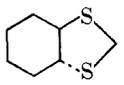
direct, high yield synthesis of IV from readily available starting material.

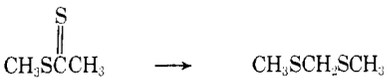
To determine whether this hydrogenolysis reaction was general for a variety of trithiocarbonates, we prepared *trans*-1,2-cyclohexane trithiocarbonate (I) using the method of Culvenor, Davies, and Pausacker.[8] Hydrogenation of I under similar conditions (MoS_3, 160°, 1900 psi) afforded *trans*-methylenedithiocyclohexane (V)[5] in 50% yield. The infrared (1439 cm^{-1}) pmr



V

[δ (CCl_4) 3.78 (singlet, 2 H, $-SCH_2S-$), 2.86 (multiplet, 2 H, >CHS), 1.16–2.36), multiplet (8 H, $-CH_2-$)], and mass spectrum [m/e 160 (M^+)] are consistent with our structural assignment.

In addition, we have found noncyclic trithiocarbonates can also be converted into the corresponding 1,3-disulfides. Thus dimethyl trithiocarbonate (VI), pre-



VI VII

pared from methyl chloride and sodium trithiocarbonate, was reduced using cobalt sulfide and molybdenum disulfide as catalyst at 2500 psi and 150°. In addition to recovered starting material, 2,4-dithiapentane (VII)[9] [infrared spectrum 1435, 1421 cm^{-1}; δ (neat) 3.65 (singlet, 2 H, $-SCH_2S-$), 2.13 (singlet, 6 H, $-SCH_3$)] was isolated in ~10–15% yield.

Experimental Section

All boiling points are uncorrected. Infrared spectra were recorded with a Perkin-Elmer Infrared or Model 21 spectrophotometer. Pmr spectra were determined at 27° (probe temperature) with a Varian Associates Model A-60A spectrometer using tetramethylsilane (TMS) as an internal standard. For each compound, chemical shifts cited are the centers of the multiplet. Numbers in parentheses refer to the multiplicity of the observed resonance.

Reagents.—Ethylene trithiocarbonate, molybdenum di- and trisulfide, cobalt sulfide and hydrogen (CP grade) were obtained from commercial sources and used without further purification. *trans*-1,2-Cyclohexane trithiocarbonate[8] and dimethyl trithiocarbonate[10] were prepared by known literature methods.

General Procedure.—The experimental conditions for the hydrogenations are recorded in Table II. A typical laboratory procedure for the preparation of 1,3-dithiolane follows.

TABLE II

Compd	Amt, mol	Catalyst (g)	Benzene, ml	H_2, psi
I	0.37	MoS_3 (5)	200	2000
III	0.11	MoS_3 (3)	50	1900
VI	0.36	MoS_2 (5) CoS (5)	100	2500

1,3-Dithiolane.—Ethylene trithiocarbonate (50 g, 0.37 mol) dissolved in 200 ml of benzene and 5.0 g of molybdenum trisulfide were placed in a 300-ml stainless steel autoclave. The autoclave was pressured to 2000 psi with hydrogen and heated to 150° for 12 hr while maintaining a constant hydrogen pressure of 2000 psi. After cooling to 25°, the autoclave was vented through a 20% sodium hydroxide solution; filtration of the clear solution followed by removal of the solvent at 15 mm afforded 37.0 g of 1,3-dithiolane (93% purity). Distillation yielded a malodorous, colorless liquid: bp 75° (25 mm); $n^{23}D$ 1.5980 [lit.[2] bp 61° (11 mm), $n^{15}D$ 1.5975]; infrared 2960, 2919, 1415, 1270, 858, 728, 680 cm^{-1}; pmr (CS_2) δ 3.83 (SCH_2S, 1), 3.13 (CH_2S, 1).

Registry No.—I, 16166-42-0; III, 822-38-8; IV, 4829-04-3; V, 5673-01-8; VI, 2168-84-5; VII, 1618-26-4.

Acknowledgment.—The technical assistance of Mr. Richard Eletto is gratefully acknowledged.

(8) C. C. J. Culvenor, W. Davies, and K. H. Pausacker, *J. Chem. Soc.*, 1050 (1946).
(9) H. Bohme and R. Marx, *Ber.*, **74**, 1667 (1941).
(10) E. Wertheim, *J. Amer. Chem. Soc.*, **48**, 826 (1926); **53**, 4037 (1931). This compound was kindly provided by Professor N. Remes.

Nitrogen Mustard Reactions by Nuclear Magnetic Resonance Spectroscopy[1]

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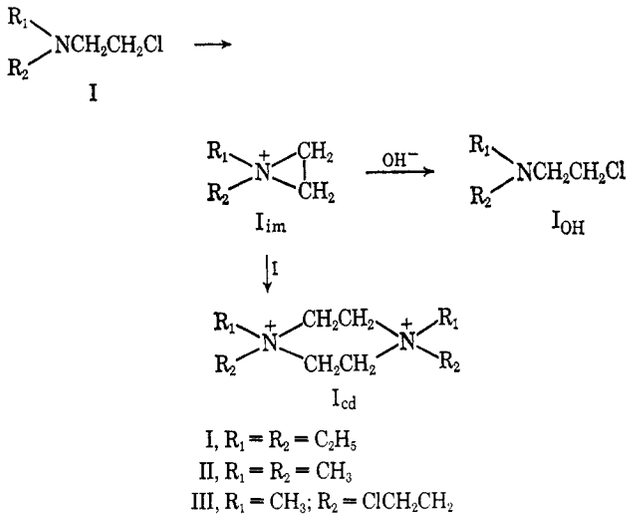
Classical chemical studies have shown that the reactions of many 2-chloroethylamines in aqueous solvent systems proceed through the formation of reactive ethyleneimonium ion intermediates.[3,4]



I, $R_1 = R_2 = C_2H_5$
II, $R_1 = R_2 = CH_3$
III, $R_1 = CH_3$; $R_2 = ClCH_2CH_2$

Levins and Papanastassiou[5] have recently shown that, for a number of primary and secondary 2-haloethylamines and for one tertiary amine, methylbis(2-chloroethyl)amine (HN-2), nmr studies in ^2H_2O can be useful for studying the rate of formation and

(1) Supported in part by U. S. Public Health Service Grant No. Ca-08485.
(2) From the Ph.D. Dissertation of J. R. Sowa, University of Pennsylvania, 1964.
(3) C. Golumbic, J. S. Fruton, and M. Bergman, *J. Org. Chem.*, **11**, 578 (1946).
(4) P. D. Bartlett, S. D. Ross, and C. G. Swain, *J. Amer. Chem. Soc.*, **71**, 1415 (1949).
(5) P. L. Levins and Z. B. Papanastassiou, *ibid.*, **87**, 826 (1965).

disappearance of aziridine and aziridinium intermediates. Before this publication we had also found[2] that nmr studies of solutions of 2-chloroethyl tertiary amines in ^2H_2O fully confirm the presence of the ethylenimonium intermediates and, in fact, serve as simple and useful means of measuring the rate of formation and disappearance of these important reactive intermediates.

In the case of the imonium ions I_{im} and II_{im}, the four hydrogens on the aziridinium ring are equivalent and appear as a singlet. For the case of III_{im}, two aziridinium hydrogens are *cis* to the N-methyl and the other two are *trans*, leading to a weak splitting of these hydrogens to a doublet (J = 2.4 cps). The chemical shifts for the aziridinium methylene hydrogens (δ 3.1–3.3) is upfield from methylenes in the cyclic dimer (4.2–4.4) or protonated bases (3.4–3.7). This is in accord with the normal upfield shift of methylene groups in three-membered rings.

The marked influence of steric hindrance at the nitrogen is indicated by the marked differences in the case of dimer formation from the several mustards. Thus, while II (Table I) cyclizes so readily that the concentration of II_{im} never exceeds 22% and III cyclizes well enough so that the maximum concentration of III_{im} reaches 57% (Table II), for I, conversion into I_{im} is rapid and quantitative, with no detectable formation of the piperazinium dimer (I_{cd}) which we synthesized by an alternate route. Evidently the only reaction which I_{im} in water undergoes is a very slow hydrolysis to the alcohol (I_{OH}).

The data in Tables I, III, and IV are in accord with the hypothesis that the rate of cyclization is related to the base strength, with I > II > III.

TABLE I

CONVERSION OF II (0.1 M), pH 9, 27°, IN D_2O BY NMR SPECTRA

Time, min	% II[a]	% II_{im}	% dimer	k_d[b]
0	79	12.5	8.5	
1	53	19	28	0.25
2	34	21	45	0.23
5	18	22	60	0.20
7	12	22	66	0.22
10	6.7	20	73	
21	5.8	13	81	

[a] $k_1 = 3.25 \times 10^{-3}$ sec^{-1}, based on % II remaining. [b] Rate of dimer formation, k_d[II][II_{im}], in l. mol^{-1} sec^{-1}, was estimated graphically from the slope of a plot of [dimer] *vs.* time.

TABLE II

CONVERSION OF III (1 M), pH 10, 30°, IN WATER AND ALSO IN SODIUM CARBONATE BY NMR SPECTRA

Time, min	% III	% III_{im}	% dimer	k_d[a] × 10^5
5	72	27		
6	55	36	8.4	8.5
8	49	41	9.6	8.3
10	41	47	11.7	8.6
15	31	52	17	10.3
20	22	57	20	12.8
25	15	57	28	
30	9.4	52	38	
45	3.4	48	47	
60		44	56	
24 hr			100	

[a] Rate of dimer formation = k_d[III][III_{im}], in l. mol^{-1} sec^{-1}, was estimated graphically. The values increase at high conversion, probably owing to more rapid reaction of III_{im} with amino alcohol formed by hydrolysis.

TABLE III

CYCLIZATION OF I (0.09 M), pH 10.5, 0°, IN SODIUM CARBONATE (0.2 M)

Time, min	% I_{im}
15	50[a]
30	84[a]
45	~100
690 (at 32°)[b]	~100

[a] $k \sim 4 \times 10^{-4}$ sec^{-1}. [b] pH 5.

TABLE IV

REACTION OF I_{im} (0.1 M), pH 9, 21°, WITH SODIUM THIOSULFATE (0.1 M)

Time, min	% I_{im}[a]
3	57
6	40
8	31
10	27
15	13.5
19	9.6
22	7.6
35	3.5

[a] k_2 = 0.041 l. mol^{-1} sec^{-1}.

Experimental Section

Cyclization of **diethyl-2-chloroethylamine** (I) to the imonium ion, I_{im}, was readily followed in a Varian Model 4300, HR-60 nmr spectrophotometer using 5-mm-o.d. precision tubes. In ^2H_2O at pH 5, 0.07 M I was protonated and stable, the ion showing a triplet (6 H) at δ' −3.44 (with respect to H_2O in the ^2H_2O) (J = 7 cps), a quadruplet (4 H) at −1.42 (J = 7 cps), a triplet (2 H) at −1.16 (J = 5.6 cps), and a triplet (CH_2Cl) at −0.75 (J = 5.6 cps). When the proton was removed from the nitrogen by adjusting the pH to 10.5, these four absorptions shifted to δ' −3.63, −2.00, −1.80, and −1.10, respectively. Even at 0°, the spectrum at pH 10.5 changed within a few minutes (see Table III), developing absorption characteristics of I_{im} at δ' −3.38 [triplet, J = 6.0 (6 H)], −1.50 [quadruplet, J = 6.0 (4 H)], and −1.69 [singlet (4 H)]. This conversion was essentially complete in 30 min and was unchanged after 20 hr at room temperature at pH 5.0; at pH 10.5, the half-life for the disappearance of I_{im} was 6 hr at 0° and 1.5 hr at 33°. On heating to 100° at pH 5.0, the spectrum of I_{im} changed to a spectrum similar to protonated I, presumably $Et_2N^+HCH_2$-CH_2OH, with a half-life of *ca.* 15 min. A ^2H_2O solution of I (0.1 M) brought to pH 12 by 2 M NaO^{2}H solution, cyclized within a few minutes at 27°, but I_{im} was 40% hydrolyzed to the amino alcohol within 40 min: δ' −3.78 [triplet, J = 7 cps (6 H)], −2.18 [quadruplet, J = 7 cps (4 H)], −1.44 [triplet, J = 7 cps (2 H)], and −1.03 [triplet, J = 7 cps (2 H)].

The nmr spectra of the hydrochloride at pH 5 and pH 7 and of I_{im} at pH 7 and pH 8 in ^2H_2O were checked against sodium trimethylsilylpropanesulfonate; the shifts reported here as δ' should be corrected by adding 4.68 ppm to give values in δ with respect to the trimethylsilyl group of this reference.

Reaction of I_{im} with thiosulfate ion could also be followed by nmr (see Table IV), the Bunte salt of I showing absorption at δ' −3.64 [triplet, J = 7.2 cps (6 H)], −1.93 [quadruplet, J = 7.2 cps (4 H)], and −1.54 [singlet (4 H)].

The **cyclic dimer of I**, N,N,N′,N′-tetraethylpiperazinium diiodide was prepared from N,N′-diethylpiperazine in excess ethyl iodide and recrystallized from methanol: mp <320°.

Anal. Calcd for $C_{12}H_{28}N_2I_2$: C, 31.73; H, 6.21; N, 6.17. Found: C, 31.68; H, 6.19; N, 6.12.

In ^2H_2O this ion showed absorption at δ' −2.47 [triplet, J = 5.0 cps (3 H)], −1.07 [quadruplet, J = 5.0 cps (2 H)],

and −0.96 (2 H). None of this product was observed in any of the reaction conditions above.

Dimethyl-2-chloroethylamine hydrochloride (II HCl) in ^2H_2O (0.1 *M*, pH 5) showed nmr absorption at δ' −1.71 (6 H), −1.10 [triplet, J = 6.0 cps (2 H)], and −0.66 [triplet, J = 6.0 cps (2 H)]. On adjustment of the pH to 9 with sodium bicarbonate, these shifted to δ' −2.34, −1.85, and −0.91, respectively. The singlet for the aziridinium methylenes in II_{im}, δ' −1.51, developed rapidly but was quickly converted to the cyclic dimer, N,N,N′,N′-tetramethylpiperazinium ion, δ' −1.20 (3 H) and −0.64 (2 H). Data on rate of conversion are summarized in Table I.

For the **Bunte salt from II**, prepared from 0.2 *M* II and 2 *M* sodium thiosulfate in ^2H_2O by heating to 75° for 2.5 hr, nmr absorption was observed as sharp singlets at δ' −1.78 (6 H) and δ' −1.17 (4 H).

For **methylbis(2-chloroethyl)amine (III)** about 1 *M* in water and also 1 *M* in sodium bicarbonate, nmr spectra showed absorption at δ' −2.67 (3 H), −2.18 [triplet, J = 8.4 cps (4 H)], and −1.25 [triplet, J = 8.4 cps (4 H), CH_2Cl], rapidly developing absorption for III_{im} at δ' −1.74 (3 H) and −1.60 [doublet, J = 2.4 cps (4 H)] and for the cyclic dimer, N,N′-dimethyl-N,N′-bis(2-chloroethyl)piperazinium dichloride (III_{cd}), at δ' −1.30 (singlet, 6 H) and −0.52 (singlet, 8 H). These spectra were useful for following the course of reaction, as summarized in Table II. Our values for nmr chemicals shifts and rates of reaction are not in full agreement with those of Levins and Papanastassiou,[5] perhaps owing to some differences in pH. Our reaction mixtures were buffered by 1 *M* bicarbonate, theirs were "neutralized by a predetermined amount of sodium hydroxide."

Registry No.—I, 100-35-6; cyclic dimer of I, 18386-47-5; II, 107-99-3; III, 51-75-2.

Branched-Chain Sugar Nucleosides. Synthesis of a Purine Nucleoside of 4-*O*-Acetyl-L-arcanose

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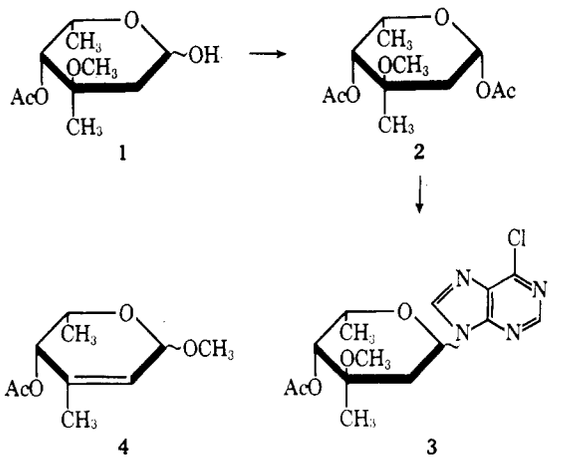
Arcanose is a dideoxy branched-chain sugar which occurs naturally as its 4-*O*-acetyl derivative in lankamycin,[1] a medium-spectrum macrolide antibiotic produced by *Streptomyces violaceoniger*.[2] By a combination of nmr and degradative studies, the 2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-L-*xylo*-hexose structure **1** was proposed for arcanose (Scheme I).[3] This assignment has been corroborated recently by us[4] by the synthesis of the D-enantiomer. We report now the utilization of L-arcanose in the preparation of 6-chloro-9-(4′-*O*-acetyl-2′,6′-dideoxy-3′-*C*-methyl-3′-*O*-methyl-β-L-*xylo*-hexopyranosyl)purine (**3**), the first synthetic nucleoside containing a naturally occurring branched-chain sugar.

SCHEME I



Attempts to obtain a glycosyl chloride derivative of **1** by treatment of its methyl glycoside with methylene chloride saturated with hydrogen chloride were unsuccessful. Although thin layer chromatography (tlc) showed that predominantly one compound had been formed, the nuclear magnetic resonance (nmr) spectrum of the crude product indicated the loss of a methoxyl group and the H-2ax hydrogen, and a downfield shift from τ 8.9 to 8.5 of the signal attributable to the C-3 tertiary methyl group. These data are consistent with the loss of methanol between C-2 and C-3 to give the unsaturated derivative **4**.

Treatment of 4-*O*-acetyl-L-arcanose[4] with acetic anhydride and pyridine gave a syrupy diacetate (**2**), which was assigned the β-L configuration by nmr spectroscopy. Condensation of 1,4-di-*O*-acetyl-2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-β-L-*xylo*-hexopyranose (**2**) with 6-chloropurine was achieved by fusing an intimate mixture of the two compounds in the presence of a trace of *p*-toluenesulfonic acid at 100° for 5 min. Fractionation of the complex mixture of products by preparative tlc on silica gel afforded the pure branched-chain sugar nucleoside **3**. The anomeric configuration has not been established. The ultraviolet absorption, uv max (EtOH) 264 mμ (ε 11,000), is in agreement with a 9-substituted purine.[5]

Experimental Section[6]

1,4-Di-*O*-acetyl-2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-β-L-*xylo*-hexopyranose (2).—A solution of **1** (105 mg) in pyridine (3 ml) and acetic anhydride (2 ml) was kept at ambient temperature overnight. The reaction mixture was poured into water, and the product isolated in the usual manner. Fractionation of the crude product on silica gel (100 × 2 cm column) with 2:3 ethyl acetate–petroleum ether as eluent gave 100 mg (80%) of diacetate **2** as a colorless mobile oil: $[\alpha]_D$ +35° (*c* 1.1, EtOAc); ir (film) 5.75 μ (OAc); nmr ($CDCl_3$) τ 4.1 (one-

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(2) E. Gäumann, R. Hütter, W. Keller-Schierlein, L. Neipp, V. Prelog, and H. Zähner, *ibid.*, **43**, 601 (1960).

(3) G. Roncari and W. Keller-Schierlein, *ibid.*, **49**, 705 (1966).

(4) G. B. Howarth, W. A. Szarek, and J. K. N. Jones, *Chem. Commun.*, 62 (1968); *Carbohyd. Res.*, **7**, 284 (1968).

(5) E. E. Leutzinger, W. A. Bowles, R. K. Robins, and L. B. Townsend, *J. Amer. Chem. Soc.*, **90**, 127 (1968).

(6) Optical rotations were measured with a Perkin-Elmer Model 141 polarimeter at 20 ± 2°. Infrared spectra were measured on a Beckman-IR5A spectrophotometer. Ultraviolet spectra were measured with a Unicam SP 800B spectrophotometer. Nmr spectra were determined with a Varian A-60 spectrometer; the freshly prepared compounds were examined in chloroform-*d* with tetramethylsilane as the internal standard. Thin layer chromatography was performed using silica gel G and 2:3 ethyl acetate–petroleum ether (bp 60–80°), with indication by sulfuric acid.