Registry No.—*myo*-Inositol, 87-89-8; **2**, 17278-21-6; **3**, 17231-20-8; **4**, 17231-21-9; **5**, 17231-22-0; **6**, 17231-23-1; **7**, 17231-24-2; **8**, 17278-22-7; **9**, 13445-86-8.

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Intramolecular Displacement by Neighboring Thiolbenzoate. Formation of Sugar Episulfides[1]

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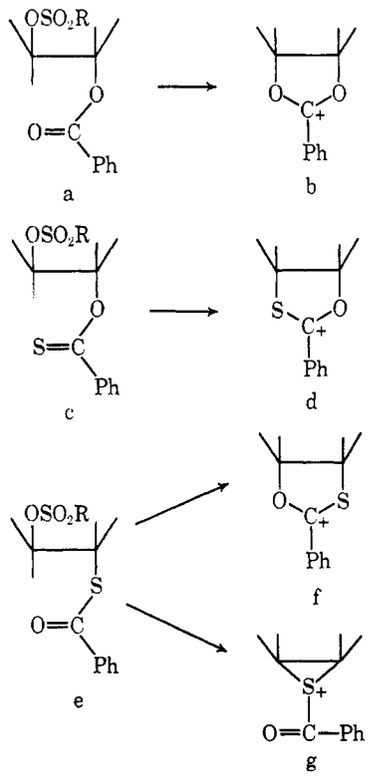
The epoxide ring of methyl 2,3-anhydro-5-*O*-trityl-β-D-lyxofuranoside was attacked nearly equally at C-2 and C-3 on fusion with pyridine–thiolbenzoic acid. The resultant 2-benzoylthio-*xylo* and 3-benzoylthio-*arabino* isomers were separated by chromatography. The tosylates of these were treated with sodium benzoate–*N*,*N*-dimethylformamide at 110°, and methyl 2,3-thioanhydro-5-*O*-trityl-β-D-ribofuranoside was formed as the only product. Sulfur participation through a three-membered cyclic intermediate thus occurred to the exclusion of oxygen participation through a five-membered cyclic intermediate.

The displacement of sulfonates with configurational inversion is a useful process for the synthesis of new sugars, but, when the sulfonate is attached to a furanose ring, direct SN2 displacement is often difficult. Internal displacement is then required, with the participation of a *trans* substituent adjacent to the sulfonate.[2] When the displacement is assisted by an *O*-benzoyl group (as in a), the result is the conversion of a *trans* into a *cis* glycol system, *via* the acylonium ion b. Syntheses of furanose derivatives of 5-deoxy-D-ribose,[3] homoribose (5-deoxy-D-allose),[4] and L-ribose[5] have been achieved, using sodium benzoate–*N*,*N*-dimethylformamide as the reaction medium. When the displacement is assisted by an *O*-thionobenzoyl group (as in c), the *trans* glycol system is converted into a *cis*-mercapto alcohol, by attack of sulfur to form the cyclic ion d, as in the recent synthesis of 3′-thioadenosine.[6] It was of interest to compare the participation of a neighboring *S*-benzoyl group (as in e) and its synthetic utility. Two possibilities seemed likely, either oxygen participation or sulfur participation, through the intermediate five-membered or three-membered cyclic ions (f and g), respectively. Occurrence of benzoylepisulfonium ions (g) has been postulated in a few cases in the literature,[2] but has not been demonstrated conclusively. If displacement were found to occur *via* the thioacylonium ion (f) on the other hand, it would constitute another synthesis of the relatively inaccessible *cis*-mercapto alcohol system. In the present study, inversion by sulfur participation is established by isolation of episulfide derived from g.



The *trans*-mercapto alcohol system required for this study is readily obtained from the opening of sugar epoxides with sulfur nucleophiles. Since we were interested in a compound which might lead, *via* the pathway e → f, to 2-thioribofuranose derivatives, we sought to obtain a 2-benzoylthioxylofuranose (precursor to e) from methyl 2,3-anhydro-β-D-lyxofuranoside[7] (**1**). The recently described fusion of epoxides with pyridinium thiolbenzoate[8] appeared to be a promising procedure, and we were encouraged to expect extensive attack at C-2 of **1**, since reaction of this epoxide with sodium benzyl mercaptide[9] gave 2-

(1) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service, Contract No. PH-43-64-500. The opinions expressed in this paper are those of the authors and not necessarily those of the Cancer Chemotherapy National Service Center.

(2) L. Goodman, *Advan. Carbohyd. Chem.*, **22**, 109 (1967).

(3) K. J. Ryan, H. Arzoumanian, E. M. Acton, and L. Goodman, *J. Amer. Chem. Soc.*, **86**, 2497 (1964).

(4) K. J. Ryan, H. Arzoumanian, E. M. Acton, and L. Goodman, *ibid.*, **86**, 2503 (1964).

(5) E. M. Acton, K. J. Ryan, and L. Goodman, *ibid.*, **86**, 5352 (1964).

(6) K. J. Ryan, E. M. Acton, and L. Goodman, *J. Org. Chem.*, **33**, 1783 (1968); E. M. Acton, K. J. Ryan, and L. Goodman, *J. Amer. Chem. Soc.*, **89**, 467 (1967).

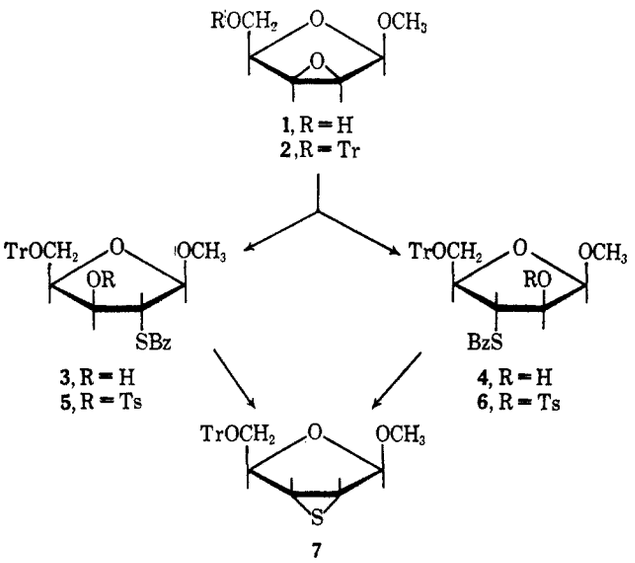
(7) B. R. Baker, R. E. Schaub, and J. H. Williams, *ibid.*, **77**, 7 (1955).

(8) J. Kocourek, *Carbohyd. Res.*, **3**, 502 (1967).

(9) G. Casini and L. Goodman, *J. Amer. Chem. Soc.*, **86**, 1427 (1964).

benzylthio-*xylo* and 3-benzylthio-*arabino* sugars in a 60:40 proportion (the first example where attack of a 2,3-anhydrofuranoside was not very predominantly at C-3).

Methyl 2,3-anhydro-β-D-lyxofuranoside (**1**) was converted into the 5-*O*-trityl derivative **2**, and this was fused with pyridine and thiolbenzoic acid. The reaction was complete after 6 hr at 110°, and nearly equal amounts of the isomeric products were formed. These were readily separated by chromatography on silica gel. The products were nearly identical in infrared spectra and exhibited the expected hydroxyl and *S*-benzoyl bands, but one product surprisingly had a chromatographic mobility greater than that of the starting epoxide **2**. The other, as expected for a monohydroxy sugar, moved more slowly than **2**. It



Tr = trityl = triphenylmethyl
Bz = benzoyl
Ts = tosyl = *p*-toluenesulfonyl

was expected that identification could be made from the nmr spectra, since the 1-H,2-H relationship would be *trans* for the *xylo* isomer and *cis* for the *arabino* isomer. Assignments based on the furanose anomeric proton are considered unambiguous when $J_{1,2}$ for the *trans* case is 1.0 Hz or less.[10] The singlet ($J \leq 0.5$ Hz) observed for the anomeric proton of the chromatographically more mobile isomer identified it as the *xylo* compound (**3**). The other then was the *arabino* compound (**4**), and it showed an uneven, broadened doublet for the anomeric proton. The unexpected mobility of **3** on silica gel was regarded as supporting evidence that it was the *xylo* isomer, since the proximity of the 3-hydroxyl to the bulky trityl group might hinder its interaction with the adsorbent; the 2-hydroxyl in **4** would be relatively unhindered, especially in the preferred twist or envelope conformation.[9,11,12]

That the trityl group was indeed involved and that its presence was crucial for the practical separation of isomers was emphasized when the reactions of 5-*O*-benzoyl[13] and 5-*O*-*p*-nitrobenzoyl epoxides (**8** and **9**) were studied. In each case, fusion with pyridine–thiolbenzoic acid gave a mixture of isomers which were only poorly resolved by thin layer chromatography; column chromatography was quite impractical. Just as with **2**, nearly equal quantities of the isomers were formed (the mixture from **8** was resolved by chromatography; that from **9** was analyzed by the nmr spectrum). Though the trityl group of **3** may hinder adsorption of the 3-hydroxyl, the trityl group of **2** apparently had little effect in directing attack of the epoxide to C-2 (about 50% *xylo* was formed from **2**, about 45% from **8**).

The hydroxy *S*-benzoates (**3** and **4** in the trityl series) were treated with tosyl chloride. The *xylo* tosylate **5** was obtained as a crystalline solid, and the *arabino* tosylate **6** was obtained as a chromatographically purified gum. Intramolecular displacement of these tosylates was carried out at 110° in *N*,*N*-dimethylformamide containing sodium benzoate. The reaction of the *xylo* isomer **5** was complete in 8 hr, according to nmr spectral evidence for absence of tosylate (after 6 hr in a trial experiment 10–15% of tosylate remained); the absence of tosylate and *S*-benzoate was confirmed qualitatively in the infrared spectrum. The nmr spectrum was readily identified as that of the episulfide **7**, by comparison with the spectrum of an authentic sample.[13] The only indication of significant impurity in the crude product was an excess of aryl protons (presumably benzoyl) upon integration. This and weak–medium carbonyl bands at 5.6 and 5.8 μ in the infrared required explanation. The 5.6-μ band suggested that benzoic anhydride was a contaminant, possibly formed from the intermediate *S*-benzoylepisulfonium ion g by reaction with sodium benzoate. The 5.8-μ band suggested some *O*-benzoyl ester, but instead was probably due to a little *S*-benzoylepisulfonium ion still present in the crude product (carbonyl absorption at 5.80 μ was previously indicative of a cyclopentene *S*-benzoylepisulfonium ion).[14] Though a benzoate might have been obtained if any inversion with oxygen participation had occurred (the intermediate thioacylonium ion f would probably have been hydrolyzed, like d, to an *O*-benzoyl mercapto sugar), there were never any nmr signals indicative of an extraneous methyl furanoside in the crude product to which a benzoate could be attached. The product seemed to be exclusively the episulfide; it was purified chromatographically and crystallized on seeding with an authentic sample.

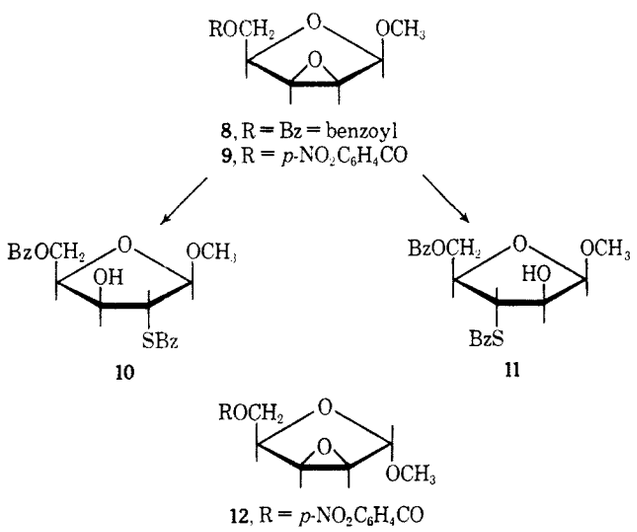
No evidence for oxygen participation could be obtained. In an attempt to isolate any possible amount of a hydrolysis product from f as the di-*O*,*S*-benzoate, the crude inversion product was immediately treated with benzoyl chloride–pyridine; again only the episulfide **7** could be isolated, after processing, in 60% yield.

Similar results were obtained on inversion of the *arabino* tosylate **6**, except that reaction was a little slower. After 6 hr at 110°, about 30% of the tosylate **6** remained unreacted; after 4 hr more at 110°, about 10% unreacted **6** still remained. The somewhat lessened reactivity supported its identity as the *arabino* isomer. In a previously studied pair of *xylo* and *ara-*

(10) R. U. Lemieux and D. R. Lineback, *Ann. Rev. Biochem.*, **32**, 156 (1963).
(11) L. D. Hall, *Chem. Ind.* (London), 950 (1963).
(12) C. T. Bishop and F. P. Cooper, *Can. J. Chem.*, **41**, 2743 (1963).
(13) L. Goodman, *Chem. Commun.*, 219 (1968).
(14) L. Goodman, A. Benitez, and B. R. Baker, *J. Amer. Chem. Soc.*, **80**, 1680 (1958).

bino compounds,[9] involving sulfur participation, the *xylo* isomer was considerably more reactive after tosylation than the *arabino* isomer. The difference was explained[9] by the twist or envelope conformations of the furanose ring.[11,12] Assuming the preferred conformers are those with the 1-methoxyl *quasi*-axial and with C-5 *quasi*-equatorial, *xylo* 2,3 substituents are in the reactive *trans* diaxial orientation, and *arabino* 2,3 substituents are diequatorial. After removal of the small amount of unreacted **6** by chromatography, a 61% yield of episulfide was obtained. As with **5**, there was no evidence for any other product. That both of the isomeric *S*-benzoyl tosylates reacted exclusively with sulfur participation may be explained simply by the greater nucleophilic character of sulfur compared to oxygen.

It may be noted that whenever the optical rotations of two isomeric D sugars were compared in this work, the rotation of the *arabino* isomer was the more negative. This was also the case with the parent D-*xylo* and D-*arabino* methyl furanosides,[12,15] but just the opposite was found[9] with some isomeric pairs of 2-benzylthio xylosides with 3-benzylthio arabinosides. This illustrates that simple comparison of optical rotations is insufficient to distinguish two such isomers.[16]



An α-methyl epoxide was studied briefly for comparison with **2**. Methyl 2,3-anhydro-α-D-lyxofuranoside[7] was converted into the 5-*O*-*p*-nitrobenzoate **12**, and this was fused with pyridine–thiolbenzoic acid. It was not practical to study the reaction further, since the α-methoxyl offered considerable hindrance to the attacking reagent. After 18 hr nearly half the starting material was unreacted, and apparently none of the attack was at C-2. The product was poorly resolved from the starting epoxide **12** on thin layer chromatography; a small sample was isolated and identified as methyl 3-*S*-benzoyl-5-*O*-*p*-nitrobenzoyl-3-thio-D-arabinofuranoside by the nmr spectrum (1-H was a singlet at τ 4.98, $J \leq 1$ Hz).

Experimental Section[17]

Methyl 2,3-Anhydro-5-*O*-triphenylmethyl-β-D-lyxofuranoside (2).—A solution of 7.5 g (51 mmol) of methyl 2,3-anhydro-β-D-lyxofuranoside[7] in 100 ml of dry pyridine was treated with 17 g (61 mmol) of trityl chloride and stirred at room temperature for 3 days. Water (1 ml) was added, and the mixture was stirred for 30 min, poured into 200 ml of ice-cold 1 *M* hydrochloric acid, and extracted with 200 ml of chloroform. The extract was washed with 200 ml of bicarbonate solution and with 200 ml of water, dried, and concentrated. The residue was recrystallized twice from 100 ml of 95% ethanol to form 12 g (62%) of white solid: mp 156–157°; $[\alpha]^{24}D$ −76° ($CHCl_3$); nmr, τ 2.4–2.85 (m, 15, C_6H_5), 5.10 (s, 1, 1-H; on expanded scale, $J_{1,2}$ = 0.6 Hz), 6.02 (*pseudo* t, 4-H, J = ~6 Hz), 6.31 and 6.45 (two doublets comprising an AB quartet, 2-H and 3-H, $J_{2,3}$ = 3 Hz; further splitting of each signal could be measured on expanded scale, $J_{1,2}$ = 0.6 Hz, $J_{3,4}$ = 1 Hz), 6.5–6.7 (m, 2, 5-H_2), 6.58 (s, 3, OCH_3); tlc with 2% ether in benzene, R_f 0.48 (upon detection by charring with dilute sulfuric acid, some samples showed a yellow spot near the solvent front, due to triphenylcarbinol detectable in trace amounts).

Anal. Calcd for $C_{25}H_{24}O_4$: C, 77.3; H, 6.23. Found: C, 77.3; H, 6.12.

Reaction of 2 with Pyridinium Thiolbenzoate.—To a mixture of 3.6 g (26 mmol) of thiolbenzoic acid (Eastman, redistilled) and 2.9 g (35 mmol) of pyridine were added 7.4 g (19 mmol) of methyl 2,3-anhydro-5-*O*-trityl-β-D-lyxofuranoside and 10 ml of tetrahydrofuran. To obtain a good melt the mixture, under nitrogen, was boiled and heated to *ca.* 110°, then evacuated for 5 min to complete the removal of tetrahyrofuran and excess pyridine. The fused mixture was heated under nitrogen at 110° for 6 hr and then *in vacuo* for 0.5 hr. The residual red glass (10.5 g) was dissolved in 20 ml of $CHCl_3$. The solution was washed with 20 ml of bicarbonate solution and with 20 ml of water, dried, and concentrated. The residual glass (10.2 g) showed only a trace of starting epoxide **2** (R_f 0.5) by tlc with 10% ether in benzene; there were two strong spots due to the products (R_f 0.4 and R_f 0.6) and one due to triphenylcarbinol (R_f 0.7). From a preliminary reaction (550 mg of epoxide) which had not gone to completion, the two products were isolated by preparative tlc in nearly equal amounts, 238 and 245 mg, respectively (33% yield, each); the former with R_f 0.4 was shown by nmr spectroscopy (*cis* C-1–C-2, $J_{1,2}$ = 2–3 Hz; see below) to be the *arabino* isomer, and the latter with R_f 0.6 (*trans* C-1–C-2, $J_{1,2} \leq 0.5$ Hz) was shown to be the *xylo* isomer.

Methyl 2-*S*-Benzoyl-2-thio-5-*O*-triphenylmethyl-β-D-xylofuranose (3) and Methyl 3-*S*-Benzoyl-3-thio-5-*O*-triphenylmethyl-β-D-arabinofuranose (4).—A solution of 10 g of the glassy mixture of isomers in 300 ml of benzene was added to a chromatographic column (40 × 5.0 cm) of 300 g of silica gel (90–200 mesh) in benzene. The eluate was examined by tlc. Elution with 1-l. portions of benzene, 0.5% ether in benzene, and 1% ether in benzene afforded triphenylcarbinol. Elution with 2% ether in benzene gave the following fractions: (a) 1.2 l. containing 3.7 g of the *xylo* isomer **3** (contamination with 30–40% of triphenylcarbinol was estimated from the excess of aryl H upon integration of the nmr spectrum; contamination with the *arabino* isomer rose from 0–10% during this elution); (b) 1.0 l., containing 1.5 g of a 1:1 mixture of **3** and **4**, with a few per cent unreacted epoxide **2** (identified by tlc, measured in the nmr spectrum); (c) 2.8 l., containing 3.5 g of the *arabino* isomer **4** (purity of 80–90% was estimated from the integrated nmr spectrum; no *xylo* isomer was detected).

Further purification was accomplished from the 1:1 mixture (300 mg) by preparative tlc on two plates, with 10% ether in benzene; each plate was dried and developed a second time; and the products were eluted with chloroform and recovered as syrups by evaporation. The faster band was **3** (65 mg): $[\alpha]^{24}D$

(15) I. Augestad and E. Berner, *Acta Chem. Scand.*, **8**, 251 (1954).

(16) For example, identification of the isomers obtained by opening a 2,3-epimino sugar with sodium azide was regarded as tentative: J. Cleophax, S. D. Gero, and J. Hildesheim, *Chem. Commun.*, 94 (1968).

(17) Melting points were determined on a Fisher-Johns hot stage and are uncorrected. Nmr spectra were determined with Varian A-60 and HR-100 spectrometers, using chloroform-*d* solutions containing 4% tetramethylsilane (τ 10.00) as an internal standard; accuracy is ±0.05 ppm for chemical shifts and ±0.2 Hz for coupling constants. Optical rotations were measured on 1% solutions in 1-dm tubes with a Perkin-Elmer Model 141 automatic polarimeter. Thin layer chromatography (tlc) was carried out with silica gel HF (E. Merck, Darmstadt) on 5 × 20 cm glass plates. Benzene–ether mixtures were used as developing solvents. Spots were detected under ultraviolet light or by spraying with dilute sulfuric acid and charring. Preparative tlc was done on 20 × 20 cm plates with 2 mm of silica gel (100 mg of compound/plate). Sample solutions were applied with the Rodder streaker, Rodder Instrument Co., Los Altos, Calif. The bicarbonate solution used in processing was saturated aqueous sodium bicarbonate. Organic solutions were dried with magnesium sulfate, which was removed by filtration; the concentration of solutions was done *in vacuo*.

$-1.9°$ ($CHCl_3$); ir (Nujol), 2.84 (OH), 5.97, 8.27, and 11.05 μ (SBz); nmr, τ 1.9–2.15 (m, 2, *o*-H's of benzoyl), 2.3–2.8 (m, 18, trityl C_6H_5's and *m*- and *p*-H's of benzoyl), 4.92 (s, 1, 1-H), 5.4–5.7 (uneven q, 1, 4-H), 5.7–5.85 (m, 2, 2-H and 3-H), 6.4–6.7 (m, 2, 5-H_2), 6.60 (s, 3, OCH_3).

Anal. Calcd for $C_{32}H_{30}O_5S \cdot 57CHCl_3$: C, 64.7; H, 5.10; Cl, 10.3; S, 5.33. Found: C, 64.2; H, 5.22; Cl, 9.98; S, 5.49.

The slower band was **4** (30 mg): $[\alpha]^{24}D$ $-62°$ ($CHCl_3$); ir (Nujol), 2.85 (OH), 5.97, 8.28, 11.05 μ (SBz); nmr, τ 2.05–2.25 (m, 2, *o*-H's of benzoyl), 2.35–2.95 (m, 18, trityl C_6H_5's and *m*- and *p*-H's of benzoyl), 5.1–5.2 (broad d, 1, 1-H, $J_{1,2}$ = 2–3 Hz), 5.7–5.9 (broad s, 3, H on C-2, C-3, and C-4), 6.61 (s, 3, OCH_3), 6.55–6.75 (m, 2, 5-H_2).

Anal. Calcd for $C_{32}H_{30}O_5S \cdot 0.24CHCl_3$: C, 69.7; H, 5.49; Cl, 4.60; S, 5.78. Found: C, 70.1; H, 5.45; Cl, 4.57; S, 5.88.

Methyl 2-*S*-Benzoyl-2-thio-3-*O*-*p*-tolylsulfonyl-5-*O*-triphenylmethyl-β-D-xylofuranoside (5).—To 1.10 g of methyl 2-*S*-benzoyl-2-thio-5-*O*-trityl-β-D-xylofuranoside (**3**, contaminated with 30% triphenylcarbinol, *i.e.*, estimated 60% purity from the integrated nmr spectrum; *ca.* 1.26 mmol) in 20 ml of dry pyridine was added 1.0 g (5.2 mmol) of tosyl chloride. The reaction mixture was stirred at room temperature for 3 days. Water (0.5 ml) was added; the mixture was stirred for 30 min and was poured into 50 ml of cold 1 *M* hydrochloric acid. The product was extracted with two 30-ml portions of chloroform. The combined extract was washed with 50 ml of saturated aqueous sodium bicarbonate and with 50 ml of water, dried, and concentrated. The residue was crystallized from 50 ml of boiling ethanol by chilling to 5° to yield 0.51 g (60%): mp 117–119° dec (capillary); $[\alpha]^{23}D$ $+1.1°$ ($CHCl_3$). The ir and nmr spectra were identical with those of an analytical sample [mp 120–120.5° dec (capillary); $[\alpha]^{21}D$ + 0.9° ($CHCl_3$)] obtained in 30% yield from a separate experiment (**3** was of 75% purity) after three recrystallizations: ir (Nujol), 5.98, 8.27, 11.12, and 14.56 (*S*-benzoyl), 7.32, 8.40 and 8.51 μ (tosyl); nmr, τ 2.0–2.9 (m, 24, aryl H), 4.92 (q, 1, 3-H, $J_{2,3}$ = 2.8 Hz, $J_{3,4}$ = 5.1 Hz), 5.00 (d, 1, 1-H, $J_{1,2}$ = 2.1 Hz), 5.35–5.7 (*pseudo* q, 1, 4-H), 5.86 (t, 1, 2-H, $J_{1,2}$ = 2.1 Hz, $J_{2,3}$ = 2.8), 6.45–6.7 (m, 2, 5-H_2), 6.61 (s, 3, OCH_3), 7.67 (s, 3, tosyl CH_3).

Anal. Calcd for $C_{39}H_{36}O_7S_2$: C, 68.8; H, 5.32; S, 9.42. Found: C, 68.9; H, 5.40; S, 9.65.

Methyl 3-*S*-Benzoyl-3-thio-2-*O*-*p*-tolylsulfonyl-5-*O*-triphenylmethyl-β-D-arabinofuranoside (6).—To 1.0 g (1.9 mmol) of methyl 3-*S*-benzoyl-3-thio-5-*O*-trityl-β-D-arabinofuranoside (**4**, purified by preparative tlc) in 20 ml of dry pyridine was added 1.2 g (6.3 mmol) of tosyl chloride. After 24 hr, the mixture was processed as for **5** to yield 1.04 g (81%) of a residual gum, homogeneous by tlc with 4% ether in benzene, R_f 0.6 The ir and nmr spectra were identical with those of an analytical sample obtained (33% yield) by preparative tlc from a separate experiment using crude (80–90% pure) **4**: $[\alpha]^{22}D$ $-29°$ ($CHCl_3$); ir (Nujol), 5.94, 8.27, 11.07, and 14.52 (SBz), 7.25, 8.39, and 8.49 μ (tosyl); nmr, τ 2.15–3.05 (m, 24, aryl H), 4.95–5.15 (m, 2, 1-H and 2-H), 5.7–5.9 (m, 2, 3-H and 4-H), 6.6–6.8 (m, 2, 5-H_2), 6.68 (s, 3, OCH_3), 7.82 (s, 3, tosyl CH_3).

Anal. Calcd for $C_{39}H_{36}O_7S_2$: C, 68.8; H, 5.53; S, 9.42. Found: C, 68.4; H, 5.52; S, 9.28.

Methyl 2,3-Thioanhydro-5-*O*-triphenylmethyl-β-D-ribofuranoside (7). I. From 5.—To a solution of 100 mg (0.147 mmol) of methyl 2-*S*-benzoyl-2-thio-3-*O*-tosyl-5-*O*-trityl-β-D-xylofuranoside (**5**) in 15 ml of *N*,*N*-dimethylformamide (dried by storing over alumina of Brockman activity I) was added 80 mg (0.56 mmol) of sodium benzoate. The mixture, under nitrogen, was heated at 110–115° for 8 hr and then was concentrated. The dry residue was partitioned with 25 ml of water and 25 ml of ethyl ether. The ether layer was washed with two 25-ml portions of bicarbonate solution and with 25 ml of water, dried, and concentrated. The residual oil, 80 mg (140% of theory, as **7**), showed no infrared absorption near 3.0 (OH) or 3.9 μ (SH) and little or no tosyl absorption near 7.25 μ; there was C=O absorption at 5.6 (weak, probably benzoic anhydride) and 5.8 μ (medium, probably *S*-benzoylepisulfonium salt). The nmr spectrum indicated that the latter band was not a sugar benzoate; though there were extraneous signals near τ 2.1 (indicative of benzoyl, *ca.* 30%), the nmr spectrum was otherwise identical with that of authentic episulfide[14] (see method II). Purification by tlc (as in II) afforded homogeneous gum, which was crystallized from hexane with seeding, mp 128–132°; the mixture melting point with authentic **7** was 128–133°.

II. From 6.—Methyl 3-*S*-benzoyl-3-thio-2-*O*-tosyl-5-*O*-trityl-β-D-arabinoside (**6**, 0.750 g, 1.10 mmol) and 0.50 g (3.5 mmol) of sodium benzoate in 50 ml of dimethylformamide was treated at 110–115°, as in I. Processing after 6 hr afforded 0.491 g (112%, as **7**). The presence of unreacted **6** was indicated by infrared absorption bands (medium) at 7.3, 8.4, and 8.5 μ (tosyl) and 5.95, 8.3 μ (*S*-benzoyl). There were no OH or SH bands, but there were C=O bands at 5.6 (weak) and 5.8 μ (medium), as in method I. The presence of both unreacted **6** (R_f 0.4) and episulfide **7** (R_f 0.6) was observed by tlc with 10% ether in benzene (trace contaminants were at R_f 0.01 and R_f 0.55). Integration of the nmr spectrum (diagnostic signals: OCH_3 and tosyl CH_3 due to unreacted **6**; 1-H and OCH_3 due to episulfide **7**) indicated the amounts present were 30 and 60%, respectively.

Further treatment with 0.40 g of sodium benzoate in 30 ml of *N*,*N*-dimethylformamide, as before, for 4 hr afforded 0.401 g (92%); 8–10% of unreacted **6** remained in the episulfide, according to the spectral measurements. Separation by preparative tlc (four plates, 20 × 20 cm; 2-mm thickness) with 10% ether in benzene and elution of the episulfide with chloroform afforded 0.270 g of homogeneous oil (61%); the nmr spectrum was identical with that of an authentic sample,[13] τ 2.4–2.9 (m, 15, aryl H), 5.07 (s, 1, 1-H), 5.72 (q, 1, 4-H, J = 5.5 Hz, J = 7.2 Hz), 6.5–6.9 (m, 4, H on C-2, C-3, C-5), 6.82 (s, 3, OCH_3). Crystallization from 10 ml of boiling hexane afforded 0.145 g (34%), mp 132–134°; mixture melting point with authentic **7** (lit.[13] mp 134–136.5°) was 132–134°, $[\alpha]^{22}D$ $-56°$ (lit.[13] $-55°$, $CHCl_3$).

Methyl 2,3-Anhydro-5-*O*-benzoyl-β-D-lyxofuranoside (8).—A solution of the epoxide **1** (2.4 g, 16 mmol) in 10 ml of dry pyridine was treated slowly, with chilling, with 2.5 ml of benzoyl chloride and then stirred overnight. Water (0.5 ml) was added; the mixture was stirred for 1 hr and was diluted with 40 ml of chloroform. The chloroform solution was washed with 50 ml of ice-cold 1 *M* hydrochloric acid, with two 50-ml portions of bicarbonate solution, and with water, dried, and concentrated to form 3.8 g (94%) of a residual oil: nmr, τ 1.8–2.1 (m, 2, *o*-H's of benzoyl), 2.35–2.80 (m, 3, *m*- and *p*-H's of benzoyl), 4.93 (s, 1, 1-H), 5.45 and 5.8 (5-H_2 as doublet plus singlet and 4-H as irregular quartet, AB_2 system, J_{AB} = 7 Hz), 6.26 (AB quartet resembling a triplet, 2, 2-H and 3-H, $J_{2,3}$ = 3 Hz), 6.48 (s, 3, OCH_3).

Methyl 5-*O*-Benzoyl-2-*S*-benzoyl-2-thio-β-D-xylofuranoside (10) and Methyl 5-*O*-Benzoyl-3-*S*-benzoyl-3-thio-β-D-arabinofuranoside (11).—Treatment of the epoxide **8** with pyridine–thiolbenzoic acid at 100–110° for 5 hr, as was done with **2**, afforded the crude mixture in quantitative yield as a red oil. Absence of **8** could be determined by the absence of its methoxyl singlet in the nmr spectrum. Peak heights of two new methoxyl singlets and integration of the two distinct 1-H signals indicated the ratio of **10** to **11** was about 3:4.

There was partial overlapping of the two products on preparative tlc in ether–benzene (3:7), but a portion of each could be separated. The *xylo* isomer **10** traveled slightly faster (R_f *ca.* 0.5) and was obtained as a gum: $[\alpha]^{22}D$ $+16°$ ($CHCl_3$); ir (film), 2.87 (OH), 5.79, 7.85, 14.05 (OBz), 5.97 8.26, 11.0, 14.53 μ (SBz); nmr, τ 4.93 (s, 1, 1-H), 6.52 (s, 3, OCH_3).

Anal. Calcd for $C_{20}H_{20}O_6S$: C, 61.8; H, 5.19; S, 8.26. Found: C, 61.0; H, 5.44; S, 9.11.

The *arabino* isomer **11** could be crystallized from methanol: mp 102–104.5°; $[\alpha]^{23}D$ $-62°$ ($CHCl_3$); ir (Nujol) 2.90 (OH), 5.79, 7.82, 13.98 (OBz), 5.99, 8.25, 11.1, 14.4 μ (SBz); nmr, τ 5.03–5.12 (rough triplet, 1, 1-H), 6.54 (s, 3, OCH_3).

Anal. Found: C, 62.0; H, 5.26; S, 8.41.

Methyl 2,3-Anhydro-5-*O*-*p*-nitrobenzoyl-α-D-lyxofuranoside (12).—Methyl 2,3-anhydro-α-D-lyxofuranoside[7] was treated with *p*-nitrobenzoyl chloride–pyridine, and the mixture was processed as described for **8**. The product crystallized from 95% ethanol: mp 126.5–127.5°; $[\alpha]D$ $+33°$ ($CHCl_3$); ir (Nujol), 5.78 (C=O), 6.52 (NO_2), 7.8 and 7.85 μ (C—O—C); nmr, τ 1.71 (s, 4, C_6H_4), 4.99 (s, 1, 1-H), 5.4 and 5.67 (5-H_2 as doublet plus singlet and 4-H as irregular quartet, AB_2 system, J_{AB} = 5 Hz), 6.17 and 6.29 (two doublets comprising an AB quartet, 2-H and 3-H, $J_{2,3}$ = 3 Hz), 6.53 (s, 3, OCH_3).

Anal. Calcd for $C_{13}H_{13}NO_7$: C, 52.9; H, 4.44; N, 4.74. Found: C, 53.2; H, 4.75; N, 4.81.

Methyl 2,3-Anhydro-5-*O*-*p*-nitrobenzoyl-β-D-lyxofuranoside (9) was recrystallized from hexane: mp 89–91°; nmr, τ 1.75 (s,

4, C_6H_4), 4.88 (s, 1, 1-H; on expanded scale, $J_{1,2}$ = 0.5 Hz), 5.4 and 5.75 (5-H_2 as doublet plus singlet and 4-H as quartet of doublets), 4.20 (AB quartet resembling a triplet, 2-H and 3-H, $J_{2,3}$ = 3.5 Hz), 6.48 (s, 3, OCH_3).

Anal. Found: C, 52.4; H, 4.48.

Registry No.—**2**, 17229-98-0; **3**, 17229-99-1; **4**, 17230-00-1; **5**, 17278-14-7; **6**, 17230-01-2; **8**, 17230-02-3; **9**, 17230-03-4; **10**, 17230-04-5; **11**, 17230-05-6; **12**, 17230-06-7.

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A Novel Furanoside Synthesis. Conversion of Methyl 6-Deoxy-6-nitro-α-D-glucopyranoside into Methyl 3-Deoxy-3-nitro-β-L-ribo- and -arabinofuranosides and Corresponding Amino Sugars[1]

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A novel way of synthesizing methyl 3-amino-3-deoxypentofuranosides is described. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-nitro-α-D-glucopyranoside (**1**) was prepared by an improved procedure and methanolized by catalysis with methyl *p*-toluenesulfonate to give crystalline methyl 6-deoxy-6-nitro-α-D-glucopyranoside (**2**). Periodic acid oxidation of **2** to dialdehyde **3** (not isolated), internal nitroalkane–aldehyde addition in the latter at pH 7.5 to a mixture of stereoisomeric methyl 5-aldo-3-deoxy-3-nitro-pentofuranosides (**4**, not isolated), and subsequent sodium borohydride reduction gave crystalline methyl 3-deoxy-3-nitro-β-L-ribofuranoside (**5**, major isomer) and methyl 3-deoxy-3-nitro-β-L-arabinofuranoside (**6**, minor isomer). The sequence constitutes a shortening of a sugar chain "from within," without chemical involvement of the glycosidic center. Catalytic hydrogenation and derivatization by standard procedures led, from **5**, to the corresponding amine hydrochloride (**7**), the amine **8**, and the acetamido derivative **9**. Acid hydrolysis of **7** gave known 3-amino-3-deoxy-L-ribose hydrochloride (**10**). A similar sequence performed with **6** gave the corresponding amino (**11**), isopropylidenamino (**12**), and acetamido (**13**) derivatives and finally, known 3-amino-3-deoxy-L-arabinose hydrochloride (**14**).

The nitromethane cyclization of "sugar dialdehydes," introduced 10 years ago[2] and often since employed for the synthesis of deoxynitro and thence aminodeoxy sugars,[3] is encumbered by a structural limitation inherent in the dialdehydes which are obtained by glycol cleavage of ordinary glycosides of both the pyranoid and the furanoid types. Ring closure by nitromethane addition leads to 3-deoxy-3-nitroaldopyranosides[2,3] (or, departing from ketosides, to 4-deoxy-4-nitroketopyranosides[4]), but nitro*furanosides* cannot be so prepared.[5] In fact, whereas some 3-amino-3-deoxyaldofuranosides have been synthesized *via* other routes,[6] no representative of an analogous group of nitro compounds is known. Interest in such 3-deoxy-3-nitroaldofuranosides appears warranted, however, and is derived mainly from two considerations. First, they would presumably be capable of reduction and thereby serve to complement existing ways of entry into the series of amino furanosides, of which some members, notably puromycin and 3′-aminoadenosine, have drawn considerable biochemical and medicinal attention. Secondly, certain further chemical properties expected to occur in 3-deoxy-3-nitroaldofuranosides should be worthy of examination. For example, one would predict these compounds to constitute yet another variety of that class of glycosides which undergo facile cleavage by alkali. It is known that 2-nitroethyl β-D-glucopyranoside[7] as well as methyl 6-deoxy-6-nitrohexopyranosides[8] suffer fission of their glycosidic bonds in alkaline medium, and with these structures the 3-deoxy-3-nitroaldofuranosides would have in common an activating nitro substituent in β position to one of the acetal oxygens.

For these and similar reasons a synthesis of nitro furanosides was sought, and it was found that methyl 6-deoxy-6-nitro-α-D-glucopyranoside may be converted into two methyl 3-deoxy-3-nitro-β-L-pentofuranosides in a simple operation based on the nitroalkane–aldehyde reaction.

Preparation of Methyl 6-Deoxy-6-nitro-α-D-glucopyranoside (**2**).—To prepare the required starting material, the 6-nitro glucoside **2**, two approaches were considered. We have recently reported[8] the methanolysis of 1,2-*O*-isopropylidene-6-deoxy-6-nitro-α-D-glucofuranose, a compound that can be synthesized without much trouble by the nitromethane method of Grosheintz and Fischer.[9] However, the methanolysis gives a syrupy, anomeric mixture of methyl 6-deoxy-6-nitro-D-glucopyranosides rather than the single ano-

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