sulfonyl-6-*O*-triphenylmethyl-α-D-glucofuranose (II) in 67% yield. Desulfonyloxylation and β-elimination of compound II with sodium methoxide affords crystalline 5-deoxy-1,2-*O*-isopropylidene-6-*O*-triphenylmethyl-α-D-*xylo*-hexofuran-5-enose (III) in 90% yield. A complete structure proof of compound III is described elsewhere.[7]

Hydrogenation of compound III, with palladium-on-carbon catalyst, produces pure, crystalline 5-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (5-deoxymonoacetone-D-glucose, IV) in 80% yield. This compound on hydrolysis of the isopropylidene group with Amberlite IR-120(H$^+$) resin produces 5-deoxy-D-*xylo*-hexose.

Experimental

Analytical Methods.—Purity of crystalline products was determined by thin layer chromatography on silica gel G-coated[8] glass plates, irrigated with (A) chloroform-acetone (1:1 v./v.) and (B) 1-butanol saturated with water. Plates were sprayed with 5% ethanolic sulfuric acid and charred at 110° until permanent spots were visible. A calibrated Fisher-Johns apparatus was used for melting point determinations. Evaporations were done at reduced pressure.

3-*O*-Acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose (I).—Acetylation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose in acetic anhydride and pyridine gave 3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose.[6] The acetyl derivative was dissolved in a 60% solution of aqueous acetic acid, allowed to stand for 5 hr. at 37°, and evaporated below 50° to a sirup which crystallized as a solid white mass of compound I. This was recrystallized from warm ethyl acetate, m.p. 126°, lit.[6] m.p. 125–126°.

3-*O*-Acetyl-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-6-*O*-triphenylmethyl-α-D-glucofuranose (II).—Compound I (180 g.) was dissolved in 900 ml. of dry pyridine to which was added 200 g. of trityl chloride (chlorotriphenylmethane). After 2 days at 25°, 400 ml. of pyridine was added and the solution was cooled to 5°. While the mixture was continuously stirred, 500 ml. of alcohol-free chloroform containing 350 g. of tosyl chloride (*p*-tolylsulfonyl chloride) was slowly added. After 3 days at 37°, the reaction mixture was cooled to 0° and 20 ml. of water was added to hydrolyze excess tosyl chloride. Within 0.5 hr., the solution was poured into a mixture of ice and water. The water layer was drawn off, extracted twice with chloroform, and the chloroform solution washed free of pyridine with several portions of chilled 15% aqueous acetic acid. Upon neutralization with a solution of sodium bicarbonate, the chloroform was washed free of salts and dried over anhydrous magnesium sulfate. After filtration and evaporation, a dark brown sirup was obtained; the yield was 450 g. which contained 300 g. of solids (compound II).

5-Deoxy-1,2-*O*-isopropylidene-6-*O*-triphenylmethyl-α-D-*xylo*-hexofuran-5-enose (III).—A 225-g. portion of this dark brown sirup, obtained above was dissolved in 1685 ml. of chloroform. While this solution was stirred continuously and externally cooled, 900 ml. of a methanol solution containing 12.5% of sodium methylate was added. After 2 hr., the reaction mixture was slowly warmed to 25° where it was held for 16 hr. Then 100 ml. of a saturated solution of potassium bicarbonate was added and the mixture evaporated to remove methanol. The residue was extracted four times with chloroform, the chloroform was washed with water, dried over anhydrous magnesium sulfate, and evaporated. The residue was crystallized from a mixture of benzene and petroleum ether (b.p. 40–60°) yielding 90 g. (90%), of III, m.p. 83°, $[\alpha]^{25}\mathrm{D}$ −15.4° (*c* 1.4, chloroform).

Anal. Calcd. for $C_{28}H_{28}O_5$ (444.50): C, 75.66; H, 6.34. Found: C, 75.4; H, 6.42.

5-Deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (IV).—Compound III (45 g.) was dissolved in 325 ml. of absolute ethanol to which was added 325 ml. of an ethanol slurry containing 20 g. of 5% palladium on carbon. This mixture was subjected to 600 p.s.i. of hydrogen pressure and stirred for 2 hr. at 60°. During this period, the pressure dropped about 400 p.s.i. The pressure was again adjusted to 600 p.s.i. and the hydrogenation continued at 60° for 18 hr. The mixture was filtered and evaporated to a sirup which was dissolved in a mixture of petroleum ether and water. Triphenylmethane was reclaimed from the ether phase. The water phase contained compound IV. This solution was evaporated to a colorless sirup which was crystallized from a mixture of benzene and petroleum ether yielding 16 g. of IV, m.p. 94°, $[\alpha]^{25}\mathrm{D}$ −10.0° (*c* 0.71, chloroform). The yield from compound I was 48%. The product migrated as a single component in irrigants A and B. An X-ray powder diffraction pattern of compound IV and an authentic sample[9] was identical.

Anal. Calcd. for $C_9H_{16}O_5$ (204.22): C, 52.94; H, 7.89. Found: C, 53.0; H, 7.98.

5-Deoxy-D-*xylo*-hexose.—Two grams of compound IV was dissolved in 50 ml. of water and stirred for 2.5 hr. at 60° with 8 g. of Amberlite IR-120(H$^+$) resin. The solution was filtered and concentrated to a colorless sirup, $[\alpha]^{25}\mathrm{D}$ +40° (*c* 1.7, in water). The sugar was converted to the known[10] crystalline 5-deoxy-D-*threo*-hexose phenylosazone, m.p. 151°.

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3-Deoxy-D-*glycero*-D-*ido*-octonic γ-Lactone

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Recently Richtmyer and Bodenheimer[2] described an octosaccharinic lactone isolated from the mother liquors of the sodium amalgam reduction of D-*erythro*-L-*talo*-octonic lactone, it being the first higher carbon saccharinic acid obtained from a sugar–alkali reaction.[3] The lactone[4] consumed 3 moles of sodium periodate in 15 min. and this value remained constant for 8 hr. Since Richards, *et al.*,[5] have shown that D-glucoisosaccharinic lactone is rapidly and completely degraded by periodate ion, the isosaccharinic acid structure is excluded for Richtmyer's lactone, 1. The decision between the metasaccharinic acid and the saccharinic acid structure was made by comparing the proton magnetic resonance spectra of 3-deoxy-D-*arabino*-hexonic γ-lactone[6a] (β-D-glucometasaccharin),[6b] 2-*C*-methyl-D-*ribo*-pentonic γ-lactone[7a] (α-D-glucosaccharin),[7b] and the octonic lactone in the region τ 8.0–

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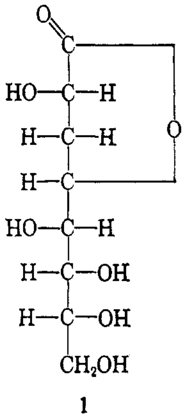
10.0. Both 3-deoxy-D-*arabino*-hexonic γ-lactone and 1 were devoid of resonance signal in this region while 2-*C*-methyl-D-*ribo*-pentonic γ-lactone showed the expected *C*-methyl signal as a singlet at τ 8.08. The lack of *C*-methyl signal in the p.m.r. spectrum of 1 eliminates the saccharinic acid structure and the metasaccharinic acid structure is established.

That 1 is a γ-lactone is indicated by its lack of mutarotation[2] and the presence of a band at 1765 cm.$^{-1}$ in the infrared.[8] The phenylhydrazide derivative of the octonic lactone is levorotatory and, by the phenylhydrazide rule,[9] the hydroxyl on C-2 is to the left in the Fischer projection formula. If one assumes the formation of the lactone *via* the Nef–Isbell mechanism,[6b,10] 1 is then 3-deoxy-D-*glycero*-D-*ido*-octonic γ-lactone.



1

It is interesting to note that Hudson's lactone rule[11] predicts the metasaccharinic acid structure as the only possibility for the octonic lactone. Its specific optical rotation was reported as +27° [2]; the γ-lactones of the two branched chain structures would both have negative optical rotations.

Experimental[12]

3-Deoxy-D-*glycero*-D-*ido*-octonic Phenylhydrazide.—A mixture of 3-deoxy-D-*glycero*-D-*ido*-octonic lactone (20 mg.), phenylhydrazine (25 mg.), and acetic acid (0.40 ml.) in water (1 ml.) was heated at 100° for 1 hr. The solution was cooled and concentrated *in vacuo* at 60° to an oil which crystallized upon addition of ethanol. The crystals (18 mg.) were collected, washed with ethanol, and dried. Two recrystallizations from methanol produced pure product, m.p. 153–154°, $[\alpha]^{20}D$ −8.8° (H_2O, *c* 1).

Anal. Calcd. for $C_{14}H_{22}O_7N_2$: C, 50.90; H, 6.71; N, 8.48. Found: C, 50.67; H, 6.68; N, 8.70.

Acknowledgment.—This work was done in the laboratories of Dr. H. E. Carter and was supported by Public Health Service grants.

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[12] Proton magnetic resonance spectra were taken in deuterium oxide on a Varian A-60 instrument by the spectroscopy laboratory, Department of Chemistry.

Nucleosides. V. The Monomesylates of 1-(2′-Deoxy-β-D-lyxofuranosyl)thymine[1,2]

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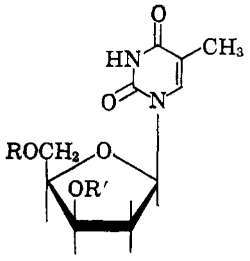
A recent study in this laboratory corrected the identity of 3′-*O*-mesyl- and 5′-*O*-mesylthymidine.[3] Efforts were then directed toward the synthesis of the corresponding mesylates of the 2′-deoxylyxosyl epimer (4) of thymidine. In fact, an unsuccessful attempt to prepare 1-(2′-deoxy-5′-*O*-mesyl-β-D-lyxofuranosyl)thymine (5) has since been recorded.[4] However, the simultaneous disclosure[4,5] of a practical route to 1-(2′-deoxy-β-D-lyxofuranosyl)thymine (4) by two laboratories provided an approach to the desired monomesyloxy derivatives.



1, R = $(C_6H_5)_3C$; R′ = H
2, R = $(C_6H_5)_3C$; R′ = CH_3SO_2
3, R = H; R′ = CH_3SO_2
4, R = R′ = H
5, R = CH_3SO_2; R′ = H

The mesylation of 1-(2′-deoxy-5′-*O*-trityl-β-D-lyxosyl)thymine (1), the direct precursor[4,5] of 4, afforded the sulfonate 2 in high yield. Detritylation of 2 with anhydrous hydrogen chloride in chloroform at −5° gave 1-(2′-deoxy-3′-*O*-mesyl-β-D-lyxofuranosyl)thymine (3) in 66% yield. Unimolar mesylation of 4 in a mixture of chloroform and pyridine at −5° produced a single[6] monomesylate (73% yield) with chromatographic (*cf.* Table I) and spectral (infrared) properties distinctly different from those of 3. Accordingly, it is concluded that selective esterification of the primary (C′-5) alcohol function in 4 was effected and structure 5 is assigned to the product.

The acquisition of 2 provided the opportunity of studying the replacement of the mesyloxy group by nucleophiles such as azide, iodide, and benzoate ions. These transformations are of interest in view of the fact that recent studies have emphasized the difficulty of promoting the displacement of secondary sulfonates

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[2] Presented, in part, before the Division of Medicinal Chemistry, 144th National Meeting, American Chemical Society, Los Angeles, Calif., April, 1963.

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[6] The same reaction conditions applied to thymidine produced a mixture of mesylates.