New C(2)-Substituted 8-Alkylsulfanyl-9-phenylmethyl-hypoxanthines III

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Title compounds were obtained starting from the key imidazole intermediate, 5-amino-1-phenylmethyl-2-mercapto-1*H*-imidazole-4-carboxylic acid amide **5**, readily derived from the base catalyzed rearrangement of a thiazole, 5-amino-2-phenylmethylaminothiazole-4-carboxylic acid amide **4**. Alkylation of the thiol function on **5** with phenylmethyl and allylic chlorides gave compounds **6** and **7** respectively. Cyclization of **6** with a variety of esters afforded 8-phenylmethylthiohypoxanthines, **8**-**11**. Similarly, **7** was cyclized to 8-allylthiohypoxanthines, **20**-**21**. Compound **5** was also cyclized, but formed 8-mercaptohypoxanthines, **22**-**24**. Alkylation of 8-mercaptohypoxanthines afforded 8-alkylthiohypoxanthines, **8**, **9**, **25** and **26** (see Scheme 2). Chlorination of **9**-**11** afforded **16**-**18**; adenine **19** was derived from **16**. Oxidation of hypoxanthines **8**-**11** with *m*-chloroperbenzoic acid gave the corresponding 8-phenylmethylsulfonyl derivatives **12**–**15**. These derivatives proved resistant to nucleophilic displacement reactions with primary amines.

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In previous papers in this series [1,2], we reported the preparation of polysubstituted purine derivatives with a phenylmethylsulfanyl group attached to the 2 or the 6 position. The sulfides were synthesised as potential precursors to the corresponding 2-amino and 6-aminopolysubstituted purines after their oxidation to sulfones. In this paper, a logical extension to our earlier studies, we wish to report a synthetic route to 8-alkylsulfanylpolysubstituted purines **A** as depicted in Figure 1.

A literature survey reveals few examples of known structures as depicted in Figure 1. Only 2,9-dimethyl-8-methylsulfanyl-1,9-dihydropurine-6-one, **B** [3], 6-(dimethylamino)-9-(4-methylphenylmethyl)-8-methylthio-2-(trifluoromethyl)-9*H*-purine **C** [4] and 8-(phenylmethylthio)-6-dimethylamino-9-(4-methylphenylmethyl)-2-(trifluoromethyl)-9*H*-purine **D** [4] are known. Other tetrasubstituted purines are known but they have the 2-alkylthio group at the 2 position, not the 8 position [2 and references cited therein].

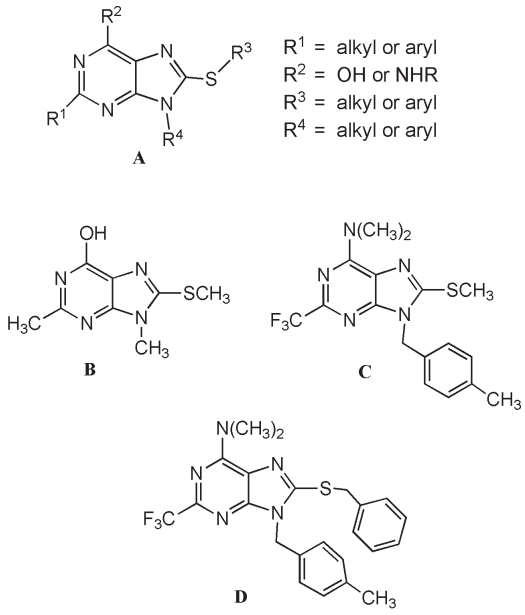


Figure 1. Tetrasubstituted purines

We have devised a synthetic pathway to produce new 8-alkylthiopurines with additional substituents in the 2, 6, and 9-positions. The various substituents at these sites are intended to explore possible interactions with a diverse array of purinoreceptors.

Inspection of the retrosynthetic pathway displayed in Figure 2, clearly indicates that an imidazole derivative with a thiol function in the 2-position **H**, would be an ideal starting point for the synthesis of polysubstituted purines **E** having a thioether at the 8-position.

Further, imidazoles **G** or **H** could be annulated to **F** (R_3=H or alkyl) trying the Yamazaki reaction conditions

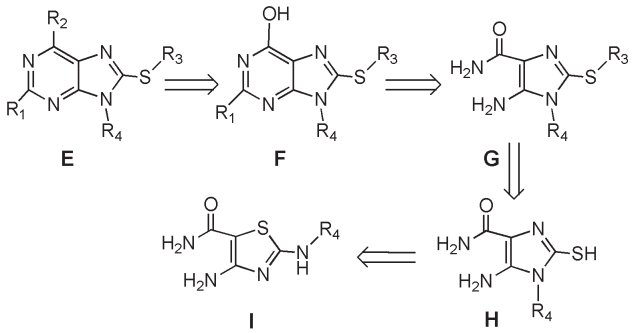
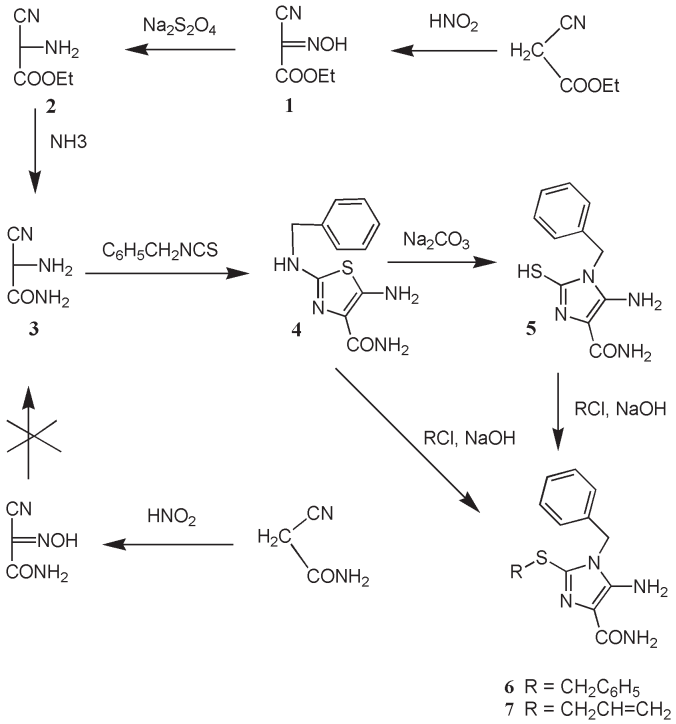


Figure 2. Retrosynthetic pathway for synthesis of the purines E.

[5] which, to date, have never been applied to the synthesis of compounds **F**.

The base catalyzed rearrangement of suitably substituted thiazoles to imidazoles was described by Cook *et al*. [6] and Sen *et al.* [7]. Cook *at al*. reported that 5-amino-2-methylamino or 2-allylamino-thiazole-4-carboxamide **I** (R_4=CH_3, or CH_2=$CHCH_2$), prepared from 2-amino-2-cyanoacetamide and methyl or allyl isothiocyanato, can be transposed to 1-methyl or 1-allyl-5-amino-2-thioxo-2,3-dihydro-1*H*-imidazole-4-carboxamide **H** (R_4= CH_3 or CH_2=$CHCH_2$) [6]. Sen *et al*., instead, described the condensation of 2-amino-2-cyanoacetamide with 3-diethylamino-propyl-1-isothiocyanate to the corresponding 2-thioxoimidazol **H** (R=$(CH_3)_2N(CH_2)_2CH_3$) [7]. To expand the scope of the base-catalyzed rearrangement, we placed the thiazole **4**, a phenylmethyl analog of **I** in an alkaline environment, which permitted the realization of the phenylmethyl derivative of the imidazole **5** [7] (Scheme 1). The latter, on reaction with phenylmethyl and allyl halides formed **6** and **7** respectively. Thiazole **4** was prepared starting from ethyl cyanoacetate which was nitrosated in a solution whose pH was controlled, to obtain the hydroxyimino derivative **1** (Aldrich Chem. Co.). Reduction of the oxime to the primary amine **2** was carried out with sodium hydrosulfite in a saturated solution of sodium bicarbonate [8]. Compound **2** proved unstable and was used immediately on preparation. So, to an ethereal solution of **2**, cooled to -18 °C in a steel vial, ammonia dissolved in ethanol was added. Under these conditions, the amide **3** [8] was obtained in good yield. In contrast, we attempted to obtain **3** in a more direct approach involving only two steps. 2-Cyanoacetamide was nitrosated using identical conditions employed for the nitrosation of ethyl cyanoacetate [9]. But subsequent reductions with sodium hydrosulfite, or freshly prepared aluminum amalgam, or hydrogenation at 3 atm with Raney nickel [9] did not give a satisfactory yield of **3**. The reaction of **3** with phenylmethylisothiocyanate gave the *N*-phenylmethylthiazole derivative **4** [7]. This product was initially insoluble in 5% sodium carbonate solution, but after heating for a brief time, was converted to a soluble product **5** *via* rearrangement, which was isolated upon neutralization with hydrochloric acid. We also discovered that the thiazole **4** can be converted directly to compounds **6** and **7**, without isolation of the intermediate thiol **5**, by addition of sodium hydroxide and the appropriate alkylating agent to the reaction mixture (Scheme 1).

Scheme 1

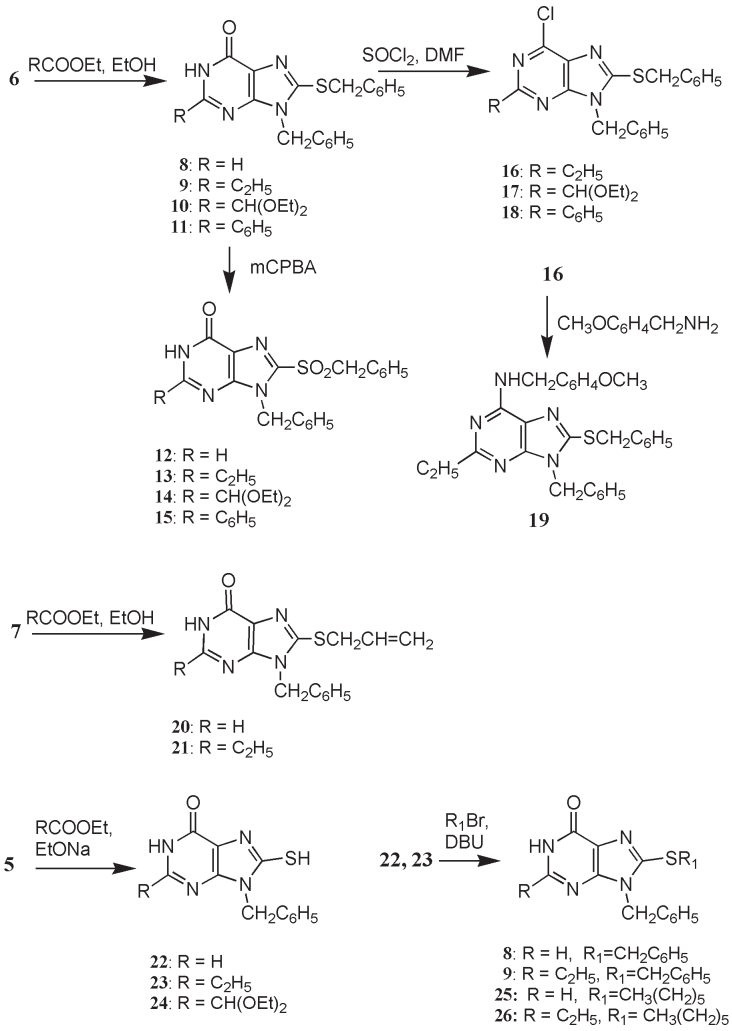


Cyclization of compounds **6** and **7** (Scheme 2) to form the purine nucleus was performed according to the Yamazaki procedure [5] by use of sodium ethoxide and a variety of esters. The base catalysis activated the amino group in the 5-amino-1-benzyl-2-thioxo-2,3-dihydro-1*H*-imidazole-4-carboxamide that reacted with the carbonyl group of the ester which looses ethoxide ion. Subsequently intramolecular cyclization occured between the 4-carboxamide group and the acylamino group formed with elimination of water. All these reactions produced 8-alkylthiopolysubstituted hypoxanthines, **8**-**11** and **20**, **21**. Chlorination of **9**-**11** afforded **16**-**18**; these compounds are instable and soon decomposed; from **16**, the adenine **19** was derived by immediate treatment with *p*-methoxyphenylmethylamine. Oxidation of hypoxanthines **8**-**11** with *m*-chloroperbenzoic acid gave the corresponding 8-phenylmethylsulfonyl derivatives **12**-**15**. These derivatives proved resistant to nucleophilic displacement reactions with primary amines.

Compound **5** was annulated with sodium ethoxide and various esters to form 8-mercaptopolysubstituted hypoxanthines, **22**-**24**. The alkylation of **22** and **23** on the HS-C(8) function formed 8-alkylthiopolysubstituted hypoxanthines **8** and **9** or **25** and **26**; benzyl bromide to **8** and **9** or hexyl bromide to **25** and **26** in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were used.

Chemical structures of the intermediates and final compounds were assigned on the basis of the well known mechanism of the reactions carried out and were confirmed by their ms, ir, ^{1}H and ^{13}C nmr spectra which were

Scheme 2



consistent with the proposed structures. ^{13}C nmr spectra of the compounds **8-15** and **19-26** evidenced in the 165-118 δ region the five signals attributable to purine nucleus carbon atoms and the signals attributable to phenyl carbons; the signals between 99 and 11 δ are due to other carbon atoms as specified in Table 3. Infrared spectra (Table) of same compounds showed a carbonyl absorption in the 1676-1699 cm^{-1} region, typical of hypoxanthine derivatives. Molecular mass of compounds **5-7** were confirmed by their ms spectra. Finally, ^{1}H nmr spectra of all synthesized compounds (**5-26**) were consistent with the structure assigned.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected; ir spectra in Nujol mulls were recorded on a ATI Mattson Genesis Series FTIR spectrometer. ^{1}H and ^{13}C nmr spectra were recorded on a Varian Gemini 200 spectrometer; chemical shifts are expressed in δ units from TMS as an internal standard; solvents employed are specified in the Table 2 and 3. Mass spectra were performed with a Hewlett Packard GC/MS System 5988A. TLC was performed on precoated silica gel F_{254} plates (Merck). Microanalyses (C H N) were carried out on a Carlo Erba elemental analyser (Model 1106) and were within ±0.4% of the theoretical values.

5-Amino-2-mercapto-1-phenylmethyl-1*H*-imidazole-4-carboxylic Acid Amide (**5**).

The product was prepared as described in the literature [5] for the alkaline catalyzed rearrangement of the thiazole ring to an imidazole nucleus. A 10% solution of sodium carbonate (300 mL) was added to 5-amino-2-phenylmethylamino-thiazole-4-carboxylic acid amide (**4**) (10.4 g, 0.042 mole) and the mixture was stirred under reflux until complete dissolution of the starting product (about 30 minutes). After cooling, the solution was neutralized with hydrochloric acid. The solid precipitated was collected by filtration: yield 70%, m.p. 240 °C (lett.242-243°C). See Table 2 for nmr and ms data.

Table 1
Chemical and physical properties of the compounds **6**-**26**.

Compound	Yield %	Cryst. solvent	M.p.(°C)	R_f	Formula	Analyses C, H, N Calc. % / Found %
6	60/70[a]	90% Ethanol	150	0.30[§]	$C_{18}H_{18}N_4OS$	63.88 5.36 16.56
						63.86 5.13 16.28
7	65/75[b]	Ethanol	115	0.11[§]	$C_{14}H_{16}N_4OS$	58.31 5.59 19.43
						58.18 5.55 19.20
8	65/50[c]	Ethanol	214-216	0.30[§]	$C_{19}H_{16}N_4OS$	65.50 4.63 16.08
						65.21 4.58 15.86
9	89/70[d]	Ethanol	207-209	0.15[§]	$C_{21}H_{20}N_4OS$	67.00 5.35 14.88
						66.83 5.14 14.68
10	60	Ethanol	167	0.46[§]	$C_{24}H_{26}N_4O_3S$	63.98 5.82 12.44
						63.70 5.76 12.17
11	52	Ethanol	243	0.40[§]	$C_{25}H_{20}N_4OS$	70.73 4.75 13.20
						70.59 4.65 13.04
12	65	Isopropanol	198-200	0.14[§]	$C_{19}H_{16}N_4O_3S$	59.99 4.24 14.73
						60.14 4.48 14.89
13	70	Isopropanol	132-135	0.20[§]	$C_{21}H_{20}N_4O_3S$	61.75 4.94 13.72
						61.51 4.67 13.44
14	65	Isopropanol	150	0.30[§]	$C_{24}H_{26}N_4O_5S$	59.74 5.43 11.61
						59.91 5.66 11.72
15	60	Isopropanol	260	0.40[§]	$C_{25}H_{20}N_4O_3S$	65.77 4.42 12.27
						65.48 4.33 12.14
16	50	Ethanol	106-108	0.43[§]	$C_{21}H_{19}ClN_4S$	63.87 4.85 14.19
						63.98 4.95 14.23
17	54	Ethanol	150	0.50[†]	$C_{24}H_{25}ClN_4O_2S$	61.46 5.37 11.95
						61.63 5.54 11.80
18	52	Ethanol	175	0.77[†]	$C_{25}H_{19}ClN_4S$	67.79 4.32 12.65
						67.84 4.41 12.52
19	95	Ethanol	103-105	0.69[§]	$C_{29}H_{29}N_5OS$	70.27 5.90 14.13
						70.40 5.99 14.21
20	58	Ethanol	237	0.13[§]	$C_{15}H_{14}N_4OS$	60.38 4.73 18.78
						60.13 4.59 18.72
21	62	Ethanol	200-201	0.10[§]	$C_{17}H_{18}N_4OS$	62.55 5.56 17.16
						62.28 5.50 17.08
22	70	Ethanol	313-315	0.17[§]	$C_{12}H_{10}N_4OS$	55.80 3.90 21.69
						55.62 3.86 21.45
23	68	Ethanol	335 (dec.)	0.11[§]	$C_{14}H_{14}N_4OS$	58.72 4.93 19.57
						58.54 4.66 19.40
24	65	Ethanol	215	0.13[§]	$C_{17}H_{20}N_4O_3S$	56.65 5.59 15.54
						56.37 5.50 15.28
25	45	Isopropanol	120	0.15[§]	$C_{18}H_{22}N_4OS$	63.13 6.48 16.36
						62.88 6.33 16.25
26	70	Isopropanol	165-167	0.16[§]	$C_{20}H_{26}N_4OS$	64.83 7.07 15.12
						64.55 6.85 15.01

[a] Yield 60% starting from **5**, yield 70% starting from **4**; [b] Yield 65% starting from **5**, yield 75% starting from **4**; [d] Yield 89% starting from **7**, yield 70% starting from **23**; [§] eluent: chloroform-methanol 10:0.5; [†] eluent: chloroform.

5-Amino-1-phenylmethyl-2-substitutedsulfanyl-1*H*-imidazole-4-carboxylic Acid Amides **6** and **7**.

Method A.

The appropriate chloride, phenylmethyl or allyl, (0.034 mole) was added to a solution of 5-amino-1-phenylmethyl-2-mercapto-1*H*-imidazole-4-carboxylic acid amide **5** (2.9 g, 0.017 mole) in 1 *N* sodium hydroxide (12 mL). The reaction mixture was stirred at room temperature for 1 hour. The solid obtained (compound **6** or **7**) was filtered and washed with water and ethyl ether, then crystallized. See Table 1 for yields, crystallization solvent, physicochemical properties and elemental analysis; see Table 2 for nmr and ms data.

Method B.

5-Amino-2-phenylmethylamino-thiazole-4-carboxylic acid amide (**4**) (10.4 g, 0.042 mole) was added to a solution of 1 *N* sodium hydroxide (300 ml) and the mixture heated at 80 °C until a clear solution was obtained. After cooling, phenylmethyl or allyl chloride (0.084 mole) was added and the mixture stirred for 1 h at room temperature. The solid obtained was (compound **6** or **7**) was collected by filtration and washed with water and ethyl ether, then crystallized. See Table 1 for yields, crystallization solvent, physicochemical properties and elemental analysis; see Table 2 for nmr and ms data.

9-Phenylmethyl-8-substitutedsulfanyl-1,9-dihydropurin-6-one **(8**, **20)** and 9-Phenylmethyl-2-substituted-8-substitutedsulfanyl-1,9-dihydropurin-6-one **(9**-**11**, **21)**.

5-Amino-1-phenylmethyl-2-substitutedsulfanyl-1*H*-imidazole-4-carboxylic acid amide (**6**) or (**7**) (1.47 mmoles) was added to a solution prepared from sodium (0.23 g, 0.01 mole) dissolved in 8.5 mL of absolute ethanol. The mixture was refluxed with stirring for 1 hour. Then a solution of the appropriate ester (7.5 mmoles) in 5 mL of ethanol was added dropwise and the solution was stirred under reflux for 48 hours. After cooling, ice was

Table 2
Spectroscopic data of the compounds **5**-**26**.

Compound (solvent)	ms (m/z, %)	ir cm^{-1} (C=O)	^{1}H nmr (, ppm) aromatic H	benzylic H	aliphatic H	exch. H
5 (DMSO-d_6)	248 (M^+, 10)		7.30 (m, 5H + 2H exch)	5.23 (s, 2H)		6.12 (br s, 1H) 6.90 (br s, 2H) 7.30 (br s, 2H)
6 ($CDCl_3$)	338 (M^+, 5.7)		6.94 (m, 2H) 7.12 (m, 2H) 7.28 (m, 6H)	4.09 (s, 2H, S-*CH_2*) 4.72 (s, 2H, N-*CH_2*+ 2H exch)		5.10 (br s, 1H) 6.70 (br s, 1H)
7 ($CDCl_3$)	288 (M^+, 7)		7.14 (m, 2H) 7.36 (m, 3H)	5.14 (s, 2H, N-*CH_2* + 2H exch)	5.05 (d, 2H, S*CH_2* J= 9.4 Hz) 5.85 (m, 1H, *CH*=CH_2) 3.51 (d, 2H, CH=*CH_2*, J= 7.4Hz)	4.79 (br s, 2H)
8 ($CDCl_3$)		1683	7.28 (m, 10H) 8.04 (s, 1H)	4.62 (s, 2H, S-*CH_2*) 5.24 (s, 2H, N-*CH_2*)		12.96 (br s, 1H)
9 ($CDCl_3$)		1676	7.28 (m, 10H)	4.56 (s, 2H, S-*CH_2*) 5.21 (s, 2H, N-*CH_2*)	1.34 (t, 3H, CH_2*CH_3*, J=7.6 Hz) 2.32 (q, 2H, *CH_2*CH_3, J=7.6 Hz)	12.01 (br s, 1H)
10 ($CDCl_3$)		1683	7.29 (m, 10H)	4.60 (s, 2H, S-*CH_2*) 5.22 (s, 2H, N-*CH_2*)	1.27 (t, 6H, CH_2*CH_3*, J=7.0 Hz) 3.68 (m, 4H, O-*CH_2*CH_3) 5.37 (s, 1H, *CH*O$(Et)_2$)	9.72 (br s, 1H)
11 ($CDCl_3$)		1678	7.31 (m, 10H) 7.58 (m, 3H) 8.12 (m, 2H)	4.60 (s, 2H, S-*CH_2*) 5.29 (s, 2H, N-*CH_2*)		10.85 (br s, 1H)
12 ($CDCl_3$)		1684	7.28 (m, 10H+ H exch) 8.24 (s,1H)	4.76 (s, 2H, SO_2-*CH_2*) 5.49 (s, 2H, N-*CH_2*)		
13 ($CDCl_3$)		1685	7.32 (m, 10H)	4.70 (s,2H, SO_2-*CH_2*) 5.43 (s, 2H, N-*CH_2*)	1.41 (t, 3H, CH_2-*CH_3*, J=7.4 Hz) 2.92 (q, 2H, *CH_2*-CH_3, J=7.4 Hz)	12.24 (br s, 1H)
14 (DMSO-d_6)		1689	7.26 (m, 10H)	4.87 (s,2H,SO_2-*CH_2*) 5.30 (s, 2H, N-*CH_2*)	1.14 (t, 6H, CH_2-*CH_3*, J=6.8 Hz) 3.62 (m, 4H, *CH_2*-CH_3) 5.33 (s, 1H, C*H*$(OEt)_2$)	12.62 (br s, 1H)
15 (DMSO-d_6)		1698	8.12 (m, 2H) 7.54 (m, 3H) 7.25 (m, 10H)	4.87 (s,2H,SO_2-*CH_2*) 5.30 (s, 2H, N-*CH_2*)		12.75 (br s, 1H)
16 ($CDCl_3$)			7.30 (m, 10H)	4.66 (s, 2H, SO_2-*CH_2*) 5.30 (s, 2H, N-*CH_2*)	1.40 (t, 3H, CH_2-*CH_3*, J=7.6 Hz) 3.04 (q, 2H, *CH_2*-CH_3, J=7.6 Hz)	
17 (DMSO-d_6)			7.28 (m, 10H)	4.59 (s, 2H, S-*CH_2*) 5.22 (s, 2H, N-*CH_2*)	1.29 (t, 6H, CH_2*CH_3* , J=7.2 Hz) 3.68 (m, 4H, O-*CH_2*CH_3) 5.35 (s, 1H, *CH*O$(Et)_2$)	
18 ($CDCl_3$)			8.53 (m, 2H) 7.36 (m, 13H)	4.70 (s, 2H, S-*CH_2*) 5.38 (s, 2H, N-*CH_2*)		
19 (DMSO)		1693	7.13-7.34 (m, 12H) 6.85 (d, 2H)	5.17 (s, 2H, N-*CH_2*) 4.47 (s, 2H, S-*CH_2*) 3.31 (d, 2H, CH_2-NH)	1.22 (t, 3H, CH_2*CH_3*, J=7.6 Hz) 2.67 (q, 2H, *CH_2*CH_3, J=7.6 Hz) 3.70 (s, 3H, O*CH_3*)	8.05 (br s, 1H)
20 ($CDCl_3$)		1685	7.97 (s, 1H) 7.27 (m, 5H)	5.27(s, 2H, N-*CH_2*)	3.99 (d, 2H, CH=*CH_2*, J=7.2 Hz) 4.70 (d, 2H, S*CH_2*, J=5.6 Hz) 5.90 (m, 1H, *CH*=CH_2)	

added and then the mixture was neutralized with 50% acetic acid. The precipitate that formed was collected by filtration and crystallized. See Table 1 for yields, crystallization solvent, physicochemical properties and elemental analysis; see Table 2 and 3 for ir and nmr data.

9-Phenylmethyl-8-phenylmethanesulfonyl-1,9-dihydropurin-6-one **(12)** and 9-Phenylmethyl-2-substituted-8-phenylmethanesulfonyl-1,9-dihydropurin-6-one **(13-15)**.

A mixture of **8** (or **9** or **10** or **11**) (2.6 mmoles) and *meta*-chloroperoxybenzoic acid (5.2 mmoles) in dichloromethane (20 ml) was stirred at room temperature overnight. The reaction mixture was treated with 5% sodium bicarbonate and extracted with dichloromethane. The organic phase was evaporated *in vacuo* to obtain a white solid which was purified by crystallization. See Table 1 for yields, crystallization solvent, physicochemical properties and elemental analysis; see Table 2 and 3 for ir and nmr data.

6-Chloro-9-phenylmethyl-8-phenylmethylsulfanyl-2-substituted-1*H*-purine (**16-18**).

A mixture **9** (or **10** or **11**) (0.015 mole), chloroform (76 mL), *N*,*N*-dimethylformamide (2.9 mL) and thionyl chloride (13.2 mL) was heated slowly up to 70 °C, and then refluxed with stirring for 2 hours. The reaction mixture was evaporated *in vacuo* at a temperature maintained below 35 °C. The residue was triturated with ethyl ether, fliltered and crystallized from ethanol. See Table 1 for yields, crystallization solvent, physicochemical properties and elemental analysis; see Table 2 for nmr data.

(2-Ethyl-9-phenylmethyl-8-phenylmethylsulfanyl-1*H*-purin-6-yl)-(4-methoxy-phenylmethyl)-amine (**19**).

To a mixture consisting of 6-chloro-2-ethyl-9-phenylmethyl-8-phenylmethylsulfanyl-1*H*-purine (**16**) (0.60 g, 1.52 mmoles), *p*-methoxyphenylmethylamine (0.42 g, 3.04 mmoles), and absolute

Table 3

^{13}C nmr data (, ppm, DMSO-d_6) of the compounds **8**-**15** and **19**-**26**.

Compound	Purine and phenyl carbons	Others
8	155.3; 149.9; 146.3; 145.3; 136.8; 135.6; 128.7; 128.5; 128.3; 127.6; 127.3; 127.0; 123.9	45.8 (CH_2-N); 35.9 (CH_2-S)
9	159.2; 156.1; 150.4; 145.6; 137.0; 135.8; 128.9; 127.7; 127.4; 127.3; 118.3	45.7 (CH_2-N); 35.9 (CH_2-S); 27.4 (CH_2); 11.6 (CH_3)
10	156.3; 154.0; 150.2; 147.6; 137.6; 136.4; 129.6; 129.3; 129.1; 128.5; 128.1; 127.9; 124.2	99.3 (O-CH-O); 63.1 (CH_2-O); 46.6 (CH_2-N); 36.7 (CH_2-S); 15.7 (CH_3)
11	156.9; 153.4; 151.1; 147.6; 137.7; 136.6; 132.8; 132.0; 129.6; 129.4; 129.2; 128.5; 128.4; 128.2; 128.1; 123.4	46.6 (CH_2-N); 36.7 (CH_2-S)
12	166.0; 156.3; 148.9; 143.0; 135.7; 131.3; 129.0; 128.8; 128.5; 127.9; 127.8; 127.0; 123.7	60.5 (CH_2-SO_2); 47.1 (CH_2-N)
13	162.7; 156.9; 149.9; 142.6; 135.8; 131.3; 128.9; 128.7; 128.5, 127.8; 127.3; 126.6; 120.9	60.5 (CH_2-SO_2); 46.9 (CH_2-N); 27.6 (CH_2); 11.2 (CH_3)
14	156.6; 156.5; 149.0; 143.3; 135.7; 131.3; 128.9; 128.5; 128.4; 127.8; 127.2; 126.5; 123.1	98.5 (O-CH-O); 62.5 (CH_2-O); 60.5 (CH_2-SO_2); 47.1 (CH_2-N); 15.0 (CH_3)
15	156.5; 156.6; 149.8; 143.0, 136.9, 135.7; 131.6; 131.2; 128.8; 128.5; 128.4; 127.9; 127.6; 127.4; 127.2; 126.5; 118.1	60.5 (CH_2-SO_2); 46.9 (CH_2-N)
19	164.0; 158.0; 146.1; 136.2; 132.0; 128.9; 128.5; 128.4; 127.5; 127.4; 127.1; 113.9; 113.5	55.0 (CH_3-O); 45.2 (CH_2-N); 35.9 (CH_2-S); 32.0 (CH_2); 12.9 (CH_3)
20	168.4; 150.9; 150.2; 143.0; 136.6; 128.3; 127.4; 127.0; 118.1	133.4 (CH=);118.0 (CH_2=); 45.3 (CH_2-N); 34.7 (CH_2-S)
21	159.5; 156.3; 150.1; 145.6; 136.5; 128.9; 128.0; 127.6; 122.3	133.5 (CH=);118.6 (CH_2=); 46.1 (CH_2-N); 35.6 (CH_2-S); 27.7 (CH_2); 11.8 (CH_3)
22	166.4; 150.5; 147.1; 146.4; 136.1; 128.3; 127.6; 127.4; 112.3	45.4 (CH_2-N)
23	166.1; 160.2; 151.1; 147.5; 136.2; 128.3; 127.9; 127.4; 110.1	45.3 (CH_2-N); 27.3 (CH_2); 11.4 (CH_3)
24	166.7; 154.2; 150.8; 146.6; 136.1; 128.3; 127.8; 127.4; 111.8	98.3 (O-CH-O); 62.4 (CH_2-O); 45.5 (CH_2-N); 15.0 (CH_3)
25	155.2; 149.3; 147.8; 147.2; 135.8; 128.6; 127.7; 127.1; 119.3	45.9 (CH_2-N); 30.8, 29.1, 27.7, 25.6, 21.9 (5 CH_2); 13.9 (CH_3)
26	159.2; 156.3; 150.0; 146.1; 136.0; 128.6; 127.7; 127.2; 121.9	45.7 (CH_2-N); 31.9, 30.7, 28.9, 27.7, 27.5, 22.0 (6 CH_2); 13.9, 11.7 (2 CH_3)

ethanol (0.5 mL), some drops of *N*,*N*-diethylaniline were added. The mixture was stirred at 110 °C in a stopped vial for 2 hours; after cooling, the precipitate was collected by filtration and crystallized. See Table 1 for yields, crystallization solvent, physicochemical properties and elemental analysis; see Table 2 and 3 for ir and nmr data.

8-Mercapto-9-phenylmethyl-1,9-dihydropurin-6-one (**22**) and 8-Mercapto-9-phenylmethyl-2-substituted-1,9-dihydropurin-6-one (**23**-**24**).

5-Amino-2-mercapto-1-phenylmethyl-1*H*-imidazole-4-carboxylic acid amide (**5**) (0.365 g, 1.47 mmoles) was added to a solution of sodium ethoxide prepared from sodium (0.23 g, 0.01 mole) in 8.5 mL of absolute ethanol. The mixture was then refluxed with stirring for 1 hour. A solution of the appropriate ester (7.5 mmoles) in 5 mL of ethanol was added dropwise and the solution was stirred under reflux for 48 hours. After cooling, ice was added and then the mixture was neutralized with 50% acetic acid. The precipitate formed was collected by filtration and crystallized. See Table 1 for yields, crystallization solvent, physicochemical properties and elemental analysis; see Table 2 and 3 for ir and nmr data.

8-Hexylsulfanyl-9-phenylmethyl-1,9-dihydro-purin-6-one (**25**) and 2-Ethyl-8-hexylsulfanyl-9-phenylmethyl-1,9-dihydro-purin-6-one (**26**).

A solution consisting of **22** or **23** (1.19 mmoles), the minimal amount of *N*,*N*-dimethylformamide, 1-bromohexane (1.18 mmoles) and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.18 mmoles) was stirred to a room temperature for 1 hour. Then the mixture reaction was diluted with water and extracted with chloroform. The organic phase was evaporated and the residue was triturated with ethyl ether. The solid was collected by filtration and crystallized. See Table 1 for yields, crystallization solvent, physicochemical properties and elemental analysis; see Table 2 and 3 for ir and nmr data.

8-Benzyl-9-phenylmethyl-1,9-dihydro-purin-6-one (**8**), 2-Ethyl-8-benzyl-9-phenylmethyl-1,9-dihydropurin-6-one (**9**) from **22** and **23** Respectively.

A solution consisting of **22** or **23** (1.19 mmoles), the minimal amount of *N*,*N*-dimethylformamide, benzyl bromide (1.18 mmoles) and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.18 mmoles) was stirred to a room temperature for 1 hour. Then the mixture reaction was diluted with water and extracted with chloroform. The organic phase was evaporated and the residue was triturated with ethyl ether. The solid was collected by filtration and crystallized. See Table 1 for yields, crystallization solvent, physicochemical properties and elemental analysis; see Table 2 and 3 for ir and nmr data.

Treatment of Compounds **12**-**15** with Amines.

Compounds **12**-**15** (1 mmol) were treated in turn with an excess of *n*-butylamine or benzylamine (3 ml); the mixture was heated at 120° for 2 h. The following dilution with cold 10% hydrochloric acid allowed the nearly complete recovering of the starting products.

REFERENCES AND NOTES

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