was copious evolution of nitric oxide, after which the solution was heated for 1.5 hr. at 50°. The cooled solution was treated with sufficient ice to hydrolyze the acetyl chloride, made basic slowly with solid sodium carbonate and extracted with 20 ml. portions of chloroform. This was dried overnight with potassium carbonate, filtered, taken to dryness and the residue recrystallized from acetone to give 1.7 g. of *4-chloro-3-picoline-1-oxide* (I), m.p. 120–122° d.

Anal. Calcd. for C_6H_6NOCl: C, 50.19; H, 4.21; N, 9.76, Cl, 24.70. Found: C, 50.39; H, 4.44;N, 9.71; Cl, 24.58%.

This material appears to be reasonably stable under ordinary conditions and shows only slight coloration after standing one year. An attempt to prepare the 4-bromo analog using acetyl bromide gave similar appearing white crystals when the chloroform was removed from the final extraction solution but these suddenly and spontaneously decomposed before they could be dissolved in acetone.

Attempts to prepare the deuterated picoline by direct reduction of I with zinc and D_2SO_4 were not successful. Therefore 4.168 g. of I were dissolved in 85 ml. of chloroform and 18 ml. of phosphorus trichloride added with the solution at 0°.[26] This was stirred for 45 minutes, then poured onto about 100 g. of ice. The solution was slowly made basic with 20% sodium hydroxide, then extracted with three 50 ml. portions of chloroform and the combined extracts dried over sodium sulfate. The solution was filtered, the sulfate washed with ether and the filtrate treated with dry hydrogen chloride; cloudiness appeared and then cleared again during this treatment. The solution was taken to dryness under vacuum and the residue was taken up in 95% ethanol and filtered to remove some insoluble yellow material. Ether was added to the warm solution until it started to grow turbid. Cooling overnight in a refrigerator produced 2.957 g. of *4-chloro-3-picoline HCl*, m.p. 165–170° (instantaneous, sealed capillary).

Anal. Calcd. for $C_6H_7NCl_2$: C, 43.93; H, 4.30; N, 8.54; Cl, 43.23. Found: C, 44.13; H, 4.48; N, 8.54; Cl, 43.25.

This material (1.39 g.) was dissolved in 25 ml. of 2 *N* D_2SO_4 in D_2O, 1.3 g. of zinc dust was added and the mixture heated at 100° for 2 hr.[27] After cooling, the solution was filtered and slowly made basic with potassium hydroxide pellets, an equal volume of water added and the solution (with suspended zinc hydroxide) extracted two days with ether in a continuous extractor. The ether solution was dried with Drierite, filtered, treated with dry hydrogen bromide and then taken to dryness. An oil was produced, which was dissolved in 150 ml. of water, taken to *p*H 6.5 and 3.57 g. of potassium permanganate added in small portions while the solution refluxed gently for 6 hr. The excess permanganate was destroyed with hydrogen peroxide and the basic solution was extracted overnight with ether. The manganese dioxide was then dissolved by the addition of conc. hydrochloric acid and the acid solution extracted with ether for 8 hr. Extraction for one day at *p*H 2.5–3 gave material which was transferred to a small vacuum sublimer with dimethylformamide and sublimed to give 263 mg. of nicotinic acid. This was recrystallized from 3 ml. of 95% ethanol before use.

The water from a dry combustion[18] of this compound was reduced over zinc at 650° in a sealed tube and the hydrogen submitted for mass spectrometer analysis.

Anal. Atom% D calcd., 20.0%; found, 19.7%, 20.1%.

The 1-methylnicotinamide iodide prepared from a diluted sample of this acid showed 0.49 atom% D. The 2- pyridone prepared from this material showed 0.54 atom% D, while the 6-pyridone contained 0.52 atom% D; the calculated value for these compounds, based on the iodide, is 0.55 atom% D.

Acknowledgments.—Drs. Eduardo Penna-Franca and Ulrich Weiss aided in the initial phases of the study. Miss P. R. Hansell contributed some of the assays and aided in the development of the column method for separation of pyridones.

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Potential Purine Antagonists. XXII. The Preparation and Reactions of Certain Derivatives of 2-Amino-6-purinethiol[1]

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RECEIVED OCTOBER 1, 1959

A number of 6-alkylthio-2-aminopurines have been prepared by two routes: (1) *via* cyclization of certain 6-alkylthio-2,4,5-triaminopyrimidines with ethyl orthoformate and acetic anhydride, and (2) by alkylation of 2-amino-6-purinethiol. A new synthesis of 2-amino-6-purinethiol has been accomplished in which thiation and ring closure of 2,4-diamino-5-formylamino-6-hydroxypyrimidine is achieved in one step with phosphorus pentasulfide in pyridine. 2-Amino-8-methyl-6-purinethiol has been similarly prepared from 5-acetylamino-2,4-diamino-6-hydroxypyrimidine. The preparation of 2-amino-6-chloropurine is reported.

A study of the antitumor activity of various 6-alkylthiopurines[3–6] against Adenocarcinoma 755[7,8] has revealed that several 6-alkylthiopurines possess a better therapeutic index than does 6-purinethiol. 6-Ethylthiopurine (National Service Center No. 11588) and 6-*n*-propylthiopurine (National Service Center No. 11595) had been previously prepared[9] and submitted for antitumor screening. The antitumor activity of this series of compounds suggested the extension of synthetic work to include

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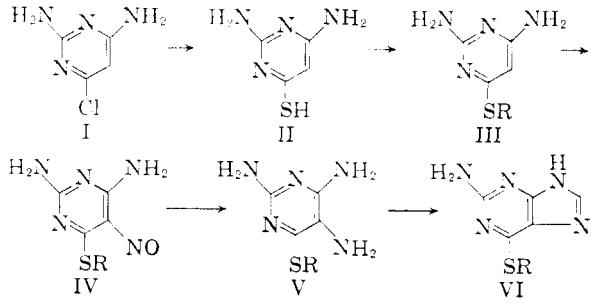
the preparation of the corresponding 6-alkylthio derivatives of 2-amino-6-purinethiol. The recent work of Sartorelli and LePage[10] has shown that 2-amino-6-purinethiol (VIII, R = H) acts as an antitumor agent by inhibition of the biosynthesis of nucleic acid at more than one site. Thus, variation in the structure could result in a drug with greater specificity, less toxicity, and a better therapeutic index over the parent compound by acting at fewer enzyme sites. The fact that 2-amino-9-β-D-ribofuranosyl-6-purinethiol[11] possesses a better therapeutic index than 2-amino-6-purinethiol[8] against Adenocarcinoma 755 would seem to support this view.

When the present work was essentially complete, a report[12] of the activity of several 6-alkylthio-2-aminopurines against Sarcoma 180 appeared. This work was followed by a recent report[13] describing the preparation of several of these compounds.

Montgomery and Holum[14] have reported the preparation of 2-amino-6-methylthiopurine by the alkylation of 2-amino-6-purinethiol with dimethyl sulfate in the presence of sodium hydroxide. Early efforts in this Laboratory to prepare a large number of the desired 6-alkylthio-2-aminopurines by this procedure were greatly hindered because 2-amino-6-purinethiol (VIII, R = H) was not readily available. The preparation of VIII, R = H, from guanine as described by Elion and Hitchings[15] could not be satisfactorily accomplished in this Laboratory on a large scale. In view of this difficulty, a new synthetic route was devised which did not require 2-amino-6-purinethiol as a necessary intermediate. This route is shown by reaction scheme I.

Ulbricht and Price[16] reported that 2,4-diamino-6-pyrimidinethiol (II) could not be prepared from 6-chloro-2,4-diaminopyrimidine (I) and thiourea in ethanol. The preparation of II, however, was successfully accomplished in good yield when compound I was heated to 140–150° with sodium hydrosulfide in ethylene glycol. 2,4-Diamino-6-pyrimidinethiol (II) was conveniently isolated from the reaction mixture as the sulfate. Treatment of II with the appropriate alkyl halide in the presence of potassium hydroxide readily gave the corresponding 6-alkylthio-2,4-diaminopyrimidine (III),[17] which was treated with nitrous acid to yield the corresponding 5-nitrosopyrimidine IV. The reduction of IV was accomplished with sodium hydrosulfite, and the purified 6-alkylthio-2,4,5-triaminopyrimidine (V)[17] was cyclized with ethyl orthoformate and acetic anhydride to the desired 6-alkylthio-2-aminopurine (VI). The first seven 6-alkylthio-2-aminopurines listed in Table II were prepared according to this general method. This method gave the desired purines in an over-all yield of 40 to 60% from 2,4-diamino-6-pyrimidinethiol (II).

REACTION SCHEME I



A rather extended study of the reaction of guanine with phosphorus pentasulfide in pyridine[15] revealed that maximum yields of 2-amino-6-purinethiol were obtained after 18 hours of reaction time and with approximately 2.5 moles of phosphorus pentasulfide per mole of guanine. Under these reaction conditions, the isolation and purification of 2-amino-6-purinethiol was greatly simplified since no unreacted guanine was found to be present. The treatment of 200 g. of guanine in this manner gave 88 g. of analytically pure 2-amino-6-purinethiol (VIII, R = H).

A much superior and rather novel preparation of 2-amino-6-purinethiol was finally accomplished directly in one step from 2,4-diamino-5-formamido-6-hydroxypyrimidine (VII, R = H)[18] and phosphorus pentasulfide in which thiation and cyclization to the desired purine were accomplished in one step. Since 2,4-diamino-5-formamido-6-hydroxypyrimidine (VII, R = H) can be prepared from 2,4-diamino-6-hydroxypyrimidine directly in essentially a one-step process by the elegant method of Pfleiderer,[18] this represents by far the best method of preparation of 2-amino-6-purinethiol. By this method VII, R = H, could be converted to 2-amino-6-purinethiol in approximately 50% yield.

To test the generality of the cyclization and thiation reaction, 5-acetamido-2,4-diamino-6-hydroxypyrimidine[19,20] was similarly treated with phosphorus pentasulfide in pyridine to give 2-amino-8-methyl-6-purinethiol (VIII, R = CH_3) in essentially 50% yield. To check on the identity of the structure assigned to the product of this reaction, 5-acetamido-2,4-diamino-6-hydroxypyrimidine was converted to 2-amino-6-hydroxy-8-methylpurine (IX, R = CH_3[21,22]) with refluxing acetamide. Treatment of 2-amino-6-hydroxy-8-methylpurine (IX, R = CH_3) with pyridine and phosphorus pentasulfide gave 2-amino-8-methyl-6-purinethiol (VIII, R = CH_3) identical to the product obtained from VII, R = CH_3, but in lower yield. Elion, *et al.*,[13] reported the preparation of several 6-alkylthio-2-aminopurines from 2-amino-6-purinethiol by treatment of VIII, R = H with an alkyl halide in the

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(14) J. A. Montgomery and L. B. Holum, *ibid.*, **79**, 2185 (1957).

(15) G. B. Elion and G. H. Hitchings, *ibid.*, **77**, 1676 (1955).

(16) T. L. V. Ulbricht and C. C. Price, *J. Org. Chem.*, **21**, 567 (1956).

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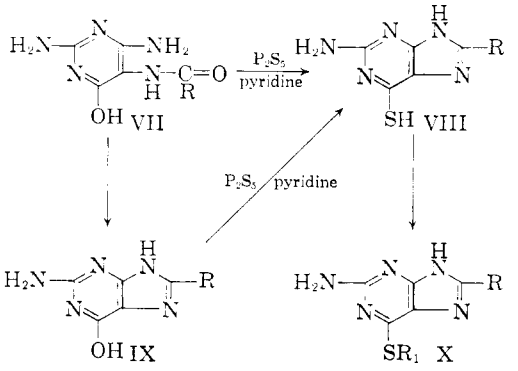
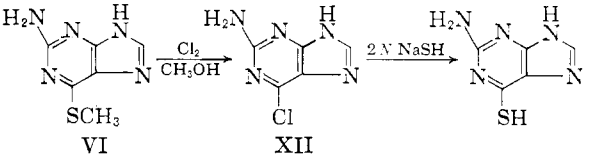
REACTION SCHEME II



presence of 0.3 *N* sodium hydroxide in a sealed tube heated at 120° for 18 hours. 2-Amino-6-methylthiopurine prepared by this method was reported[13] to melt at 205–206°. The same compound previously prepared by Montgomery and Holum[14] from 2-amino-6-purinethiol and dimethyl sulfate is reported to melt at 239–239.5°. 2-Amino-6-methylthiopurine has recently been prepared by the methylation of 2-amino-6-purinethiol with iodomethane[23] in the presence of sodium hydroxide at room temperature. The melting point of this product is recorded[23] as 237–241° dec. 2-Amino-6-methylthiopurine (VI, R = CH_3) has now been prepared by an unambiguous method from 2,4-diamino-6-methylthiopyrimidine (III, R = CH_3). It has been shown to possess a melting point of 239–241° and to be identical with the compound reported by Montgomery and Holum[14] and that reported by Leonard, *et al.*[23] The general method of synthesis of 6-alkylthio-2-aminopurines devised in this Laboratory and listed in Table II is similar to that of Leonard, *et al.*,[23] in that the alkylations were run at room temperature. A sealed tube[13] is unnecessary and probably undesirable since an alkyl halide in the presence of sodium hydroxide heated in a sealed tube has been reported as suitable conditions for the alkylation of purine derivatives in the 7- or 9-position.[21,24,25] Concentrated aqueous ammonia was found to be the best reaction medium for these alkylation reactions since 2-amino-6-purinethiol is soluble in this solvent while the resulting 6-alkylthio-2-aminopurine is insoluble and usually crystallizes from the reaction mixture. Thus, an effective separation of product from starting material can usually be made. If the reaction mixture is simply acidified or neutralized with acid, the product in most instances is contaminated with starting material which is difficult to remove. The presence of a small amount of contaminating 2-amino-6-purinethiol is indeed enough to render the antitumor screening results valueless since 2-amino-6-purinethiol is above 90% inhibitory[8] against Adenocarcinoma 755 at 0.5 mg./kg. per day in the mouse and is toxic at levels of 3 mg./kg. per day.

In the case where the alkyl group contained a carboxylic acid function, the (2-amino-6-purinylthio)-alkanoic acid was separated from 2-amino-6-purinethiol by the use of aqueous sodium bicarbonate, in which the latter is insoluble at room temperature. A number of 6-alkylthio-2-aminopurines were prepared utilizing several branch-chained iodoalkanes. In these instances a higher temperature and longer reaction time were necessary to effect alkylation. Several slightly more complex 2-amino-6-substituted thiopurines were prepared from certain pyrimidines possessing an active chlorine group, such as 6-chloro-4-methylamino-5-nitropyrimidine, which reacted readily to give 2-amino-6-(4′-methylamino-5′-nitro-6′-pyrimidinylthio)-purine. Several 6-alkylthio-2-amino-8-methylpurines (X, R = CH_3) were prepared from 2-amino-8-methyl-6-purinethiol (VIII, R = CH_3) in a similar manner. These derivatives are listed in Table III.

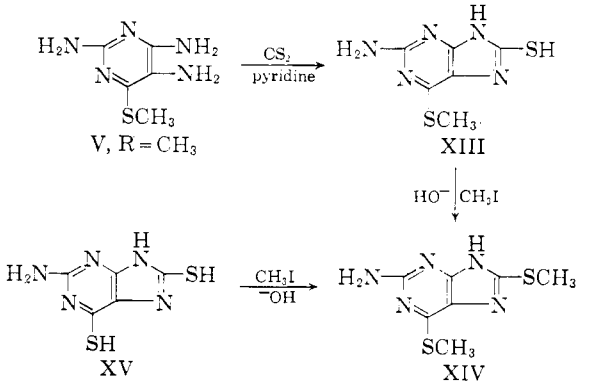
Recent studies[26] in this Laboratory have shown that a methylthio group in position 6 of the purine nucleus can be replaced by a chlorine atom by means of chlorine gas in methanol. Extension of this work to 2-amino-6-methylthiopurine (VI, R = CH_3) resulted in a good yield of 2-amino-6-chloropurine (XII). The preparation of this compound



has previously been reported only in a patent.[27] Adams and Whitmore[28] have reported that attempts to chlorinate guanine to obtain 2-amino-6-chloropurine were unsuccessful.

Treatment of 2-amino-6-chloropurine (XII) with boiling aqueous sodium hydrosulfide provided another method of preparing 2-amino-6-purinethiol in good yield. As might be expected, 2-amino-6-chloropurine in refluxing 1 *N* hydrochloric acid gave guanine. Treatment of 2-amino-6-chloropurine in refluxing 1 *N* potassium hydroxide for one hour gave only starting material. It would thus

REACTION SCHEME III



appear that the presence of the 2-amino group makes the 6-chloro atom less susceptible to nucleophilic attack since 6-chloropurine is converted to

(23) E. O. Leonard, C. G. Skinner, E. M. Lansford, Jr., and W. Shive, THIS JOURNAL, **81**, 907 (1959).
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(25) J. M. Gulland, *J. Chem. Soc.*, 662 (1933).
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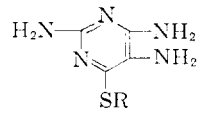
TABLE I

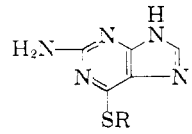
6-ALKYLTHIO-2,4,5-TRIAMINOPYRIMIDINES (III)



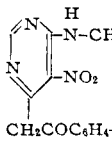
R	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Yield from II, %	Meth. of prepn.	Recrystn. solvent	Alkyl halide employed
CH_3	191–192	35.0	35.3	5.3	5.2	40.9	41.5	67	A	MeOH–water	Methyl iodide
C_2H_5	150–151					37.8	38.0	52	A	Water	Ethyl iodide
n-C_3H_7	145–146	42.2	42.4	6.5	6.5	35.2	35.6	50	B	MeOH–water	n-Propyl iodide
n-C_4H_9	89–90					32.8	32.8	47	B	Heptane–EtAc	n-Butyl iodide
$CH_2CH{=}CH_2$	149–151	42.7	42.4	5.6	5.7	35.5	35.6	56	B	Dil. NH_4OH	Allyl chloride
$CH_2C_6H_4Cl$-p	173–175	46.9	47.3	4.3	4.2	24.8	24.7	83	C	MeOH–water	p-Chlorobenzyl-chloride
$CH_2C_6H_5$	177–178					28.3	28.1	76	C	MeOH–water	Benzyl chloride

TABLE II

2-AMINO-6-SUBSTITUTED THIOPURINES



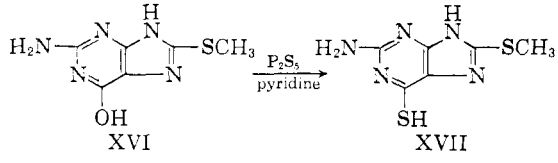
R	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Yield, %	Meth. of prepn.	Recrystn. solvent	pH 1 λmax, mμ		pH 11 λmax, mμ		Alkyl halide employed
CH_3[12,14,23]	238–241	39.8	39.9	3.9	3.6	38.7	38.6	89	E	Water	242 273 318	6,300 9,200 12,000	312	10,000	
C_2H_5[13]	206–208	43.1	43.4	4.6	4.2	35.8	36.1	86	E	MeOH–EtAc	242 276	6,400 9,600	229 316	18,900 11,300	
n-C_3H_7[13]	191–193	45.8	45.5	5.3	5.5	33.5	33.3	92	E	MeOH–EtAc	320 277 321	13,300 10,200 13,600	229 316	25,300 11,100	
n-C_4H_9[13]	204–206	48.3	48.5	5.8	5.7	31.3	31.5	76	E	MeOH–EtAc	278 321	9,400 13,800	230 316	18,100 11,600	
$CH_2C_6H_4Cl$-p[13]	238–239	49.4	49.4	3.4	3.4	24.0	24.0	87	E	MeOH–water	276 320	11,700 17,500	316	12,000	
$CH_2C_6H_5$[23]	212–214					27.2	27.0	79	E	MeOH–water	277 320	9,500 14,600	316	12,600	
								56.1	A	Ethanol					
$(CH_2)_4CH_3$	202	50.6	51.0	6.3	6.1	29.5	29.2	65.7	A	MeOH–water	277 320	10,900 15,400	316	10,400	I
CH_2COOH	>300	37.3	36.9	3.1	3.0	31.1	30.8	69.0	C	Reppd.	269 318	9,000 11,900	313	11,500	Cl
$(CH_2)_5CH_3$	180–182	52.7	52.8	6.8	6.7	27.9	27.6	55.6	A	EtAc–benzene	242 277 320	9,300 14,000 19,800	316	16,100	I
$(CH_2)_3CH(CH_3)_2$	201–203	50.6	50.5	6.3	6.3	29.5	29.5	36.8	A	EtAc–benzene	242 277 320	7,600 11,400 15,600	316	10,000	I
$CHCH_2CH_3$ $\vert$ CH_3	158–160	48.5	48.5	5.8	5.5	31.4	31.7	59.4	B	EtAc–heptane	278 322	9,800 14,300	317	11,000	I
$CH_3CH(CH_2)_2$	188–191	48.5	48.6	5.5	5.7	31.4	31.7	66.3	B	EtAc–heptane	243 278 320	5,800 10,500 15,000	316	11,800	I
$CH_2C_6H_4F$-p	245–246	52.3	52.7	3.6	3.6	25.4	25.2	78.1	A	EtOH–dimethyl-formamide	274 320	14,000 21,400	317	10,400	Cl
$CHCH_3COOH$	Dec. 250	40.1	40.1	3.8	3.9	29.2	28.9	56.1	C	Reppd.	242 270 320	7,900 8,800 12,000	314	11,000	Br
$(CH_2)_2C_6H_5$	190–192	57.6	57.9	4.8	4.8	25.8	25.4	28.4	A	Ethanol	316	22,500	316	16,500	Br
$CH(CH_2)_2CH_3$ $\vert$ $COOH$	223–228	45.0	44.8	4.9	5.4	24.6	24.4	62.5	C	Reppd.	272 320	9,300 12,500	315	10,100	Br
$CH_2C{\equiv}CH$	214–216	46.8	47.4	3.4	3.5	33.9	33.7	51.3	A	Water	321	15,400	320	16,400	Br
$(CH_2)_3CH_3$	204–206	48.5	48.6	5.8	5.6	31.4	31.8	60.1	A	EtAc–benzene	242 277 320	6,300 9,600 13,300	316	10,700	I
$(CH_2)_6CH_3$	153–155	54.4	54.4	7.2	6 8	26.4	26.1	81.7	A	EtAc–heptane	242 277 320	6,100 9,300 13,200	316	10,300	I
$CH_2CH{=}CHC_6H_5$	204–205	59.4	59.4	4.6	4.8	24.7	24.4	36.7	A	Ethanol	256 321	22,600 16,700	317	11,600	Cl

$CH_2C_6H_3Cl_2$-2,4	246–248	44.4	44.0	2.8	2.5	21.5	21.4	50.7	A	EtOH–dimethyl-formamide	275 320	10,100 14,300	3..,	13,000	Cl
$CH_2C_6H_4Cl$-*o*	205	49.4	49.4	3.4	3.3	24.0	24.0	74.2	A	Ethanol	276 320	9,000 13,400	316	11,000	Cl
CH_2CN	Dec. 265	40.7	41.0	2.9	3.2	40.7	40.3	45.1	A	EtOH–water	241 267 319	9,100 9,500 12,800	313	10,900	Cl
$CH(CH_3)_2 \cdot H_2O$	164–165	42.3	42.3	5.7	5.7			48.8	B	EtAc–heptane	242 277 320	5,600 9,800 13,800	317	11,500	I
CH_2CONH_2	Dec. 285	37.5	37.4	3.6	3.8	37.5	37.4	79.8	A	Water	269 319	8,300 11,400	313	10,300	Cl
$CH_2COC_6H_5$	208–209	54.7	55.2	3.7	4.1	24.5	24.5	40.2	A	Water	328	12,200	318	11,900	Cl
$CH_2CH{=}CH_2$	198–200	46.4	46.3	4.4	4.5	33.7	34.0	45.3	A	Ethyl acetate	243 276 320	5,800 9,700 13,500	316	10,000	Br
$(CH_2)_2OH$	Dec. 240	39.8	39.8	4.3	4.5	33.2	33.4	64.3	A	Water	242 275 320	6,500 9,700 12,200	315	10,100	Br
	Dec. 200	37.7	38.0	2.8	3.6	40.0	40.0	78.1	D	H_2O–dimethyl-formamide	256 336	10,800 29,700	270 322	8,600 30,000	Cl
$CH_2COC_6H_4$–Br-*p*	231–232	42.8	43.3	2.7	3.1	19.4	19.7	54.6	D	H_2O–dimethyl-formamide	250 347	14,600 16,000	322	12,700	Br
Cyclohexyl	258–261	52.8	52.4	6.0	6.0	28.1	28.3	36.9	I	Ethyl acetate	279 320	8,700 15,100	317	10,200	I
$CHCH(CH_3)_2 \cdot H_2O$ COOH	Dec. 200	42.2	42.7	5.3	5.4	24.6	24.8	48.7	C	Reppd.	272 320	8,800 11,600	315	10,300	Br
$CH(CH_2)_4CH_3$ COOH	215–217	48.9	48.2	5.8	5.8	23.7	23.4	47.2	C	Reppd.	242 271 320	6,500 8,300 11,500	315	10,000	Br
$CH_2CH_2CH_2C_6H_5$	121–123	59.0	59.0	5.3	5.4	24.5	24.2	62.0	A	Ethyl acetate	242 277 320	6,300 9,200 14,800	316	11,700	Cl
$CH_2C_6H_4$–NO_2-*p*	Dec. 265	47.8	47.7	3.3	3.8	27.8	27.8	78.0	A	H_2O–dimethyl-formamide	268 336	14,800 16,900	271 318	14,500 19,300	Cl
$CH_2C_6H_4$–NO_2-*o*	235–236	47.8	48.0	3.3	3.4	27.8	27.8	76.0	A	EtOH–dimethyl-formamide	272 320	18,100 20,500	314	13,300	Cl

hypoxanthine[29] by boiling 0.1 *N* sodium hydroxide.

Treatment of 6-methylthio-2,4,5-triaminopyrimidine (V, R = CH_3) with carbon disulfide in pyridine gave 2-amino-6-methylthio-8-purinethiol (XIII), which with iodomethane in the presence of base gave 2-amino-6,8-bis-methylthiopurine (XIV). This compound, XIV, was also obtained from 2-amino-6,8-purinedithiol (XV)[13] by methylation under similar conditions.

Treatment of 2-amino-6-hydroxy-8-methylthiopurine (XVI)[13] with phosphorus pentasulfide in pyridine gave 2-amino-8-methylthio-6-purinethiol (XVII) in good yield.



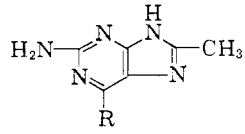
XVI XVII

It is interesting to note that XVI and phosphorus pentasulfide in tetralin has previously been reported[13] to yield 2-amino-6,8-purinedithiol.

Experimental[30]

Preparation of 2,4-Diamino-6-pyrimidinethiol (II).—Sodium hydrosulfide ($NaSH \cdot 3H_2O$) (320 g.) was added to 520 ml. of ethylene glycol. The temperature of the solution was raised to 60°, and 120 g. of 6-chloro-2,4-diaminopyrimidine[31] was added with stirring. The reaction temperature was then raised to 140–150° over a period of 30 min. and then maintained at 140–150° for an additional 30 min. The solution was cooled to 60°, and the mixture was stirred into 1600 ml. of water. The straw-colored solution was carefully acidified to *p*H 1 with 1:1 aqueous sulfuric acid. The mixture was cooled, and the sulfate salt was filtered and washed with water followed by acetone. The sulfate was suspended in 1600 ml. of water and enough concentrated aqueous ammonia at 50°. The solution was treated with charcoal and filtered. The filtrate was acidified with glacial acetic acid and cooled. The precipitate was filtered, washed with water, and dried to yield 85 g. of product. Recrystallization from water (100 g./1.) gave a pure product which gradually decomposed above 230°. The ultraviolet absorp-

TABLE III



R	*p*H 1 λ_{max}, mμ	*p*H 1 ε	*p*H 11 λ_{max}, mμ	*p*H 11 ε
OH	249	11,900	276	7,700
	276	7,700		
SH	350	20,000	323	17,200
	256	8,000		
SCH_3	320	14,600	317	12,700
	268	9,000		
	242	10,900		
$SCH_2C_6H_5$	322	14,200	318	11,700
	270	7,300		
	242	9,200		

(29) A. Bendich, P. J. Russell, Jr., and J. J. Fox, THIS JOURNAL, **76**, 6073 (1954).

(30) All melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected.

(31) Purchased from Francis Earle Laboratories, Inc., Peekskill, New York.

tion spectra at *p*H 11 showed λ_{max} 237 (ϵ_{max} 16,500) and 298 (ϵ_{max} 17,500) and at *p*H 1, λ_{max} 244 (ϵ_{max} 8,100) and 320 (ϵ_{max} 28,100).

Anal. Calcd. for $C_4H_6N_4S$: C, 33.8; H, 4.2; N, 39.4. Found: C, 33.7; H, 4.8; N, 39.3.

2,4-Diamino-6-methylthiopyrimidine (III, R = CH_3).[17]—Fifty grams of 2,4-diamino-6-pyrimidinethiol (II) was dissolved in 500 ml. of water containing 30 g. of potassium hydroxide. Then, 55 g. of iodomethane was added, and the mixture was stirred 1 hr. at room temperature. The precipitate that formed was filtered, washed with a small portion of very dilute aqueous ammonia, then ice-water, and dried to yield 46 g. of product. Recrystallization from dilute aqueous ammonia yielded a pure sample, m.p. 202–204°.

Anal. Calcd. for $C_5H_8N_4S$: C, 38.5; H, 5.1; N, 35.8. Found: C, 38.5; H, 5.1; N, 35.8.

2,4-Diamino-6-*n*-propylthiopyrimidine (III, R = *n*-C_3H_7).—Twenty grams of 2,4-diamino-6-pyrimidinethiol (II) was dissolved in 200 ml. of water containing 15 g. of potassium hydroxide. Then, 25 g. of 1-iodopropane, dissolved in 50 ml. of dioxane, was added, and the mixture was stirred 1.5 hr. at 80°. It was then stirred and cooled in an ice-bath for approximately 1 hr. and filtered. The product was washed with cold water and dried at 60° to yield 22 g. of the desired 2,4-diamino-6-*n*-propylthiopyrimidine. One recrystallization from dilute aqueous ammonia gave a pure sample, m.p. 107–109°.

Anal. Calcd. for $C_7H_{12}N_4S$: C, 45.7; H, 6.5; N, 30.4. Found: C, 45.5; H, 6.8; N, 30.1.

6-Benzylthio-2,4-diaminopyrimidine (III, R = $CH_2C_6H_5$).—To 20 g. of 2,4-diamino-6-pyrimidinethiol (II) and 18 g. of anhydrous potassium carbonate, in 70 ml. of N,N-dimethylformamide, was added 18 g. of α-chlorotoluene. The mixture was stirred and maintained at 60° for 1 hr. Then, 300 ml. of water was added, and the mixture was allowed to cool to room temperature. The precipitate was filtered, washed with water, then benzene, and dried to yield 30 g. of white powder, m.p. 143–145°. One recrystallization from benzene gave a product, m.p. 146–148°.

Anal. Calcd. for $C_{11}H_{12}N_4S$: C, 56.8; H, 5.2; N, 24.1. Found: C, 57.2; H, 5.2; N, 23.9.

Preparation of 6-Alkylthio-2,4,5-triaminopyrimidines (V) (See Table I). **Method A.**—2,4-Diamino-6-pyrimidinethiol (II) (100 g.) was dissolved in 1 l. of 1 *N* potassium hydroxide. Then, 0.73 mole of the appropriate alkyl halide was added, and this mixture was vigorously stirred for 1 hr. at room temperature. The precipitate was filtered, washed with cold water, and then added to 200 ml. of glacial acetic acid and 400 ml. of water. To this solution was added (dropwise) 60 g. of sodium nitrite in 150 ml. of water, with vigorous stirring, so that the temperature did not rise above 30°. The mixture was allowed to stir 1 hr. longer, and the purple nitroso compound was filtered and washed with cold water. The wet 5-nitrosopyrimidine was then placed in 1 l. of water at 60°, and sodium hydrosulfite was added, with stirring, until the solution had completely decolorized. The clear solution was boiled with charcoal and filtered, and the filtrate was adjusted to *p*H 8–9 with ammonium hydroxide. After the solution had been thoroughly chilled, the precipitate was filtered, washed with water, and carefully dried at 60° to yield the appropriate 4,5-diaminopyrimidine listed in Table I.

Method B.—Twenty-five grams of 2,4-diamino-6-pyrimidinethiol (II) in 250 ml. of water, containing 15 g. of potassium hydroxide, was stirred. Then, 0.18 mole of the appropriate alkyl halide, dissolved in 50 ml. of dioxane, was added. The temperature was raised to 80° for 3 hr. The stirred mixture was cooled, and the precipitate was filtered and added to 100 ml. of water and 50 ml. of glacial acetic acid. To this mixture was added, dropwise, a solution of 10 g. of sodium nitrite in 25 ml. of water, and the solution was stirred for 1 hr. The purple nitrosopyrimidine was filtered, washed, and suspended in 800 ml. of water at 70°. Sodium hydrosulfite was added, with stirring, until the solution had completely decolorized. The solution was then adjusted to *p*H 8–9 with aqueous ammonia and allowed to cool. The precipitate was filtered, washed with water, and dried to yield the appropriate 4,5-diaminopyrimidine as indicated in Table I.

Method C.—To 40 g. of 2,4-diamino-6-pyrimidinethiol (II) and 36 g. of potassium carbonate, in 140 ml. of N,N-dimethylformamide, was added 0.29 mole of the appropriate alkyl halide. This mixture was stirred and maintained at 70° for 1 hr. then added to 600 ml. of water and allowed to stand. The precipitate was filtered, washed with water, and added to 200 ml. of glacial acetic acid and 400 ml. of water. Thirty grams of sodium nitrite, in 80 ml. of water, was added dropwise. The mixture was allowed to stir 1 hr. The purple nitrosopyrimidine was reduced with sodium hydrosulfite and isolated as in method B.

Preparation of 6-Alkylthio-2-aminopurines Listed in Table II. Method E.—Twenty grams of the 6-alkylthio-2,4,5-triaminopyrimidine (V) was placed in 250 ml. of a 1:1 mixture of ethyl orthoformate and acetic anhydride. The solution refluxed for 2–3 hr., and the excess solvent was removed under reduced pressure with a water-bath as the source of heat. The residue was covered with 200 ml. of water, and then solid potassium hydroxide was added until the solution was strongly basic. The solution was boiled, treated with charcoal, and filtered. The filtrate was neutralized with acetic acid and allowed to cool. The precipitate was filtered, washed with water, and dried at 70° to yield the desired product. Purification was effected by recrystallization from the solvents indicated in Table II.

2-Amino-6-chloropurine (XII).—Absolute methanol (150 ml.) was cooled to 15° in an ice-bath, and chlorine gas was passed into the solution at a moderate rate for approximately 10 min. The flow of chlorine was then slowed somewhat, and small portions of 2-amino-6-methylthiopurine (VI, R = CH_3) were added at such a rate that the temperature did not exceed 25°. The 2-amino-6-methylthiopurine readily dissolved, and gradually a white precipitate appeared. After 10 g. of IV, R = CH_3, had been added, the flow of chlorine was discontinued, and the mixture was stirred and cooled in an ice-bath for 20 min. It was then filtered, washed with methanol, and dried at 70° to yield 4 g. of product. Recrystallization from water gave pure white crystals which gradually decomposed above 275° when heated slowly on the melting point block. XI at *p*H of 1 exhibited λ_{max} 316 mμ, ε 6,800, λ_{max} 237 mμ, ε 6,100 at *p*H of 11, λ_{max} 308 mμ, ε 6,300, λ_{max} 273, ε 3,800.

Anal. Calcd. for $C_5H_4N_5Cl$: C, 35.4; H, 2.4; N, 41.3. Found: C, 35.5; H, 2.3; N, 41.5.

2-Amino-6-methylthio-8-purinethiol (XIII).—Twenty grams of 6-methylthio-2,4,5-triaminopyrimidine (V, R = CH_3) was covered with 120 ml. of pyridine. Carbon disulfide (30 ml.) was added, and the mixture was refluxed for 2 hr., then allowed to cool to room temperature. The precipitate was filtered and washed with water, followed by acetone. The pale-yellow crystals were dried at 110° to yield 19.6 g. of product. An analytically pure sample was obtained by reprecipitating the product from boiling dilute aqueous ammonia with glacial acetic acid.

Anal. Calcd. for $C_5H_7N_5S_2$: C, 33.8; H, 3.3; N, 32.8. Found: C, 33.8; H, 3.2; N, 32.6.

2-Amino-6,8-bis-methylthiopurine (XIV). **Method A.**—Thirty grams of 2-amino-6-methylthio-8-purinethiol (XIII) was dissolved in 900 ml. of water containing 27 g. of potassium hydroxide. Then, 21.0 g. of iodomethane was added. The mixture was stirred for 1.5 hr. at room temperature and then acidified with glacial acetic acid. The precipitate was filtered, washed with water, and dried at 120° to give 31.8 g. colorless product. Recrystallization from methanol–water gave an analytically pure sample, m.p. 283–284°.

Anal. Calcd. for $C_6H_9N_5S_2$: C, 33.5; H, 4.2; N, 32.6. Found: C, 33.9; H, 4.0; N, 32.0.

Method B.—Thirty grams of 2-amino-6,8-purinedithiol (XV) was prepared as in method A, except that 43 g. of iodomethane was used. This gave 34.5 g. of product which did not depress the melting point of the same product prepared by method A. The ultraviolet absorption spectra of the two preparations were identical.

General Methods of Preparation of 2-Amino-6-substituted thiopurines. (See Table II). **Method A.**—To 150–200 ml. of 28% aqueous ammonia was added 10 g. of 2-amino-6-purinethiol (0.06 mole). This solution was stirred mechanically, and 0.065–0.07 mole of the appropriate alkyl halide, in 25 ml. of dioxane, was added slowly over a 15–30-min. period. During this period the solution was warmed carefully to 35–40° then allowed to cool to room temperature with continuous stirring for 2–5 hr. The precipitate, which gradually appeared in the reaction mixture, was filtered and

washed with water. The product was dried and purified by recrystallization from the solvent indicated in Table II.

Method B.—To 150 ml. of 1 *N* potassium hydroxide was added 10 g. of 2-amino-6-purinethiol (0.06 mole) and 0.065–0.07 mole of the appropriate alkyl halide. The reaction mixture was refluxed with continuous stirring until only one phase was present. The hot solution was acidified to *p*H 5 with acetic acid and allowed to cool. The crude product was filtered, dried, and recrystallized from the solvent indicated in Table II.

Method C.—To 200 ml. of 1 *N* potassium hydroxide was added 10 g. of 2-amino-6-purinethiol (0.06 mole) and 0.065–0.07 mole of the appropriate α-bromo-alkanoic acid. This solution was refluxed for 2–3 hr. then acidified to *p*H 3 with 6 *N* hydrochloric acid and allowed to cool. The crude product was filtered and suspended in 300 ml. of water. To this solution was added an excess of sodium bicarbonate, and the solution was stirred at room temperature for 2 hr. The unreacted 2-amino-6-purinethiol and the excess sodium bicarbonate were filtered. The filtrate was treated with charcoal and filtered. This filtrate was boiled, the *p*H was adjusted to 3 with 6 *N* hydrochloric acid, and the solution was allowed to cool. The product was filtered, washed with 500 ml. of water, and dried at 125° for 2 hr. before analysis.

Method D.—This procedure is identical to that described for method A, except that dioxane was not added to the reaction mixture.

2-Amino-6-hydroxy-8-methylpurine (IX, R = CH_3).–A mixture of 50 g. of 5-acetamido-2,4-diamino-6-hydroxypyrimidine[20] and 200 g. of acetamide was heated in a Wood metal-bath under reflux for 3 hr. using an air-cooled condenser. The hot solution was poured slowly with stirring into 800 ml. of boiling water. This solution was allowed to cool. The precipitate which appeared was filtered and suspended in 800 ml. of boiling water, and enough 6 *N* hydrochloric acid was added to effect solution. This solution was treated with charcoal, and the filtrate, when cooled, yielded white needles of 2-amino-6-hydroxy-8-methylpurine hydrate.

Anal. Calcd. for $C_6H_7N_5O \cdot HCl \cdot H_2O$: C, 32.9; H, 3.2; N, 31.9. Found: C, 33.0; H, 3.5; N, 31.9.

This salt was suspended in 800 ml. of boiling water, and enough hydrochloric acid was added to effect solution. The boiling solution was carefully neutralized with aqueous ammonia and allowed to cool. The product was filtered and dried to yield 29 g. (64.4%) of pure 2-amino-6-hydroxy-8-methylpurine, m.p. >300°. The ultraviolet absorption spectra of the product was identical to that previously reported.[22]

2-Amino-8-methyl-6-purinethiol, VIII, R = CH_3. **Method A.**—A mixture of 25 g. of 2-amino-6-hydroxy-8-methylpurine and 87 g. of phosphorus pentasulfide was suspended in 600 ml. of pyridine, and the solution was refluxed for 8 hr. The excess pyridine was distilled under reduced pressure using a water bath as a source of heat. To the residue was added 800 ml. of water, and the mixture was allowed to stand 12 hr. The precipitate was filtered, washed with 1 l. of water, and finally dissolved in 800 ml. of 10–15% boiling, aqueous ammonia. The solution was treated with charcoal and filtered. The boiling filtrate was neutralized with acetic acid. The product was filtered and recrystallized from water to yield 10.1 g. (36.9%) of pure product. This product lost only part of its water of hydration even after heating at 130° for 6 hr.

Anal. Calcd. for $C_6H_7N_5S \cdot {}^1/_2H_2O$: C, 37.9; H, 4.2; N, 36.9. Found: C, 38.3; H, 4.3; N, 36.7.

Method B.—A mixture of 10 g. of 5-acetamido-2,4-diamino-6-hydroxypyrimidine and 35 g. of phosphorus pentasulfide was suspended in 400 ml. of pyridine and refluxed for 8 hr. The excess pyridine was distilled under reduced pressure using a water-bath as a source of heat. To the residue was added 400 ml. of water, and the reaction mixture was allowed to stand for 12 hr. The precipitate was filtered, and the product was purified in the manner described in method A to yield 5.1 g. (51.8%) of 2-amino-8-methyl-6-purinethiol. Comparison of the ultraviolet and infrared spectra show this compound to be identical with that prepared by method A.

Anal. Calcd. for $C_6H_7N_5S \cdot {}^1/_2H_2O$: N, 36.9. Found: N, 37.0.

2-Amino-8-methyl-6-methylthiopurine.—To 50 ml. of 1 *N* potassium hydroxide were added 4 g. of 2-amino-8-methyl-6-purinethiol and 3.2 g. of iodomethane. This solution was stirred continuously at room temperature for 4 hr. The precipitate which gradually appeared during the reaction time was finally filtered and dried in an oven at 60°. This crude product was recrystallized from absolute ethanol to yield 2.7 g. (62.8%) of colorless needles, m.p. 292–293°.

Anal. Calcd. for $C_7H_9N_5S$: C, 43.1; H, 4.6; N, 35.9. Found: C, 42.8; H, 4.6; N, 36.2.

2-Amino-6-benzylthio-8-methylpurine.—To 60 ml. of 1 *N* potassium hydroxide were added 5 g. of 2-amino-8-methyl-6-purinethiol and 3.6 g. of α-chlorotoluene. This solution was stirred continuously for 6 hr. at a temperature of 50°. After cooling, the precipitate was filtered and dried in an oven at 60°. This crude product was recrystallized from absolute ethanol to yield 4.3 g. (58.6%) of pure, white needles, m.p. 185–186°.

Anal. Calcd. for $C_{13}H_{13}N_5S$: C, 57.6; H, 4.8. Found: C, 58.0; H, 4.8.

2-Amino-6-purinethiol. Method A.—A mixture of 200 g. of guanine and 700 g. of phosphorus pentasulfide was suspended in 3500 ml. of pyridine, and the solution was refluxed for 18 hr. The excess pyridine was distilled under reduced pressure using a water-bath as a source of heat. To the residue was added 4 l. of water, and the mixture was allowed to stand for 12 hr. The precipitate was filtered and washed with 3 l. of water. This product was carefully added to 3 l. of 10–15% boiling, aqueous ammonia. Decolorizing carbon was added, and the solution was boiled for 10–15 min. The charcoal was filtered and retained. The excess ammonia was removed by boiling the filtrate until *p*H 7 was reached. The volume was maintained by the successive addition of water. The solution was then allowed to cool, and the product was filtered. The charcoal previously used was extracted with 2 l. of boiling 10% aqueous ammonia, and the solution was filtered. The crude 2-amino-6-purinethiol obtained from the original solution was added to the hot filtrate, and the resultant solution was boiled until approximately *p*H 7 was reached. A constant volume again was maintained by the addition of water. The solution was then cooled, and the product was filtered, washed with water, and dried to yield 88 g. of light-tan needles, m.p. >300°.

Anal. Calcd. for $C_5H_5N_5S$: C, 35.9; H, 3.0; N, 41.8. Found: C, 36.0; H, 3.0; N, 41.5.

Five grams of this product was dissolved in boiling dilute hydrochloric acid. This solution was boiled with charcoal, filtered, and cooled to yield 4.5 g. of white needles of the hydrochloride of 2-amino-6-purinethiol.

Anal. Calcd. for $C_5H_5N_5S \cdot HCl \cdot H_2O$: C, 27.1; H, 3.6. Found: C, 26.7; H, 3.5. Calcd. for $C_5H_5N_5S \cdot HCl$ (after heating at 140°): N, 34.5. Found: N, 34.4.

The hydrochloride (4.5 g.) was suspended in 300 ml. of boiling water, and enough hydrochloric acid was added to effect solution. The boiling solution was neutralized with aqueous ammonia, and this solution was cooled and filtered. The product was dried to yield 3.4 g. of white needles of 2-amino-6-purinethiol. This product was found to exhibit the ultraviolet spectra as recorded by Fox,[11] *et al.*

Method B.—A mixture of 20 g. of 2,4-diamino-5-formamido-6-hydroxypyrimidine[18] and 70 g. of phosphorus pentasulfide was suspended in 600 ml. of pyridine, and the solution was refluxed for 8 hr. The excess pyridine was distilled under reduced pressure using a water-bath as the source of heat. Water (800 ml.) was added to the residue, and the mixture was allowed to stand 12 hr. The precipitate was filtered and dissolved in 1 l. of 15% boiling aqueous ammonia. The solution was treated with charcoal and filtered. The boiling filtrate was neutralized with acetic acid. After the solution was allowed to cool, the product was filtered and further purified by reprecipitation from boiling aqueous ammonia to yield 9.6 g. (47.7%) of white needles, m.p. >300°. Comparison of ultraviolet and infrared absorption spectra show this compound to be identical to that prepared by method A.

Anal. Calcd. for $C_5H_5N_5S$: N, 41.8. Found: N, 42.2.

Method C.—Two grams of 2-amino-6-chloropurine (XII) was added to 100 ml. of 2 *N* sodium hydrosulfide, and the solution was refluxed for 2 hr. then acidified with acetic acid. This solution was cooled and filtered. The solid was

washed with water and dried to yield 1.7 g. of 2-amino-6-purinethiol, identified by its ultraviolet absorption data.[11]

Preparation of Guanine from 2-Amino-6-chloropurine (XII).—2-Amino-6-chloropurine (0.5 g.) was added to 100 ml. of 1 *N* hydrochloric acid. The solution was refluxed for 1 hr. and allowed to cool. The precipitate was filtered, washed with water, and dried to give 0.4 g. of guanine hydrochloride.

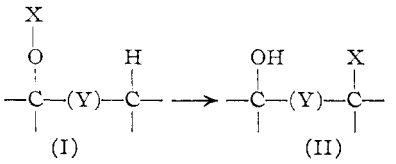
TEMPE, ARIZ.

COMMUNICATIONS TO THE EDITOR

A NEW PHOTOCHEMICAL REACTION

Sir:

It was conceived by one of us (D.H.R.B.) that the exchange process [(I) → (II)], where Y represents a chain of atoms so disposed as to bring (—C—O—X) and the non-activated (—C—H) bond into close (or potentially close) juxtaposition, might be feasible especially if photochemically induced. Such an exchange for (—O—X) bonds is without precedent, although other methods of attacking unactivated (—C—H) intramolecularly already are known.[1,2] Of the various systems possible (*e.g.*, X = halogen, $-NO_2$, $-NO$, $-OR$, *etc.*) the nitrites appear to be most suitable. The exchange reaction [(I) → (II) (X = NO)]



(I) (II)

cannot be induced in good yield thermally but acceptable and, in some cases, high yields can be secured by irradiation with ultraviolet light. The following are two illustrations for the case where (Y) = —C—C—.

3β-Acetoxy-5α-pregnan-20β-ol (III) in dry pyridine at −20 to −30°, treated with nitrosyl chloride in slight excess, gave the 20β-nitrite[3] (94%), m.p. (from methanol) 162–164.5°, $[\alpha]^{25}D$ −16° (*c*, 1.1, all rotations in $CHCl_3$ unless stated otherwise). Photolysis of this nitrite (10.0 g.) in a Pyrex vessel in dry benzene (200 ml.) at 10° under pure nitrogen for 2–5 hr. (disappearance of nitrite bands in the infrared) using a 200-watt Hanovia high pressure mercury arc lamp with a Pyrex filter sleeve gave on chromatography (III) (0.27 g.) and 18-oximino-5α-pregnane-Cβ,20β-diol 3-acetate (IV, R = Ac) (3.42 g., 34.2%), m.p. (needles from acetone–hexane) 192–195°, $[\alpha]^{25}D$ + 19° (*c*, 0.7), ν_{max}^{KBr} at 1635 cm.$^{-1}$ (oxime).

With acetone–H_2O (5:1) containing approx. 2% of concd. HCl at room temperature for 18 hr. the oxime afforded the masked aldehyde (V, R = Ac) (78%), m.p. (from methylene dichloride–methanol) 171–179°, $[\alpha]^{22}D$ +17° (*c*, 1.1), no aldehyde absorption in the infrared. Wolff–Kishner reduction of (V, R = Ac) gave 5α-pregnane-3β, 20β-diol (m.p., mixed m.p., rotation and infrared spectrum) in high yield (93%).

The oxime (IV, R = Ac) with pyridine–Ac_2O on the steam-bath for 15 min. and then with Ac_2O–AcONa at reflux for 30 min. gave 3β,20β-diacetoxy-5α-pregnane-18-nitrile (VI, R = Ac), m.p. (from hexane) 131–132°, $[\alpha]^{25}D$ +5° (*c*, 1.0), ν_{max}^{KBr} at 2250 (nitrile) and 1740 and 1250 cm.$^{-1}$ (acetate). The corresponding diol (VI, R = H) had m.p. (from methylene dichloride–hexane) 229.5–231.5°, $[\alpha]^{25}D$ −2° (*c*, 1.0), $\nu_{max}^{CHCl_3}$ at 2250 cm.$^{-1}$ (nitrile).

Treatment of (VI, R = H) with 4:1 EtOH-concd. HCl under reflux for 15 min. gave the iminolactone (VII, X = NH, R = H) (89%), m.p. 171–174°, $[\alpha]^{26}D$ +3° (*c*, 1.0), $\nu_{max}^{CHCl_3}$ at 1670 cm.$^{-1}$ (C=N), which on heating with 2 *N* hydrochloric acid on the steam-bath for 24 hr. furnished the lactone (VII, X = O, R = H), m.p. 217–218°, $[\alpha]^{25}D$ +12° (*c*, 1.0 in Me_2CO), $\nu_{max}^{CHCl_3}$ at 1750 cm.$^{-1}$ (γ-lactone). The corresponding acetate[2] (VII, X = O, R = Ac), prepared with pyridine–Ac_2O, had m.p. (from acetone–hexane) 207–209°, $[\alpha]^{24}D$ −9° (*c*, 1.0), $\nu_{max}^{CCl_4}$ at 1765 (γ-lactone) and at 1745 and 1240 cm.$^{-1}$ (acetate). This acetate (VII, X = O, R = Ac) also was obtained (m.p., mixed m.p. and infrared spectrum) by oxidation of (V, R = Ac) with pyridine–CrO_3.

Similarly the nitrite of 6β-hydroxycholestanyl acetate (VIII, R = NO, X = H_2), m.p. (from methanol) 153–154°, $[\alpha]D$ −31° (*c*, 0.56) (32.2 g.), irradiated in toluene (700 ml.), gave a crystalline precipitate of the nitroso-dimer (16.5 g.) corresponding to the oxime (VIII, R = H, X = NOH). Refluxing the dimer in 2-propanol furnished this

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(2) G. Cainelli, M. L. Mihailović, D. Arigoni and O. Jeger, *ibid.*, **42**, 1124 (1959); B. Kamber, G. Cainelli, D. Arigoni and O. Jeger, *ibid.*, **43**, 347 (1960).

(3) Satisfactory analytical data have been secured for all compounds described in this communication.