Steroid Derivatives of Purine-6(1*H*)-thione (1a-c)

F. I. Carroll, Abraham Philip, Anna M. Ferguson and Monroe E. Wall

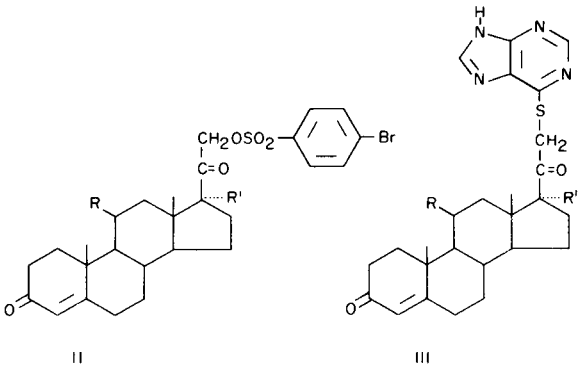
The Chemistry and Life Sciences Laboratory, Research Triangle Institute

The products obtained as a result of the alkylation of purine-6(1*H*)-thione, and 6-alkylthiopurines with steroidal-21-(*p*-bromobenzenesulfonates) (II) and 3-methoxy-16α-bromoestra-1,3,5(10)-triene-17-one (IV) is reported. The ratio of 9-alkylated to 7-alkylated purine in the alkylation of 6-methylthiopurine (VI) is presented. The use of the *S*-diphenylmethylprotecting group in the syntheses of sensitive 9-steroidal-9*H*-purine-6(1*H*)-thiones is discussed.

The anticancer agent purine-6(1*H*)-thione (1, 6-mercaptopurine) is ineffective against leukemia L1210 implanted intracerebrally in mice (2). Since steroid molecules with appropriate substituents are known to penetrate to all body areas, including the brain and other portions of the central nervous system, it became of interest to study the synthesis of some steroid derivatives of purine-6(1*H*)-thione that might penetrate the blood-brain barrier (3,4).

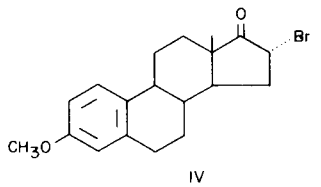
6-Alkylthiopurines have usually been prepared by the alkaline catalyzed reaction of 1 with the desired alkyl halide (5). When 1 was treated with deoxycorticosterone brosylate (IIa) in *N*,*N*-dimethylformamide (DMF) containing anhydrous potassium carbonate, 92% of 21-(purin-6-ylthio)pregn-4-ene-3,20-dione (IIIa), which gave one spot on thin layer chromatograms (tlc) (6), was obtained. The infrared spectrum showed absorption at 3108 (NH), 1717 (20 C=O), and 1665 cm^{-1} (3 C=O) and the ultraviolet spectrum showed a double peak due to the purine ring system at λ max (methanol) 284 ($\epsilon \times 10^{-1}$ = 16.8) and 281 mμ (17.2) which gave a bathochromic shift to 288 mμ and coalesced to one peak in both acid and alkaline medium. An absorption peak was also present at 240 mμ (18.6), which was due to the Δ^4-3-ketone function of the steroid moiety. The nmr spectrum showed two singlets at δ 8.70 and 8.53 ppm for the purine 2- and 8-hydrogens in addition to the typical steroid resonances. The results obtained with other steroidal brosylates and steroidal bromides are given in Table I.

The alkylation of 6-alkylthiopurines would be expected to give a mixture of 9-alkyl- and 7-alkyl-6-alkylthiopurines.

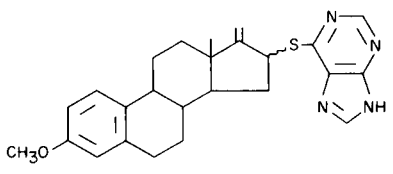


II III

where a, R = R' = H
b, R = R' = OH
c, R = O, R' = OH



IV



V

TABLE I

6-Steroidalthiopurines

Compound (a)	Yield (b) %	M.P. °C	Ultraviolet abs. (c) λ max (methanol)	ε x 10^{-3}	NMR Resonances $(CD_3)_2SO$, δ Purine-2H	Purine-8H	Other Resonances	Molecular Formula	Calcd. % (Found %) C	H	N	S
IIIa (d)	92	212-215	284	16.8	8.70	8.53	0.68 (18-CH_3)	$C_{26}H_{32}N_4O_2S$	65.29	7.31	11.28	6.46
			281	17.2			1.15 (19-CH_3)	$\cdot CH_3OH$	(65.43)	(7.53)	(11.03)	(6.49)
			240	18.6			4.36 (SCH_2CO)					
IIIb	77	238-240	286	17.7	8.75	8.50	0.88 (18-CH_3)	$C_{26}H_{32}N_4O_4S$	62.87	6.50	11.28	6.46
			282	17.7			1.43 (19-CH_3)		(62.91)	(6.50)	(11.31)	(6.68)
			241	18.2			4.37 (SCH_2CO)					
IIIc (e)	86	190-192	287	17.5	8.70	8.52	0.57 (18-CH_3)	$C_{26}H_{30}N_4O_4S$	60.91	6.29	10.93	6.26
			282	17.6			1.38 (19-CH_3)	$\cdot H_2O$	(61.05)	(6.37)	(10.67)	(6.12)
			244	19.9			4.58 (SCH_2CO)					
V (f,g)	90	188-194	287	20.1	8.80	8.55	0.93, 1.00 (18-CH_3)	$C_{24}H_{26}N_4O_2S$	66.35	5.99	12.90	7.37
			282	19.7					(66.14)	(6.10)	(12.72)	(7.25)
			217 (s)	20.9			3.73 (CH_3O)					

(a) A general procedure is given in the Experimental Section. (b) Based on pure compounds isolated. (c) (s) represents shoulder. (d) obtained as the mono-methanol solvate. The methanol could be removed at 130° but slight decomposition occured along with removal of the methanol, (e) obtained as the mono-hydrate. (f) This prosuct was obtained as a mixture of 16α- and 16β-isomers. (g) It was found that 16α-bromoestra-1,3,5(10)-triene-17-one (A) isomerized to a mixture of A and 16β-bromoestra-1,3,5(10)-triene-17-one under the conditions used for alkylation.

TABLE II

9- or 7-Steroidal-6-alkylthiopurines

Compound (a)	Yield (b) %	M.P. °C	Ultraviolet abs. (c) λ max (methanol)	ε x 10^{-3}	NMR Resonances $(CD_3)_2SO$, δ Purine-2H	Purine-8H	Other Resonances	Molecular Formula	Calcd. % (Found %) C	H	N	S
VIIa (d)	80	209-214	289	19.8	8.73	8.40	0.68 (18-CH_3)	$C_{27}H_{34}N_4O_2S$ (e)	67.76	7.16	11.71	6.70
			283	20.7			1.15 (19-CH_3)		(67.57)	(7.24)	(11.45)	(6.67)
			240	19.1			2.72 (CH_3S)					
			227	22.0			5.27 (NCH_2CO)					

TABLE II (continued)

VIIIa (f)	13	134-137	297 (s) 291 238 230 (s)	11.6 13.4 21.8 21.1	8.84	8.56	0.73 (18-CH_3) 1.15 (19-CH_3) 2.71 (CH_3S) 5.47 (NCH_2CO)	$C_{27}H_{34}N_4O_2S$	67.76 (67.61)	7.16 (7.07)	11.71 (11.52)	6.70 (6.49)
VIIb (d)	76	262 dec	289 283 240(s) 227	18.7 19.3 18.2 21.0	8.73	8.30	0.84 (18-CH_3) 1.40 (19-CH_3) 2.70 (CH_3S-) 5.25 (NCH_2CO)	$C_{27}H_{34}N_4O_4S$	63.50 (63.39)	6.71 (6.90)	10.97 (11.24)	6.28 (6.23)
VIIIb (d)	5	303-308	299 (s) 292 233- 238 (P) 244	11.2 13.6 20.1 20.9	g	g	g	$C_{27}H_{34}N_4O_4S$ ·H_2O	61.34 (61.67)	6.86 (6.73)	g	g
IX (h)	56	192-196	289 283	19.4 21.9	8.76	8.48	1.13 1.25 } (18-CH_3) 2.70 (CH_3S) 3.75 (CH_3O)	$C_{25}H_{28}N_4O_2S$	66.96 (66.71)	6.25 (6.28)	12.50 (12.39)	7.14 (7.08)
XIa (i,j)	66	146-149										
XIb (k)	80	259-261	293 286 244 224	22.6 22.7 20.3 27.3	8.75	8.43	0.88 (18-CH_3) 1.43 (19-CH_3) 5.30 (NCH_2CO) 6.83 [$SCH(Ar)_2$]	$C_{39}H_{42}N_4O_4S$	70.70 (70.60)	6.34 (6.58)	8.46 (8.63)	4.83 (4.83)
XIII (l)	54	113-115	293 286 224	16.5 16.1 22.6	8.73	8.53	1.13 1.26 } 18-CH_3 3.72 (CH_3O) 6.81 [$SCH(Ar)_2$]	$C_{37}H_{36}N_4O_2S$	74.00 (73.73)	6.00 (6.00)	9.33 (9.51)	5.43 (5.56)

(a) A general procedure is given in the Experimental Section. (b) Based on pure compound isolated. (c) (s) represents shoulder; (P) plateau. (d) Recrystallized from methanol. (e) The analytical sample was dried at 130°. (f) Recrystallized from an ether and hexane mixture. (g) Insufficient material was available to obtain a complete analysis or nmr spectrum. However, a mass spectrum showed M^+ at m/e 510.2311, calcd. for $C_{27}H_{34}N_4O_4S$, 510.2302. (h) Recrystallized from a methylene chloride and methanol mixture. (i) Taken from ref. 10. (j) Recrystallized from a chloroform and petroleum ether mixture. (k) Recrystallized from acetonitrile. (l) Recrystallized from ethanol.

TABLE III

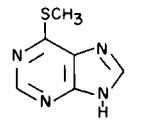
Comparison of Ultraviolet Absorption Spectra (a,b)

Compound	*p*H 1		*p*H 7		*p*H 11	
	λ max	$\epsilon \times 10^{-3}$	λ max	$\epsilon \times 10^{-3}$	λ max	$\epsilon \times 10^{-3}$
VIIa	293	20.4	292	21.1	292	20.7
	287	19.3	286	21.2	286	21.1
VIIIa	315 (c)	10.5	300 (c)	12.2	300 (c)	12.0
	303	12.9	294	13.2	294	13.0
	297	12.3				
VIIb	293	19.6	292	19.3	291	19.7
	287	18.8	286	19.3	286	19.8
VIIIb	315 (c)	6.7	302 (c)	11.9	301 (c)	10.5
	303	11.8	295	13.5	293	11.2
	297 (c)	11.4				
9-benzyl-6-benzylthiopurine (d)	295	18.9	289 (c)		289 (c,e)	
			294	20.4	294 (e)	20.5
7-benzyl-6-benzylthiopurine (f)	304	13.1	298	13.8	298	13.9
9-ethyl-6-methylthiopurine (g)	286 (h)	17.7	286	17.6	296 (i)	16.5
	290 (c,h)	17.4	290 (c)	17.1	222 (i)	10.6
7-ethyl-6-benzylthiopurine (f)	295 (c)		295	15.7	294 (e)	15.7
	302	15.2	300 (c)		300 (c,e)	
	315 (c)					

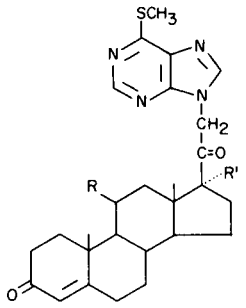
(a) Only absorption above 250 mμ is recorded. (b) λ max given in mμ. (c) Shoulder. (d) Taken from ref. 5. (e) Run at *p*H 13. (f) J. A. Montgomery and K. Henson, *J. Org. Chem.*, 26, 4469 (1961). (g) J. A. Montgomery and C. Temple, Jr., *J. Am. Chem. Soc.*, 79, 5238 (1957). (h) Run in 0.1 *N* HCl. (i) Run in 0.1 *N* NaOH.

However, in general the isolation of only the 9-isomer has been reported and no attempt has been made to determine the ratio of isomers obtained (7,8). We found that the alkylation of 6-methylthiopurine (VI) with IIa in DMF containing anhydrous potassium carbonate gave 80% of 21-[6-(methylthio)-9*H*-purin-9-yl]pregn-4-ene-3,20-dione (VIIa) and 13% of 21-[6-(methylthio)-7*H*-purine-7-yl]-pregn-4-ene-3,20-dione (VIIIa). Similarly the alkylation of VI with IIb gave 76% of VIIb and 5% of VIIIb. The structural assignments were based mainly on a comparison of the ultraviolet spectra of these compounds with those of appropriate model compounds (Table III). The 9-isomer showed higher R_f on the chromatograms and the nmr spectra showed singlets at higher field than the 7-isomer for the 2- and 8-hydrogens of the purine ring (Table II). The alkylation of VI with IV gave 56% of a product which showed one spot on tlc chromatograms and analyzed correctly for $C_{25}H_{28}N_4O_2S$. A comparison of the ultraviolet and nmr spectra of this compound with those of VIIa and VIIIa indicated that this compound was a 9-substituted purine. In the nmr spectrum the product displays two singlets at δ 1.13 and 1.25 ppm attributable to steroid 18-CH_3 protons in a ratio of 28:72. On the basis of the foregoing information the product is believed to be a mixture of 16β- and 16α-[6-(methylthio)-9*H*-purin-9-yl]-3-methoxyestra-1,3,5-triene-17-one (IX). Since we

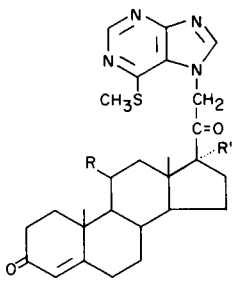
found that the 16α-bromo compound (IV) was partially isomerized to the 16β-isomer under the conditions of the reaction, the mixture IX probably results from displacement by VIa on the separate 16α- and 16β-bromoketones. Alternatively, the mixture of isomers could result by initial formation of 16β-[6-(methylthio)-9*H*-purin-9-yl]-3-methoxyestra-1,3,5-triene-17-one which partially isomerizes to the 16α-epimer in the alkaline medium. The latter explanation seems less likely since Hassner and Catsoulacos found that 16α-piperidino-17-ketones were isomerized to the 16β-epimer in the presence of excess amine (9a,b).



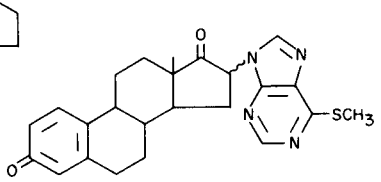
VI



VII



VIII

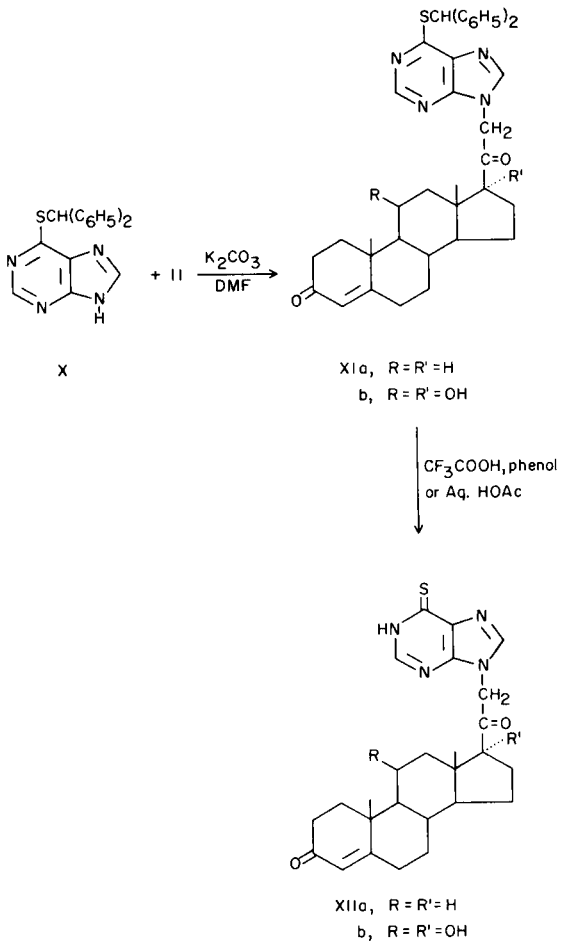


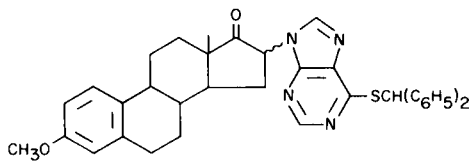
IX

where a, R = R' = H
b, R = R' = OH

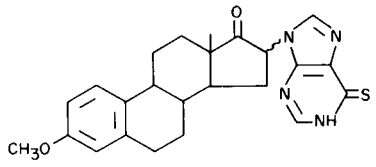
Recently Carroll and Philip reported the preparation of 21-(1,6-dihydro-6-thioxo-9*H*-purin-9-yl)-pregn-4-ene-3,20-dione (XIIa) by the procedure shown in Chart 1 (10). The procedure involves the alkylation of 6-diphenylmethylthiopurine (X) to give XIa which affords XIIa on removal of the diphenylmethyl (DPM) protecting group. In a similar fashion, the alkylation of X with IIb and IV gives XIb and XIII respectively (11). Treatment of XIb and XIII with refluxing trifluoroacetic acid containing a small amount of phenol gave 97% and 80% yields respectively of the corresponding 9-steroidal-9*H*-purine-6(1*H*)-thiones, XIIb and XIV. In order to show that no D-homoannulation (12) of IIb, which contains an acid-labile 17α-hydroxyl function, had occured, we treated XIIb with methyl iodide in DMF containing potassium carbonate and obtained VIIb. This product was identical to VIIb obtained by the alkylation of VI with IIb. In addition XIb could be converted to XIIb in 60% yield by treatment with aqueous acetic acid at room temperature. The elemental analysis and spectral data recorded in the experimental section are in agreement with these assignments.

Chart I





XIII



XIV

EXPERIMENTAL

Melting points were determined on a Kofler hot stage microscope using a calibrated thermometer. Ultraviolet and visible spectra were measured on a Cary Model 14 Spectrophotometer. Nmr spectra were recorded on a Varian Model A-60, using tetramethylsilane as an internal standard. Infrared spectra were measured with a Perkin Elmer 221 Spectrophotometer; samples were prepared in the form of pressed potassium bromide disks. Mass spectra were determined on a AEI MS-902 spectrometer. Microanalyses were carried out by Micro-Tech Laboratories, Skokie, Illinois.

General Method for the Preparation of Steroid-21-(*p*-bromobenzenesulfonates) II (13).

To a 0.1 *M* solution of the steroid in freskly distilled tetrahydrofuran at 0° was added 1.5 equivalents of triethylamine and 1.5 equivalents of *p*-bromobenzenesulfonyl chloride. After solution was complete, the solution was allowed to stand at 5-10° for 24-72 hours. The cold solution was evaporated to dryness *in vacuo*. Chloroform and a cold saturated sodium bicarbonate solution were added to the residue and the resulting two phase system was shaken vigorously. The organic layer was washed several times with cold bicarbonate solution and with cold water. After drying over sodium sulfate, the solvent was removed *in vacuo* and the residue was crystallized from a suitable solvent. The following steroid *p*-bromobenzenesulfonates were obrained in 45-81% yield. Deoxycorticosterone-21-(*p*-bromobenzenesulfonate) (IIa) recrystallized from a methylene chloride and methanol mixture had m.p. 148-150°.

Anal. Calcd. for $C_{27}H_{33}BrO_5S$: C, 59.01; H, 6.05; Br, 14.54; S, 5.84. Found: C, 59.29; H, 6.00; Br, 14.48; S, 5.79. Hydrocortisone-21-(*p*-bromobenzenesulfonate) (IIb) recrystallized from a methylene chloride and ether mixture had m.p. 113-115°.

Anal. Calcd. for $C_{27}H_{33}BrO_7S$: C, 55.76; H, 5.72; Br, 13.74; S, 5.51. Found: C, 55.75; H, 5.87; Br, 13.80; S, 5.50.

Cortisone-21-(*p*-bromobenzenesulfonate) (IIc) was used without recrystallization.

3-Methyl-16α-bromoestra-1,3,5(10)-triene-17-one (IV).

3-Methoxy-16α-bromoestra-1,3,5(10)-triene-17-one was prepared from the enol acetate of estrone 3-methyl ether according to the procedure reported by Johnson and Johns (14), m.p. 173-175°; ν max (carbon tetrachloride) 1758 cm^{-1} (C=O). Lit. (14) m.p. 176-177°.

Preparation of 6-Steroidalthiopurines.

A mixture of 0.17 g. (1.0 mmole) of purine-6(1*H*)-thione monohydrate, 0.14 g. (1.01 mmoles) of anhydrous potassium carbonate and 1 ml. of purified *N,N*-dimethylformamide (DMF) was stirred at room temperature for 15 minutes while protected by a Drierite drying tube. With continued stirring, 1 mmole of steroidal brosylate or steroidal bromide was added in one portion. The stirred mixture was then heated to 60° and kept at this temperature for 2 hours. The reaction was allowed to cool to room temperature and poured into 20 ml. of water. The mixture was adjusted to *p*H 5-6 with acetic acid. The resulting precipitate was separated by filtration, washed with water and dried *in vacuo* at 42° and recrystallized from a methanol and methylene chloride mixture. The results obtained with individual compounds are given in Table I.

Preparation of Steroidal-6-alkylthiopurines.

A mixture of the 6-alkylthiopurine, anhydrous potassium carbonate and the steroidal brosylate or steroidal bromide (1 mmole of each) in 1 ml. of DMF was stirred at 60° for 2-4 hours (until a tlc (6) indicated that the reaction was complete). The reaction mixture was cooled and diluted with 20 ml. of water. The resulting precipitate was filtered, washed with water, dried and recrystallized to give the pure 9-isomer. The solvent used for recrystallization along with the yield, spectral data and analytical results for individual compounds is given in Table II. In the cases where 7-steroidal-6-methylthiopurines were obtained, these were separated from the 9-isomer by preparative tlc on silica gel HF using hexane:chloroform:methanol (4:4:1) as the eluent. The two bands were detected by UV quenching, separated and extracted with acetone. Concentration of the extracts followed by recrystallization from the appropriate solvent (Table II) gave the pure 9- and 7-isomer.

21-(1,6-Dihydro-6-thioxo-9*H*-purin-9-yl)-11β,17α-dihydroxypregn-4-ene-3,20-dione (XIIb).

A solution of 0.223 g. (0.34 mmole) of XIb in 3 ml. of trifluoroacetic acid containing 0.020 g. of phenol was refluxed for 0.25 hour. The reaction mixture was cooled, concentrated on a rotary evaporator and triturated with ether. The solid obtained was filtered, washed with ether, recrystallized from a methylene chloride and methanol mixture and dried to give 0.162 g. (97%) of XIIb, m.p. 234-237°. The analytical sample prepared by further recrystallization from the same solvent mixture had m.p. 232-235°; ν max (potassium bromide) 1728 (17 C=O) 1655 (3 C=O), 1599 and 1540 (purine C=C and C=N), and 1200 cm^{-1} (C=S); λ max (methanol) in mμ (ε x 10^{-3}); 323 (24.2); *p*H 7, 319 (22.8); *p*H 11, 310 (22.2). Nmr [$(CD_3)_2SO$] showed a singlet at δ 0.83 (18 CH_3-), a singlet at 1.42 (19-CH_3), a multiplet at 4.32 ($COCH_2N$), a singlet at 5.63 and two singlets at 8.20 and 8.25 ppm (purine 8- and 2-H); Mass spectrum showed M^+ at *m/e* 496.2140, calcd. for $C_{26}H_{32}N_4O_4S$: 496.2144.

Anal. Calcd. for $C_{26}H_{32}N_4O_4S$: C, 62.88; H, 6.50; N, 11.28; S, 6.46. Found: C, 62.79; H, 6.42; N, 11.15; S, 6.58.

In a separate experiment 1.5 g. (2.26 mmoles) of XIb was dissolved in 8 ml. of aqueous acetic acid and stirred at 25° for 4 days. The reaction mixture was filtered and the filtrate diluted with ether. The resulting precipitate was recrystallized from a methylene chloride and methanol mixture to give 0.63 g. (56%) of product, m.p. 234-237°. The infrared spectrum of this product was

identical to XIIb obtained above.

Preparation of 21-[6-(Methylthio)-9*H*-purin-9-yl]-11β,17α-dihydroxypregn-4-ene-3,20-dione (VIIb) from XIIb.

To a mixture of 0.224 g. (0.45 mmole) of XIIb and 0.069 g. (0.5 mmole) of anhydrous potassium carbonate was added 0.064 g. (0.45 mmole) of iodomethane and the contents were stirred at 25° for 1.5 hours. The mixture was diluted with water. The resulting solid was filtered and dried to give 0.21 g. Recrystallization from a methanol and methylene chloride mixture gave 0.16 g. (70%) of VIIb, m.p. 232-235°. The infrared spectrum of this sample was identical to the spectrum of VIIb prepared by alkylating VI with IIb.

16-(1,6-Dihydro-6-thioxo-9*H*-purin-9-yl)-3-methoxyestra-1,3,5-(10)-triene-17-one (XIV).

This compound was prepared from XIII in 80% yield using a procedure similar to the procedure used to prepare XIIb. The product recrystallized from DMF had m.p. 320-325°. ν max (potassium bromide) 1760 (C=O) 1598 and 1540 (purine C=C and C=N) and 1202 cm^{-1} (C=S), λ max (methanol) 312 mμ (ε x 10^{-3} = 22.6), 228 (19.4).

Anal. Calcd. for $C_{24}H_{26}N_4O_2S$: C, 66.36; H, 5.99; N, 12.90; S, 7.37. Found: C, 66.14; H, 6.07; N, 12.76; S, 7.13.

REFERENCES

(1a) Steroids LXXXII. Previous paper in this series: Steroids LXXXI. G. S. Abernethy, Jr., and M. E. Wall, submitted to *J. Org. Chem.* (b) This research was carried out under Contract No. SA-43-ph-4351 of the Endocrine Evaluation Branch, General Laboratories and Clinics, National Institutes of Health. (c) Part of this work was presented at the 19th Southeastern Regional Meeting of the Americal Chemical Society, Atlanta, Georgia, November, 1967; Abstract No. 326.

(2) H. E. Skipper, F. M. Schabel, Jr., M. W. Troder, and J. R. Thomson, *Cancer Res.* 21, 1154 (1961).

(3) W. Damashek and F. Grunz "Leukemia", 2nd Ed., Grune and Strutton, N. Y., 1964, p. 496.

(4) F. M. Schabel, Jr., J. P. Johnston, G. S. McCaleb, J. A. Montgomery, W. R. Laster and H. E. Skipper, *Cancer Res.*, 23, 725 (1963).

(5) T. P. Johnston, L. B. Holum, and J. A. Montgomery, *J. Am. Chem. Soc.*, 80, 6265 (1958).

(6) Thin layer plates were prepared using silica gel HF. The plates were eluted with hexane:chloroform:methanol (4:4:1) and developed by spraying with a 5% solution of phosphomolybdic acid in ethanol followed by heating to 100°.

(7) D. E. O'Brien, J. D. Westover, R. K. Robins and C. C. Cheng, *J. Med. Chem.*, 8, 182 (1965) reported that the alkylation of 6-benyzlthiopurine with ethylene bromohydrin in DMSO catalyzed by potassium carbonate gave a 57% yield of 6-benzylthio-9-(β-hydroxyethyl)purine but did not report the formation of any 6-benzylthio-7-(β-hydroxyethyl)purine.

(8) Johnston and co-workers (ref. 5) reported that the treatment of purine-6(1*H*)-thione with two equivalents of α-chlorotoluene in DMF containing 2.2 moles of potassium carbonate gave an 82% yield of dibenzylated product which contained both 9-benzyl and 7-benzyl-6-benzylthiopurine. These products were presumably formed *via* the intermediate 6-benzylthiopurine; however, the 7-isomer was not obtained in pure form.

(9a) A. Hassner and P. Catsoulacos, *J. Org. Chem.*, 32, 549 (1967). (b) Since 16β-alkylamino-17-ketones appear to be more stable than this isomeric 16α-alkylamino-17-ketones, (see ref. 9a) we believe that the major isomer of II is 16β[6-(methylthio)-9*H*-purin-9-yl]2-methoxyestra-1,3,5-triene-17-one. The nmr spectrum which shows a resonance for the 18-CH_3 at δ 1.25 ppm approximately 3 times as large as the resonance at δ 1.13 is in accord with this assignment.

(10) F. I. Carroll and A. Philip, *J. Org. Chem.*, 33, 3776 (1968).

(11) Tlc chromatograms indicated that the amount of 7-isomer present was less than that formed in similar alkylations of 6-methylthiopurine. The pure 9-isomer was obtained by recrystallization and no attempt was made to isolate the 7-isomer from the filtrates.

(12) L. F. Fieser and M. Fieser, "Steroids", Reinhold Publishing Corporation, New York, N. Y., 1959, p. 577.

(13) These compounds were prepared by G. S. Abernethy, Jr., as part of a separate program.

(14) W. S. Johnston and W. F. Johns, *J. Am. Chem. Soc.*, 79, 2005 (1957).

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Research Triangle Park, North Carolina 27709