

A Feasibility Study for Application to Solid-Phase Synthesis. I [1]

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A suitably substituted pyrimidine **1** was converted to a number of title compounds. Nucleophilic substitution involving the chlorine atoms in **1** by treatment with phenylmethanethiol yielded **2** or **3**, depending on the reaction temperature. Treatment of **3** with an amine afforded 6-phenylmethanesulfanyl-N⁴-substituted-2-phenyl-pyrimidine-4,5-diamines **4-7**. These pyrimidines were converted into 2-phenylpurines **8-11** and 2-phenyl-8-azapurines **12-14**, by treatment with triethyl orthoformate in the presence of hydrochloric acid (or acetic anhydride), or with potassium nitrite and acetic acid respectively. The thioether function on C(6) was then converted into a sulfonyl group by oxidation with *m*-chloroperoxybenzoic acid affording purines **15-18** and their 8-azaanalogs **19-21**; these compounds, as crude products, were treated with an amine to yield the corresponding adenines **22-25** or 8-azaadenines **26-31**. All reactions were performed under conditions compatible with the possible use of a thiomethyl resin in place of phenylmethanethiol to bind the pyrimidine ring of **1** to a solid phase.

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The preparation of purines or their analogs constitutes an important target for medicinal chemists, as compounds of these classes can interact with many biological processes or modulate many physiological functions. Solid-phase synthesis is a relatively recent method to obtain libraries of biologically active compounds which belong to the same class but differ about various substituents. A number of preparative methods for purine library synthesis have been reported in the literature [2-6]. These methods utilized the intact purine nucleus and were based on the formation of a covalent bond between a resin and an appropriately substituted purine, followed by the introduction of various substituents on the purine ring, and finally, cleavage to the desired products. In another approach, the manipulation of the pyrimidine core on a solid phase and subsequent conversion to a purine nucleus was reported [7]. This technique utilized 4,6-dichloro-5-nitropyrimidine for linkage to the solid phase.

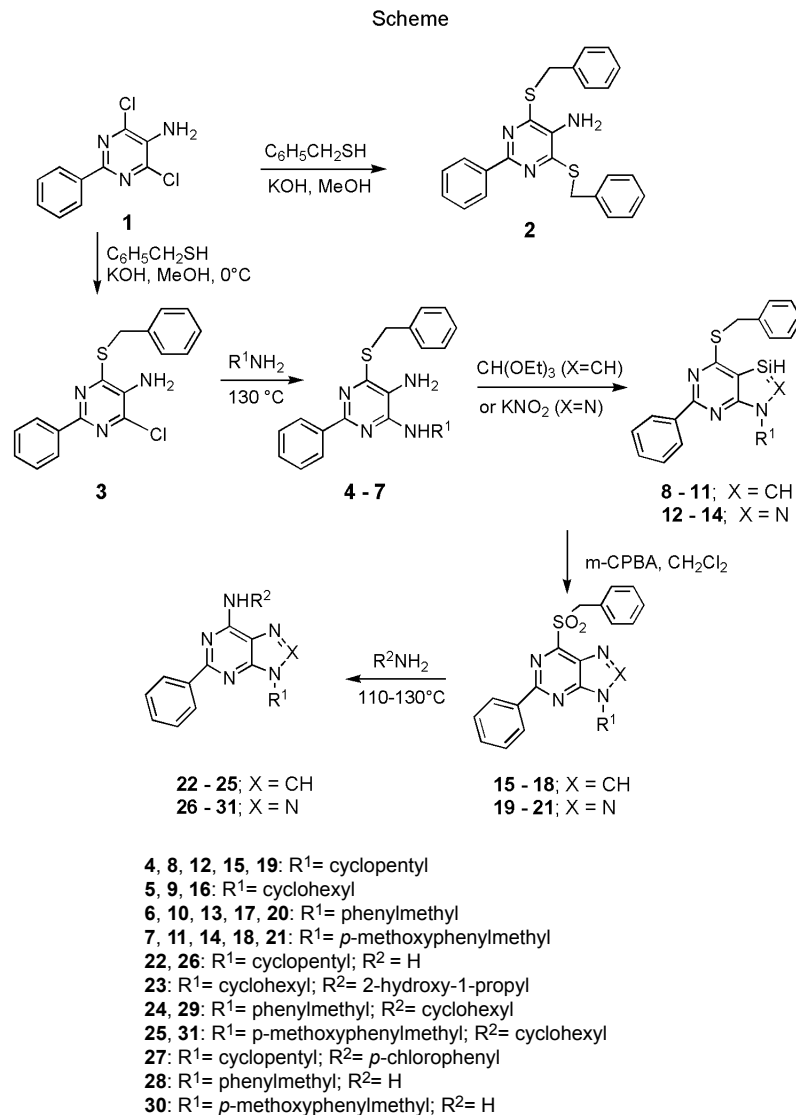
We wish to report the manipulation of a pyrimidine core, 5-amino-4,6-dichloro-2-phenylpyrimidine **1** [11] to N⁶,9-disubstituted-2-phenyladenines or 8-azaadenines. The conditions shown in the Scheme are compatible with the possible utilization of a thiomethyl resin [8] for covalent bonding to pyrimidine **1**. In our method, we used a phenylmethanesulphonyl group, later oxidized to a phenylmethanesulfonyl moiety for detachment, as a model for such a resin. In previous papers, we reported the positive effect of a phenyl group on C(2) of the adenine nucleus with regard to activity of such compounds as ADA enzyme inhibitors and/or A₁ receptor ligands [9-11].

The reaction of starting material **1** [12] with phenylmethanethiol, which would mimic the thiomethyl resin, deserves some comments. The reaction of **1** with phenyl-

methanethiol in the presence of methanolic KOH, at room temperature, yielded compound **2** in nearly pure form. When the reaction was carried out at 0 °C the monosubstituted derivative **3** was obtained in moderately good yield. In contrast, the analogous 2,4-dichloro-3-nitro-6-phenylpyrimidine, which is far more reactive than **1** toward nucleophilic aromatic substitution, [13] consistently afforded disubstituted products, even at low temperatures. Furthermore, 5-amino-4-chloro-2-phenyl-6-phenylmethanesulphonylpyrimidine **3** showed a relative high stability toward nucleophilic agents such as phenylmethylamine, *p*-methoxyphenylmethylamine, cyclopentylamine and cyclohexylamine, which required an elevated temperature of 130 °C in xylene to convert **3** to tetrasubstituted pyrimidines, **4-7**.

Compounds **4-7**, in turn, were transformed into the corresponding purines **8-11** in moderately good yield, by treatment with a mixture of acetic anhydride and triethyl orthoformate at 120 °C for 1.5 hour. Alternatively, treatment of the cyclohexylamine derivative **5**, with triethyl orthoformate in the presence of 37% hydrochloric acid afforded the corresponding purine **9** in good yield after 12 hours at room temperature. In comparison, the latter reaction at room temperature, though it required a longer time for cyclization, allowed a much easier isolation of the final product.

Some 9-substituted 8-azaanalogs of **8-11**, such as 9-cyclopentyl- (**12**) or 9-phenylmethyl- (**13**), or 9-*p*-methoxyphenylmethyl-2-phenyl-6-phenylmethanesulphonyl-8-azapurine (**14**), were prepared in moderately good yields by the dropwise addition of aqueous potassium nitrite to a solution of the corresponding 4,5-diaminopyrimidine in tetrahydrofuran and acetic acid at 0 °C.



Compounds **8-11** and 8-azaanalogs **12-14** were treated with *m*-chloroperoxybenzoic acid in dichloromethane, at room temperature, to obtain sulfones **15-18** and **19-21**, respectively, which exhibited a marked instability. Therefore they were converted as soon as prepared into the final compounds **22-25** and **26-31**. This conversion was accomplished by use of 33% aqueous ammonia in ethanol or an appropriate amine in a vial with a stopper at 110° C for 5-16 hours (Table 1). A similar reaction was described starting from a 6-phenylsulfanylpurine [3]. Methoxyethanol was used as solvent, in place of ethanol, when the 8-azaanalogs **19** and **21** reacted. Isolation of reaction products was realized by dilution of the reaction mixture with chloroform, washing of the organic layer with dilute hydrochloric acid and water followed by evaporation. Alternatively, simple acidification of the reaction mixture with dilute hydrochloric acid yielded the products.

The structures of all the new prepared compounds were assigned based on known reaction pathways and were confirmed by analytical and spectroscopic methods (ms and ¹H nmr, Table 2).

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra in Nujol mulls were recorded on a Mattson Genesis series FTIR spectrometer. ¹H nmr spectra were recorded on a Varian Gemini 200 spectrometer; chemical shifts are expressed in ppm (δ) from TMS as an internal standard; the compounds were dissolved in deuteriochloroform. Mass spectra were measured on a Hewlett-Packard GC/MS System 5988A. TLC was performed on precoated silica gel F₂₅₄ plates (Merck). Flash-column chromatography was performed using Merck Kieselgel 60 (230-400 mesh). Microanalyses (C H N) were carried out on a Carlo Erba elemental analyser (Model

Table 1
Chemical and Physical Properties of Compounds **2-14** and **22, 23, 25, 27, 30, 31**

Compound	Yield %	Cryst. solvent	M.p.(°C)	R _f [b]	Formula	Analyses C, H, N Calcd.% / Found%		
2	40	95% Ethanol	148-149	0.39[+]	C ₂₄ H ₂₁ N ₃ S ₂	69.36	5.09	10.11
						69.47	5.21	10.31
3	62	95% Ethanol	118-119	0.36[+]	C ₁₇ H ₁₄ ClN ₃ S	62.28	4.30	12.82
						62.36	4.33	12.93
4	66	2-Propanol	130	0.40 [#]	C ₂₂ H ₂₄ N ₄ S	70.18	6.42	14.88
						70.25	6.43	15.01
5	61	2-Propanol	128	0.40 [#]	C ₂₃ H ₂₆ N ₄ S	70.74	6.71	14.35
						70.41	6.69	14.44
6	77	2-Propanol	132	0.37[§]	C ₂₄ H ₂₂ N ₄ S	72.33	5.56	14.06
						72.40	5.77	14.36
7	50	Dichloromethane- 2-propanol	96	0.28[§]	C ₂₅ H ₂₄ N ₄ OS	70.07	5.64	13.07
						69.83	5.92	12.88
8	64	Absolute ethanol	122	0.20[§]	C ₂₃ H ₂₂ N ₄ S	71.47	5.74	14.50
						71.30	5.61	14.21
9	70	95% Ethanol	132-135	0.20[§]	C ₂₄ H ₂₄ N ₄ S	71.97	6.04	13.99
						71.81	6.34	13.61
10	72	Absolute ethanol	125	0.39[§]	C ₂₅ H ₂₀ N ₄ S	73.50	4.93	13.71
						73.86	4.68	13.91
11	37	Absolute ethanol	148	0.20[§]	C ₂₆ H ₂₂ N ₄ OS	71.21	5.06	12.78
						71.20	5.02	12.59
12	70	2-Propanol	138	0.37[+]	C ₂₂ H ₂₁ N ₅ S	68.19	5.46	18.07
						67.92	5.11	17.79
13	71	2-Propanol	123	0.40[+]	C ₂₄ H ₁₉ N ₅ S	70.39	4.68	17.10
						70.25	4.44	17.06
14	56	Dichloromethane- 2-propanol	100	0.38[§]	C ₂₅ H ₂₁ N ₅ OS	68.32	4.82	15.93
						68.07	4.58	15.85
22	63	95% Ethanol	162-165	0.30[°]	C ₁₆ H ₁₇ N ₅	68.79	6.13	25.07
						68.88	6.18	25.32
23	60	95% Ethanol	190	0.39[°]	C ₂₀ H ₂₅ N ₅ O	68.35	7.17	19.93
						68.24	7.12	19.60
25	45	95% Ethanol	132-135	0.36[⊥]	C ₂₀ H ₂₅ N ₅ O	72.61	6.58	16.94
						72.32	6.44	17.06
27	80	95% Ethanol	225	0.32[†]	C ₂₁ H ₁₉ ClN ₆	64.53	4.90	21.50
						64.85	5.17	21.74
30	73	95% Ethanol	145	0.30[⊥]	C ₁₈ H ₁₆ N ₆ O	65.05	4.85	25.29
						64.98	4.73	25.05
31	60	2-Propanol	170	0.30[§]	C ₂₄ H ₂₆ N ₆ O	69.54	6.32	20.27
						69.80	6.40	20.33

Eluents: [+] petroleum ether-chloroform 3:2; [#] petroleum ether-chloroform 4:1; [§] dichloromethane; [†] petroleum ether-dichloromethane 1:2; [°] dichloromethane-methanol 9.5:0.5; [⊥] chloroform-methanol 9.8:0.2.

1106) and were within $\pm 0.4\%$ of the theoretical values. Petroleum-ether corresponds to fraction boiling at 40-60 °C.

4,6-Bis(phenylmethanesulphonyl)-2-phenylpyrimidine-5-ylamine (**2**).

To a solution of 5-amino-4,6-dichloro-2-phenylpyrimidine **1** (1.25 g, 5.2 mmoles) and phenylmethanethiol (0.6 mL) in methanol (4 mL), a solution of potassium hydroxide (0.3 g, 5.8 mmoles) in methanol (10 mL) was added dropwise. The resulting mixture was stirred for 1 hour at room temperature. Then water (2-3 mL) was added to give a pink precipitate that was collected by filtration and dissolved in dichloromethane. This solution was washed with water, filtered and evaporated to dryness to give compound **2**, which was crystallized. Experimental and analyti-

cal data are reported in Tables 1 and 2.

5-Amino-4-chloro-2-phenyl-6-phenylmethanesulphonylpyrimidine (**3**).

To a solution of 5-amino-4,6-dichloro-2-phenylpyrimidine **1** (1.25 g, 5.2 mmoles) in methanol (4 mL) and phenylmethanethiol (0.6 mL), cooled in an ice-bath, a solution of potassium hydroxide (0.3 g, 5.8 mmoles) in methanol (10 mL) was added dropwise. The resulting mixture was stirred for 1 hour at 0 °C and for another 1 hour at room temperature. Then water (2-3 mL) was added to give a pink precipitate that was collected by filtration and dissolved in dichloromethane. This solution was washed with water, filtered and evaporated to dryness to give pure **3**. Experimental and analytical data are reported in Tables 1 and 2.

Table 2

Mass and ^1H nmr Spectra of Compounds **2-14** and **22, 23, 25, 27, 30, 31**

Compound	Mass m/z		^1H nmr (δ , ppm)
	M^+ (%)	Base	
2	415(1.5)	91	8.45 (m, 2H, arom); 7.48-7.27 (m, 13H, arom); 4.69 (s, 4H, benz CH_2); 3.67 (s, 2H, exch)
3	327(5)	91	8.37 (m, 2H, arom); 7.45 (m, 5H, arom); 7.39 (m, 3H, arom); 4.70 (s, 2H, benz CH_2); 4.11 (s, 2H, exch)
4	376(4)	91	8.45 (m, 2H, arom); 7.43-7.25 (m, 8H, arom); 4.80 (d, 1H, exch); 4.63 (s, 2H, benz CH_2); 4.51 (m, 1H, aliph); 2.95 (br s, 2H, exch); 2.24 (m, 2H, aliph); 1.92-1.24 (m, 6H, aliph)
5	390(22)	91	8.43 (m, 2H, arom); 7.44 (m, 5H, arom); 7.27 (m, 3H, arom); 4.71 (d, 1H, exch); 4.63 (s, 2H, benz CH_2); 4.15 (m, 1H, aliph); 2.93 (br s, 2H, exch); 2.14 (m, 2H, aliph); 1.92-1.20 (m, 8H, aliph)
6	398(8)	91	8.46 (m, 2H, arom); 7.44-7.25 (m, 13H, arom); 5.17 (br t, 1H, exch); 4.83 (d, 2H, benz CH_2); 4.65 (s, 2H, benz CH_2); 2.95 (br s, 2H, exch)
7	428(2)	121	9.85 (br t, 1H, exch); 8.03 (m, 2H, arom); 7.42-7.18 (m, 10H, arom); 6.74 (d, 2H, arom); 5.80 (br s, 2H, exch); 4.75 (d, 2H, benz CH_2); 4.65 (s, 2H, benz CH_2); 3.69 (s, 3H, aliph)
8	386(30)	91	8.57 (m, 2H, arom); 7.98 (s, 1H, arom); 7.51 (m, 5H, arom); 7.32 (m, 4H, 3 arom + 1 exch); 5.04 (m, 1H, aliph); 4.80 (s, 2H, benz CH_2); 2.34 (m, 2H, aliph); 2.16-1.81 (m, 6H, aliph)
9	400(48)	91	8.58 (m, 2H, arom); 8.03 (s, 1H, arom); 7.49 (m, 6H, 5 arom + 1 exch); 7.31 (m, 3H, arom); 4.81 (s, 2H, benz CH_2); 4.58 (m, 1H, aliph); 2.23 (m, 2H, aliph); 2.01-1.54 (m, 8H, aliph)
10	408(11)	91	8.58 (m, 2H, arom); 7.92 (s, 1H, arom); 7.50 (m, 8H, arom); 7.35 (m, 5H, arom); 5.48 (m, 2H, benz CH_2); 4.81 (s, 2H, benz CH_2)
11	438(2)	121	8.57 (m, 2H, arom); 7.89 (s, 1H, arom); 7.50 (m, 8H, arom); 7.35 (d, 2H, arom); 6.89 (d, 2H, arom); 5.41 (s, 2H, benz CH_2); 4.81 (s, 2H, benz CH_2); 3.80 (s, 3H, aliph)
12	387(29)	91	8.58 (m, 2H, arom); 7.53 (m, 5H, arom); 7.29 (m, 3H, arom); 5.43 (m, 1H, aliph); 4.84 (s, 2H, benz CH_2); 2.34 (m, 4H, aliph); 2.10 (m, 2H, aliph); 1.84 (m, 2H, aliph)
13	409(9)	91	8.60 (m, 2H, arom); 7.53 (m, 8H, arom); 7.33 (m, 5H, arom); 5.88 (s, 2H, benz CH_2); 4.84 (s, 2H, benz CH_2)
14	439(1)	121	8.60 (m, 2H, arom); 7.53 (m, 8H, arom); 7.31 (d, 2H, arom); 6.87 (d, 2H, arom); 5.88 (s, 2H, benz CH_2); 4.81 (s, 2H, benz CH_2); 3.77 (s, 3H, aliph)
23	351(7)	225	8.43 (m, 2H, arom); 8.02 (s, 1H, arom); 7.48 (m, 3H, arom); 4.55 (m, 1H, aliph); 4.17 (m, 1H, aliph), 3.91 (m, 1H, aliph); 3.70 (m, 1H, aliph); 2.23-1.32 (m, 13H aliph, + 2H, exch)
25	413(14)	91	8.50 (m, 2H, arom); 7.68 (s, 1H, arom); 7.45 (m, 3H, arom); 7.33 (d, 2H, arom); 6.88 (d, 2H, arom); 5.68 (br s, 1H, exch); 5.36 (s, 2H, benz CH_2); 4.34 (m, 1H, aliph); 3.80 (s, 3H, aliph); 2.18-1.25 (m, 10H, aliph)
27	390(21)	41	8.51 (m, 2H, arom); 8.28 (br s, 1H, exch); 7.93 (d, 2H, arom); 7.51 (m, 3H, arom); 7.45 (d, 2H, arom); 5.42 (m, 1H, aliph); 2.28-1.80 (m, 8H, aliph)
30	332(6)	121	8.51 (m, 2H, arom); 7.52 (m, 5H, arom); 6.88 (d, 2H, arom); 5.77 (s, 2H, benz CH_2); 3.79 (s, 3H, aliph); 2.13 (br s, 2H, exch)
31	414(3)	121	8.51 (br s, 1H, exch); 8.10 (m, 2H, arom); 7.63 (m, 2H, arom) 7.49 (m, 3H, arom); 6.88 (m, 2H, arom); 5.73 (s, 2H, benz CH_2); 4.42 (q, 1H, aliph); 2.28-1.80 (m, 8H, aliph)

N^4 -Cycloalkyl-2-phenylpyrimidine-6-phenylmethanesulfanyl-4,5-diamines (**4,5**).

A mixture of **3** (0.40 g, 1.22 mmole), xylene (1 mL) and the appropriate amine (2.23 mmoles) was stirred at reflux temperature for 16 hours. The resulting solution was evaporated and the residue was dissolved in chloroform and washed successively with 10% hydrochloric acid and water. After evaporation of the organic layer, the residue was crystallized to yield the title compound. Experimental and analytical data are reported in Tables 1 and 2.

N^4 -Alkyl-2-phenylpyrimidine 6-phenylmethanesulfanyl-4,5-diamines (**6,7**).

A mixture of **3** (0.20 g, 0.61 mmole), xylene (1 mL) and the appropriate amines (2.11 mmoles) was stirred at reflux temperature for 4 hours. The resulting solution was evaporated and the residue was dissolved in chloroform and washed successively with 10% hydrochloric acid and water. After evaporation of the organic layer, the residue was crystallized. Experimental and analytical data are reported in Tables 1 and 2.

9-Alkyl(cycloalkyl)-2-phenyl-6-phenylmethanesulphanylpurines (**8,10,11**).

A mixture of acetic anhydride (0.86 g, 8.4 mmoles), triethyl orthoformate (1.25 g, 8.4 mmoles) and **4** (or **6** or **7**) (0.84 mmole) was stirred at reflux for 1.5 hour. The resulting solution was evaporated to dryness and the residue crystallized. Experimental and analytical data are reported in Tables 1 and 2.

9-Cyclohexyl-2-phenyl-6-phenylmethanesulphanylpurines (**9**).

A mixture of **5** (0.20 g, 0.47 mmole), triethyl orthoformate (0.70 g, 4.7 mmoles) and 12 *N* hydrochloric acid (0.14 mL) was stirred at room temperature overnight. The precipitate obtained was collected by filtration and crystallized. Experimental and analytical data are reported in Tables 1 and 2.

9-Alkyl(cycloalkyl)-2-phenyl-6-phenylmethanesulphanyl-8-azapurines (**12-14**).

To an iced mixture of **4** (or **6** or **7**) (0.28 mmole), acetic acid (0.4 mL), water (0.9 mL) and tetrahydrofuran (3.2 mL) an iced solution of potassium nitrite (0.3 mmole) in water was added dropwise. The mixture was stirred for 3 hours and the precipitate formed was collected by filtration, washed with water, and dried to give compounds **12**, **13** and **14** respectively. Experimental and analytical data are reported in Tables 1 and 2.

General Procedure for 9-Alkyl(cycloalkyl)-2-phenyl-6-phenylmethanesulphonyl purines (**15-18**) or 8-Azapurines (**19-21**).

A mixture of the appropriate 9-alkyl(cycloalkyl)-2-phenyl-6-phenylmethanesulphonyl purine (**8, 9, 10** or **11**) or 8-azapurine (**12, 13, or 14**) (0.25 mmole), *m*-chloroperoxybenzoic acid (0.55 mmole) and dichloromethane (2.2 mL) was stirred at room temperature overnight. The reaction mixture was treated with 5% aqueous sodium bicarbonate and extracted with dichloromethane. The organic phase was evaporated to dryness at room temperature to yield a solid residue which was used without purification as soon as possible for the next reaction.

9-Cyclopentyl-2-phenyladenine (**22**) [14].

A mixture of **15** (0.15 g, 0.36 mmole), 35% aqueous ammonia (0.7 mL) and ethanol (2 mL) was stirred at 110 °C in a Pyrex vial with stopper in place for 6 hours. The resulting mixture was diluted with chloroform and washed successively with 10% hydrochloric acid and water. The organic phase was evaporated to obtain an oil that crystallized from ethanol. The melting point and nmr data of **22** are consistent with the literature data [14].

9-Cyclohexyl-N⁶-(2-hydroxy-1-propyl)-2-phenyladenine (**23**).

A mixture of 9-cyclohexyl-2-phenyl-6-phenylmethanesulphonyl purine (**16**) (0.2 mmole) and 1-amino-2-propanol (0.4 mL) was stirred at 110 °C in a Pyrex vial with stopper in place for 5 hours. The resulting mixture was worked up as described for the previous reaction. Experimental and analytical data are reported in Tables 1 and 2.

N⁶-Cyclohexyl-2-phenyl-9-phenylmethyladenine (**24**) [15].

A mixture of 2-phenyl-9-phenylmethyl-6-phenylmethanesulphonyl purine (**17**) (0.2 mmole) and cyclohexylamine (0.4 mL) was stirred at 110 °C in a Pyrex vial with stopper in place for 8 hours. The resulting mixture was worked up as described for the previous reaction. The melting point and nmr data of **24** are consistent with the literature data [15].

N⁶-Cyclohexyl-9-(4-methoxyphenylmethyl)-2-phenyladenine (**25**).

A mixture of 9-(4-methoxyphenylmethyl)-2-phenyl-6-phenylmethanesulphonyl purine (**18**) (0.2 mmole) and cyclohexylamine (0.4 mL) was stirred at 110 °C in a Pyrex vial with stopper in place for 5 hours. The resulting mixture was worked up as described for the previous reaction. Experimental and analytical data are reported in Tables 1 and 2.

9-Cyclohexyl-2-phenyl-8-azapurine (**26**) [14].

A mixture of 9-cyclohexyl-2-phenyl-6-phenylmethanesulphonyl-8-azapurine (**19**) (0.2 mmole), 35% aqueous ammonia (0.4 mL) and ethanol (1 mL) was stirred at 110 °C in a Pyrex vial with stopper in place for 6 hours. The reaction mixture was treated with 10% hydrochloric acid and the precipitate formed was collected by filtration, washed with water and dried to give compound **26** which was crystallized. The melting point and nmr data of **26** are consistent with the literature data [14].

N⁶-(4-Chlorophenyl)-9-cyclohexyl-2-phenyl-8-azapurine (**27**).

A mixture of 9-cyclohexyl-2-phenyl-6-phenylmethanesulphonyl-8-azapurine (**19**) (0.2 mmole), 4-chloroaniline (80 mg, 0.63 mmole) and 2-methoxyethanol (0.5 mL) was stirred at 110 °C in a Pyrex vial with stopper in place for 6 hours. The reaction mixture

was worked up as described for the previous reaction. Experimental and analytical data are reported in Tables 1 and 2.

9-Phenylmethyl-2-phenyl-8-azapurine (**28**) [10].

A mixture of 2-phenyl-9-phenylmethyl-6-phenylmethanesulphonyl-8-azapurine (**20**) (0.2 mmole), 35% aqueous ammonia (0.4 mL) and ethanol (1 mL) was stirred at 110 °C in a Pyrex vial with stopper in place for 6 hours. The reaction mixture was worked up as described for the previous reaction. The melting point and nmr data of **28** are consistent with the literature data [10].

N⁶-Cyclohexyl-2-phenyl-9-phenylmethyl-8-azapurine (**29**) [16].

A mixture of **20** (0.2 mmole) and cyclohexylamine (0.4 mL) was stirred at 110 °C in a Pyrex vial with stopper in place for 6 hours. The reaction mixture was worked up as described for the previous reaction. The melting point and nmr data of **29** are consistent with the literature data [16].

9-(4-Methoxyphenylmethyl)-2-phenyl-8-azaadenine (**30**).

A mixture of **21** (0.2 mmole), 35% aqueous ammonia (0.4 mL) and 2-methoxyethanol (0.5 mL) was stirred at 110 °C in a Pyrex vial with stopper in place for 6 hours. The reaction mixture was worked up as described for the previous reaction. Experimental and analytical data are reported in Tables 1 and 2.

N⁶-Cyclohexyl-9-(4-methoxyphenylmethyl)-2-phenyl-8-azaadenine (**31**).

A mixture of **21** (0.2 mmole) and cyclohexylamine (0.4 mL) was stirred at 110 °C in a Pyrex vial with stopper in place for 6 hours. The reaction mixture was worked up as described for the previous reaction. Experimental and analytical data are reported in Tables 1 and 2.

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