after 4 hr.; λ_{max}^{KBr} 5.90 μ (OAc); $\lambda_{max}^{C_2H_5OH}$ 210 (1215), 256 mμ (ϵ 731); X-ray powder diffraction data[19]: 12.81 w, 11.19 s (2), 9.83 s (2,2), 8.93 s (2,2), 6.61 vw, 6.24 vw, 5.19 m (3), 4.85 s (1), 4.48 m, 4.11 s (1,1), 3.71 w, 3.56 w.

Anal. Calcd. for $C_{14}H_{19}BrO_9S$: C, 37.92; H, 4.28; Br, 18.05; S, 7.22. Found: C, 38.18; H, 4.74; Br, 18.00; S, 7.48.

The product could be stored unchanged in a desiccator for 2 days at 25°, but it changed to an oil during the third or fourth day.

Preparation of Some *trans*-Aminomercaptofuranose Sugars[1]

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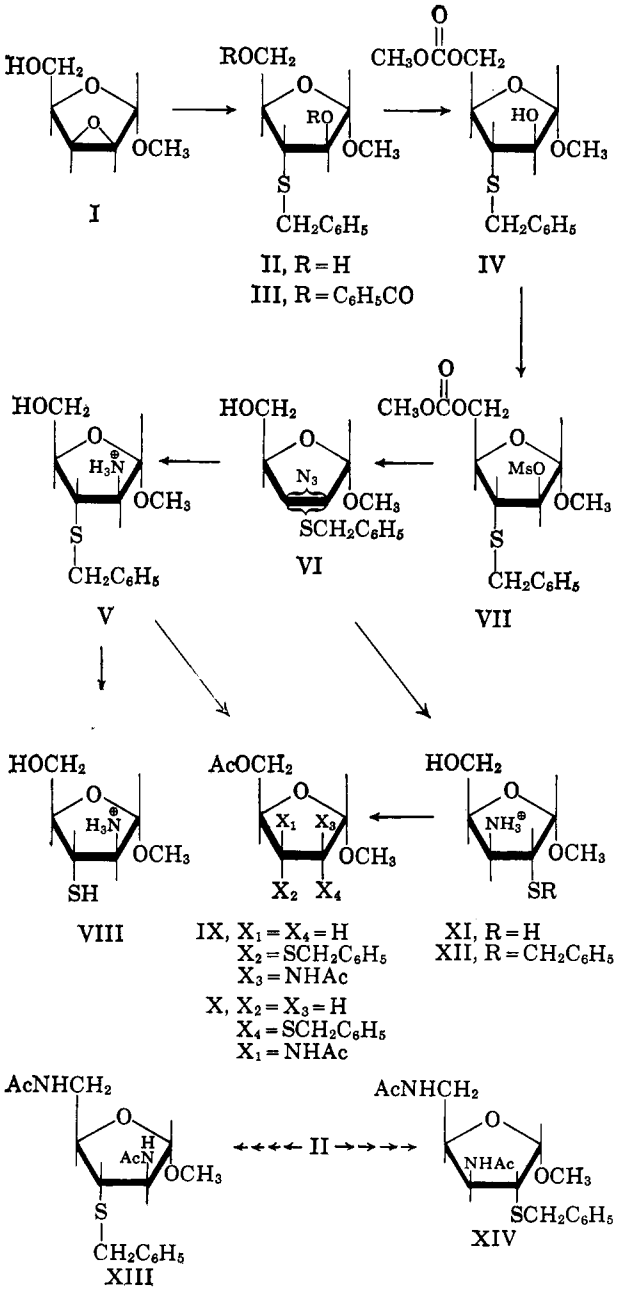
Two *trans*-aminomercapto glycosides, methyl 2-amino-2-deoxy-3-thio-α-D-arabinofuranoside hydrochloride (VIII) and methyl 3-amino-3-deoxy-2-thio-α-D-xylofuranoside hydrochloride (XI), have been prepared using the benzylthio neighboring group approach. Assignments of structure of the intermediates to the final products were made on the basis of n.m.r. interpretation. An estimate is made of the relative amount of ring-opening at the two carbons of an episulfonium ion intermediate.

Use of the benzylthio moiety as a neighboring group permitted the synthesis of two *trans*-aminomercaptopyranose glycosides.[2] The extension of these techniques to some furanosides has now led to the preparation of methyl 2-amino-2-deoxy-3-thio-α-D-arabinofuranoside hydrochloride (VIII) and the isomeric *trans*-aminomercaptan, methyl 3-amino-3-deoxy-2-thio-α-D-xylofuranoside hydrochloride (XI).

Both glycosides VIII and XI were derived from methyl 2,3-anhydro-α-D-lyxofuranoside (I).[3] Treatment of I with sodium benzyl mercaptide gave an excellent yield of a sirup that could be converted, in good yield, to a crystalline dibenzoate. Ring opening of 2,3-anhydrofuranosides has been generally observed to occur predominantly at C-3[4] and, on this basis, the diol II that formed the dibenzoate III was the expected major product. The structure assignment for III was verified by the nuclear magnetic resonance spectrum which showed the C-1 proton as a sharp singlet not visibly coupled to the *trans*-proton at C-2; the 2-benzylthio isomer of III would be expected to show its C-1 proton as a doublet with $J \cong 5$ c.p.s. according to its n.m.r. spectrum.[5b] The situation with the α-anhydrolyxoside (I) contrasts with that in the reaction of methyl 2,3-anhydro-β-D-lyxofuranoside and sodium benzyl mercaptide where the predominant product results from attack at C-2 of the epoxide.[5a] It seems probable that steric factors decide the position of attack in these two anomers; the bulky mercaptide ion's access to C-2 is seriously hindered by the C-1 methoxyl group in I but not in the β-anomer of I.

It was necessary to block the C-5 hydroxyl of II and this was done conveniently by reaction of II with slightly more than one equivalent of methyl chloroformate to give IV, which contained some II as shown by subsequent reactions. Use of the trityl blocking group for the C-5 hydroxyl gave poorer results. Treat-



(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.

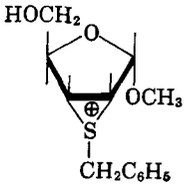
(2) (a) J. E. Christensen and L. Goodman, *J. Am. Chem. Soc.*, **83**, 3827 (1961); (b) L. Goodman and J. E. Christensen, *J. Org. Chem.*, **28**, 158 (1963).

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

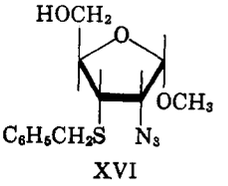
(4) For leading references, see C. D. Anderson, L. Goodman, and B. R. Baker, *ibid.*, **80**, 5247 (1958).

(5) (a) G. Casini and L. Goodman, *ibid.*, **85**, 235 (1963); (b) see K. L. Rinehart, Jr., W. S. Chilton, M. Hichens, and W. von Phillipsborn, *ibid.*, **84**, 3216 (1962), for a discussion of this point.

ment of IV with methanesulfonyl chloride afforded the methanesulfonate VII, again as a sirup, contaminated with some 2,5-di-*O*-methanesulfonate as a result of the presence of II in the starting material. When the crude methanesulfonate VII was treated with sodium azide in aqueous 2-methoxyethanol, the methoxycarbonyl group was cleaved and a mixture of azides (VI) was formed that also contained the 2(3),5-diazide mixture derived from the dimethanesulfonate of II. The azide mixture (VI) results from opening of a derived episulfonium ion intermediate (XV), at least predominantly. Although a direct SN2 displacement of the methanesulfonate of VII by azide ion, a strong nucleophile, to give the azide XVI with a ribose configuration represents a



XV

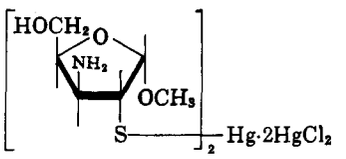


XVI

real possibility, no compounds derivable from XVI could be detected in the subsequent work. The n.m.r. spectra of the 3-benzylthiofuranosides isolated showed either a C-1 proton singlet or a C-1 proton doublet with $J \sim 1.5$ c.p.s., absorptions that are generally characteristic for *trans* C-1–C-2 proton couplings in a furanose sugar. Using these considerations as the basis, no evidence was found for the formation of XVI in the reaction of VII with azide ions since compounds derived from XVI should possess a *cis* relationship of the C-1–C-2 protons and would be expected to show coupling constants for these protons of about 4–5 c.p.s.[5b]

Reduction of the azide mixture (VI) with sodium borohydride in isopropyl alcohol[6] gave a mixture of amines (and diamines) that was acetylated yielding a mixture of IX, X, XIII, and XIV, the latter two compounds being derived from the dimethanesulfonate contaminant of VII. Chromatography using silicic acid served to separate the mixture of diamides XIII and XIV from the mixture of IX and X. Saponification of the mixture of monoamides IX and X yielded the amine mixture that was converted to a mixture of amine hydrochlorides, V and XII, easily separated into its components by recrystallization. The lower melting hydrochloride was converted to a crystalline N,O-diacetate whose n.m.r. spectrum identified it as the amide IX that was derived from the amine hydrochloride V. Thus, the C-1 proton of IX appeared at τ 5.18 as a singlet not detectably coupled to the *trans*-proton at C-2. The higher melting hydrochloride XII was converted to a crystalline N,O-diacetate X whose n.m.r. spectrum showed the C-1 proton as a doublet centered at τ 5.16 with $J = 5$ c.p.s. as a result of spin-coupling to the *cis*-proton at C-2.

Reduction of the free benzylthio amines derived from V and XII with sodium in liquid ammonia afforded the aminomercaptans, isolated as their mercaptides by precipitation with mercuric chloride. The mercaptide from XII gave an analysis consistent with structure XVII. Decomposition of the mercury salts derived from V and XII using hydrogen sulfide afforded the



XVII 2HCl

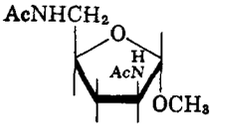
trans-aminomercaptans (VIII and XI, respectively) isolated as analytically pure, crystalline solids.

It was not apparent from the relative amounts of XII and V that were isolated whether the opening of the episulfonium ion XV had occurred predominantly at C-2 as would be predicted from purely steric considerations or at C-3, and the complexity of the reaction products prevented any reasonable estimation of the ratio of products derived from XV. In order to get a more quantitative idea of the position of ring opening of an ion such as XV, the diol II, was converted to the 2,5-dimethanesulfonate which was then treated with sodium azide in 2-methoxyethanol by the reaction conditions used in preparing VI. The diazide mixture was converted by reduction and acetylation to a mixture of the diamides XIII and XIV which was not completely pure because of some elimination of benzyl mercaptan that took place in the sodium azide reaction. However, the purity of the mixture was such that a reasonably reliable estimate of the composition of the mixture could be made on the basis of rotation data, and this suggested that 78% of the arabinoside XIII, formed by attack on the ion intermediate at C-2, was present.

The n.m.r. spectrum of the mixture showed clearly the resonances associated with the C-1 proton of XIII and the C-1 proton of XIV, and from the relative areas of these absorptions it was estimated that the mixture contained 69% of XIII and 31% of XIV; this estimate was subject to greater error than that from the rotation data. If the assumption is reasonable that the ring opening of the ion derived from the dimethanesulfonate of II is comparable with that of XV, the ratio, V/XII, formed from VII *via* XV should be about 3.

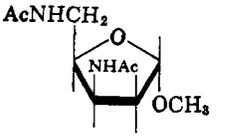
The pure diamides XIII and XIV required for reference rotations and n.m.r. spectra were easily obtained from the diamide mixture by fractional recrystallization. Again the n.m.r. spectra of the compounds served to assign their structures. Thus, the predominant diamide XIII showed the C-1 proton as a doublet at τ 5.12 with $J = 1.5$ c.p.s. as would be predicted for the poorly coupled C-1, C-2 *trans*-protons of a methyl furanoside. The xylose isomer XIV showed the C-1 proton as a doublet centered at τ 5.22 with $J = 4.5$ c.p.s. consistent with the *cis* arrangement of the C-1 and C-2 protons. These structure assignments for

XIII →



XVIII

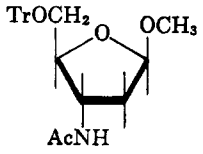
XIV →



XIX

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

XIII and XIV received further confirmation by a study of the n.m.r. spectra of the crystalline diamides XVIII and XIX, respectively, obtained by Raney nickel desulfurization of XIII and XIV. The C-1 proton of the 3-deoxyglycoside XVIII appeared as a singlet at τ 5.12 (in deuteriochloroform), and the C-1 proton of the 2-deoxyglycoside XIX appeared as a symmetrical triplet centered at τ 4.98 with $J = 4$ c.p.s. (in deuterated dimethyl sulfoxide) as a result of equal coupling of the C-1 proton to both C-2 protons. The appearance of a triplet for C-1 in XIX parallels the situation with 2′-deoxyadenosine,[7] but stands in contrast with that of the monoamide XX where the C-1 proton appears as a



XX

pair of doublets, one representing *cis* coupling with J = 5 c.p.s. and the other the result of *trans*-proton coupling with J = 1 c.p.s.[8]

Experimental[9]

Methyl 3-Benzyl-3-thio-α-D-arabinofuranoside (II) and Its Dibenzoate (III).—To a chilled (0°) solution containing 1.69 g. (13.6 mmoles) of benzyl mercaptan, 0.74 g. (13.7 mmoles) of sodium methoxide, and 30 ml. of methanol was added 1.00 g. (6.84 mmoles) of the epoxide I, and the resulting solution, under nitrogen, was heated at reflux for 18 hr. The mixture was adjusted to pH 7 with glacial acetic acid, then poured into 50 ml. of water and extracted with two 25-ml. portions of dichloromethane. The combined extracts were washed with two 25-ml. portions of water, then dried over magnesium sulfate. The solvent was evaporated, and the residue was washed by decantation with two 5-ml. portions of petroleum ether (b.p. 62–70°), then dried *in vacuo* to yield 1.73 g. (94%) of a pale yellow sirup that was suitable for further use.

The dibenzoate III was prepared from 34.8 g. (0.128 mole) of II, 250 ml. of pyridine, and 54.4 g. (0.387 mole) of benzoyl chloride to afford, after decomposition of the reaction mixture, 63.2 g. (102%) of cream-colored, crystalline product. Recrystallization from 1 l. of petroleum ether (b.p. 88–99°) gave 53.6 g. (87%) of product, m.p. 110–112°. The analytical sample, prepared in another experiment, had m.p. 110–111°; λ_{max}^{Nujol} 5.77, 5.81 (ester C=O), 7.79 (ester C–O–C), 14.05, and 14.26 μ (monosubstituted phenyl); $[\alpha]^{28}D$ +133°.

Anal. Calcd. for $C_{27}H_{26}O_6S$: C, 67.8; H, 5.48; S, 6.70. Found: C, 67.8; H, 5.90; S, 6.82.

A mixture of 25.9 g. of the dibenzoate III, 154 g. of potassium hydroxide, 400 ml. of methanol, and 75 ml. of water was heated at reflux for 4 hr., then cooled and evaporated *in vacuo*. The white residue was dissolved in 200 ml. of water, and the solution was extracted with one 200-ml. and one 100-ml. portion of dichloromethane. The combined extracts were washed with three 100-ml. portions of water, dried over potassium carbonate, and evaporated *in vacuo*, yielding 10.2 g. (70%) of pale yellow sirup II, $n^{23}D$ 1.5580. The analytical sample, $n^{23}D$ 1.5560, $[\alpha]^{26}D$ +145°, was obtained similarly from another run after decolorizing the sirup with Norit A in benzene. In the infrared it had λ_{max}^{film} 2.91 (OH), 14.20 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{13}H_{18}O_4S$: C, 57.8; H, 6.71; S, 11.9. Found: C, 58.0; H, 6.72; S, 11.7.

Methyl 3-Benzyl-5-*O*-methoxycarbonyl-3-thio-α-D-arabinofuranoside (IV).—To a chilled (0°) solution of 12.0 g. (44.4 mmoles) of II in 100 ml. of dry pyridine was added dropwise, with stirring, a solution of 4.94 g. (52.2 mmoles) of methyl chloroformate in 50 ml. of chloroform. The mixture was stirred for 1 hr. at 0° and at room temperature for 18 hr., then was poured, with stirring, into 400 ml. of cold saturated aqueous sodium bicarbonate. The organic layer was separated and the aqueous layer was extracted with 100 ml. of chloroform. The combined solutions were washed with 100 ml. of water, dried over magnesium sulfate, and evaporated *in vacuo*. Pyridine was removed from the residue by the addition and evaporation of portions of toluene until the pyridine odor was gone. The residue, 14.5 g. (100% yield), was a sirup; λ_{max}^{film} 2.90 (OH), 5.70 (ester C=O), 7.82 (ester C–O–C), 14.19 μ (monosubstituted phenyl).

Methyl 3-Benzyl-5-*O*-methoxycarbonyl-2-*O*-methylsulfonyl-3-thio-α-D-arabinofuranoside (VII).—To a chilled (0°), stirred mixture of 14.5 g. (44.2 mmoles) of IV in 100 ml. of dry pyridine was added dropwise 13.4 g. (0.116 mole) of methanesulfonyl chloride. The solution was stirred at 0° for 1 hr. and at room temperature for 18 hr. and then was poured into 500 ml. of cold saturated aqueous sodium bicarbonate. The aqueous mixture was extracted with two 100-ml. portions of dichloromethane; the combined extracts were washed with two 100-ml. portions of water, then decolorized with Norit A, and dried over magnesium sulfate. After removal of the solvent *in vacuo*, toluene was added and evaporated to remove all the pyridine, leaving 17.4 g. (97%) of amber sirup; λ_{max}^{film} 5.70 (ester C=O), 7.33 and 8.50 (sulfonate ester), 7.83 (ester C–O–C), 14.15 μ (monosubstituted phenyl); there was no 3.0-μ –OH band.

Methyl 2(3)-Azido-3(2)-benzyl-3(2)-thio-α-D-arabino(xylo)furanoside (VI).—A mixture of 17.4 g. (42.8 mmoles) of VII, 28 g. (0.43 mole) of sodium azide, and 300 ml. of 95:5 2-methoxyethanol–water was heated with stirring under nitrogen at 110–120° for 18 hr., then cooled, and evaporated *in vacuo*. The residue was partitioned between 200 ml. of water and 200 ml. of dichloromethane. The aqueous layer was extracted with two 50-ml. portions of dichloromethane; the combined extracts were washed with two 100-ml. portions of water and then dried over magnesium sulfate. Evaporation *in vacuo* gave 11.9 g. (94%) of a dark oil; λ_{max}^{film} 2.90 (OH), 4.77 (N_3), 14.22 μ (monosubstituted phenyl); there was no ester C=O band at 5.70 μ.

Anal. Calcd. for $C_{13}H_{17}N_3O_3S$: N, 14.2. Found: N, 14.9.

Methyl 2-Amino-3-benzyl-2-deoxy-3-thio-α-D-arabinofuranoside Hydrochloride (V) and Methyl 3-Amino-2-benzyl-3-deoxy-2-thio-α-D-xylofuranoside (XII).—A mixture of 30.3 g. (0.102 mole) of VI, 9.0 g. (0.239 mole) of sodium borohydride, and 350 ml. of isopropyl alcohol was heated at reflux for 15 hr., then cooled, and evaporated *in vacuo*. The residue was partitioned between 400 ml. of dichloromethane and 350 ml. of water, the resulting emulsion being broken after filtration through Celite. The dichloromethane extract was washed with 250 ml. of water, dried over magnesium sulfate, and evaporated *in vacuo*, affording 27.5 g. (100%) of orange sirup; λ_{max}^{film} 2.99, 3.04 (OH, NH_2), 6.25 (NH_2 and aryl), 14.20 μ (monosubstituted phenyl). The sirup was dissolved in 130 ml. of cold (0°) pyridine containing 15 ml. (0.108 mole) of triethylamine, and this solution was treated with 67 ml. of acetic anhydride. The reaction mixture was kept at 5° for 18 hr., then stirred at room temperature for 1 hr., then added to 1 l. of ice–water. The mixture was neutralized with solid sodium carbonate and extracted with two 100-ml. portions of dichloromethane; the combined extracts were washed with two 100-ml. portions of water, then dried over magnesium sulfate. Evaporation *in vacuo* left 35.5 g. (98%) of a solid that was a mixture of the amides (IX and X) which contained some of the diamides (XIII and XIV).

This amide mixture was applied to a column of silica gel, 90–200 mesh (250 × 35 mm.). Elution with 200 ml. of ethyl acetate gave 1.26 g. (A) of orange liquid as a forerun which showed no amide bands in its infrared spectrum. A second portion of 800 ml. of ethyl acetate eluted 22.0 g. (B) of solid which was a mixture of the amides IX and X. Elution with 800 ml. of chloroform yielded no product, and finally 200 ml. of methanol eluted the crude diamide mixture (C).

Fraction B, 22.0 g., was dissolved in a mixture of 1 l. of methanol, 250 ml. of water, and 300 g. of potassium hydroxide,

(7) W. W. Lee, A. Benitez, C. D. Anderson, L. Goodman and B. R. Baker, *J. Am. Chem. Soc.*, **83**, 1906 (1961).

(8) C. D. Anderson, W. W. Lee, L. Goodman, and B. R. Baker, *ibid.*, **83**, 1900 (1961).

(9) 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 run by the descending technique on Whatman No. 1 paper using solvent systems A, 1-butanol–acetic acid–water (5:2:3), and B, isopropyl alcohol–2 *N* hydrochloric acid (65:35). Spots were detected with the sodium azide–iodine[10] spray and were located relative to adenine (R_f adenine = 1.00). The n.m.r. spectra were obtained either with the Varian A-60 spectrometer or the Varian V-4311 spectrometer operated at 60 Mc.

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

and the solution was heated at reflux, under nitrogen, for 40 hr., then evaporated *in vacuo*. The residue was dissolved in 300 ml. of water and extracted with two 200-ml. portions of dichloromethane; the extracts were washed with water until neutral, then dried over magnesium sulfate and evaporated *in vacuo*, leaving 13.0 g. (77%) of yellow sirup which contained no N-acetate according to the infrared spectrum. Two grams (7.43 mmoles) of this residue was dissolved in 10 ml. of anhydrous ether, and a saturated solution of ethereal hydrogen chloride was added, dropwise, until precipitation was complete. The ether was decanted and the semisolid residue washed by decantation with several small portions of fresh ether leaving, after removal of the last traces of ether *in vacuo*, 2.04 g. (89%) of solid. This was dissolved in a minimum amount of methanol, and 25 ml. of ether was added. After chilling the solution, the white needles, 0.47 g. (21%), m.p. 211–213° dec., were collected and shown to be the 2-amine salt XII by infrared spectral comparison with the analytical sample. The filtrate from XII was evaporated *in vacuo* and the residue crystallized from 30 ml. of acetonitrile to give 0.68 g. (30%) of white needles, m.p. 159–162°, whose infrared spectrum showed it to be V, free from XII.

The analytical sample of XII, prepared in an earlier experiment, had m.p. 210–212° dec.; $[\alpha]^{25}D$ +59° (1% in methanol); λ_{max}^{Nujol} 2.99 (OH), 3.29, 3.66–3.82 (NH_3^+), 14.09 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{13}H_{20}ClNO_3S$: C, 51.1; H, 6.59; Cl, 11.6; N, 4.58; S, 10.5. Found: C, 51.2; H, 6.71; Cl, 11.4; N, 4.53; S, 10.4.

The analytical sample of V, prepared in an earlier experiment, had m.p. 159–162°; $[\alpha]^{25}D$ +104° (1% in methanol); λ_{max}^{Nujol} 2.99 (OH); 3.21, 3.7–4.2 (NH_3^+), 13.95 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{13}H_{20}ClNO_3S$: C, 51.1; H, 6.59; Cl, 11.6; N, 4.58; S, 10.5. Found: C, 51.3; H, 6.54; Cl, 11.6; N, 4.55; S, 10.5.

Methyl 2,5-Diacetamido-3-benzyl-2,5-dideoxy-3-thio-α-D-arabinofuranoside (XIII) and Methyl 3,5-Diacetamido-2-benzyl-3,5-dideoxy-2-thio-α-D-xylofuranoside (XIV).—Fraction C was stirred with 30 ml. of ethyl acetate. The insoluble white solid, 2.14 g., m.p. 190–231°, was recrystallized from chloroform to give 1.08 g. of white crystals, m.p. 235–236°, which was shown to be XIV by comparison with the analytical sample. Petroleum ether (30–60°) was added to the ethyl acetate liquors which precipitated 2.54 g. of solid with m.p. 157–166°. Recrystallization from 50 ml. of ethyl acetate gave 1.01 g. of white crystals, m.p. 163–165°, which proved to be XII.

The analytical sample of XIV had m.p. 231–235°; $[\alpha]^{24}D$ −19.6°; λ_{max}^{Nujol} 3.01, 3.03, 6.40 (NH), 6.03 (amide C=O), 13.02, 14.27 μ (monosubstituted phenyl). The n.m.r. spectrum, in deuteriochloroform, showed resonances at τ 2.68 (aromatic), 4 (broad NH), 5.22 (C-1, doublet, J = 4.5 c.p.s.), 6.23 (benzyl CH_2), 6.65 (OCH_3), 7.98, and 8.10 (CH_3CO).

Anal. Calcd. for $C_{17}H_{24}N_2O_4S$: C, 57.9; H, 6.86; N, 7.95; S, 9.10. Found: C, 58.0; H, 6.98; N, 7.96; S, 9.01.

The analytical sample of XIII had m.p. 163–166°; $[\alpha]^{24}D$ +43.7°; λ_{max}^{Nujol} 3.02, 3.03, 6.40 (NH), 6.01, 6.03 (amide C=O); 13.07, 14.03 μ (monosubstituted phenyl). The n.m.r. spectrum, determined in deuteriochloroform, showed resonances at τ 2.70 (aromatic), 4 (broad, NH), 5.12 (C-1, doublet, J = 1.5 c.p.s.), 6.18 (benzyl CH_2), 6.66 (OCH_3), 7.99 and 8.12 (CH_3CO).

Anal. Calcd. for $C_{17}H_{24}N_2O_4S$: C, 57.9; H, 6.86; N, 7.95; S, 9.10. Found: C, 57.9; H, 6.82; N, 7.98; S, 9.09.

Methyl 2-Acetamido-5-*O*-acetyl-3-benzyl-2-deoxy-3-thio-α-D-arabinofuranoside (IX).—A mixture of 0.35 g. (1.14 mmoles) of V, 4 ml. of dry pyridine, 0.30 ml. of triethylamine, and 5 ml. of acetic anhydride was maintained at room temperature for 18 hr. then poured into ice–water. The solid was collected and dried yielding 0.28 g. (69%) of white crystals. Recrystallization from water afforded 0.26 g. (64%) of needles, m.p. 134–136°; $[\alpha]^{24}D$ +194°; λ_{max}^{Nujol} 3.11 and 6.40 (NH), 5.75 (ester C=O), 6.08 (amide C=O), 8.07 (ester C-O-C), 14.13 μ (monosubstituted phenyl). The n.m.r. spectrum, in deuteriochloroform, showed resonances at τ 2.70 (aromatic), 4–5 (broad, NH), 5.18 (C-1, singlet), 6.16 (benzyl CH_2), 6.64 (OCH_3), 7.96 and 8.06 (CH_3CO).

Anal. Calcd. for $C_{17}H_{23}NO_5S$: C, 57.8; H, 6.56; N, 3.96; S, 9.07. Found: C, 57.9; H, 6.62; N, 3.96; S, 9.21.

Methyl 3-Acetamido-5-*O*-acetyl-2-benzyl-3-deoxy-2-thio-α-D-xylofuranoside (X).—Acetylation of 0.35 g. (1.14 mmoles) of XII by the procedure described for the preparation of IX gave after recrystallization from water 0.37 g. (92%) of white crystals, m.p. 138–139°; m.m.p. 113–116° with IX; $[\alpha]^{24}D$ +133°; λ_{max}^{Nujol} 3.09 and 6.62 (NH), 5.74 (ester C=O), 6.05 (amide C=O), 8.14 (ester C–O–C), 14.40 μ (monosubstituted phenyl). The n.m.r. spectrum, in carbon tetrachloride, showed resonances at τ 2.66 (aromatic), 4–5 (broad, NH), 5.16 (C-1, doublet, J = 4.5 c.p.s.), 6.21 (benzyl CH_2), 6.63 (OCH_3), 7.98 and 8.11 (CH_3CO).

Anal. Calcd. for $C_{17}H_{23}NO_5S$: C, 57.8; H, 6.56; N, 3.96; S, 9.07. Found: C, 58.1; H, 6.61; N, 2.94; S, 9.26.

Methyl 2-Amino-2-deoxy-3-thio-α-D-arabinofuranoside Hydrochloride (VIII).—The free base of V was generated by dissolving 1.45 g. (4.73 mmoles) of V in 30 ml. of saturated aqueous sodium bicarbonate. The solution was extracted with three 15-ml. portions of dichloromethane; the extracts were washed with water, dried over magnesium sulfate, and evaporated *in vacuo*, giving 1.23 g. (96%) of the free amine. A solution of the amine in 8 ml. of dry 1,2-dimethoxyethane was added dropwise to a well stirred solution of 0.55 g. (24 mg.-atoms) of sodium in 25 ml. of liquid ammonia. The mixture was stirred for 30 min., then the excess sodium was decomposed by adding absolute ethanol to discharge the blue color. The ammonia was evaporated under nitrogen and the residue was dissolved in 8 ml. of water. The aqueous solution was adjusted to pH 7 with glacial acetic acid and was then treated with excess aqueous mercuric chloride solution. The white precipitate was washed with water and dried, then thoroughly triturated with dichloromethane to remove bibenzyl, affording finally 2.51 g. of white solid mercaptide.

The mercaptide was suspended in 25 ml. of methanol and hydrogen sulfide was bubbled through the well stirred suspension for 20 min. The reaction mixture was filtered through Celite and the filtrate was evaporated *in vacuo*, affording 0.86 g. (84%) of a tan, crystalline residue. The residue was dissolved in 15 ml. of methanol and precipitated with excess ether, giving a gummy product that solidified to a foam after being treated *in vacuo*. The nitroprusside-positive solid, 0.59 g. (58%), had $[\alpha]^{24}D$ +100.8° (1% in methanol); λ_{max}^{Nujol} 2.87, 2.96 (OH), 3.82 (SH), 5.0, 6.22 and 6.55 μ (NH_3^+); there was no phenyl absorption near 14 μ. It was homogeneous on paper chromatography in solvents A and B with R_{Ad} 0.96 and 1.38, respectively.[9]

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, 33.4; H, 6.63; Cl, 16.7; N, 6.31; S, 14.8.

A portion (0.50 g.) of amorphous, but analytically pure, solid from another run was crystallized from 15 ml. of acetonitrile to give 0.13 g. of a crystalline solid, m.p. 138–145°; $[\alpha]^{22}D$ +94.6 (1% in methanol).

Anal. Found: C, 33.6; H, 6.43; Cl, 16.5; N, 6.39; S, 15.0. Iodometric thiol titration indicated the material to contain 93% of the theoretical mercaptan.

Methyl 3-Amino-3-deoxy-2-thio-α-D-xylofuranoside Hydrochloride (XI).—The salt XII, 2.40 g. (7.83 mmoles), was converted to its free base and thence to its mercaptide using the procedure described for the similar conversion of V. The mercaptide was a brown solid, 4.81 g. In a previous run the mercaptide had been analyzed and appeared to be the bismercury compound XVII.

Anal. Calcd. for $C_{12}H_{26}Cl_4Hg_3N_2O_6S_2$: C, 13.1; H, 2.38, Cl, 12.9, N, 2.55. Found: C, 12.7; H, 1.84; Cl, 12.9; N, 2.51.

The mercaptan was generated from XVII with hydrogen sulfide and gave 1.00 g. (59%) of crystalline solid, which was reprecipitated from methanol with ether to give 0.73 g. (43%) of the nitroprusside-positive analytical sample, $[\alpha]^{24}D$ +73.5° (1% in methanol); λ_{max}^{Nujol} 3.02 3.17, (OH), 3.83 (SH), 6.22, 6.40, 6.60 μ (NH_3^+); there was weak and unexpected absorption at 14.3 μ. The product was homogeneous on paper chromatography in solvents A and B with R_{Ad} 0.98 and 1.36, respectively.

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, 33.5; H, 6.78; Cl, 16.7; N, 6.73; S, 14.6.

From another run the analytically pure solid showed 96% of the theoretical mercaptan content according to iodometric titration and gave a solid, m.p. 156–161°, after recrystallization from methanol–ether.

Conversion of the Diol II to the Mixture of Diamides XIII and XIV.—The diol II, 2.04 g. (7.53 mmoles) in 30 ml. of dry pyridine was treated conventionally with 2.96 g. (25.9 mmoles) of methanesulfonyl chloride yielding 3.39 g. (105%) of the dimethanesulfonate as a yellow oil whose infrared spectrum showed no

–OH absorption near 3.0 μ. The dimesylate, 3.2 g. (7.5 mmoles), was treated with excess sodium azide in 2-methoxyethanol as described for the preparation of VI, affording 2.09 g. (87%) of a yellow oil whose infrared spectrum showed little or no sulfonate ester absorption. The diazide, 2.0 g. (6.23 mmoles), was reduced with excess sodium borohydride in isopropyl alcohol to furnish 1.54 g. (92%) of a sirup whose infrared spectrum showed the absence of covalent azide absorption. Acetylation of 1.50 g. of the amine mixture in pyridine containing triethylamine afforded 1.57 g. (79%) of a yellow crystalline solid whose analysis showed it to be deficient in nitrogen and to contain excess sulfur as calculated for the diamide mixture. Chromatography of 1.50 g. of the solid over silicic acid gave 0.12 g. of a fraction eluted with ethyl acetate which appeared to be mostly dibenzyl disulfide and 1.27 g. of material eluted with methanol whose infrared spectrum indicated it to be a mixture of the diamides XIII and XIV, $[\alpha]^{24.5}D$ +29.8°.

Anal. Calcd. for $C_{17}H_{24}N_2O_4S$: C, 57.9; H, 6.86; N, 7.95; S, 9.10. Found: C, 57.5; H, 6.80; N, 7.24, 7.30, S, 8.63.

Methyl 2,5-Diacetamido-2,3,5-trideoxy-α-D-*threo*-pentofuranoside (XVIII).—A stirred mixture of 1.00 g. (2.83 mmoles) of XIII, approximately 12 g. of Raney nickel[11] (thoroughly washed with dioxane), and 50 ml. of dioxane was heated at reflux for 4.5 hr., then was cooled, and filtered through Celite with adequate washing. The filtrate and the washings were evaporated *in vacuo* leaving 0.75 g. (115%) of a sirup whose infrared spectrum showed the absence of benzyl absorption near 14.3 μ. Four recrystallizations of the residue using first benzene–petroleum ether (30–60°), then ethyl acetate afforded 0.23 g. (35%) of the analytical sample, m.p. 127–132°; $[\alpha]^{24.5}D$ +32°; λ_{max}^{Nujol} 3.03, 3.27 and 6.43 (NH), 6.09 μ (amide C=O).

Anal. Calcd. for $C_{10}H_{18}N_2O_4$: C, 52.2; H, 7.88; N, 12.2. Found: C, 52.1; H, 7.88; N, 12.4.

Methyl 3,5-Diacetamido-2,3,5-trideoxy-α-D-*threo*-pentofuranoside (XIX).—Desulfurization of 1.08 g. (3.06 mmoles) of XIV using the conditions described for preparation of XVIII gave, after four recrystallizations of the residue from ethyl acetate, 0.11 g. (15%) of the analytical sample, m.p. 200–206°; $[\alpha]^{26}D$ +172° (1% in dimethyl sulfoxide); λ_{max}^{Nujol} 3.04, 3.22, 6.39 (NH), 6.05 μ (amide C=O); there was no S-benzyl absorption at 14.3 μ.

Anal. Calcd. for $C_{10}H_{18}N_2O_4$: C, 52.2; H, 7.88; N, 12.2. Found: C, 52.5; H, 7.87; N, 12.0.

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(11) Sponge nickel catalyst, Davison Chemical Co., Cincinnati 29, Ohio.

Syntheses with Partially Benzylated Sugars. II.[1] The Anomeric 1-*O*-Benzoyl-L-arabinopyranoses and 1-*O*-Benzoyl-L-arabinofuranoses and Their Tendencies to Undergo Acyl Migration

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The four 1-*O*-benzoyl-L-arabinoses have been prepared in pure form and their behavior in aqueous pyridine studied. Under the conditions chosen, both 1-*O*-benzoyl-α-L-arabinopyranose and 1-*O*-benzoyl-α-L-arabinofuranose are stable while the corresponding anomeric esters readily undergo acyl migration to yield 2-*O*-benzoyl-L-arabinopyranose. The rate of mutarotation of 1-*O*-benzoyl-β-L-arabinofuranose in aqueous pyridine is much faster than that of 1-*O*-benzoyl-β-L-arabinopyranose; since the rate of mutarotation of 2-*O*-benzoyl-β-L-arabinopyranose in aqueous pyridine is faster than either of the preceding mutarotations, it is concluded that the rates observed actually represent the acyl migration step in each of the two cases.

In 1956 Ness and Fletcher[3] observed that the 1-*O*-benzoyl group in 1,3,5-tri-*O*-benzoyl-α-D-ribofuranose readily migrates under mildly alkaline conditions to the C-2 position, giving 2,3,5-tri-*O*-benzoyl-D-ribofuranose. The ease with which this rearrangement takes place stands in marked contrast to the stability of 1-*O*-benzoyl-β-D-glucopyranose[4] under such conditions and suggested that 1-*O*-acyl aldoses may fall into two classes, *viz.*, those with a hydroxyl group at C-2 *cis* to the 1-*O*-acyl group and a second, more stable class having a *trans* arrangement. Recent researches by various workers have tended to support this view. Lemieux and Brice[5] predicted that 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose ought to rearrange to 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose and Bonner[6] later showed that such a rearrangement did indeed take place.

While a variety of 1-*O*-acyl-β-D-glucopyranoses have been discovered in nature, it is significant that no α-anomers having the acyl group *cis* to the hydroxyl at C-2 have been found. The first attempt to make a representative of this class, 1-*O*-mesitoyl-α-D-glucose,[7] clearly showed that the ester of even a sterically hindered acid readily undergoes migration from the C-1 to the C-2 position in α-D-glucopyranose.[8] It was only through the reaction of ethyl 1-thio-β-D-glucopyranoside with silver mesitoate that Pedersen and Fletcher[9] finally succeeded in synthesizing 1-*O*-mesitoyl-α-D-glucopyranose, the first 1-*O*-acyl-α-D-glucopyranose. When silver benzoate was used in this reaction only 2-*O*-benzoyl-D-glucose was obtained, indicating the

(1) The paper by R. Barker and H. G. Fletcher, Jr., entitled "2,3,5-Tri-*O*-benzyl-D-ribosyl- and -L-arabinosyl bromides" [*J. Org. Chem.*, **26**, 4605 (1961)] is regarded as I of this series.

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(3) R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **78**, 4710 (1956).

(4) L. Zervas, *Ber.*, **64**, 2289 (1931).

(5) R. U. Lemieux and C. Brice, *Can. J. Chem.*, **33**, 109 (1955).

(6) W. A. Bonner, *J. Org. Chem.*, **24**, 1388 (1959), found that the methylation of 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose with methyl iodide in the presence of silver oxide gives methyl β-D-glucopyranoside tetraacetate in 81.2% yield. It should be noted that the anomeric tetraacetate gave the same product under these conditions but in significantly lower yield (51%), demonstrating that migration between *trans* positions may indeed take place. However, the possibility of anomerization preceding acyl migration does not seem to be excluded here.

(7) H. B. Wood, Jr., and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **78**, 2849 (1956).

(8) As far as we are aware, this represents the only known case of an O → O migration of a mesitoyl group.

(9) C. Pedersen and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **82**, 3215 (1960).