Syntheses and Reactions of some 1-Substituted-7-alkyl-2-thioxopurines: X-Ray Structure of 6-Methylamino-7-nonyl-2-thioxopurine

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Several 1-substituted-7-alkyl-2-thioxopurines **8,9,10** were synthesized by the reaction of isothiocyanates with 1-alkyl-4-amino-5-cyanoimidazoles **3**. Treatment of **3** with methyl isothiocyanate gave the Dimroth rearranged product 6-methylamino-7-alkyl-2-thioxopurines **11**. The structure of **11** was unambiguously defined by X-ray crystallography.

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Introduction.

A relatively simple nucleoside has recently been detected and isolated from three different marine organisms in geographically different areas; from the sponge *Tedania digitata* found in an Australian reef [1], from the Californian dorid nudibranch *Anisodoris nobilis* [2] and from the coral *Madracis mirabilis* collected off the coast of Barbados [3].

This nucleoside, identified as 1-methyl-9-ribosylisoguanine, as well as its hitherto unknown aglycone, were synthesized by three groups, all using essentially the same methodology [4-5]. In view of the potent pharmacological properties of nucleosides **1** [6-9] we were interested in studying the chemistry of its analogues.

In particular we have focused our attention on the variation of the N-9 and N-7 substituents, specifically by replacing the naturally-occuring sugar with other groups.

In a previous paper [3] we described the syntheses of 7-and 9- substituted *N*-methylisoguanines **7** (Scheme 1). Here we report the syntheses of 2-thioxo analogues which display a chemistry different from that of the 2-oxo compounds.

Syntheses of Starting Materials.

Substituted 4(5)-amino-5(4)-cyanoimidazoles are versatile starting materials for the synthesis of purine ring systems. The combination of an electrophilic cyano group proximate to a nucleophilic amino function results in a one-step addition-cyclization reaction of electrophiles to give purine analogues. Alkylation of 4(5)-amino-5(4)-cyanoimidazole resulted in a mixture of two isomers which could not be identified easily unless the synthesis to a known purine structure was carried out. We now report that each of the isomers **3** and **4** has a characteristic nmr spectrum. The C-2 proton of 1-alkyl-4-amino-5-cyanoimidazole **3** in DMSO-d_6 resonates at 7.4-7.7 ppm; in contrast, in the other isomer, 1-alkyl-5-amino-4-cyanoimidazole **4**, the resonance is at 7.1-7.3 ppm. Similarly the ^{13}C-nmr spectra of the two isomers are distinct for the C-2, C-4 and C-5 signals and therefore can be used for structural identification. We found that the resonances of the C-2, C-4 and C-5 signals in DMSO-d_6 are at 138, 157 and 82 ppm, respectively, for isomer **3** and at 132, 147, and 90 ppm for isomer **4** (see Table 1). In addition, from the alkylation mixture we isolated and identified the previously unknown 1-alkyl-4-alkylamino-5-cyanoimidazoles **5**. The site of alkylation was unequivocally established by the alkylation of **3** with one equivalent of alkylating agent. Careful chromatographic separation of the alkylation mixture of **3a** did not show any of the isomeric 1-methyl-5-methylamino-4-cyanoimidazole.

Results and Discussions.

In this paper we report the results of the reaction of **3** with a number of isothiocyanates. Since **3** and **4** behave differently, we will describe the reaction of **4** with methyl isothiocyanate in a separate paper.

The purine formation *via* reaction of **3** with alkyl isothiocyanate is different from and more complicated than the corresponding reaction of **3** with alkyl isocyanates. In the latter case the ureas **6** could be isolated and cyclized to the purines **7** (Scheme 1). However, using isothiocyanates, the corresponding open thioureas could not be isolated and immediate ring closure to the purine derivative was observed to take place. The reaction is further complicated by the occurrence of isomerization during the reaction and also by the number of theoretically possible reaction products, many of which would be difficult to characterize unambiguously by conventional spectroscopic methods (ir, ^{1}H-nmr and ms). For this reason we undertook the X-ray analysis of **11d**, a product of one of these reactions. Figure 1, a perspective view of **11d**, establishes that the reaction of 1-nonyl-4-amino-5-cyanoimidazole with methyl iosthiocyanate ultimately give 6-methylamino-7-nonyl-2-thioxopurine.

Reaction of 4(5)-amino-5(4)-cyanoimidazole (**2**) with methyl isothiocyanate gave **8** (R = H) in 37% yield. This structure was conclusively established by desulfurization to 1-methyladenine (**12**) [10]. Treatment of 1-methyl-4-amino-5-cyanoimidazole (**3a**) with methyl isothiocyanate in pyridine gave two products; one of which exhibited an ultraviolet absorption spectrum identical to that observed for **8**, R = H. The second product was determined to be 6-methylamino-7-methyl-2-thioxopurine, **11a**, because its uv spectra in 0.1 *N* hydrochloric acid and in 0.1 *N* sodium hydroxide were identical to the one obtained for **11d** whose structure was obtained by X-ray crystallography. The conversion of **8** to **11** is an additional example of the 1,3-exoannular rearrangement which has been observed in the reactions of phenyl isocyanate with anthranilonitrile [11] and also with 4-amino-5-cyano-1- and 3-substituted-1,2,3-triazoles [12]. The thermal conversion is catalyzed by excess isothiocyanate and proceeds *via* a ring opening, ring closure sequence to **13**. An attempt to effect the rearrangement with one mole of isothiocyanate resulted in lower yields and the isolation of unreacted starting materials.

The intermediates **13** were isolated and converted to products **11** by the elimination of one mole of methyl isothiocyanate. This reversible reaction between **13** and **11** was studied in a nmr experiment in DMSO-d_6. For example, with R = $-CH_2C_6H_5$, at 20° **13** is the only product observed. As the temperature is increased to 90°, **11** is formed, together with methyl isothiocyanate. On cooling to ambient temperature **13** is regenerated. Preparation of **11a-i** is facilitated by heating **13a-i** in methanol containing a trace of aqueous hydrochloric acid to prevent reformation of **13a-i** on cooling.

In all but one of the examples studied, treatment of 1-alkyl-4-amino-5-cyanoimidazole with methyl isothiocyanate gave the Dimroth rearranged product **13** which was converted to **11**. The exception was **3a** where a mixture of 1,7-dimethyl-6-imino-2-thioxopurine (**8a**) and the Dimroth rearranged product **11a** was obtained. Treatment of **3a** and **3j** with ethyl- or phenyl isothiocyanate resulted in formation of 6-imino-2-thioxopurines **9,10** only. This suggests a steric involvement of the substituent on the N-1 position which prevents the Dimroth rearrangement if the substituent is larger than a methyl group.

The X-ray analysis of **11d** established the molecular constitution of the ultimate products in the reaction sequence when substituents **b-i** were used.

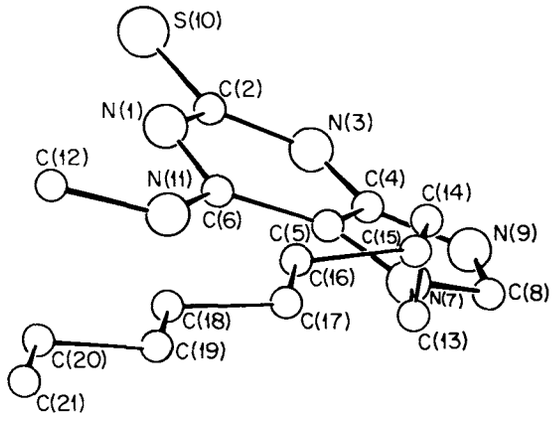
The purine skeleton of 6-methyl-amino-7-nonyl-2-thioxopurine is planar with the maximum deviation from the mean plane being 0.069 Å. Except for the rather short 1.331(7) Å N(7)-C(8) distance the bond lengths compare well with related compounds [13-16].

Because both C(6) and N(7) bear substituents which are larger than hydrogen the extra-annular C(6)-C(5)-N(7) angle is substantially opened (137.3(5)°). The pattern of valency angles in the five-membered ring is normal [13-16]. Since N(7) bears the extra-annular substituent C(5)-N(7)-C(8) angle is larger than the C(4)-N(9)-C(8) angle [17] and the C(6)-C(5)-N(9) angle is larger than the C(5)-C(6)-N(7) angle.

The methylamino group is nearly coplanar with the rings (N(1)-C(6)-N(11)-C(12) 8.1(5)°) in order to extend the conjugation. The nonyl group, which adopts an almost totally extended conformation, lies well out of the plane of the rings (C(5)-N(7)-C(13)-C(14) −70.3(5)°). The torsion angle about the C(14)-C(15) bond is −79.0(6)° and is probably due to packing forces.

The molecules aggregate as hydrogen bonded dimers about centers of symmetry. Molecules in a dimer are held together by very strong N(3)-H(3)...N(9)′ hydrogen bonds (N(3)...N(9)′ 2.88 Å, N(9)′ is in the molecule at 2-x, −y, 1-z). The sulfur atom in the molecule at x, 1+y, z approaches N(11) at 3.31 Å. With H(11) calculated to lie in the C(6), N(11), C(12) plane, the N(11)-H(11)...S(10)′ angle is 116.0°.

The molecules pack in layers along the x direction alternating double layers of purine skeletons, hydrogen-bonded to one another, with double layers of nonyl "tails".



View of 6-methyl-7-nonyl-2-thioxopurine with the numbering scheme. Hydrogen atoms have been omitted for clarity.

Crystallography.

Crystal Data. $C_{15}H_{25}N_5S$, M = 307.5, Monoclinic, a = 17.225(4), b = 7.624(1), c = 14.302(2) Å, β = 109.38(1) Å^3, Z = 4, D_c = 1.152 g cm^{-3}, D_m = 1.15 g cm^{-3}, F(000) = 672. Cu-Kα radiation (λ = 1.5418 Å), μ = 15.8 cm^{-1}. Space group $P2_1/c$ (C_{2h}) by systematic absences: $h0\ell$ when $\ell = 2n$, $0k0$ when $k = 2n$. Specimen: 0.15 × 0.03 × 0.65 mm.

Crystallographic Measurements and Structure Analysis.

A quadrant of data $\theta = 65°$ was collected on a Syntex $P2_1$ automated diffractometer using variable speed, $\theta/2\theta$ scans. The standard reflection, measured every 99 reflections, showed a maximum variation of 4%. Of the 2773 reflections collected, 1583 reflections with $I \geq 2\sigma(I)$ were corrected for Lorentz and polarization effects and used in the structure solution and refinement. The structure was solved by direct phasing methods (MULTAN 80) and the non-hydrogen atoms were refined by full-matrix least squares to an R of 0.071 [18]. Hydogen atoms, except for those on methyl groups were included in calculated positions.

Supplementary Materials.

Listings of final atomic positional and thermal parameters are given in Tables II-IV. Bond distances and valency angles are in Table V and torsion angles are in Table VI.

EXPERIMENTAL

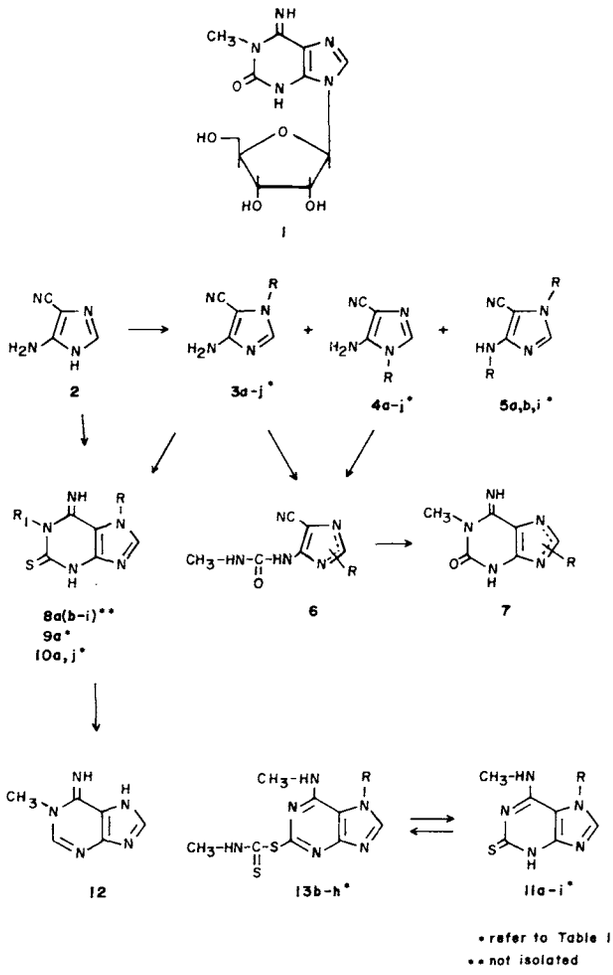
Melting points are uncorrected and were run on a Buchi 520 capillary melting point apparaturs. The nmr spectra were determined with a Brucker WM250 spectrometer with TMS as the internal standard. Ultraviolet spectra were recorded on a Perkin-Elmer 320 spectrometer. Low-resolution mass spectra were obtained with a Finnigan 4023 GC/MS/DS at 70 e.v. and probe temperatures were noted. Microanalyses were performed by Micro Tech, Inc., Skokie, IL. Silica gel was obtained from Fisher 60-200 mesh.

1-Methyl-6-imino-2-thioxopurine Hydrochloride **8** R = H.

To a solution of 5.4 g (5 mmoles) of 4(5)-amino-5(4)-cyanoimidazole (**2**) in 100 mℓ of pyridine was added 7.3 g (10 mmoles) of methyl isothiocyanate. Refluxing was carried out for 1 hour before the resulting pale yellow solid was collected by filtration and washed with water. The solid was dissolved in warm 1*N* hydrochloric acid and concentrated until crystals separated; addition of methanol precipitated more product. The solid was filtered, washed with methanol, and dried *in vacuo* (60°C) to give 4.0 g (37%) of **8** where R = H, mp 272°-274°; nmr (DMSO-d_6): δ 2.50 (s, 3H), 3.9 (s, 3H), 8.4 (s, 1H), 9.7 (m, 1H), 10.5 (m, 1H), 14.3 (m, 1H); uv (0.1*N* hydrochloric acid): λ max 239 (ϵ 19,200), 286 (ϵ 18,700); (0.1*N* sodium hydroxide): 237 nm (ϵ 19,700), 287 nm (ϵ 15,100).

Anal. Calcd. for $C_6H_7N_5S \times HC\ell$: C, 33.10; H, 3.70; N, 32.17; S, 14.73; Cℓ, 16.29. Found: C, 33.04; H, 3.67; N, 31.95; S, 14.81; Cℓ, 16.03.

Scheme I



Picric Acid Salt of 1-Methyladenine (**12**) from 1-Methyl-6-amino-2-thioxopurine (**8**, R = H).

A suspension of 1.0 g (4.6 mmoles) of 1-methyl-6-amino-2-thioxopurine hydrochloride (**8**, R = H) and a 50% aqueous Raney Ni slurry (2 mℓ) in 250 mℓ of water was refluxed for 6 hours. The reaction mixture was cooled and filtered and the filter was washed with ethanol. The filtrate was

Table I

Alkylation of 4(5)-amino-5(4)-cyanoimidazole (**2**) to **3** and **4** in DMSO-d_6

Compound		1-alkyl-4-amino-5-cyanoimidazole (3)						1-alkyl-5-amino-4-cyanoimidazole (4)					
		Yield	mp	^{1}H-NMR	^{13}C-NMR			Yield	mp	^{1}H-NMR	^{13}C-NMR		
No.	R	%	°C	N-HC=N	C-2	C-4	C-5	%	°C	(N-CH=N)	C-2	C-4	C-5
a	methyl	27.5	175-177	7.41	138.8	157.1	83.7	22.1	201-203	7.14	132.9	147.7	90.5
b	benzyl	35.3	204-205	7.69	138.5	157.5	82.3	23.7	202-203	7.29	132.5	147.3	90.9
c	2-ethylthioethyl	44.8	71-72	7.50	138.7	157.2	82.1	35.5	133-134	7.20	132.7	147.0	90.7
d	nonyl	25.5	97-98	7.48	138.5	157.5	82.3	18.1	156-157	7.18	132.5	147.4	90.5
e	2-cyclohexylthioethyl	23.8	109-111	7.50	138.7	157.3	82.1	40.0	189-191	7.20	132.7	147.0	90.8
f	2-(*p*-chlorophenyl)thioethyl	20.1	135-137	7.48	138.7	157.2	82.1	10.0	213-215	7.15	132.6	147.9	91.0
g	3-[4-(*p*-chlorobenzyl)piperazin-1-yl]propyl	33.0	136-138	7.42	138.2	157.1	82.3	22.0	212-213	7.20	132.3	147.2	90.4
h	2-methoxyethyl	33.0	100-101	7.45	138.9	157.3	82.5	49.0	115-116	7.12	133	147	90
i	*p*-chlorobenzyl	25.0	190-192	7.70	138.7	157.6	82.2	12.0	192-194	7.32	132.4	147.2	90.8
j	2-(*N,N*-dimethylamino)ethyl	6.7	100-102	7.47	138.5	157.0	82.6	13.4	163-165	7.16	132.9	147.5	90.4

concentrated to 30 mℓ. The resulting precipitate was filtered and the filter cake was dissolved in water and an ethanolic picric acid solution was added to give a yellow crystalline solid. Recrystallization from methanol/water gave a fine yellow powder mp 257°-258°. The ir and uv spectra λ max (*p*H 4): 259 nm; (*p*H 13): (270 nm) were identical with the ones made from a commercial sample [10] of 1-methyladenine.

Table II

Fractional atomtic coordinates (× 10⁴) for the non-hydrogen atoms, with estimated standard deviations in parentheses.

Atom	x/a	y/b	z/c
N(1)	8624(3)	1506(5)	6891(3)
C(2)	9042(3)	164(7)	6685(3)
N(3)	9398(3)	288(5)	5958(3)
C(4)	9296(3)	1794(6)	5420(3)
C(5)	8853(3)	3167(6)	5593(3)
C(6)	8561(3)	3046(7)	6413(3)
N(7)	8862(3)	4407(5)	4889(3)
C(8)	9290(3)	3704(7)	4360(3)
N(9)	9576(3)	2113(6)	4653(3)
S(10)	9142(1)	−1776(2)	7308(1)
N(11)	8198(3)	4410(6)	6689(3)
C(12)	7954(3)	4351(8)	7595(3)
C(13)	8425(3)	6099(7)	4676(3)
C(14)	7514(4)	5839(8)	4196(4)
C(15)	7033(4)	7572(10)	4102(5)
C(16)	6909(4)	8149(9)	5066(5)
C(17)	6508(4)	9968(10)	4989(6)
C(18)	6327(5)	10476(11)	5915(6)
C(19)	5935(5)	12251(12)	5868(7)
C(20)	5699(6)	12719(16)	6769(7)
C(21)	5347(7)	14607(15)	6649(10)

Table III

Anisotropic temperature factor parameters* (× 10³), with estimated standard deviations in parentheses.

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	87(2)	30(2)	52(2)	5(2)	34(2)	1(2)
C(2)	80(3)	39(3)	45(2)	−4(2)	27(2)	−4(2)
N(3)	92(2)	27(2)	55(2)	6(2)	38(2)	−1(2)
C(4)	79(3)	29(3)	48(2)	0(2)	30(2)	−2(2)
C(5)	75(3)	34(3)	48(2)	−4(2)	25(2)	4(2)
C(6)	71(3)	38(3)	50(2)	0(2)	25(2)	−2(2)
N(7)	88(2)	28(2)	55(2)	2(2)	35(2)	0(2)
C(8)	93(3)	36(3)	54(2)	0(3)	36(2)	3(2)
N(9)	94(2)	39(2)	53(2)	7(2)	40(1)	2(2)
S(10)	111.4(8)	26.8(7)	54.7(6)	3.2(7)	39.4(5)	3.5(6)
N(11)	103(3)	37(2)	66(2)	14(2)	48(2)	1(2)
C(12)	126(3)	63(3)	74(2)	19(3)	65(2)	3(3)
C(13)	96(3)	40(3)	63(2)	9(3)	36(2)	10(2)
C(14)	110(4)	63(4)	79(3)	9(3)	33(3)	4(3)
C(15)	105(4)	105(5)	94(3)	36(4)	37(3)	42(4)
C(16)	103(4)	87(5)	108(4)	15(4)	40(3)	4(4)
C(17)	107(4)	93(5)	125(5)	9(4)	43(3)	2(4)
C(18)	120(5)	95(5)	134(5)	2(4)	48(4)	−13(4)
C(19)	111(5)	114(6)	155(6)	5(5)	45(4)	−25(5)
C(20)	166(6)	166(8)	203(6)	−11(6)	107(4)	−57(6)
C(21)	205(8)	159(8)	256(10)	48(7)	80(7)	−64(7)

*In the form: $B \sin^2\theta/\lambda^2 = 2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}\ell^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}h\ell a^*c^* + 2U_{23}k\ell b^*c^*)$

Table IV

Hydrogen atom fractional coordinates (× 10³) and unrefined isotropic thermal parameters (× 10³)

Atom	x/a	y/b	z/c	U
H(3)	975	−82	582	44
H(8)	940	430	378	44
H(11)	814	567	631	50
H(131)	865	687	418	63
H(132)	853	682	537	63
H(141)	729	492	464	63
H(142)	739	527	345	63
H(151)	643	744	352	63
H(152)	738	860	387	63
H(161)	750	814	566	89
H(162)	650	717	525	89
H(171)	594	998	435	89
H(172)	694	1093	486	89
H(181)	689	1042	656	101
H(182)	588	950	604	101
H(191)	540	1237	519	101
H(192)	639	1326	579	101
H(201)	624	1265	744	114
H(202)	523	1181	684	114

Table V

Interatomic distances (Å) and valency angles (deg), with estimated standard deviations in parentheses.

a) Bond lengths

N(1)-C(2)	1.339(7)	N(7)-C(13)	1.473(7)
N(1)-C(6)	1.344(6)	C(8)-N(9)	1.324(7)
C(2)-N(3)	1.375(6)	N(11)-C(12)	1.490(7)
C(2)-S(10)	1.706(5)	C(13)-C(14)	1.502(8)
N(3)-C(4)	1.360(6)	C(14)-C(15)	1.542(10)
C(4)-C(5)	1.365(7)	C(15)-C(16)	1.527(10)
C(4)-N(9)	1.359(6)	C(16)-C(17)	1.537(10)
C(5)-C(6)	1.424(7)	C(17)-C(18)	1.508(11)
C(5)-N(7)	1.386(6)	C(18)-C(19)	1.504(12)
C(6)-N(11)	1.339(7)	C(19)-C(20)	1.517(14)
N(7)-C(8)	1.331(7)	C(20)-C(21)	1.548(17)

b) Valency angles

C(2)-N(1)-C(6)	120.9(4)	C(5)-N(7)-C(9)	106.2(4)
N(1)-C(2)-N(3)	121.5(4)	C(5)-N(7)-C(13)	128.3(4)
N(1)-C(2)-S(10)	121.1(4)	C(8)-N(7)-C(13)	125.2(4)
N(3)-C(2)-S(10)	117.5(4)	N(7)-C(8)-N(9)	114.0(4)
C(2)-N(3)-C(4)	118.6(4)	C(4)-N(9)-C(8)	103.1(4)
N(3)-C(4)-C(5)	121.3(4)	C(6)-N(11)-C(12)	121.8(4)
N(3)-C(4)-N(9)	126.4(4)	N(7)-C(13)-C(14)	111.3(4)
C(5)-C(4)-N(9)	112.2(4)	C(13)-C(14)-C(15)	112.1(5)
C(4)-C(5)-C(6)	118.1(4)	C(14)-C(15)-C(16)	113.6(5)
C(4)-C(5)-N(7)	104.5(4)	C(15)-C(16)-C(17)	113.0(6)
C(6)-C(5)-N(7)	137.3(5)	C(16)-C(17)-C(18)	112.9(6)
N(1)-C(6)-C(5)	119.0(4)	C(17)-C(18)-C(19)	114.4(7)
N(1)-C(6)-N(11)	119.6(4)	C(18)-C(19)-C(20)	114.7(8)
C(5)-C(6)-N(11)	121.3(4)	C(19)-C(20)-C(21)	109.3(9)

Table VI

Torsion angles (deg), with estimated standard deviations in parentheses.

C(6)-N(1)-C(2)-N(3)	-2.2(5)	C(4)-C(5)-N(7)-C(8)	0.5(5)
C(6)-N(1)-C(2)-S(10)	178.5(5)	C(4)-C(5)-N(7)-C(13)	174.7(5)
C(2)-N(1)-C(6)-C(5)	8.2(5)	C(6)-C(5)-N(7)-C(8)	175.9(6)
C(2)-N(1)-C(6)-N(11)	-174.6(5)	C(6)-C(5)-N(7)-C(13)	-9.9(5)
N(1)-C(2)-N(3)-C(4)	-2.2(5)	N(1)-C(6)-N(11)-C(12)	8.1(5)
S(10)-C(2)-N(3)-C(4)	177.1(4)	C(5)-C(6)-N(11)-C(12)	-174.8(5)
C(2)-N(3)-C(4)-C(5)	0.2(5)	C(5)-N(7)-C(8)-C(9)	-0.8(5)
C(2)-N(3)-C(4)-N(9)	-177.2(5)	C(13)-N(7)-C(8)-C(9)	-175.2(6)
C(3)-C(4)-C(5)-C(6)	5.6(5)	C(5)-N(7)-C(13)-C(14)	-70.3(5)
C(3)-C(4)-C(5)-N(7)	-177.9(4)	C(8)-N(7)-C(13)-C(14)	102.8(5)
N(9)-C(4)-C(5)-C(6)	-176.6(5)	N(7)-C(8)-N(9)-C(4)	0.7(4)
N(9)-C(4)-C(5)-N(7)	-0.1(4)	N(7)-C(13)-C(14)-C(15)	171.9(5)
N(3)-C(4)-N(9)-C(8)	177.3(5)	C(13)-C(14)-C(15)-C(16)	-79.0(6)
C(5)-C(4)-N(9)-C(8)	-0.3(4)	C(14)-C(15)-C(16)-C(17)	174.0(6)
C(4)-C(5)-C(6)-N(1)	-9.8(5)	C(15)-C(16)-C(17)-C(18)	175.6(7)
C(4)-C(5)-C(6)-N(11)	173.0(5)	C(16)-C(17)-C(18)-C(19)	180.0(7)
N(7)-C(5)-C(6)-N(1)	175.2(6)	C(17)-C(18)-C(19)-C(20)	176.1(8)
N(7)-C(5)-C(6)-N(11)	-2.0(5)	C(18)-C(19)-C(20)-C(21)	177.0(9)

1-Phenyl-6-imino-2-thioxopurine (**10**, R = H).

A mixture of 5.4 g (5 mmoles) of 4(5)-amino-5(4)-cyanoimidazole (**2**), 13.4 g (10 mmoles) of phenyl isothiocyanate and 100 mℓ of dry pyridine was heated and refluxed for 2 hours. After cooling the mixture, the precipitate was filtered and dissolved in hot DMF. Addition of water gave 4.5 g (37%) of **10**, R = H mp 300°; nmr (DMSO-d_6): δ 7.15 (t, 1H), 7.4 (t, 2H), 7.85 (d, 2H), 8.10 (s, 1H), 9.85 (br s, 1NH), 12.4 (br s, 1NH), 13.2 (br s, 1NH); uv (0.1*N* hydrochloric acid): λ max 243 nm (ε 1,580), 287 nm (ε 3,090); (0.1*N* sodium hydroxide): 240 nm (ε 17,600), 272 nm (ε 22,900), 314 nm (ε 15,900).

Anal. Calcd. for $C_{11}H_9N_5S$: C, 54.28; H, 3.72; N, 28.78; S, 13.17. Found: C, 54.07; H, 3.75; N, 29.00; S, 13.16.

4-Amino-1-methyl-5-cyanoimidazole (**3a**), 5-Amino-1-methyl-4-cyanoimidazole (**4a**) and 4-Methylamino-1-methyl-5-cyanoimidazole (**5a**).

A mixture of 2.16 g (20 mmoles) of 4(5)-amino-5(4)-cyanoimidazole (**2**), 3.3 g (24 mmoles) of potassium carbonate and 3.4 g (24 mmoles) of methyl iodide in 30 mℓ of tetrahydrofuran and 15 mℓ of *N,N*-dimethylformamide was stirred at room temperature for 48 hours. The inorganic salts were filtered off and washed with tetrahydrofuran. The combined filtrates were evaporated and purified by column chromatography on silica gel. Compound **5a** was eluted with 2% ethanol in methylene chloride (0.15 g, 5.5%) mp 161°-163°; nmr (DMSO-d_6): δ 2.77 (d, CH_3, J ~ 4-5 Hz), 3.55 (s, CH_3), 6.30 (d, 1 NH, J ~ 4-5 Hz), 7.47 (s, 1H).

Anal. Calcd. for $C_6H_8N_4$: C, 52.92; H, 5.92; N, 41.15. Found: C, 52.67; H, 5.81; N, 41.26.

The more polar **3a** eluted next yielding 0.5 g, (22%) mp 174°-176°; nmr (DMSO-d_6): δ 3.52 (s, CH_3), 5.85 (s, NH_2), 7.41 (s, 1H).

Anal. Calcd. for $C_5H_6N_4$: C, 49.17; H, 4.95; N, 45.88. Found: C, 48.81; H, 4.98; N, 45.56.

The last compound eluted was **4a** which yielded, after recrystallization from methanol, 0.86 g (35%) mp 199°-202°; nmr (DMSO-d_6): δ 3.40 (s, CH_3), 6.20 (s, NH_2), 7.14 (s, 1H).

Anal. Calcd. for $C_5H_6N_4$: C, 49.17; H, 4.95; N, 45.88. Found: C, 49.82; H, 4.94; N, 45.89.

1,7-Dimethyl-6-imino-2-thioxopurine (**8a**) and 7-Methyl-6-methylamino-2-thioxopurine (**11a**).

A mixture of 8.5 g (7 mmoles) of 4-amino-1-methyl-5-cyanoimidazole (**3a**), 100 mℓ of pyridine and 20.5 g (28 mmoles) of methyl isothiocyanate was stirred at reflux temperature for 2 hours. After cooling, 100 mℓ of ether was added and the resulting solid filtered off. The solid was dissolved in a mixture of 20 mℓ of 4*N* hydrochloric acid and 150 mℓ of methanol. After neutralizing with ammonium hydroxide a white crystalline solid precipitated. The solid was dissolved in 16 ℓ of hot water, cooled to room temperature and the crystals were collected by filtration to give 6 g (44%) of **8a**, mp 276-278°; nmr (TFA-d: δ 4.20 (s, 3H), 3.38 (s, 3H), 8.70, (s, 1H); uv (0.1*N* hydrochloric acid): λ max 243 nm (ε 21,700), 286 nm (ε 19,800); (0.1*N* sodium hydroxide): 234 nm (ε 17,500), 284 nm (ε 13,900).

Anal. Calcd. for $C_7H_9N_5S$: C, 43.07; H, 4.65; N, 35.89; S, 16.40. Found: C, 42.84; H, 4.66; N, 35.59; S, 16.49.

The above filtrate was concentrated to 1 ℓ using a rotary evaporator. The white precipitate which separated was filtered, recrystallized from boiling water and dried at 130° to give 2 g (15%) of **11a**, mp 274°-275°; nmr (DMSO-d_6): δ 3.00 (d, 3H, J ~ 5-6 Hz), 3.95 (s, 3H), 7.40 (d, 1NH), J ~ 5-6 Hz), 7.95 (s, 1H), 12.85 (s, 1H); uv (0.1*N* hydrochloric acid): λ max 245 nm (ε 22,500), 287 nm (ε 21,700); (0.1*N* sodium hydroxide): 251 nm (ε 20,000).

Anal. Calcd. for $C_7H_9N_5S$: C, 43.07; H, 4.65; N, 35.89; S, 16.40. Found: C, 42.98; H, 4.71; N, 36.25; S, 16.43.

1-Ethyl-6-imino-7-methyl-2-thioxopurine (**9a**).

A mixture of 2.44 g (2 mmoles) of 4-amino-1-methyl-5-cyanoimidazole (**3a**), 5.22 g (6 mmoles) of ethyl isothiocyanate, and 20 mℓ of pyridine was heated to reflux for 1.5 hours. After cooling the solution, the pale yellow solid was filtered and dissolved in a mixture of 50 mℓ water and 5 mℓ 4*N* hydrochloric acid. After neutralizing with ammonium hydroxide 2.5 g (60%) of crystals were obtained, mp 252°-253°C; nmr (TFA-d): δ 1.55 (t, 3H, J ≈ 5 Hz), 4.40 (s, 3H), 4.90 (q, 2H, J ≈ 5 Hz), 8.70 (s, 1H); uv (0.1*N* hydrochloric acid): λ max 244 nm (ε 20,300), 288 nm (ε 22,200); (0.1*N* sodium hydroxide): 235 nm (ε 20,500), 286 nm (ε 17,000).

Anal. Calcd. for $C_8H_{11}N_5S$: C, 45.93; H, 5.30; N, 33.48; S, 15.30. Found: C, 45.82; H, 5.25; N, 33.11; S, 15.67.

7-Methyl-6-imino-1-phenyl-2-thioxopurine (**10a**).

A mixture of 2.44 g (2 mmoles) of 4-amino-1-methyl-5-cyanoimidazole (**3a**), 20 mℓ of pyridine and 4.05 g (6 mmoles) of phenyl isothiocyanate was heated to reflux for 2 hours. The mixture was allowed to cool to room temperature and was then filtered. The solid was recrystallized from 0.5 ℓ of *N,N*-dimethylformamide and dried under vacuum at 130° to give 4.3 g (84%) mp 278°-279° of **10a**; nmr (TFA-d): δ 4.40 (s, 3H), 7.5-7.7 (m, 5H), 8.67 (s, 1H); uv (0.1*N* hydrochloric acid): λ max 249 nm (ε 15,500), 288 nm (ε 20,500); (0.1*N* sodium hydroxide): 237 nm (ε 16,600), 274 nm (ε 18,200); ms: (300°) m/e 257 (M^+), 224 (M^+ -SH), 199 (M^+ -CSNH), 180 (M^+ -C_6H_6).

Anal. Calcd. for $C_{12}H_{11}N_5S$: C, 56.02; H, 4.31; N, 27.23; S, 12.44. Found: C, 56.36; H, 4.46; N, 27.15; S, 12.37.

4-Amino-1-benzyl-5-cyanoimidazole (**3b**), 5-Amino-1-benzyl-4-cyanoimidazole (**4b**) and 1-Benzyl-4-benzylamino-5-cyanoimidazole (**5b**).

A mixture of 10.8 g (0.1 mole) of **2**, 13.8 g (0.1 mole) of potassium carbonate, 50 mℓ of THF, 100 mℓ of DMF and 17.1 g (0.1 mole) of benzyl bromide was stirred at reflux for 7 hours. After cooling the mixture to room temperature the insoluble material was filtered off, and the filtrate was concentrated under vacuum to a partially solid residue which was triturated with ethanol. The solid was collected by filtration. Recrystallization from methanol afforded 6.5 g (33%) of colorless crystals of **3b**, mp 204-205°; nmr (DMSO-d_6): δ 5.10 (s, 2H), 5.90 (s, 2H, NH_2), 7.2-7.4 (m, 5H), 7.69 (s, 1H).

Anal. Calcd. for $C_{11}H_{10}N_4$: C, 66.65; H, 5.09; N, 28.27. Found: C, 66.72; H, 5.13; N, 28.41.

The above ethanol filtrate and mother liquor were evaporated *in vacuo* and the residue was subjected to column chromatography on silica gel with dichloromethane/ethanol (ratio 95:5) as the eluent. The first fraction gave 2.2 g (7.5%) of **5b**, mp 140-141°; nmr (DMSO-d_6): δ 4.40 (d, 2H, J = 3.5 Hz), 5.10 (s, 2H), 6.92 (q, 1H, NH, J ~ 3.5 Hz), 7.1-7.4 (m, 5H), 7.72 (s, 1H).

Anal. Calcd. for $C_{18}H_{16}N_4$: C, 74.97; H, 5.59; N, 19.43. Found: C, 75.30; H, 5.84; N, 19.41.

The second fraction eluted gave 4.7 g (24%) of **4b**, mp 202-203; nmr (DMSO-d_6): δ 5.07 (s, 2H), 6.30 (s, 2H, NH_2), 7.17-7.30 (m, 5H), 7.29 (s, 1H).

Anal. Calcd. for $C_{11}H_{10}N_4$: C, 66.65; H, 5.09; N, 28.27. Found: C, 66.39; H, 5.24; N, 28.00.

7-Benzyl-6-methylamino-2-methyldithiocarbamylpurine (**13b**).

A mixture of 3.96 g (40 mmoles) of 4-amino-1-benzyl-5-cyanoimidazole (**3b**), 50 mℓ of pyridine and 7.3 g (100 mmoles) of methyl isothiocyanate was heated at reflux for 1.5 hours. The reaction mixture was partially concentrated and triturated with 100 mℓ of ether. The solid was collected, washed with ether and dissolved in a mixture of 300 mℓ of methanol/dichloromethane (1:1) and filtered through a column of 800 g of alumina in methanol/dichloromethane (2:8). After recrystallization from methanol-ether 3.0 g (43%) mp 269-270° of **13b** was obtained. nmr (DMSO-d_6): δ 2.95 (d, 3H, J ~ 5 Hz), 3.27 (d, 3H, J ~ 5 Hz), 5.70 (s, 2H), 7.1-7.5 (m, 6H), 8.45 (s, 1H), 12.65 (d, 1NH, J ~ 5 Hz).

Anal. Calcd. for $C_{15}H_{16}N_6S_2$: C, 52.32; H, 4.68; N, 24.41; S, 18.59. Found: C, 52.83; H, 4.71; N, 24.89; S, 18.15.

7-Benzyl-6-methylamino-2-thioxopurine (**11b**).

To 2 g (5.8 mmoles) of **13b** was added 50 mℓ of methanol, containing 4 drops of a 4*N* hydrochloric acid solution, the resulting mixture was heated under reflux for 2h. After cooling the mixture was neutralized with concentrated ammonia and then concentrated to 20 mℓ. The precipitated solid was collected by filtration and dried under vacuum at 100° to yield 1.5 g (95%) of **11b**; mp (269-270°C, NMR (DMSO-d_6): δ 2.90 (d, 3H, J ~ 2 Hz), 5.62 (s, 2H), 7.0-7.4 (m, 6H, 5-arom., 1NH), 8.15 (s, 1H), 12.8 (q., 1NH); UV λ max. 0.1N HCℓ 246 nm (ε 18,500) 287 nm (ε 20,900) uv (0.1*N* hydrochloric acid): λ max 246 nm (ε 18,500), 287 nm (ε 20,900); (0.1*N* sodium hydroxide): 253 nm (ε 26,800).

Anal. Calcd. for $C_{13}H_{13}N_5S$: C, 57.56; H, 4.83; N, 25.82; S, 11.80. Found: C, 57.24; H, 4.80; N, 26.06; S, 11.70.

4-Amino-1-ethylthioethyl-5-cyanoimidazole (**3c**) and 5-Amino-1-ethylthioethyl-4-cyanoimidazole (**4c**).

A mixture of 24.8 g (0.23 mole) of 4(5)-amino-5(4)-cyanoimidazole (**2**), 31.7 g (0.23 mole) of potassium carbonate, 175 mℓ of tetrahydrofuran, 175 mℓ of *N,N*-dimethylformamide, and 50 g (0.23 mole) of 2-chloroethyl ethyl sulfide was heated under reflux for 5 hours. The reaction mixture was concentrated under vacuum to a partially solid residue which was stirred with a mixture of methylene chloride and ethanol (95:5). The insoluble material was removed by filtration, and the filtrate was added to a column of 1 kg silica gel in toluene. Elution of the column with toluene-ethanol (9:1) effected separation of **3c** and **4c**. Colorless crystals were obtained after crystallization from ethanol-petroleum ether, yield, **3c** 20.2 g (45%), mp 71-72°; NMR (DMSO-d_6): δ 1.17 (t, 3H, J ~ 8 Hz), 2.50 (q, 2H, J ~ 8 Hz), 2.85 (t, 2H, J ~ 8 Hz), 4.05, (t, 2H, J ~ 8 Hz), 5.90 (s, NH_2), 7.50 (s, 1H).

Anal. Calcd. for $C_8H_{12}N_4S$: C, 48.95; H, 6.16; N, 28.54; S, 16.34. Found: C, 48.93; H, 6.22; N, 28.50; S, 16.45.

Compound **4c** was obtained in 36% yield (16.0 g), mp 133-134°; nmr (DMSO-d_6): δ 1.15 (t, 3H, J ~ 7 Hz), 2.50 (q, 2H, J ~ 7 Hz), 2.78 (t, 2H, J ~ 7 Hz), 3.98 (t, 2H, J ~ 7 Hz), 6.20 (s, NH_2), 7.20 (s, 1H).

Anal. Calcd. for $C_8H_{12}N_4S$: C, 49.11; H, 6.16; N, 28.54; S, 16.34. Found: C, 49.11; H, 6.42; N, 28.26; S, 16.54.

7-Ethylthioethyl-6-methylamino-2-thioxopurine (**11c**) and 7-Ethylthioethyl-6-methylamino-2-methyldithiocarbamylpurine (**13c**).

Method A.

A solution of 5 g (25.5 mmoles) of **3c** and 4.4 g (60 mmoles) of methyl isothiocyanate in 25 mℓ of pyridine was heated under reflux for 2 hours and was then evaporated to dryness under reduced pressure. Addition of water to the residue resulted in the separation of a light yellow solid. Recrystallization from methylene chloride-ethanol gave 0.6 g (6.9%) of **11c**, mp 222-224°; nmr (DMSO-d_6): δ 1.10 (t, 3H, J ~ 7 Hz), 2.42 (q, 2H, J ~ 7 Hz), 2.82 (t, 2H, J ~ 7 Hz), 3.00 (d, 3H, J ~ 5 Hz), 4.52 (t, 2H, J ~ 7 Hz), 7.39 (q, 1NH, J ~ 5 Hz), 8.07 (s, 1H), 12.81 (s, NH); uv (0.1*N* hydrochloric acid): λ max 247 nm (ε 12,500), 289 nm (ε 14,500); (0.1*N* sodium hydroxide): 253 nm (ε 17,500).

Anal. Calcd. for $C_{10}H_{15}N_5O \times \frac{1}{2} H_2O$: C, 43.14; H, 5.79; N, 25.15; S, 23.03. Found: C, 43.06; H, 5.60; N, 24.96; S, 23.08.

The mother liquor was concentrated under vacuum and added to a column of 500 g of silica gel in methylene chloride. Elution of the column with 5% ethanol in methylene chloride effected purification of **13c**. Recrystallization from methylene chloride/ether gave 1.6 g (18%) mp 243-245° of **13c**; nmr (DMSO-d_6): δ 1.10 (t, 3H, J ~ 7 Hz), 2.42 (q, 2H, J ~ 7 Hz), 2.85 (t, 2H, J ~ 7 Hz), 2.99 (d, 3H, J ~ 5 Hz), 3.30 (d, 3H, J ~ 5 Hz), 4.60 (t, 2H, J ~ 7 Hz), 7.52 (q, NH, J ~ 5 Hz), 8.34 (s, 1H), 12.70 (d, NH, J ~ 5 Hz).

Anal. Calcd. for $C_{12}H_{18}N_6S_3$: C, 42.10; H, 5.30; N, 24.55. Found: C, 41.99; H, 5.30; N, 24.85.

Method B.

A solution of **13c** in ethanol containing 2 drops of 4*N* hydrochloric acid was refluxed for 10 minutes. The solution was neutralized with diluted ammonium hydroxide solution, and the precipitated solid was collected by filtration. The tlc, mp and ir characteristics were identical to those obtained by Method A.

4-Amino-1-nonyl-5-cyanoimidazole (**3d**) and 5-Amino-1-nonyl-4-cyanoimidazole (**4d**).

A mixture of 10.8 g (0.1 mole) of 4(5)-amino 5(4)-cyanoimidazole (**2**), 16.6 g (0.12 mole) of potassium carbonate and 24.8 g (0.12 mole) of 1-bromononane in 120 mℓ of THF/DMF (1:1) was heated under reflux for 4 hours. The insoluble product was filtered off and washed with DMF. The filtrate was concentrated and diluted with 500 mℓ of water. The precipitated solid was removed by filtration and the wet cake was dissolved in methylene chloride. The solution was dried over sodium sulfate and the solvent was evaporated. Addition of ethanol gave a white crystalline solid. On repeated crystallization from ethanol 2 g of pure **3d** was obtained mp 97-98°; nmr (DMSO-d_6): δ 1.85 (t, 3H, J ~ 7 Hz), 1.2-1.4 (m, 12H), 1.67 (q, 2H, J ~ 5 Hz), 3.85 (t, 2H, J ~ 5 Hz), 5.85 (s, NH_2), 7.48 (s, 1H).

Anal. Calcd. for $C_{13}H_{22}N_4$: C, 66.63; H, 9.46; N, 23.91. Found: C, 66.58; H, 9.45; N, 23.98.

Efforts to obtain more pure **3d** or pure **4d** by crystallization were unsuccessful. The mixture was separated by passing it through a silica gel column. Elution with ethyl acetate yielded 4.24 g (18%) mp 156-157° of **4d** followed by 3.93 g of **3d**; nmr (DMSO-d_6): of **4d**, δ 1.85 (t, 3H, J ~ 5 Hz), 1.1-1.3 (m, 12H), 2.59 (q, 2H, J ~ 5 Hz), 3.75 (t, 2H, J ~ 5 Hz), 6.18 (s, NH_2), 7.18 (s, 1H).

Anal. Calcd. for $C_{13}H_{22}N_4$: C, 66.63; H, 9.46; N, 23.91. Found: C, 66.57; H, 9.41; N, 23.91.

6-Methylamino-2-methyldithiocarbamyl-7-nonylpurine (**13d**).

A mixture of 2 g (8.9 mmoles) of **3d** and 3.6 g (50 mmoles) of methyl isothiocyanate in 25 mℓ of pyridine was heated at reflux for 1 hour. The solution was concentrated and addition of methylene chloride gave a precipitate which was filtered off. The product was purified by passing through a silica gel column. Crystallization from methanol/ether afforded 1.4 g (43%) mp 244-245° of **13d**; nmr (DMSO-d_6): δ 0.85 (t, 3H, J ~ 5 Hz), 1.25 (s, 12H), 1.67 (m, 2H), 3.00 (d, 3H, J ~ 5 Hz), 3.30 (d, 3H, J ~ 5 Hz), 4.40 (t, 2H, J ~ 5 Hz), 7.40 (d, NH, J ~ 5 Hz), 8.30 (s, 1H), 12.68 (d, 2NH, J ~ 5 Hz); ms: (300°) m/e 307 ($M^+ - CH_3NCS$).

Anal. Calcd. for $C_{17}H_{26}N_6S_2$: C, 53.66; H, 7.42; N, 22.09; S, 16.28. Found: C, 53.97; H, 7.41; N, 22.10; S, 16.57.

6-Methylamino-7-nonyl-2-thioxopurine (**11d**).

A solution of 2 g (5.2 mmoles) of **13d** in 100 mℓ of ethanol was allowed to stand for one week. The precipitated solid was collected by filtration and recrystallized from methanol/ether to give 0.9 g (56%), mp 242-243° of **11d**; nmr (DMSO-d_6): δ 0.85 (t, 3H, J ~ 5 Hz), 1.20 (br s, 12H), 1.64 (m, 2H), 2.98 (d, 3H, J ~ 4 Hz), 4.30 (t, 2H, J ~ 4 Hz), 7.30 (d, NH, J ~ 4 Hz), 8.05 (s, 1H), 12.85 (s, NH); uv (0.1*N* hydrochloric acid): λ max 246 nm (ε 3,350), 287 nm (ε 3,470); (0.1*N* sodium hydroxide): 252 nm (ε 22,200); ms: (300°) m/e 307 (M^+).

Anal. Calcd. for $C_{15}H_{25}N_5S$: C, 58.61; H, 8.20; N, 22.79; S, 10.41. Found: C, 58.82; H, 8.31; N, 22.25; S, 10.66.

4-Amino-1-cyclohexylthioethyl-5-cyanoimidazole (**3e**) and 5-Amino-1-cyclohexylthioethyl-4-cyanoimidazole (**4e**).

A mixture of 10.8 g (0.1 mmole) of 4(5)-amino-5(4)-cyanoimidazole (**2**) 13.8 g (0.1 mole) of potassium carbonate and 20 g (0.11 mole) of 2-chloroethyl cyclohexyl sulfide in 50 mℓ of THF and 50 mℓ of DMF was heated at reflux for 4 hours. After cooling to room temperature, 200 mℓ of water was added and the resulting mixture was stirred overnight. The precipitated crystalline product was collected, washed thoroughly with water, dried in air, and recrystallized several times from toluene/ethanol to yield 9.96 g (40%) of **4e**, mp 189-191°; nmr (DMSO-d_6): δ 1.1-1.9 (m, 10H), 2.62 (m, 1H), 2.78 (t, 2H, J ~ 6 Hz), 3.97 (t, 2H, J ~ 6 Hz), 6.20 (s, 2NH), 7.20 (s, 1H).

Anal. Calcd. for $C_{12}H_{18}N_4S$: C, 57.58; H, 7.25; N, 22.39; S, 12.78. Found: C, 57.32; H, 7.12; N, 22.37; S, 13.03.

The mother liquors of **4e** were added to a column of silica gel in toluene. Successive elution of the column with toluene, followed by a toluene/ethanol mixture (9:1) gave **3e**. Recrystallization from toluene gave 5.9 g (24%) of **3e**, mp 109-110°; nmr (DMSO-d_6): δ 1.15-1.95 (m, 10H), 2.60 (m, 1H), 2.83 (t, 2H, J ~ 6 Hz), 4.00 (t, 2H, J ~ 6 Hz), 5.88 (s, 2NH), 7.50 (s, 1H).

Anal. Calcd. for $C_{12}H_{18}N_4S$: C, 57.58; H, 7.25; N, 22.39; S, 12.78. Found: C, 57.68; H, 7.03; N, 22.26; S, 12.93.

7-Cyclohexylthioethyl-6-methylamino-2-methyldithiocarbamylpurine (**13e**).

A mixture of 4 g (16 mmoles) of 4-amino-1-cyclohexylthioethyl-5-cyanoimidazole (**3e**) and 6.0 g (82 mmoles) of methyl isothiocyanate in 50 mℓ of pyridine was heated under reflux for 1 hour. After cooling, the mixture was poured into 500 mℓ of water, and stirred overnight. The precipitated solid was collected, washed with water and dried. The crude product was purified by passing it through a column packed with silica gel. Elution with methylene chloride afforded 2.6 g (41%) mp 255-257° of **13e**; nmr (DMSO-d_6): δ 1.0-2.0 (m, 11H), 2.82 (t, 2H, J ~ 3 Hz), 3.00 (d, 3H, J ~ 2.5 Hz), 3.25 (s, H, J ~ 2.5 Hz), 4.60 (t, 2H, J ~ 3 Hz), 7.42 (q, NH, J ~ 3 Hz), 8.30 (s, 1H), 12.8 (q, NH, J ~ 3 Hz).

Anal. Calcd. for $C_{16}H_{24}N_6S_3$: C, 48.48; H, 6.10; N, 21.20; S, 24.22. Found: C, 48.76; H, 6.05; N, 21.27; S, 23.49.

7-Cyclohexylthioethyl-6-methylamino-2-thioxopurine (**11e**).

A mixture of 0.8 g (1.58 mmoles) of **13e** in 100 mℓ of methanol containing 4 drops of a 4*N* hydrochloric acid solution was stirred and heated to reflux for 45 minutes. After cooling, the mixture was adjusted to neutral *p*H with concentrated ammonium hydroxide. The precipitated product was filtered off and recrystallized from methanol to give 0.5 g (98%) mp 266-267° of **11e**; nmr (DMSO-d_6): δ 1.1-1.85 (m, 11H), 2.82 (t, 2H, J ~ 5 Hz), 3.00 (d, 3H, J ~ 5 Hz), 4.50 (t, 2H, J ~ 5 Hz), 7.38 (d, NH, J ~ 5 Hz), 8.05 (s, 1H); uv (0.1*N* hydrochloric acid): 245 nm (ε 13,400), 287 nm (ε 15,300); (0.1*N* sodium hydroxide): 253 nm (ε 21,000).

Anal. Calcd. for $C_{14}H_{21}N_5S_2$: C, 52.00; H, 6.55; N, 21.66; S, 19.79. Found: C, 51.97; N, 6.57; N, 21.34; S, 19.87.

4-Amino-1-(*p*-chlorophenylthioethyl)-5-cyanoimidazole (**3f**), and 5-Amino-1-(*p*-chlorophenylthioethyl)-4-cyanoimidazole (**4f**).

A mixture of 20.7 g (0.1 mole) of 2-chloroethyl *p*-chlorophenyl sulfide, 10.8 g (0.1 mole) of 5(4)-amino-4(5)-cyanoimidazole (**2**), 13.8 g (0.1 mole) of potassium carbonate in 50 mℓ of DMF and 50 mℓ of THF was stirred at reflux for 4 days. The solvent was evaporated and the resin stirred with 0.5 ℓ of water. The insoluble precipitate was filtered, washed with water and dried at 60°. To the mixture of isomers was added 0.5 ℓ of methlene chloride. The solution was heated to reflux and filtered hot. The filtrate was concentrated to 100 mℓ. Addition of ether gave 5.6 g (20%) mp 135-137° of **3f**; nmr (DMSO-d_6): δ 3.35 (t, 2H, J ~ 4 Hz), 4.06 (t, 2H, J ~ 4 Hz), 5.90 (s, NH_2), 7.40 (s, 4H), 7.48 (s, 1H).

Anal. Calcd. for $C_{12}H_{11}ClN_4S$: C, 51.70; H, 3.98; Cℓ, 12.72; N, 20.10; S, 11.50. Found: C, 51.52; H , 4.01; Cℓ, 12.41; N, 20.25; S, 11.76.

The methylene chloride insoluble fraction was crystallized from hot ethanol to give 2.8 g (10%) mp 213-215° of **4f**; nmr (DMSO-d_6): δ 3.30 (t, 2H, J ~ 4 Hz), 4.00 (t, 2H, J ~ 4 Hz), 6.22 (s, NH_2), 7.15 (s, 1H), 7.37 (s, 4H).

Anal. Calcd. for $C_{12}H_{11}ClN_4S$: C, 51.70; H, 3.98; Cℓ, 12.72; N, 20.10; S, 11.50. Found: C, 51.56; H, 3.99; Cℓ, 12.47; N, 20.29; S, 11.70.

7-(*p*-Chlorophenyl)thioethyl-6-methylamino-2-methyldithiocarbamylpurine (**13f**).

A mixture of 2.78 g (10 mmoles) of **3f**, and 2.92 g (40 mmoles) of methyl isothiocyanate in 25 mℓ of pyridine was heated under reflux for 2 hours and then evaporated to dryness under reduced pressure. Addition of 100 mℓ of water to the residue resulted in the separation of a solid. After filtration, the crude product was purified by crystallization from methylene chloride/ethanol to give 2 g (66%) mp 254-256° of **13f**; nmr (DMSO-d_6): δ 3.00 (d, 3H, J ~ 5 Hz), 3.30 (d, 3H, J ~ 5 Hz), 3.40 (t, 2H, J ~ 5 Hz), 4.65 (t, 2H, J ~ 5 Hz), 7.10 (br s, 4H), 7.4 (d, NH, J ~ 5 Hz), 8.15 (s, 1H), 12.8 (d, NH).

Anal. Calcd. for $C_{16}H_{17}ClN_6S_3$: C, 45.22; H, 4.03; N, 19.77; Cℓ, 8.34; S, 22.63. Found: C, 45.20; H, 4.08; N, 19.60; Cℓ, 8.85; S, 22.37.

7-(*p*-Chlorophenyl)thioethyl-6-methylamino-2-thioxopurine (**11f**).

A solution of 400 mg (0.94 mmole) of **13f** in 100 mℓ of methanol containing 5 drops of a 4*N* hydrochloric acid solution was heated under reflux for 1 hour. After neutralizing with concentrated ammonium hydroxide, the solution was concentrated under reduced pressure to 30 mℓ. The insoluble product was filtered and recrystallized from methanol. The yield of **11f** was 0.3 g (91%) mp 265-266°; nmr (DMSO-d_6): δ 2.90 (d, 3H, J ~ 3 Hz), 3.40 (t, 2H, J ~ 3 Hz), 4.60 (t, 2H, J ~ 3 Hz), 7.32 (s, 4H), 7.38 (d, NH), 7.95 (s, 1H), 12.85 (s, NH); uv (0.1*N* hydrochloric acid): λ max 254 nm (ε 15,300), 289 nm (ε 19,600); (0.1*N* sodium hydroxide): 254 nm (ε 24,400).

Anal. Calcd. for $C_{14}H_{14}ClN_5S_2$: C, 47.79; H, 4.01; N, 19.90; S, 18.22; Cℓ, 10.07. Found: C, 47.77; H, 4.02; N, 19.93; S, 18.49; Cℓ, 9.77.

4-Amino-1-[3-[4-(*p*-chlorobenzyl)piperazinyl]propyl]-5-cyanoimidazole (**3g**) and 5-Amino-1-[3-[4-(*p*-chlorobenzyl)piperazinyl]propyl]-5-cyanoimidazole (**4g**).

A suspension of 10.8 g (0.1 mole) of 4(5)-amino-5(4)-cyanoimidazole (**2**), 13.8 (0.1 mole) of potassium carbonate and 32.0 g (0.11 mole) of 1-(3-chloropropyl)-4-(4-chlorobenzyl)piperazine in 30 mℓ of DMF and 50 mℓ of THF was heated to reflux for 72 hours. The solvent was evaporated and the residue was stirred with 200 mℓ of methylene chloride for 12 hours. The insoluble product was filtered and washed with methylene chloride. The methylene chloride insoluble fraction was extracted with hot ethanol. On cooling, crystals formed which were filtered and recrystallized from ethnaol to yield 8.0 g (22%) mp 212-213° of **4g**; nmr (DMSO-d_6): δ 1.6-2.5 (m, 12H), 3.45 (s, 2H), 3.80 (t, 2H, J ~ 6 Hz), 6.2 (s, NH_2), 7.20 (s, 1H), 7.36 (s, 4H).

Anal. Calcd. for $C_{18}H_{23}ClN_6$: C, 60.24; H, 6.46; Cℓ, 9.88; N, 23.42. Found: C, 60.26; H, 6.63; Cℓ, 9.67; N, 23.41.

The above methylene chloride soluble part was worked up as follows: The solvent was evaporated and ether was added to give crude **3g**. Recrystallization from methanol, then from methylene chloride/ether gave 12.0 g (33%) of pure **3g**, mp 136-138°; nmr (DMSO-d_6): δ 1.6-2.5 (m, 12H), 3.45 (s, 2H), 3.90 (t, 2H, J ~ 6 Hz), 5.80 (s, NH_2), 7.30 (s, 4H), 7.42 (s, 1H).

Anal. Calcd. for $C_{18}H_{23}ClN_6$: C, 60.24; H, 6.46; Cℓ, 9.88; N, 23.42. Found: C, 60.16; H, 6.54; Cℓ, 10.01; N, 23.12.

7-[3-[4-(*p*-Chlorobenzyl)piperazinyl]propyl]-6-methylamino-2-methyldithiocarbamylpurine (**13g**) and 7-[3-[4-(*p*-Chlorobenzyl)piperazinyl]propyl]-6-methylamino-2-thioxopurine (**11g**).

A mixture of 1.9 g (5.3 mmoles) of 4-amino-1-[3-[4-(*p*-chlorobenzyl)-piperazinyl]propyl]-5-cyanoimidazole (**3g**) and 3.0 g (40 mmoles) of methyl isothiocyanate in 50 ml of pyridine was heated at reflux for 1.5 hours. The solvent was evaporated under reduced pressure. Addition of

water to the residue resulted in the separation of a mixture of **13g** and **11g**. The products were separated on a silica gel column. Compound **13g** was eluted with methylene chloride/ethanol (9:1) and was crystallized from methylene chloride/ether to yield 1.0 g (74%) mp 234-237°; nmr (DMSO-d_6): δ 1.85 (t, 2H, J ~ 5 Hz), 2.15-2.3 (m, 10H), 3.0 (d, 3H, J ~ 5 Hz), 3.28 (d, 3H, J ~ 5 Hz), 3.40 (s, 2H), 4.40 (t, 2H, J ~ 5 Hz), 7.35 (q, 4H), 7.50 (d, 1H, J ~ 5 Hz), 8.27 (s, 1H), 12.75 (d, NH, J ~ 5 Hz).

Anal. Calcd. for $C_{22}H_{29}ClN_8S_2$: C, 52.31; H, 5.79; Cl, 7.02; N, 22.18; S, 12.70. Found: C, 52.08; H, 5.73; Cl, 7.47; N, 21.94; S, 12.30.

Compound **11g** was eluted with methylene chloride/ethanol/ammonium hydroxide (79:20:1). Crystallization from ethanol/methylene chloride gave 0.2 g (11%) mp 234-238°; nmr (DMSO-d_6): δ 1.82 (t, 2H, J ~ 5 Hz), 2.2-2.3 (m, 10H), 2.95 (d, 3H, J ~ 5 Hz), 3.42 (s, 2H), 4.35 (s, 2H, J ~ 5 Hz), 7.25-7.40 (m, 5H), 8.00 (s, 1H), 12.85 (s, NH); uv (0.1*N* hydrochloric acid): λ max 247 nm (ε 33,000), 288 nm (ε 35,000); (0.1*N* sodium hydroxide): 253.7 nm (ε 33,000).

Anal. Calcd. for $C_{20}H_{26}ClN_7S$: C, 55.60; H, 6.07; Cl, 8.21; N, 22.70; S, 7.42. Found: C, 55.49; H, 6.15; Cl, 8.05; N, 22.65; S, 7.59.

4-Amino-1-methoxyethyl-5-cyanoimidazole (**3h**) and 5-Amino-1-methoxyethyl-4-cyanoimidazole (**4h**).

A mixture of 10.8 g (0.1 mole) of 4(5)-amino-5(4)-cyanoimidazole (**2**), 13.8 g (0.1 mole) of potassium carbonate and 9.5 g (0.1 mole) of 2-chloroethylmethyl ether in 30 mℓ of DMF and 50 mℓ of THF was heated under reflux for 18 hours and then evaporated under reduced pressure. The residue was extracted with ethanol. The ethanol soluble part was chromatographed on a silica gel column. Successive elution of the column with toluene, 2% ethanol in toluene and 5% ethanol in toluene effected separation of **3h** and **4h**. The fractions were monitored by tlc. Compound **3h** was eluted first with toluene, then was crystallized from ethanol to give 5.5 g (33%) of **3h**, mp 100-101°; nmr (DMSO-d_6): δ 3.25 (s, 3H), 3.56 (t, 2H, J ~ 5 Hz), 4.02 (t, 2H, J ~ 5 Hz), 5.85 (s, NH_2), 7.45 (s, NH).

Anal. Calcd. for $C_7H_{10}N_4O$: C, 50.59; H, 6.07; N, 33.72. Found: C, 50.52; H, 6.08; N, 33.77.

Compound **4h** was eluted with toluene/ethanol 9:1. After evaporation of the solvent and addition of ether 8.9 g (49%) of **4h** was obtained mp 115-116°; nmr (DMSO-d_6): δ 3.25 (s, 3H), 3.52 (t, 2H, J ~ 5 Hz), 3.95 (t, 2H, J ~ 5 Hz), 6.15 (s, NH_2), 7.12 (s, 1H).

Anal. Calcd. for $C_7H_{10}N_4O$: C, 50.59; H, 6.07; N, 33.72. Found: C, 50.51; H, 5.90; N, 33.73.

7-Methoxyethyl-6-methylamino-2-methyldithiocarbamylpurine (**13h**).

A mixture of 3.32 g (20 mmoles) of **3h** and 3.65 g (50 mmoles) of methyl isothiocyanate in 25 mℓ of pyridine was heated under reflux for 2 hours and then evaporated under a vacuum to dryness. The residue was dissolved in methanol and passed through a silica gel column. Elution with methylene chloride containing 2% ethanol gave 1.2 g (19%) of **13h**, mp 242-244°; nmr (deuteriochloroform): δ 3.05 (d, 3H, J ~ 5 Hz), 3.40 (d, 3H, J ~ 5 Hz), 3.42 (s, 3H), 3.80 (t, 2H, J ~ 5 Hz), 4.40 (t, 2H, J ~ 5 Hz), 6.97 (q, NH, J ~ 5 Hz), 7.80 (s, 1H), 12.80 (q, NH, J ~ 5 Hz).

Anal. Calcd. for $C_{11}H_{19}N_6S_2O$: C, 42.29; H, 5.16; N, 26.90; S, 20.53. Found: C, 42.08; H, 5.20; N, 26.92; S, 20.49.

7-Methoxyethyl-6-methylamino-2-thioxopurine (**11h**).

A solution of 510 mg (1.63 mmoles) of **13h** in 50 mℓ of methanol containing 4 drops of 4*N* hydrochloric acid solution was heated under reflux for 4 hours. The solution was concentrated to 20 mℓ and was neutralized by the addition of ammonium hydroxide. The precipitated solid was collected by filtration. Recrystallization from methanol gave 200 mg (51%) mp 234-237° of **11h**; nmr (DMSO-d_6): δ 2.97 (d, 3H, J ~ 3 Hz), 3.20 (s, 3H), 3.60 (t, 2H, J ~ 3 Hz), 4.50 (t, 2H, J ~ 3 Hz), 7.36 (q, NH, J ~ 3 Hz), 7.98 (s, 1H), 12-13 (br s, NH); uv (0.1*N* hydrochloric acid): λ max 245 nm (ε 19,000), 287.5 nm (ε 20,000); (0.1*N* sodium hydroxide): 253 nm (ε 21,000).

Anal. Calcd. for $C_9H_{13}N_5S$: C, 45.17; H, 5.48; N, 29.27; S, 13.40. Found: C, 45.02; H, 5.28; N, 28.77; S, 13.55.

4-Amino-1-(*p*-chlorobenzyl)-5-cyanoimidazole (**3i**), 5-Amino-1-(*p*-chlorobenzyl)-4-cyanoimidazole (**4i**) and 1-(*p*-Chlorobenzyl)-4-(*p*-chlorobenzylamino)-5-cyanoimidazole (**5i**).

A mixture of 28 g (0.26 mole) of **2**, 35.9 g (0.26 mole) of potassium carbonate and 41.8 g (0.26 mole) of *p*-chlorobenzyl chloride in 50 mℓ of THF and 100 mℓ of DMF was stirred at room temperature for three days. After removal of the insoluble inorganic matter by filtration, the filtrate was concentrated to a small volume and ether was added to give 15 g (25%) of **3i**). An analytical sample was obtained by recrystallization from methanol, mp 190-192°; nmr (DMSO-d_6): δ 5.12 (s, 2H), 5.96 (s, NH_2), 7.25 (d, 2H, J ~ 8 Hz), 7.46 (d, 2H, J ~ 8 Hz), 7.70 (s, 1H).

Anal. Calcd. for $C_{11}H_9ClN_4$: C, 56.78; H, 3.90; Cl, 15.24; N, 24.08. Found: C, 56.81; H, 3.94; Cl, 15.31; N, 24.00.

The mother liquors of **3i** were concentrated to a gum which gave crystals from methanol upon cooling. Two recrystallizations from methanol gave 7.2 g (12%) of **4i**, mp 192-194°; nmr (DMSO-d_6): δ 5.10 (s, 2H), 6.30 (s, NH_2), 7.22 (d, 2H, J ~ 8 Hz), 7.32 (s, 1H), 7.42 (d, 2H, J ~ 8 Hz).

Anal. Calcd. for $C_{11}H_9ClN_4$: C, 56.78; H, 3.90; Cl, 15.24;N, 24.08. Found: C, 56.39; H, 3.97; Cl, 15.34; N, 23.66.

The filtrate from the collection of **4i** was concentrated under vacuum to an oil. The oil was purified by passing it through a silica gel column. Successive elution with methylene chloride and then methylene chloride/2% ethanol gave 1.5 (1.6%) mp 120-122° of **5i**; nmr (DMSO-d_6): δ 4.35 (d, 2H, J ~ 7 Hz), 5.12 (s, 2H), 7.10 (t, NH, J ~ 7 Hz), 7.2-7.5 (m, 8H), 7.75 (s, 1H).

Anal. Calcd. for $C_{18}H_{14}Cl_2N_4$: C, 60.52; H, 3.95; Cl, 19.85; N, 15.68. Found: C, 60.73; H, 3.95; Cl, 19.80; N, 15.71.

7-(*p*-Chlorobenzyl)-6-methylamino-2-thioxopurine (**11i**).

A mixture of 2.35 g (10 mmoles) of **3i** and 3.65 g (50 mmoles) of methyl isothiocyanate in 30 mℓ of pyridine was heated under reflux for one hour. After cooling the mixture to room temperature, methylene chloride was added. The precipitate which formed was filtered, washed with ether and air dried. The product was dissolved in 75 mℓ of methanol, and acidified with a 1*N* hydrochloric acid solution and heated under reflux for 0.5 hour. The crystalline product obtained was filtered and recrystallized with DMF, and dried at 90° in a vacuum to give 1.0 g (33%) mp 275-276° of **11i**; nmr (DMSO-d_6): δ 2.90 (d, 3H, J ~ 12 Hz), 5.65 (s, 2H), 7.15 (d, 2H, J ~ 17 Hz), 7.30 (d, NH, J ~ 12 Hz), 7.45 (d, 2H, J ~ 17 Hz), 8.20 (s, 1H), 12.95 (s, NH); uv (0.1*N* hydrochloric acid): λ max 246 nm (ε 13,200), 287.5 nm (ε 14,700); (0.1*N* sodium hydroxide): 253 nm (ε 33,300).

Anal. Calcd. for $C_{13}H_{12}ClN_5S$: C, 51.06; H, 3.96; Cl, 11.59; N, 22.90; S, 10.48. Found: C, 50.54; H, 3.86; Cl, 11.82; N, 22.86; S, 10.60.

4-Amino-1-(*N,N*-dimethylaminoethyl)-5-cyanoimidazole (**3j**) and 5-Amino-1-(*N,N*-dimethylaminoethyl)-4-cyanoimidazole (**4j**).

A mixture of 54 g (0.5 mole) of 4(5)-amino-5(4)-cyanoimidazole (**2**), 138 g (1.0 mole) of potassium carbonate and 72.0 g (0.5 mole) of 2-dimethylaminoethyl chloride hydrochloride in 200 mℓ of DMF and 250 mℓ of THF was stirred at room temperature for 4 days, then heated at reflux for 8 hours. The insoluble product was filtered off and washed with ethanol. The filtrate was concentrated to dryness and the residue purified on a silica gel column. Successive elution with 2%, increasing to 10%, ethanol in methylene chloride effected separation of **3j** and **4j**. The fractions were monitored by tlc.

Compound **4j** eluted first and, after crystallization from ethanol 12.0 g (13%) mp 163-165° was obtained; nmr (DMSO-d_6): δ 2.17 (s, 6H), 2.48 (t, 2H, J ~ 4 Hz), 3.85 (t, 2H, J ~ 4 Hz), 6.25 (s, NH_2), 7.15 (s, 1H).

Anal. Calcd. for $C_8H_{13}N_5$: C, 53.61; H, 7.31; N, 39.08. Found: C, 53.59; H, 7.35; N, 39.09.

Compound **3j** was eluted next. After crystallization from methylene chloride and addition of some ether 6.0 g (6.7%) was obtained, mp 100-102°; nmr (DMSO-d_6): δ 2.17 (s, 6H), 2.55 (t, 2H, J ~ 4 Hz), 3.95 (t, 2H, J ~ 4 Hz), 5.82 (s, NH_2), 7.47 (s, 1H).

Anal. Calcd. for $C_8H_{13}N_5$: C, 53.61; H, 7.31; N, 39.08. Found: C, 53.62; H, 7.34; N, 39.29.

6-Imino-7-(*N,N*-dimethylaminoethyl)-1-phenyl-2-thioxopurine Hydrochloride (**10j**).

A mixture of 1.79 g (10 mmoles) of **3j** and 4.05 g of phenyl isothiocyanate (30 mmoles) in 25 mℓ of pyridine was heated under reflux for 2 hours. After cooling the mixture the solvent was evaporated under reduced pressure. Addition of methylene chloride gave a precipitate which was filtered and washed with ether. The free base of **11j** was suspended in 100 mℓ of methanol; addition of anhydrous hydrogen chloride gave a thick crystalline product. An analytical sample was obtained by recrystallization from hot methanol to which water was added until a clear solution resulted. On cooling 2.5 g (71%) mp 275-276° of **10j** was obtained; nmr (DMSO-d_6): δ 2.85 (s, 6H), 3.62 (t, 2H, J ~ 3 Hz), 4.80 (t, 2H, J ~ 3 Hz), 7.2-7.5 (m, 5H), 8.10 (s, 1H); uv (0.1*N* hydrochloric acid): λ max 250 nm (ε 14,700), 284 nm (ε 21,600); (0.1*N* sodium hydroxide): 237.5 nm (ε 19,700), 275 nm (ε 17,100).

Anal. Calcd. for $C_{15}H_{18}N_6S \times HCl$: C, 51.35; H, 5.46; N, 23.95; S, 9.14; Cℓ, 10.10. Found: C, 51.07; H, 5.31; N, 23.62; S, 9.13; Cℓ, 9.92.

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REFERENCES AND NOTES

[1] R. J. Quinn, R. P. Gregson, A. F. Cook and R. T. Bartlett, *Tetrahedron Letters*, **21**, 567 (1980).

[2] F. A. Fuhrman, G. J. Fuhrman, Y. H. Kim, L. A. Pavelka and H. S. Mosher, *Science*, **207**, 193 (1980).

[3] K. Grozinger, K. Freter, P. Farina and A. Galdczuk, *Eur. J. Med. Chem.*, **18**, 221 (1983).

[4] A. F. Cook, R. T. Bartlett, R. P. Gregson and R. J. Quinn, *J. Org. Chem.*, **45**, 4020 (1980).

[5] Y. H. Kim, R. J. Nachman, L. Pavelka, H. S. Mosher, F. A. Fuhrman and G. J. Fuhrman, *J. Nat. Prod.* (Lloydia) **44**, 206, (1981).

[6] J. Baird-Lambert, J. F. Marwood, L. P. Davies and K. M. Taylor, *Life Sci.*, **26**, 1069 (1980).

[7] L. P. Davies, K. M. Taylor, R. P. Gregson and R. J. Quinn, *Life Sci.*, **26**, 1079 (1980).

[8] L. P. Davies, A. F. Cook, M. S. Poonian and K. M. Taylor, *Life Sci.*, **26**, 1089 (1980).

[9] R. T. Bartlett, A. F. Cook, M. J. Holman, W. W. McComas, E. F. Nowoswait and M. S. Poonian, *J. Med. Chem.*, **24**, 947, (1981).

[10] A commercial sample of 1-methyladenine was obtained from Sigma Chem. Co.

[11] E. C. Taylor and R. V. Ravindranathan, *J. Org. Chem.*, **27**, 2622, (1962).

[12] A. Albert and C. J. Lin, *J. Chem. Soc., Perkin Trans. I.*, 210 (1977).

[13] F. Nygjerd and E. Sletten, *Acta Chem. Scand.*, **27**, 2902 (1973).

[14] U. Thewalt and C. E. Bugg, *Acta Cryst.*, **B28**, 1767, (1972).

[15] T. F. Lai and R. E. Marsh, *Acta Cryst.*, **B28**, 1982 (1972).

[16] P. L. Johnson, C. A. Maier and I. C. Paul, *J. Am. Chem. Soc.*, **95**, 5370 (1973).

[17] D. Voet, A. Rich, "Progress in Nucleic Acid Research and Molecular Biology", Vol 10, J. N. Davidson and W. E. Cohn, eds, Academic Press, New York 1970, pp 183-265.

[18] All crystallographic calculations were carried out on a VAX 11/780 computer. The principal programs used were: FMLS, anisotropic full-matrix least-squares refinement, P. L. Ganzel, R. A. Sparks and K. N. Trueblood, UCLA; modified by A. T. McPhail, Duke University; MULTAN 80, for description see G. Germain, P. Main and M. M. Woolfson, *Acta Cryst.*, **B26**, 274 1970; ORTEP, crystallographic illustration programs, C. K. Johnson, Oak Ridge, ORNL-3794.