Compound XIII in pyridine: 3150, 1750, 1385, 1365, 1335, 1275, 1235, 1083, and 1050 cm.$^{-1}$.

Nuclear Magnetic Resonance Data.—The n.m.r. spectra were recorded on a Varian Model A-60 spectrometer; pyridine was used as the solvent and tetramethylsilane as the internal reference. We are indebted to Dr. John D. Stevens of this laboratory for the following interpretation.

Nuclear magnetic resonance spectra confirmed that the hydroxyl group on C-6 was acetylated in the two sulfone monoacetates (V and XIII). The spectrum for β-D-glucopyranosyl *p*-tolyl sulfone (III) showed signals at τ 7.83 (aromatic methyl group), at 5.3 to 6.1 (broad band due to protons on C-2 to C-6), and at 4.83 (doublet, spacing 9.0 c.p.s.). The doublet at τ 4.83 arises from the anomeric hydrogen atom. Since the spacing for this doublet is typical of 1,2 diaxially oriented hydrogen atoms on a six-membered ring,[30] this observation verifies the β-D-glucopyranosidic linkage in the sulfone. A similar spectrum was obtained for the *p*-bromophenyl β-D-glucopyranosyl sulfone (XII, doublet at τ 4.77, spacing 8.6 c.p.s.). 6-*O*-Acetyl-β-D-glucopyranosyl *p*-tolyl sulfone (V) showed signals at τ 8.13 (acetyl group), 7.75 (aromatic methyl group), a series of broad peaks between 5.25 and 6.13, and a doublet (spacing 9.2 c.p.s.) at 4.89. The low-field doublet in the spectrum of this compound is attributed to the anomeric hydrogen atom and the absence of any signals downfield from this proton is strong evidence for the absence of an acetoxy group on C-2, C-3, or C-4. [For comparison, the spectrum of methyl tetra-*O*-acetyl-β-D-glucopyranoside in pyridine solution showed protons on C-2, C-3, and C-4 at τ 4.3 to 4.6 and the anomeric hydrogen at 5.2 (spacing 7.5 c.p.s.)[31]]. For tetra-*O*-acetyl-β-D-glucopyranosyl *p*-tolyl sulfone (II), signals with intensity corresponding to two protons occurred at τ 4.0 to 4.47 and another group of signals with two-proton intensity occurred at 4.5 to 4.97; thus, the signals due to protons on C-1 to C-4 all occur at τ-values less than 5. Similarly, no peaks occurred downfield from the doublet at τ 4.83 (spacing 9.0 c.p.s.) due to the anomeric hydrogen atom in the n.m.r. spectrum of 6-*O*-acetyl-β-D-glucopyranosyl *p*-bromophenyl sulfone (XIII).

Acknowledgment.—The authors wish to thank Mr. Harold G. McCann and his associates of the Analytical Services Unit of this laboratory for obtaining the infrared spectra and the microanalyses, Mr. Harold K. Miller for his advice on the infrared spectra, and Mr. Robert B. Bradley and Dr. John D. Stevens for obtaining the n.m.r. spectra.

(30) R. U. Lemieux, R. K. Kullnig, H. F. Bernstein, and W. G. Schneider, *J. Am. Chem. Soc.*, **80**, 6098 (1958).

(31) N. Mori, S. Omura, O. Yamamoto, T. Suzuki, and Y. Tsuzuki [*Bull. Chem. Soc. Japan*, **36**, 1047 (1963)] have shown that for methyl tetra-*O*-acetyl-β-D-glycopyranosides in chloroform solution the signals due to the anomeric hydrogen appear at higher field than those due to protons on C-2 to C-4.

Preparation of 6-Acetamido-1,2,3,4-tetra-O-acetyl-6-deoxy-L-idothiapyranose[1]

LEON GOODMAN AND JAMES E. CHRISTENSEN

Life Sciences Research, Stanford Research Institute, Menlo Park, California

Received December 4, 1963

Reaction of 5,6-anhydro-3-O-benzyl-1,2-O-isopropylidene-D-glucofuranose (I) with benzylmercaptide ion afforded 3-O-benzyl-6-S-benzyl-1,2-O-isopropylidene-6-thio-D-glucofuranose (II) that, with thionyl chloride, yielded 3-O-benzyl-5-S-benzyl-6-chloro-6-deoxy-1,2-O-isopropylidene-5-thio-L-idofuranose (IV) *via* the benzylepisulfonium ion (VIII). Reaction of IV with sodium azide gave the 6-azido-5-benzylthio sugar (VII) that was reduced to the 6-amino-5-benzylthio derivative (V), easily converted to the N-acetate (VI). Reduction of V or VI with sodium and liquid ammonia afforded the 6-amino-5-thiol (IX) and the 6-acetamido-5-thiol (X), respectively. Acid hydrolysis of the isopropylidene group resulted in the formation of a thiapyranose sugar, that was acetylated to the pentaacetate (XII), one anomer of which was isolated as a crystalline solid.

Since 1961 a number of articles have appeared describing sugars that contain sulfur[2] or nitrogen[3] as the heterocyclic atom of the sugar ring. In studying the relative abilities of thiol, hydroxyl, and amino groups to interact with C-1 to form a cyclic sugar it will be advantageous to have a number of sugars containing these groups properly situated for potential cyclization. This manuscript reports the preparation of a derivative (XII) of 6-amino-6-deoxy-5-thio-L-idose, such a sugar. The pentaacetate (XII) is also a derivative of a vicinal aminomercapto sugar which is of interest for comparison with other such compounds which have recently been prepared.[4]

The conversion of 1,2:5,6-di-O-isopropylidene-D-glucofuranose to 5,6-anhydro-3-O-benzyl-1,2-O-isopropylidene-D-glucofuranose (I) was carried out using the sequence described by Meyer and Reichstein.[5] Reaction of the epoxide (I) with sodium benzyl mercaptide afforded the 6-benzylthio sugar (II) (Chart I) as an oil purified by chromatography over silica gel. Previously it had been determined that treatment of I with sodium hydroxide gave 3-O-benzyl-1,2-O-isopropylidene-D-glucofuranose predominantly, if not exclusively,[5] indicating nucleophilic attack at C-6. Similar 5,6-anhydro sugars have been shown to undergo nucleophilic attack by ammonia at C-6[6]; structure II is written on the basis of these considerations. The benzylthio sugar (II) was characterized as the crystalline phenylurethan (III) and was converted to the crystalline chloro sugar (IV) by treatment with thionyl chloride. The structure of IV was assigned on the assumption of opening of an episulfonium ion intermediate (VIII, formed by the way of the chlorosulfite of II) at C-6[5,6] and on the basis of n.m.r. information. Thus, the C-6 methylene group of IV appeared as a four-peak multiplet centered at γ 6.45 as compared

(1) (a) 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) (a) J. C. P. Schwarz and K. C. Yule, *Proc. Chem. Soc.*, 417 (1961); (b) T. J. Adley and L. N. Owen, *ibid.*, 418 (1961); (c) R. L. Whistler, M. S. Feather, and D. L. Ingles, *J. Am. Chem. Soc.*, **84**, 122 (1962); (d) E. J. Reist, D. E. Gueffroy, and L. Goodman, *ibid.*, **85**, 3715 (1963).

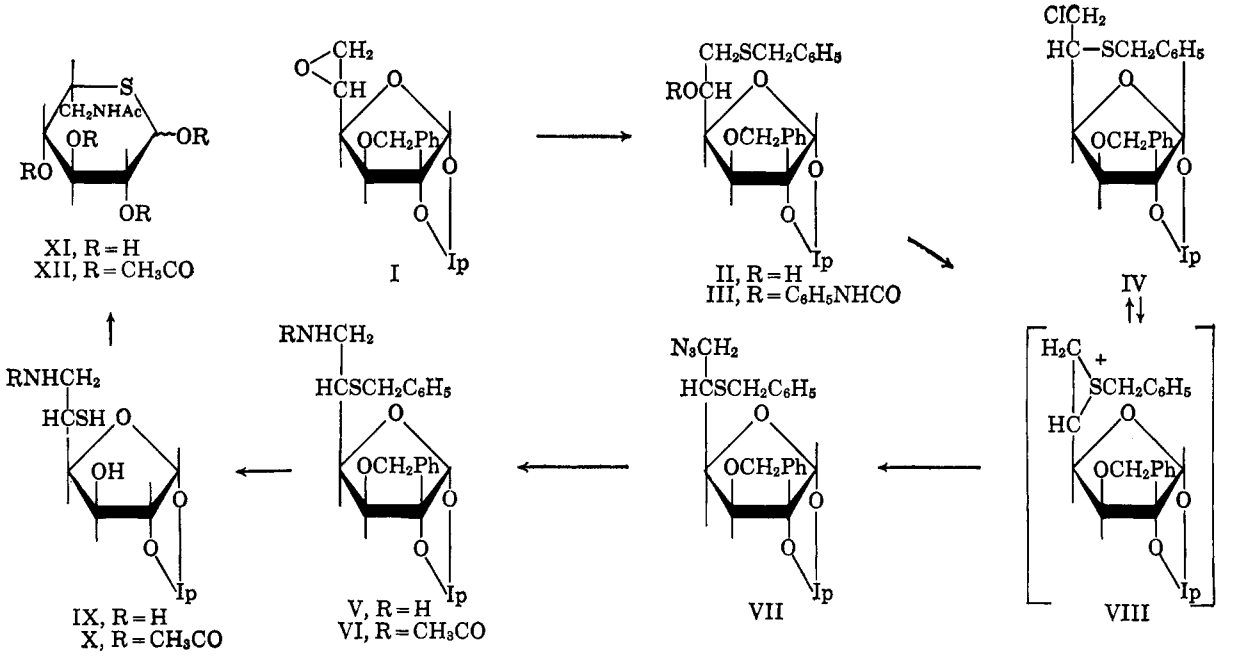
(3) (a) J. K. N. Jones and J. C. Turner, *J. Chem. Soc.*, 4699 (1962); (b) H. Paulsen, *Angew. Chem., Intern. Ed. Engl.*, **1**, 597 (1962).

(4) (a) L. Goodman and J. E. Christensen, *J. Am. Chem. Soc.*, **83**, 3823 (1961); (b) J. E. Christensen and L. Goodman, *ibid.*, **83**, 3827 (1961).

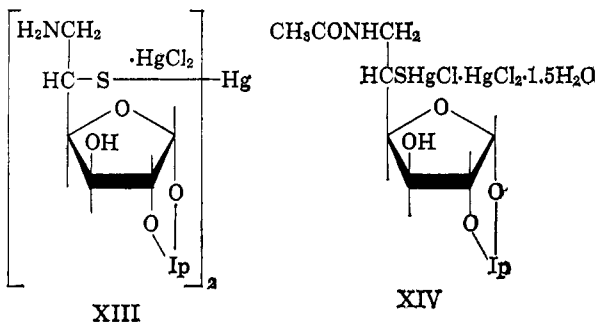
(5) A. S. Meyer and T. Reichstein, *Helv. Chim. Acta*, **29**, 152 (1946).

(6) H. Ohle and L. Vargha, *Ber.*, **62B**, 2435 (1929).

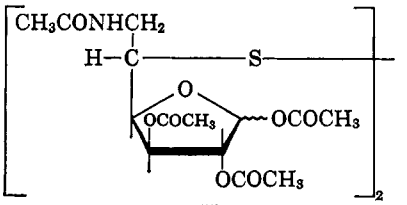
CHART I



to the C-6 methylene of III at γ 7.18; the position of the C-6 protons in IV as compared to that in III is logical when the deshielding ability of a chlorine is compared with that of a benzylthio group. Reaction of IV with sodium azide in 2-methoxyethanol gave a good yield of the azide (VII) that was reduced with sodium borohydride in isopropyl alcohol[7] to the crystalline amine (V) also characterized as the N-acetate (VI). The position of the amine group at C-6 is assumed on the basis of reaction *via* the ion VIII and opening of VIII at C-6. Reduction of either V or VI with sodium in liquid ammonia gave thiols that were isolated as complex mercaptides with mercuric chloride. The derivative from V was analyzed as the bismercurial XIII, that from VI as the chloromercuri derivative XIV. Similar complex mercaptides have been noted



in other work with mercaptoamino sugars.[4a,8] The regeneration of the free thiols from XIII and XIV with hydrogen sulfide, either in methanolic or aqueous hydrogen chloride to remove the isopropylidene group, gave solids that did not analyze well for the expected thiapyranose sugar (XI, or its methyl glycoside when methanolic hydrogen chloride was employed). It was found in later work that the isopropylidene group was unexpectedly resistant to acid hydrolysis and the presence of some deblocked compound may have been responsible for the poor analytical results. In the most favorable case the mercaptide (XIV) was treated with hydrogen sulfide in aqueous hydrochloride acid; then the removal of the isopropylidene group was completed with hot hydrochloric acid. The product of the reaction, presumably XI, was acetylated to give a low yield of a sharply melting, nitroprusside-negative, crystalline compound, probably one of the pure anomers of XII. The compound showed no infrared S-acetate absorption and its n.m.r. spectrum showed the presence of five acetyl groups, thus eliminating the furanose disulfide (XV) as a possible structure. The specific



rotation of crystalline XII, +54.5°, as compared with that of the mother liquors from crystallization of XII, −29.5°, suggests that crystalline XII is 6-acetamido-1,2,3,4-tetra-O-acetyl-6-deoxy-β-L-idothiapyranoside. The analysis of compound XII was not satisfactory according to normal analytical standards. However, the n.m.r. spectrum clearly showed the presence of about 0.4 benzene protons (benzene was one of the recrystallizing solvents); correction of the calculated values for the appropriate amount of benzene then gave completely acceptable analytical figures for solvated XII.

Experimental[9]

3-O-Benzyl-6-S-benzyl-1,2-O-isopropylidene-6-thio-D-glucofuranose (II) and Its Phenylurethan (III).—A solution of 20.53 g.

(7) P. A. S. Smith, J. H. Hall, and R. O. Kan, *J. Am. Chem. Soc.*, **84**, 485 (1962).

(8) J. E. Christensen and L. Goodman, *J. Org. Chem.*, **28**, 2995 (1963).

(9) Melting points are uncorrected and were obtained with the Fisher-Johns apparatus. Optical rotations were determined in chloroform at the sodium D line unless otherwise noted. The n.m.r. spectra were obtained with the A-60 instrument or the V-4311 spectrometer operated at 60 Mc. and were run in deuteriochloroform. Magnesium sulfate was the drying agent employed. The silica gel used in chromatography was purchased from Gallard-Schlesinger Chemical Manufacturing Corp., Garden City, N. Y.

(70.2 mmoles) of the crude epoxide (I),[5] 3.85 g. (71.2 mmoles) of sodium methoxide, 8.88 g. (71.5 mmoles) of benzylmercaptan, and 200 ml. of methanol was heated at reflux under nitrogen for 18 hr., then was cooled and adjusted to pH 7 with glacial acetic acid. The mixture was concentrated *in vacuo* to about half its volume, then was poured into 400 ml. of ice–water. The aqueous mixture was extracted with four 50-ml. portions of dichloromethane; the combined extracts were washed with 100 ml. of water, decolorized with Norit, and dried, then evaporated *in vacuo* leaving 25.6 g. of an amber sirup. This was applied to a silica gel column (90–200 mesh, 36 × 260 mm.), and elution with 500 ml. of benzene removed 9.6 g. of an oil that, according to its infrared spectrum, contained considerable dibenzyl disulfide. Further elution with benzene containing 4% ethyl acetate (800 ml.) gave 13.3 g. (45.7%) of a sirup whose infrared spectrum compared well with the analytical sample of II (see below) and which was suitable for use in subsequent work. Finally elution with 400 ml. of ethyl acetate afforded 2.5 g. of a sirup whose infrared spectrum showed too little benzylthio absorptions. The low yield of II is probably a reflection of the quality of I used; extensive decomposition accompanied efforts to purify I by distillation so that crude I was used in most of the work.

From another run, a portion of the product was acetylated with acetic anhydride and pyridine and the isolated acetate, a sirup, was deacetylated with a catalytic amount of sodium methoxide in methanol, affording II as a sirup with $n^{18}D$ 1.5663.

Anal. Calcd. for $C_{23}H_{28}O_5S$: C, 66.3; H, 6.78; S, 7.70. Found: C, 65.8, 65.9; H, 7.11, 7.18; S, 7.67.

A mixture of 0.50 g. (1.20 mmoles) of II, 0.22 g. (1.85 mmoles) of phenyl isocyanate and a drop of triethylamine, protected against moisture, was heated on the steam bath for 2.25 hr., then was extracted with three 5-ml. portions of petroleum ether (b.p. 30–60°). The sirup remaining after the petroleum ether treatment was a foamy solid that was recrystallized from 3 ml. of isopropyl alcohol giving 0.070 g. (11%) of solid, m.p. 110–133°. A second recrystallization from 2 ml. of isopropyl alcohol afforded 0.040 g. of the analytical sample, m.p. 138–139°, λ_{max}^{Nujol} 2.97 (NH) and 5.85 μ (urethan C=O). The n.m.r. spectrum showed resonances at γ 3.63 (NH singlet), 4.19 (C-1 doublet, J = 3.5 c.p.s.), 4.74 (C-5, one proton multiplet), 6.31 (benzylthio singlet), 7.18 (C-6, 2 proton multiplet), 8.54 and 8.72 (isopropylidene methyls).

Anal. Calcd. for $C_{30}H_{33}NO_6S$: C, 67.3; H, 6.21; N, 2.62; S, 5.99. Found: C, 67.1; H, 5.99; N, 2.59; S, 5.90.

3-O-Benzyl-5-S-benzyl-6-chloro-6-deoxy-1,2-O-isopropylidene-5-thio-L-idofuranose (IV).—A mixture of 15.2 g. (36.4 mmoles) of II, 17 ml. of thionyl chloride, and 150 ml. of dichloromethane was heated at reflux, with exclusion of moisture, for 1.5 hr., then poured cautiously with stirring into 900 ml. of cold (0°) saturated aqueous sodium carbonate. The layers were separated and the aqueous phase was extracted with two 100-ml. portions of dichloromethane. The combined organic solutions were washed with two 100-ml. portions of water, then dried and evaporated *in vacuo*, affording 14.7 g. (93%) of pale amber sirup whose infrared spectrum showed no –OH absorption. The sirup crystallized on standing. A portion (0.41 g.) was recrystallized from 5 ml. of isopropyl alcohol yielding 0.29 g. of needles, m.p. 62–65°. A second identical recrystallization afforded 0.18 g. of the analytical sample, m.p. 61.5–64.0°, $[\alpha]^{24}$ −70.8° (1%). The n.m.r. spectrum showed resonances at γ 4.13 (C-1 doublet, J = 3.5 c.p.s.), 6.11 (benzylthio singlet), 6.45 (C-6, 2 proton quartet), 6.85 (C-5, one proton multiplet), 8.58 and 8.73 (isopropylidene methyls).

Anal. Calcd. for $C_{23}H_{27}ClO_4S$: C, 63.5; H, 6.26; Cl, 8.15; S, 7.37. Found: C, 63.9; H, 6.64; Cl, 7.96; S, 7.36.

6-Azido-3-O-benzyl-5-S-benzyl-6-deoxy-1,2-O-isopropylidene-5-thio-L-idofuranose (VII).—A stirred mixture of 2.26 g. (5.20 mmoles) of the chloro sugar (IV), 8.5 g. (0.13 mole) of sodium azide, and 60 ml. of 95% aqueous 2-methoxyethanol was heated, under nitrogen, at 105–110° for 2 hr., then cooled, and evaporated *in vacuo*. The solid residue was partitioned between 100 ml. of dichloromethane and 150 ml. of water. The aqueous layer was extracted with two 50-ml. portions of dichloromethane, and the combined organic solutions were washed with 100 ml. of saturated aqueous sodium chloride solution, then dried. The filtrated solution was evaporated *in vacuo*, leaving 2.14 g. of a golden sirup. The sirup was extracted with 25 ml. of Skellysolve B (b.p. 62–70°), leaving a small residue. Evaporation of the Skellysolve B extract afforded 2.05 g. (90%) of a yellow sirup; λ_{max}^{film} 4.78 (N_3), 13.0, 13.56, and 14.27 μ (phenyl). Analysis was obtained on a product prepared as above.

Anal. Calcd. for $C_{23}H_{27}N_3O_4S$: C, 62.6; H, 6.16; N, 9.52; S, 7.28. Found: C, 62.5, 62.7; H, 6.41, 6.58; N, 9.82; S, 7.72.

6-Amino-3-O-benzyl-5-S-benzyl-6-deoxy-1,2-O-isopropylidene-5-thio-L-idofuranose (V) and Its N-Acetate (VI).—A stirred mixture of 3.68 g. (8.32 mmoles) of VII (as the crude sirup), 1.3 g. (34 mmoles) of sodium borohydride, and 30 ml. of isopropyl alcohol was heated at reflux for 40 hr., then cooled, and evaporated *in vacuo*. The residue was dissolved in 20 ml. of water, and the solution was extracted with 30 ml. of dichloromethane. The organic layer was washed with two 20-ml. portions of water, dried, and evaporated *in vacuo*, affording 3.38 g. (98%) of sirup. Crystallization from 30 ml. of Skellysolve C (b.p. 88–99°) afforded 2.0 g. (58%) of white crystals, m.p. 103–112°. An analytical sample was obtained from a reduction of VII with lithium aluminum hydride. After recrystallization from isopropyl alcohol it had m.p. 111–113°, $[\alpha]^{33}$ −115° (1%).

Anal. Calcd. for $C_{23}H_{29}NO_4S$: C, 66.5; H, 7.04; N, 3.37; S, 7.72. Found: C, 66.4; H, 7.31; N, 3.55; S, 7.99.

Acetylation of 0.40 g. (0.963 mmole) of V with 2 ml. of acetic anhydride and 0.30 g. of anhydrous sodium acetate at 55° for 3.5 hr. gave, after decomposition with 30 ml. of ice–water, 0.50 g. (114%) of white solid, m.p. 98–113°. Two recrystallizations from benzene–petroleum ether (b.p. 30–60°) gave 0.30 g. (68%) of white needles, m.p. 123–125°; λ_{max}^{Nujol} 2.99 (NH) and 6.05 μ (amide C=O); $[\alpha]^{22}$ −64° (*c* 1, methanol).

Anal. Calcd. for $C_{25}H_{31}NO_5S$: C, 65.6; H, 6.83; N, 3.06; S, 7.01. Found: C, 65.1; H, 6.52; N, 3.05; S, 7.23.

6-Amino-6-deoxy-1,2-O-isopropylidene-5-thio-L-idofuranose (IX) and Its Mercaptide (XIII).—To a stirred solution of 0.50 g. (21.7 mg.-atoms) of clean, dry sodium in 22 ml. of liquid ammonia was added dropwise a solution of 1.72 g. (4.14 mmoles) of the amine (V) in 7 ml. of 1,2-dimethoxyethane. The resulting solution was stirred for 30 min., then was treated with solid ammonium chloride until the blue color had disappeared. The ammonia was carefully evaporated, the residue was dissolved in 30 ml. of water, and the solution was adjusted to pH 6 with glacial acetic acid. Extraction of the solution with two 30-ml. portions of dichloromethane removed bibenzyl; then the solution was continuously extracted with chloroform for 18 hr., yielding 0.24 g. (25%) of white nitroprusside-positive solid. Continuous extraction for 48 hr. more with chloroform afforded 0.19 g. (20%) of the solid. The first crop was stirred with ether and filtered giving a white solid, m.p. 88–109°; λ_{max}^{Nujol} 3.1–3.3, 3.6–4.1, and 6.3 μ (broad absorptions, usually characteristic of amine salts).

Anal. Calcd. for $C_9H_{17}NO_4S$: C, 46.0; H, 7.28; N, 5.96; S, 13.6. Found: C, 44.4; H, 7.27; N, 5.92; S, 13.7.

When the aqueous solution containing the product from sodium and liquid ammonia treatment of 1.50 g. of V was treated with excess saturated aqueous mercuric chloride, a precipitate was formed. This was dried and triturated thoroughly with dichloromethane to remove any bibenzyl, giving 1.93 g. (44%) of white solid whose analysis is in accord with structure XIII.

Anal. Calcd. for $C_{18}H_{32}Cl_4Hg_3N_2O_8S_2$: C, 17.8; H, 2.66; Cl, 11.7; N, 2.31; S, 5.29. Found: C, 17.5; H, 3.03; Cl, 11.6; N, 2.09; S, 5.29.

Treatment of the mercaptide (XIII) with hydrogen sulfide either in methanol or water containing hydrogen chloride gave widely melting solids whose analytical figures did not agree with those for any logical structure.

6-Acetamido-6-deoxy-1,2-O-Isopropylidene-5-thio-L-idofuranose (X) and Its Mercaptide (XIV).—The amide (VI), 2.67 g. (5.84 mmoles), was treated with sodium and liquid ammonia using the procedure described for the similar treatment of V. The aqueous solution of the residue from evaporation of the ammonia was treated with excess aqueous mercuric chloride, affording 4.10 g. (90%) of cream-colored solid. From a previous run a similar solid, m.p. 123–125°, was obtained whose analysis was in accord with that for structure XIV.

Anal. Calcd. for $C_{11}H_{18}Cl_3Hg_2NO_5S \cdot 1.5H_2O$: C, 16.3; H, 2.61; Cl, 13.1; S, 3.95. Found: C, 16.2; H, 2.84; Cl, 12.9; S, 4.01.

The mercaptide (XIV), 4.10 g., was suspended in 40 ml. of cold (0°) water and the suspension was treated with hydrogen sulfide for 30 min. The suspension was filtered through Celite and the pH of the filtrate was adjusted to 5–6 with Amberlite IR 45 resin. After being filtered, the solution was evaporated

in vacuo and the residue was triturated with several portions of dry ether then maintained at 1 mm., leaving 0.75 g. (52%) of a hygroscopic, nitroprusside-positive foam which darkened on standing; λ_{max}^{film} 3.0 (OH, NH), 3.90 (SH), and 6.0–6.1 μ (amide C=O).

Anal. Calcd. for $C_{11}H_{19}NO_6S$: C, 47.6; H, 6.91; N, 5.05; S, 11.6. Found: C, 45.7; H, 6.93; N, 5.60; S, 11.8.

6-Acetamido-1,2,3,4-tetra-O-acetyl-6-deoxy-L-idothiapyranose (XII).—The mercaptide (XIV), 4.23 g. (5.40 mmoles), suspended in 40 ml. of 0.1 *N* hydrochloric acid, was treated with hydrogen sulfide as described for the preparation of IX. After the filtration through Celite, the filtrate was stirred at room temperature for 1.5 hr., then neutralized, and evaporated, yielding 0.75 g. of a foam that gave a positive reducing sugar test and a positive nitroprusside test; its infrared spectrum indicated the presence of the isopropylidene group, however. The foam was stirred in 0.1 *N* hydrochloric acid overnight, then neutralized, and evaporated, giving 0.53 g. of a glass whose n.m.r. spectrum in deuterium oxide showed the presence of about 60–70% of the original isopropylidene group. Finally, the material in 20 ml. of 0.5 *N* hydrochloric acid was stirred at 40–45° for 3.5 hr., then neutralized, and evaporated, yielding 0.41 g. of sirup whose n.m.r. spectrum showed the essential absence of the isopropylidene group.

The sirup, 0.35 g., was treated with 5 ml. of dry pyridine and the solution was decanted from some insoluble material, chilled to 0°, and 5 ml. of acetic anhydride was added. The mixture was maintained at 5° for 18 hr. and at room temperature for 2 hr., then was poured into 50 ml. of ice–water. The solution was neutralized with solid sodium carbonate, and extracted with two 20-ml. portions of dichloromethane; the extracts were washed with 20 ml. of water and dried. Evaporation left 0.26 g. of yellow sirup which crystallized on standing. It was recrystallized three times from benzene–petroleum ether (b.p. 30–60°), affording 0.065 g. of crystals, m.p. 165–166°; $[\alpha]^{24}$ +54.5° (1%); λ_{max}^{Nujol} 2.99, 3.02 and 6.42 (NH), and 5.68 (O-acetyl C=O), 6.02 μ (amide C=O); there was no appreciable absorption near 5.90 μ, suggestive of an S-acetyl carbonyl, nor near 7.40 μ, suggestive of the methyl group of the S-acetate. The n.m.r. spectrum showed absorptions at γ 2.71 (benzene solvent, 0.36 protons), 3.85 (C-1 doublet, J = 3.5 c.p.s.), 7.83, 7.91, 7.96, and 8.01 (CH_3CO protons totaling 15 protons).

Anal. Calcd. for $C_{16}H_{23}NO_9S \cdot 0.06C_6H_6$: C, 47.9; H, 5.74; N, 3.42; S, 7.84. Found: C, 48.1; H, 5.87; N, 3.45; S, 7.60.

The mother liquors from the recrystallizations were combined and evaporated *in vacuo* leaving a sirup, $[\alpha]^{25}$ −29.5° (1.1%), whose infrared spectrum was similar to that of the crystalline solid and demonstrated the same functional groups.

Acknowledgment.—The authors wish to thank Dr. Peter Lim and his group for the infrared, n.m.r., and optical rotation data, and Mr. O. P. Crews and staff for the large-scale preparation of certain intermediates.

2-Deoxy Sugars. VII. 2-Deoxy-D-allose (2-Deoxy-D-*ribo*-hexose) *via* the Fischer–Sowden Nitromethane Synthesis[1]

W. WERNER ZORBACH[2] AND ABRAHAM P. OLLAPALLY[3]

Department of Chemistry, Georgetown University, Washington 7, D. C.

Received February 3, 1964

Condensation of nitromethane with D-ribose (**1**) leads to a sirupy mixture of the nitrohexitols (**2** and **3**), which on acetylation yielded the corresponding epimeric acetylated derivatives **4** and **5**, the latter of which was crystalline. Both **4** and **5** were separately deacetylated by acid hydrolysis to regenerate the nitrohexitols (**2** and **3**), each of which underwent the Nef reaction to give D-allose (**6**) and D-altrose (**7**), respectively, thus establishing the structure of the crystalline acetylated nitrohexitol (**5**) as 2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-nitro-D-altritol. Elimination of a molecule of acetic acid from **5** gave the acetylated nitrohexene (**8**), which underwent reduction of the double bond to give the sirupy 3,4,5,6-tetra-*O*-acetyl-1,2-dideoxy-1-nitro-D-*ribo*-hexitol (**9**). Alkaline hydrolysis of **9**, followed by the Nef reaction, gave 2-deoxy-D-allose (2-deoxy-D-*ribo*-hexose) (**11**) in 20% yield. Alternately, the acetylated deoxynitrohexitol (**9**) could be deacetylated by aqueous acid giving crystalline 1,2-dideoxy-1-nitro-D-*ribo*-hexitol (**10**), which underwent the Nef reaction to give 2-deoxy-D-allose (**11**) in 38% yield. Yields of **11** by both the alkaline and acid procedure are based on the hexene (**8**).

2-Deoxy-D-allose (2-deoxy-D-*ribo*-hexose) (**11**) has not been reported to occur naturally, but may be obtained by the hydrolysis of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexoside[4] for which an improved preparation in four steps, starting with methyl α-D-glucopyranoside, has been reported.[5] Our interest in preparing both cardenolides[6] and nucleosides containing as the carbohydrate component 2-deoxy-D-allopyranose (2-deoxy-D-*ribo*-hexopyranose) prompted us to investigate an alternate and perhaps more economical procedure for synthesizing the hexose (**11**).

In a variation of their nitromethane synthesis for lengthening the carbon chain of aldoses, Sowden and Fischer described[7] a general method for producing 2-deoxy sugars, and were successful in converting D-arabinose to 2-deoxy-D-*arabino*-hexose (2-deoxyglucose). In the same paper D-ribose (**1**) was treated similarly; in this case, however, the synthesis was not carried beyond the preparation and isolation of the intermediary 3,4,5,6-tetra-*O*-acetyl-1-nitro-D-*ribo*-hexene-1 (**8**). Our own work, which is presently described, is concerned with a re-examination of the conversion of D-ribose (**1**) to the acetylated hexene (**8**) as well as with the transformation of the latter to 2-deoxy-D-allose (**11**).

Condensation of D-ribose (**1**) with nitromethane and removal of the sodium from the sodium salts of the nitro alcohols by an ion-exchange resin gave a sirupy mixture of the free, epimeric nitro alcohols **2** and **3**, from which neither epimer could be obtained in crystalline form. Whereas Sowden and Fischer, on acetylating the sirup containing **2** and **3**, obtained only a sirupy mixture of the acetylated nitro alcohols **4** and **5**[7] we were able to secure crystalline 2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-nitro-D-altritol (**5**) in 19% yield based on D-ribose (**1**). In an effort to determine

(1) This work was supported largely by U. S. Public Health Service Grants AM-02764 and CY-4288.

(2) To whom all inquiries regarding this paper should be addressed.

(3) This work was taken from a dissertation to be submitted to the Graduate School of Georgetown University in partial fulfillment of the degree of Doctor of Philosophy in Chemistry.

(4) W. W. Zorbach and T. A. Payne, *J. Am. Chem. Soc.*, **80**, 5564 (1958).

(5) D. A. Prins, *ibid.*, **70**, 3955 (1948).

(6) W. W. Zorbach and W. Buhler, *Ann. Chem.*, **670**, 116 (1963).

(7) J. C. Sowden and H. O. L. Fischer, *J. Am. Chem. Soc.*, **69**, 1048 (1947).