refluxed for 3 hr., excess reagent was decomposed by adding ethanol and the salts were filtered. The filtrate was evaporated to dryness. The residue was N-acetylated in methanol with acetic anhydride and processed as usual to give the crystalline product (1.5 g.). Recrystallization from ether–pentane gave 1.3 g. of a solvated product, m.p. 65–66°. Vapor phase chromatography indicated the presence of solvated ether and/or pentane molecules. The product melted when dried *in vacuo* at 50° or at room temperature; infrared absorption data, λ_{max}^{KBr} 1670, 1658 (amide I), and 1568 cm.$^{-1}$ (amide II).

Anal. Calcd. for $C_{17}H_{23}NO_5$: C, 63.51; H, 7.21; N, 4.31. Found: C, 62.67; H, 7.29; N, 4.48.

5-Acetamido-5-deoxy-D-ribofuranose (XXIII). A. From XXI.—A solution containing 330 mg. of XXI in 75 ml. of ethanol was hydrogenated 2.5 hr. over 20% palladium catalyst[22] (0.5 g.) at room temperature. Filtration and evaporation of the solution gave a colorless sirup (120 mg.) which showed two spots, R_f 0.34 and 0.27 in solvent A. These components were separated by preparative paper chromatography to give XXIII (80 mg.) (R_f 0.34 component) as a colorless sirup; $[\alpha]^{24}D$ 19° (constant, 24 hr.) (*c* 1.16, in water). Solutions of XXIII equilibrated in the presence of acids and bases (much faster) to a mixture consisting mainly of XXIII and XXII in minor amounts. The infrared spectrum of XXIII showed an amide I band at 1640 cm.$^{-1}$ and an amide II band at 1560 cm.$^{-1}$.

B. From XXVIII.—A solution containing 400 mg. of XXVIII in 10 ml. of 60% acetic acid was heated 1 hr. on the steam bath. Evaporation of the solution gave a residue which contained essentially the same two components as before. These were separated by chromatography over cellulose to give XXIII (200 mg.) (R_f 0.34 component) as a colorless sirup.

5-Acetamido-5-deoxy-D-ribopyranose (XXII). A. From XXI.—The component with R_f 0.27 from the hydrogenolysis of XXI was isolated by elution of the appropriate zone as described before to give XXII (20 mg.) as a colorless sirup. This product was homogeneous on paper chromatograms in several solvent systems. Solutions of XXII in the presence of acids or bases were equilibrated to give a mixture consisting predominantly of XXIII with only small amounts of XXII, as evidenced by paper chromatography experiments.

B. From XXVIII.—Fractions containing the component with R_f 0.27 from the cellulose column chromatography experiment described before, were combined and processed as usual to give XXII (13 mg.) as a colorless sirup. Its properties were identical with the product obtained from XXI.

5-Acetamido-5-deoxy-D-ribose Benzylphenylhydrazone (XXIV).—A solution of XXIII (35 mg.) in aqueous ethanol containing 50 mg. of sodium acetate and 22 mg. of benzylphenylhydrazine hydrochloride was refluxed for 2.5 hr. The resulting yellow solution was processed as usual to give a yellow sirup which was covered with 10 ml. of ether and stored at 5°. The crystals that formed were collected and washed with petroleum ether (b.p. 50–60°) to give 35 mg. of product. Recrystallization from a mixture of methanol, ether, and petroleum ether gave pure material, m.p. 143–144°; $[\alpha]^{23}D$ −36.4° (*c* 1.725, in methanol); λ_{max}^{KBr} 3450, 3290 (OH), 1627 (amide I), and 1556 cm.$^{-1}$ (amide II, shoulder). X-Ray powder diffraction data[29] gave 11.95 w, 10.59 s, 7.34 w, 6.86 m, 5.83 w, 5.44 m, 5.10 s, 4.93 w, 4.73 m, 4.51 m, 4.35s, 4.04 wb, and 3.79 w.

Anal. Calcd. for $C_{20}H_{25}N_3O_4$: C, 64.67; H, 6.78; N, 11.31. Found: C, 64.49; H, 6.66; N, 11.11.

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Use of a Complex Neighboring Group to Prepare Aminomercaptofuranose Sugars[1]

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The conversion of methyl 3-amino-3-deoxy-α-D-arabinofuranoside (I) to methyl 3-amino-3-deoxy-2-thio-α-D-ribofuranoside hydrochloride (VI) using a dithiocarbamoyl neighboring group is described. The use of an alternative procedure resulted in a C-3 to C-5 neighboring group participation and ultimately yielded methyl 3-amino-3-deoxy-2-*O*-methylsulfonyl-5-thio-α-D-arabinofuranoside hydrochloride (XIII).

The preparation of methyl 3-amino-3-deoxy-2-thio-α-D-allopyranoside hydrochloride, described previously,[2] utilized the *S*-methyldithiocarbamoyl neighboring group in going from a *trans*-amino alcohol to a *cis*-amino mercaptan; the over-all result of the synthetic work was the conversion of a D-altrose derivative to a D-allose derivative. In the course of that work it was noted that when sodium methoxide was used to effect the neighboring group participation the nitrogen atom of the group was the displacing agent, but when refluxing pyridine was employed the sulfur atom was the displacing agent. In a later article zu Reckendorf and Bonner[3] reported that the *S*-methyldithiocarbamoyl group in a suitably blocked D-glucosamine derivative gave sulfur participation when methanolic sodium methoxide was used to effect participation; these authors suggested that the conformational differences in the participating and leaving groups in the blocked 3-amino-3-deoxy-D-altrose glycoside and in the blocked 2-amino-2-deoxy-D-glucose glycoside, both pyranosides, might explain the different reaction courses in these two series. It was of interest to extend the study of the dithiocarbamoyl group to the furanose sugar system where the geometrical situation of the participating and leaving groups would be quite different from the pyranose sugars; this manuscript describes the conversion of methyl 3-amino-3-deoxy-α-D-arabinofuranoside (I) to methyl 3-amino-3-deoxy-2-thio-α-D-ribofuranoside (VI) using the complex neighboring group approach.

Methyl 3-amino-3-deoxy-α-D-arabinofuranoside (I) was prepared from methyl 2,3-anhydro-α-D-lyxofuranoside by the literature procedure.[4] The conventional reaction of I with carbon disulfide and methyl iodide furnished the dithiocarbamate II as a crystalline solid, further characterized as the dibenzoate III. The reaction of II with nearly the stoichiometric amount of methyl chloroformate yielded the 5-*O*-methoxycarbonyl derivative (IV) as an oil; use of the trityl blocking group for

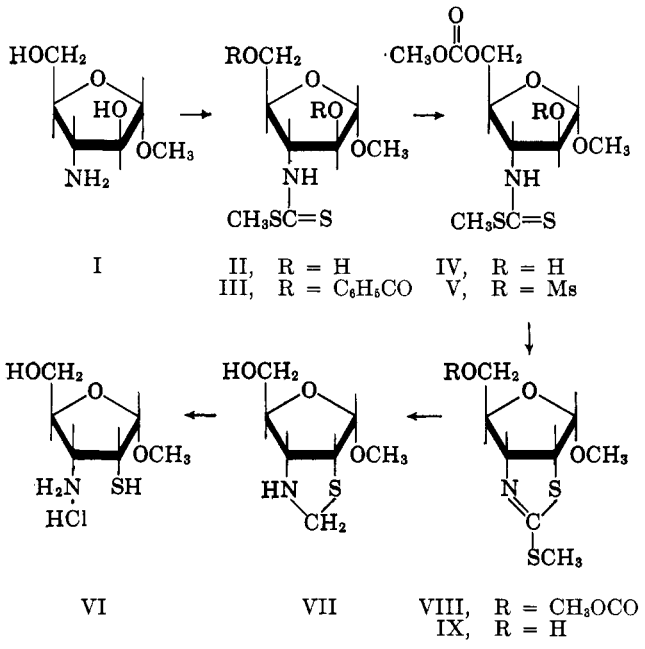
(1) This work was carried out under the joint auspices of the Office of the Surgeon General, Medical Research and Development Command, under contract no. DA 49-193-MD-2068 and of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service under contract no. SA-43-ph-1892. The opinions expressed in this article are those of the authors and not necessarily those of either sponsoring agency.

(2) L. Goodman and J. E. Christensen, *J. Am. Chem. Soc.*, **83**, 3823 (1961).

(3) W. M. zu Reckendorf and W. A. Bonner, *Proc. Chem. Soc.*, 429 (1961).

(4) B. R. Baker, R. E. Schaub, and J. H. Williams, *J. Am. Chem. Soc.*, **77**, 7 (1955).

the C-5 hydroxyl group was less satisfactory. Treatment of IV with methanesulfonyl chloride gave only a fair yield of the crystalline methanesulfonate V. The best method for converting V to the thiazoline VIII employed pyridine at reflux. Alternatively heating of V in toluene gave a sirup that appeared to be the methanesulfonic acid salt of VIII which could be converted to VI; the yields of products from V by this latter route were lower. The thiazoline VIII, an oil, was deblocked with a catalytic amount of sodium methoxide in methanol, affording IX, also as an oil. Aluminum amalgam



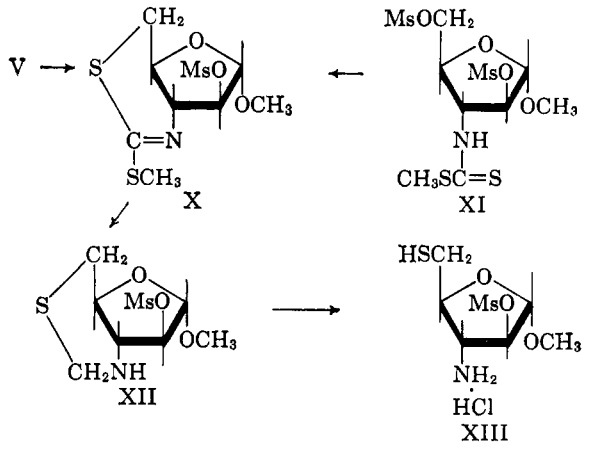
I II, R = H III, R = C_6H_5CO IV, R = H V, R = Ms

VI VII VIII, R = CH_3OCO IX, R = H

reduction of IX gave the thiazolidine VII, a sirup for which a crystalline derivative was not found. The standard decomposition of VII with mercuric chloride yielded a solid mercaptide that was converted to the aminomercaptan salt VI with hydrogen sulfide. The glycoside VI was an amorphous solid but it gave an excellent elemental analysis.

Attempts to hydrolyze the glycoside VI to the free sugar with aqueous hydrochloric acid were not successful. The hydrolysis product was an amorphous, nitroprusside-negative solid whose elemental analysis did not agree with any logical structure; however, the analysis did show the proper nitrogen to sulfur ratio.

When the dithiocarbamoyl methanesulfonate V was treated with methanolic sodium methoxide there was isolated a low yield of a crystalline compound whose infrared spectrum showed a strong C=N band at 6.4 μ and strong sulfonate ester bands. The same compound could be obtained in better yield by sodium methoxide treatment of the dimethanesulfonate XI, and since the sulfonate ester group of the product could not be displaced by benzoate ion under forcing conditions, it was probable that the new solid was the dihydro-1,3-thiazine X. Here again there is a difference in result between the reaction of sodium methoxide and refluxing pyridine on a *trans*-dithiocarbamoylmethanesulfonate. In this instance both reagents lead to sulfur participation whereas in the previous instance,[2] sodium methoxide led to nitrogen participation. The presence of some thiazoline product from the reaction of V and XI with methoxide cannot be ruled out, since

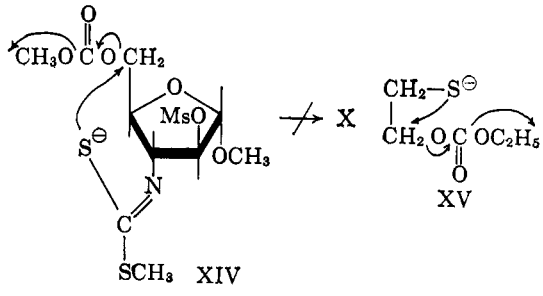


XII XIII

the yield of X in these reactions was far from quantitative. The possibility of some product of nitrogen participation cannot be eliminated.

It seems probable that the first step in the conversion of V to X is the removal of the methoxycarbonyl blocking group of V. This is followed by a transmesylation reaction between demethoxycarbonylated V and a second molecule of V to form XI, which then undergoes 3,5-cyclization giving X. A similar intermolecular transtosylation reaction was observed by Cope and Shen[5] in the case of a 1,4:3,6-dianhydrohexitol; these authors suggested that a *p*-toluenesulfonate suitable for such a transtosylation reaction must be one that is capable of undergoing an S_N2S (*i.e.*, cleavage of the sulfur–oxygen bond of the ester) type of reaction with an alkoxide ion, *e.g.*, an isolated secondary *p*-toluenesulfonate group of a carbohydrate. The methanesulfonate group in V fulfills this requirement.

The direct displacement of the methoxycarbonyloxy group by the ionized dithiocarbamoyl group in XIV represented another possible mechanism for the formation of X from V.[6] The mercaptoethylation of amines with ethyl 2-mercaptoethylcarbonate represents a situation in which a mercaptide ion probably displaces an ethoxycarbonyloxy group to form ethylene sulfide which then reacts with the amines[7]; the probable intermediate in that reaction, XV, is analogous to XIV. The treatment of IV with sodium methoxide under the



XIV XV

conditions that afforded X from V, however, merely regenerated the dithiocarbamate II. It seems highly unlikely that the change from a hydroxyl group in IV to the mesyloxy group in V could result in a change in the course of reaction of these compounds with sodium

(5) A. C. Cope and T. Y. Shen, *J. Am. Chem. Soc.*, **78**, 5912 (1956).

(6) This mechanism was suggested by Dr. Elmer J. Reist of these laboratories.

(7) D. D. Reynolds, D. L. Fields, and D. L. Johnson, *J. Org. Chem.*, **26**, 5125 (1961).

methoxide, and it seems safe to rule out this latter mechanism.

Aluminum amalgam reduction of X afforded the crystalline tetrahydro-1,3-thiazine XII which was converted to the 3,5-aminomercaptan salt XIII with mercuric chloride, followed by hydrogen sulfide.

Experimental[8]

Methyl 3-Deoxy-3-(dithiocarbomethoxy)amino-α-D-arabinofuranoside (II) and Its Dibenzoate (III).—To a chilled (0°), stirred solution of 22.3 g. (0.137 mole) of the amine I,[4] 400 ml. of dry pyridine, and 14.3 g. (0.141 mole) of dry triethylamine, was added slowly, while maintaining the temperature below 10°, 11.2 g. (0.146 mole) of carbon disulfide. The solution was stirred for 1 hr. at 0–5°, then 20.1 g. (0.141 mole) of iodomethane was added slowly while the temperature was kept below 10°. The mixture was stored at 5° for 24 hr., then was poured with stirring into 1 l. of ice–water. The product was extracted with two 250-ml. portions of dichloromethane, and the combined extracts were washed with water, dried over magnesium sulfate, and evaporated *in vacuo*, affording, after removal of all the pyridine, 32.6 g. (94%) of a yellow solid. Recrystallization of the solid from 100 ml. of benzene gave 26.7 g. (77%) of crystals, m.p. 85–90°, and a second recrystallization from 85 ml. of benzene yielded 25.2 g. (73%) of product, m.p. 88–91°. The analytical sample, recrystallized from benzene had m.p. 91–92°; $[\alpha]^{28}D$ +92° (1% in methanol); λ_{max}^{Nujol} 2.99, 3.01, 3.05 (OH, NH), 6.63 μ (NH).

Anal. Calcd. for $C_8H_{15}NO_4S_2$: C, 37.9; H, 5.97; N, 5.53; S, 25.3. Found: C, 37.9; H, 5.69; N, 5.31; S, 25.5.

A mixture of 0.97 g. (3.83 mmoles) of II and 10 ml. of pyridine was treated with 1.70 g. (12.0 mmoles) of benzoyl chloride according to standard procedures. The crude yield of solid was 1.72 g. (97%), and this was recrystallized from 15 ml. of benzene and sufficient petroleum ether (30–60°) to cause crystallization, affording 1.41 g. (80%) of plates, m.p. 118–125°. The analytical sample recrystallized from benzene had m.p. 125–127°; $[\alpha]^{24}D$ −33.0°; λ_{max}^{Nujol} 3.03, 6.53 (NH), 5.78, 5.83 (ester C=O), 7.79 (ester C—O—C), 13.90 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{22}H_{23}NO_6S_2$: C, 57.3; H, 5.02; N, 3.04; S, 13.9. Found: C, 58.0; H, 5.28; N, 2.91; S, 13.6.

Methyl 3-Deoxy-3-(dithiocarbomethoxy)amino-5-*O*-methoxycarbonyl-α-D-arabinofuranoside (IV).—To a chilled (0°), stirred solution of 13.36 g. (52.7 mmoles) of II in 80 ml. of pyridine was added dropwise a solution of 5.42 g. (57.6 mmoles) of methyl chloroformate in 40 ml. of chloroform. The resulting solution was stirred for 30 min. at 0° and for 18 hr. at room temperature, then poured, with stirring, into 500 ml. of cold saturated aqueous sodium bicarbonate. The chloroform layer was separated and the aqueous layer was extracted with 100 ml. of chloroform. The combined chloroform solutions were washed with two 100-ml. portions of water, dried over magnesium sulfate, and evaporated *in vacuo*. Toluene was then added and evaporated to remove most of the pyridine, giving 18.7 g. of yellow sirup that still contained some pyridine; λ_{max}^{film} 2.90–3.02 (OH, NH), 5.68 (ester C=O), 6.62 (NH), 7.82 μ (C—O—C).

Methyl 3-Deoxy-3-(dithiocarbomethoxy)amino-5-*O*-methoxycarbonyl-2-*O*-methylsulfonyl-α-D-arabinofuranoside (V).—The crude IV from the preceding experiment was dissolved in 200 ml. of dry pyridine, chilled in an ice–acetone bath, and treated with 12.9 g. (0.148 mole) of methanesulfonyl chloride, added dropwise with good stirring. The solution was stirred for 1 hr. in the ice–acetone bath and was stored at 5° for 18 hr., then poured with stirring into 500 ml. of cold saturated aqueous sodium bicarbonate. The product was extracted with two 100-ml. portions of dichloromethane and the extracts were washed with two 100-ml. portions of water, dried over magnesium sulfate, and evaporated *in vacuo* at room temperature. Two 50-ml. portions of toluene were added and evaporated to remove pyridine, and 50 ml. of toluene was added to the solid residue. Filtration of the mixture gave 10.92 g. (53% from II) of solid, m.p. 94–110°. The filtrate was evaporated *in vacuo* and ethanol was added to the residue, affording an additional 1.12 g. (5.5%) of product, m.p. 113–120°. From a previous run the analytical sample was obtained after several recrystallizations from ethyl acetate, m.p. 123–125°; $[\alpha]^{26}D$ +116°; λ_{max}^{Nujol} 3.06, 6.59 (NH), 5.80 (ester C=O), 7.72 (ester C—O—C), 7.40 and 8.50 μ (sulfonate ester).

Anal. Calcd. for $C_{11}H_{19}NO_8S_3$: C, 33.9; H, 4.92; N, 3.60; S, 24.7. Found: C, 33.9; H, 4.85; N, 3.34; S, 23.2, 23.5.

5′-*O*-Methoxycarbonyl-1′-*O*-methyl-2-(methylthio)-α-D-ribofurano-[3′,2′:4,5]-2-thiazoline (VIII). A. From Hot Pyridine.—A solution of 6.06 g. (15.6 mmoles) of V in 60 ml. of pyridine was heated at reflux for 3.5 hr. under a nitrogen atmosphere, then cooled, and evaporated *in vacuo*. The residue was extracted with four 30-ml. portions of hot benzene leaving a residue of pyridinium methanesulfonate. The benzene extracts from two identical runs were combined, decolorized with Norit A, dried over magnesium sulfate, and evaporated *in vacuo* leaving 8.92 g. (98%) of an amber sirup; λ_{max}^{film} 5.70 (ester C=O), 6.37 (C=N), 7.85 μ (ester C—O—C).

B. From Hot Toluene.—A solution of 2.00 g. (5.14 mmoles) of V in 50 ml. of toluene was heated at reflux for 75 min., during which time an oil separated. The mixture was chilled and the toluene decanted. The residue was washed twice by decantation with ether and dried, yielding 1.28 g. (64%) of an amber sirup that appears to be the methanesulfonate salt of VIII; λ_{max}^{film} 3.70 (NH^+), 5.69 (ester C=O), 6.40 (C=N), 7.82 (ester C—O—C), 8.38, 9.41, 9.61 μ (mesylate ion). The salt, treated with sodium methoxide, afforded 0.54 g. (70%) of IX; aluminum amalgam reduction of IX gave 0.48 g. (110%) of crude VII. The thiazolidine (VII) was converted to 0.98 g. of mercaptide and thence to 0.16 g. (55%) of analytically pure mercaptoamine salt (VI). The over-all yield of VI from V was about 15%.

1′-*O*-Methyl-2-(methylthio)-α-D-ribofurano[3′,2′:4,5]-2-thiazoline (IX).—A mixture of 8.92 g. (30.5 mmoles) of VIII, 150 ml. of methanol, and 0.3 g. of sodium methoxide was stirred at room temperature overnight, adjusted to pH 7 with glacial acetic acid, and evaporated *in vacuo*. The residue was partitioned between 100 ml. of dichloromethane and 50 ml. of water and the organic layer was washed with 50 ml. of water, then dried over magnesium sulfate. Evaporation gave 5.69 g. (79%) of a sirup; λ_{max}^{film} 2.96 (OH), 6.38 μ (C=N).

1′-*O*-Methyl-α-D-ribofurano[3′,2′:4,5]thiazolidine (VII).—Aluminum foil (14 g.) was amalgamated according to the directions of Vogel[10] and to the aluminum amalgam was added a solution of 5.69 g. (24.1 mmoles)of IX in 500 ml. of tetrahydrofuran. The well stirred mixture was chilled and 50 ml. of water was added, dropwise with stirring. The reaction mixture was stirred for 6 hr. at 55–60°, then cooled, filtered through Celite, and evaporated *in vacuo* to afford 4.2 g. (91%) of a sirup; λ_{max}^{film} 2.93–3.05 μ (OH, NH); there was no C=N absorption near 6.4 μ.

Methyl 3-Amino-3-deoxy-2-thio-α-D-ribofuranoside Hydrochloride (VI).—A solution of 2.00 g. (10.5 mmoles) of VII in 10 ml. of water was filtered through Celite to remove a small amount of insoluble material. It was then treated with excess aqueous mercuric chloride solution to give, after drying, 5.33 g. of a cream-colored solid. The solid was suspended in 50 ml. of methanol and hydrogen sulfide was bubbled through the well stirred suspension for 20 min. The mixture was filtered through Celite and the filtrate evaporated *in vacuo*. The residue was washed with ether and dried *in vacuo*, leaving 1.36 g. (85%) of a white, nitroprusside-positive foam; λ_{max}^{Nujol} 3.0–3.2 (OH), 5.0, 6.29, 6.69 μ (NH_3^+).

Anal. Calcd. for $C_6H_{14}ClNO_3S$: C, 33.4; H, 6.54; Cl, 16.4; N, 6.49; S, 14.9. Found: C, 33.2; H, 6.61; Cl, 16.6; N, 6.40; S, 14.9.

A previous analytical sample (A) had $[\alpha]^{24}D$ −78° (1% in methanol); on paper chromatography it showed two spots with R_{Ad} 0.41 and 0.97. Deliberate oxidation of a portion of the product gave material that showed only the spot with R_{Ad} 0.41 suggesting that this preparation of VI contained an appreciable quantity of disulfide. This was confirmed by iodometric titration of the product which showed 77–80% of the theoretical thiol content. Another sample (B) of analytical purity had $[\alpha]^{26}D$ −61° (1% in methanol), suggesting that different samples may have been subjected to different degrees of anomerization during preparation.

(8) Melting points are uncorrected and were obtained with the Fisher-Johns apparatus. Optical rotations are given for 1% solutions in chloroform unless otherwise noted. Paper chromatography was done by the descending technique on Whatman no. 1 paper, using the solvent system 1-butanol–acetic acid–water (5:2:3). Spots were detected with the sodium azide–iodine spray,[9] unless otherwise noted, and were located relative to adenine (R_f adenine 1.00).

(9) E. Chargaff, C. Levine, and C. Green, *J. Biol. Chem.*, **175**, 67 (1948).

(10) A. I. Vogel, "Textbook of Practical Organic Chemistry," Longmans Green and Co., Ltd., London, England, 1956, p. 198.

Anal. Found for A: C, 33.2; H, 6.55; Cl, 16.3; N, 6.30; S, 15.0. Found for B: C, 33.4; H, 6.77; Cl, 16.2; N, 6.36; S, 14.6.

Methyl 2,5-Di-*O*-methylsulfonyl-3-(dithiocarbomethoxy)amino-α-D-arabinofuranoside (XI).—A chilled (0°), stirred mixture of 5.00 g. (19.8 mmoles) of II in 80 ml. of pyridine was treated dropwise with 7.4 g. (64.7 mmoles) of methanesulfonyl chloride under standard sulfonylation conditions. After a standard work-up, utilizing extraction with dichloromethane, there was obtained 7.62 g. (94%) of a sirup; λ_{max}^{film} 3.03, 6.55 (NH), 7.35, 8.50 μ (sulfonate ester).

1′-*O*-Methyl-2′-*O*-methylsulfonyl-2-(methylthio)-α-D-arabino-furano-[5′,3′:4,5]-4,5-dihydro-6H,1,3-thiazine (X). A. From V.—A mixture of 1.00 g. (2.57 mmoles) of V in 10 ml. of methanol was treated with a solution of 0.150 g. (2.78 mmoles) of sodium methoxide in 10 ml. of methanol. The solution was stirred at room temperature for 5 min. and heated on the steam bath for 3 min., then chilled and treated with a large volume of water. The precipitate, 0.19 g. (24%), m.p. 101–103°, was recrystallized twice from petroleum ether (b.p. 88–99°) to give 0.13 g. (16%) of crystals, m.p. 111–113°; $[\alpha]^{24}D$ −93.9°; λ_{max}^{Nujol} 6.35 (C=N), 7.39, 8.43 μ (sulfonate ester); there was no OH absorption near 3.0 μ.

Anal. Calcd. for $C_9H_{15}NO_5S_3$: C, 34.5; H, 4.82; N, 4.47; S, 30.7. Found: C, 34.9; H, 4.98; N, 4.23; S, 31.0.

B. From XI.—To a stirred, chilled (−11°) solution of 4.30 g. (10.5 mmoles) of the dimethanesulfonate XI in 20 ml. of methanol was added a solution of 0.60 g. (11.1 mmoles) of sodium methoxide in 20 ml. of methanol. The solution was stirred for 10 min. then poured into about 100 ml. of water. The precipitate, 2.08 g. (64%), was recrystallized from petroleum ether to give 1.32 g. (40%) of white crystals. A second recrystallization from petroleum ether gave product with m.p. 110–112°. There was no mixture melting point depression with the product from V.

1′-*O*-Methyl-2′-*O*-methylsulfonyl-α-D-arabinofurano[5′,3′:4,5]-tetrahydro-1,3-thiazine (XII).—A chilled, stirred suspension of 3.0 g. of aluminum which had been amalgamated,[10] 1.20 g. (3.84 mmoles) of X, and 100 ml. of tetrahydrofuran was treated, dropwise, with 15 ml. of water. The mixture was heated with stirring at 50° for 18 hr. under a nitrogen atmosphere, then was cooled and filtered through Celite. The filtrate was evaporated *in vacuo*, the residue partitioned between 20 ml. of dichloromethane and 20 ml. of water, and the dichloromethane layer washed with 10 ml. of water, then dried over magnesium sulfate. Evaporation *in vacuo* left 1.20 g. (116%) of a sirup that crystallized when it was scratched. This was recrystallized from ethanol, yielding 0.45 g. (44%) of crystals, m.p. 122–125°. The analytical sample from ethanol had m.p. 125–127°; $[\alpha]^{25}D$ +80°; λ_{max}^{Nujol} 3.07 (NH), 7.37, 8.50 μ (sulfonate ester); there was no C=N absorption near 6.4 μ.

Anal. Calcd. for $C_8H_{15}NO_5S_2$: C, 35.7; H, 5.61; N, 5.20; S, 23.8. Found: C, 35.6; H, 5.69; N, 5.22; S, 23.9.

Methyl 3-Amino-3-deoxy-2-*O*-methylsulfonyl-5-thio-α-D-arabinofuranoside Hydrochloride (XII).—The tetrahydro-1,3-thiazine (XII), 1.59 g. (5.91 mmoles), was dissolved in 50 ml. of boiling water and to the hot solution was added an excess of saturated aqueous mercuric chloride. The mixture was heated for 45 min. and cooled yielding a white precipitate, 5.08 g., that was collected and suspended in 50 ml. of methanol. Hydrogen sulfide was bubbled through the well stirred suspension for 15–20 min., then the mixture was filtered through Celite, and the filtrate evaporated *in vacuo*. The residue was washed with ether and dried *in vacuo* to afford 1.20 g. (69% from XII) of a white, nitroprusside-positive foam, $[\alpha]^{23}D$ +71° (1% in methanol); λ_{max}^{film} 2.95 (OH), 4.85–5.0, 6.25, 6.69 (NH_3^+), 7.32, 8.47 μ (sulfonate ester).

Anal. Calcd. for $C_7H_{16}ClNO_5S_2$: C, 28.6; H, 5.49; Cl, 12.1; N, 4.77; S, 21.8. Found: C, 28.7; H, 5.72; Cl, 12.0; N, 4.68; S, 21.7.

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The Reaction of Ammonia with Acylated Disaccharides. III. Acetyl Derivatives of Maltose and an Interpretation

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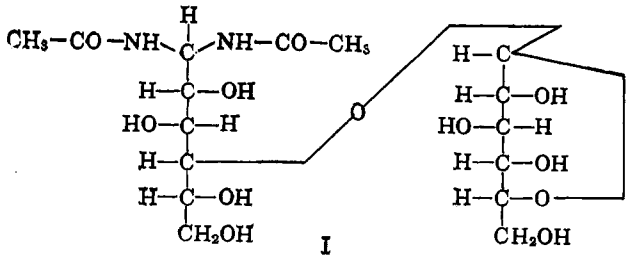
The reaction of ammonia with β-octa-O-acetylmaltose affords N,N′-diacetylmaltosylidenediamine (I), from which its acetate was prepared. A comparative study of the reaction in methanolic and in aqueous media was performed. The higher yield of I obtained in aqueous medium was qualitatively interpreted according to known kinetic studies about the reaction of ester ammonolysis, which is simultaneous and competitive with the reaction described. It is demonstrated that, in the reaction of penta-O-benzoyl-α-D-glucopyranose with methanolic ammonia, methyl benzoate is produced. Therefore, in that medium methoxide ions are formed, pointing out that, apart from the ammonolysis reaction and from the formation of "aldose-amides" by an ortho ester mechanism, a third competitive reaction takes place, by which acyl groups are split off through a transesterification mechanism.

In the previous papers of this series[1,2] it was shown that acetylated disaccharides react with methanolic ammonia affording the original free sugar in high yields and the so-called "aldobiose-diamides" (or more correctly N,N′-diacetylaldobiosylidenediamines) in yield lower than 5%, jointly with N-acetylaldobiosylamines in yields lower than 1%.

In this paper we describe the reaction of ammonia with β-octa-O-acetylmaltose. The presence of N,N′-diacetylmaltosylidenediamine (I) could be detected, in the sirup obtained in the reaction, by paper chromatography and spraying with the picric acid–sodium metaperiodate reagent.[3] It was observed that I had the same R_f of pure maltose and this coincidence persisted in different solvent systems. A charcoal column chromatography afforded crystalline maltose, but it was impossible to separate the mixture of maltose and I. The eluted fractions, which on paper chromatog-



I

(1) J. O. Deferrari and R. A. Cadenas, *J. Org. Chem.*, **28**, 1070 (1963).
(2) R. A. Cadenas and J. O. Deferrari, *ibid.*, **28**, 1072 (1963).
(3) R. A. Cadenas and J. O. Deferrari, *Analyst*, **86**, 132 (1961).