found: C, 68.48; H, 5.62; N, 19.85.

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