action mixture was left at room temperature overnight, most of the pyridine was removed under vacuum, and the residue was poured into ice–water. The oil which separated solidified after a short time. The crystals were dissolved in ethyl acetate and the solution was washed. The residue left after removal of the solvent was crystallized from ethanol to give pointed prisms, m.p. 130–133°. Two additional crystallizations raised the melting point to 134°: $[\alpha]^{21}D$ −40.0° (*c* 3.0, chloroform); infrared, 1725 (ester), 1670 (benzamide), 1625 cm.$^{-1}$ (C=N); n.m.r. 5.7 (one aldehydic hydrogen), 6.9–8.7 p.p.m. (15 aromatic hydrogens).

Anal. Calcd. for $C_{26}H_{24}N_2O_5$ (444): C, 70.27; H, 5.40; N, 6.30. Found: C, 70.23; H, 5.34; N, 6.17.

***N*-Benzyl-1-amino-1-deoxy-2,4-*O*-ethylidene-D-erythritol (XI).**—Crude 2,4-*O*-ethylidene-D-erythrose benzylamine Schiff base (20 g., 0.085 mole) was dissolved in 100 ml. of ethanol. The filtered solution was reduced in a Parr hydrogenation apparatus at room temperature with Raney nickel catalyst[26] at 55 p.s.i. When no more hydrogen was absorbed (*ca.* 24 hr.), the catalyst was filtered off, the filtrate was concentrated to dryness, and the solid residue was crystallized from ethanol (10 g., 43%). Alternate crystallizations from ether and from ethanol to constant melting point formed orthorhombic prisms, m.p. 111°, $[\alpha]^{25}D$ +23.0° (*c* 1.01, chloroform).

Anal. Calcd. for $C_{13}H_{19}NO_3$ (237): C, 65.82; H, 8.01; N, 5.90. Found: C, 65.93; H, 7.91; N, 5.83.

1-Amino-1-deoxy-2,4-*O*-ethylidene-D-erythritol (XII).—The crude 2,4-*O*-ethylidene-D-erythrose benzylamine Schiff base (VI) (23.5 g., 0.1 mole) was dissolved in 100 ml. of ethanol, filtered, and reduced with 1.5 g. of palladium-on-carbon catalyst[27] for 24 hr. as described above. The catalyst was removed by filtration and the filtrate was concentrated to dryness. The crystalline residue was recrystallized from 30 ml. of boiling dioxane to form orthorhombic prisms and pyramids. The crystals were collected by suction and washed with benzene, m.p. 140–142° (10.6 g., 72%, R_f paper 0.28), $[\alpha]^{26}D$ −62.6° (*c* 2.95, water).

Anal. Calcd. for $C_6H_{13}NO_3$ (147): C, 48.97; H, 8.84; N, 9.52. Found: C, 48.68; H, 8.85; N, 9.69.

Reduction of crude 2,4-*O*-ethylidene-D-erythrose phenylhydrazone (VII) (47.2 g., 0.2 mole, in 150 ml. of ethanol) with palladium on carbon (4.0 g.) as described above yielded the amine XII (13.5 g., 46%), m.p. 140°. Reduction of the hydrazone (23.6 g., 0.1 mole) with Raney nickel yielded the amine XII in 74% yield. Some reductions of 0.5 mole of the phenylhydrazone VII or of the Schiff base VI were performed in an autoclave at 80–85° with initial pressure of 1800 p.s.i., with 78% yield.

A solution of the secondary amine XI (12 g.) in ethanol (100 ml.) was catalytically hydrogenated with palladium on carbon. After working up as above, 6.4 g. (75%) of the primary amine XII was obtained.

1-Amino-1-deoxy-D-erythritol *p*-Toluenesulfonic Acid Salt.—A solution of 1-amino-1-deoxy-2,4-*O*-ethylidene-D-erythritol (2.94 g., 0.02 mole) and *p*-toluenesulfonic acid (5.7 g., 0.03 mole) in 100 ml. of water was refluxed for 1 hr. with a stream of air being sucked through the boiling solution. The cooled solution was concentrated under vacuum to a syrup, which was dissolved in boiling methanol, treated with Norit, and crystallized by the addition of ether to turbidity to give elongated prisms, m.p. 112° (5.1 g., 87%). Two recrystallizations from the same solvents yielded the salt of m.p. 112–113°, $[\alpha]^{23}D$ −63.2° (*c* 2.94, water), R_f (paper) 0.06.

Anal. Calcd. for $C_{11}H_{19}NO_6S$ (293): C, 45.05; H, 6.48; N, 4.77; S, 10.92. Found: C, 44.89; H, 6.40; N, 4.79; S, 10.61.

Acknowledgment.—We are greatly indebted to Dr. S. Pinhas of the Weizmann Institute of Science, Rehovoth, for the infrared and ultraviolet spectral analyses, and to Dr. Y. Shvo of the same institute for the n.m.r. analyses, both of whom are thanked too for enlightening discussions on the interpretation of the spectra. We also wish to express our thanks to Mr. J. Hoffmann of the Weizmann Institute for friendly cooperation in performing the high-pressure catalytic reductions.

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(27) 10% Palladio (catalyst on carbon), Industrie Engelhard, Roma.

Neighboring-Group Participation. The Preparation of Derivatives of D-Ribose and L-Lyxose from L-Arabinose[1]

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The selective tosylation of the 3-hydroxyl of methyl 2-O-benzoyl-β-L-arabinopyranoside (I) to give methyl 2-O-benzoyl-3-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (II) illustrates the preferential sulfonation of an equatorial hydroxyl over an axial hydroxyl. Treatment of the resulting *trans*-benzoyloxysulfonate II with sodium fluoride in N,N-dimethylformamide caused the displacement of the tosylate and gave methyl 2(3)-O-benzoyl-β-L-lyxopyranoside after hydrolysis of the intermediate ortho ester ion (XI). Similar treatment of methyl 2-O-benzoyl-3,4-di-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (III) gave methyl α-D-ribopyranoside derivatives (VII)—an inversion of both carbon atoms originally bearing tosyl groups by means of two successive ortho ester ion intermediates. An analogous series of reactions starting from D-arabinose gave derivatives of L-ribose.

The use of the N-acylate as a participating group in carbohydrates to effect the elimination of a secondary *trans* sulfonate ester and generate a *cis* amino alcohol system is well established.[3] In recent years it has been demonstrated that the O-acyl group can undergo similar reactions,[4,5] albeit not so readily as the N-acyl. There are examples of the failure of the O-acyl group to undergo participation,[6] so it is apparent that the mere occurrence of a sulfonate grouping in the *trans* relationship to an O-acyl group is not in itself sufficient to ensure a participation reaction. Two different reagents have been used successfully in this transformation—sodium benzoate in N,N-dimethylformamide (DMF)[4,5] and sodium fluoride in DMF.[4,7]

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(2) To whom inquiries should be addressed.

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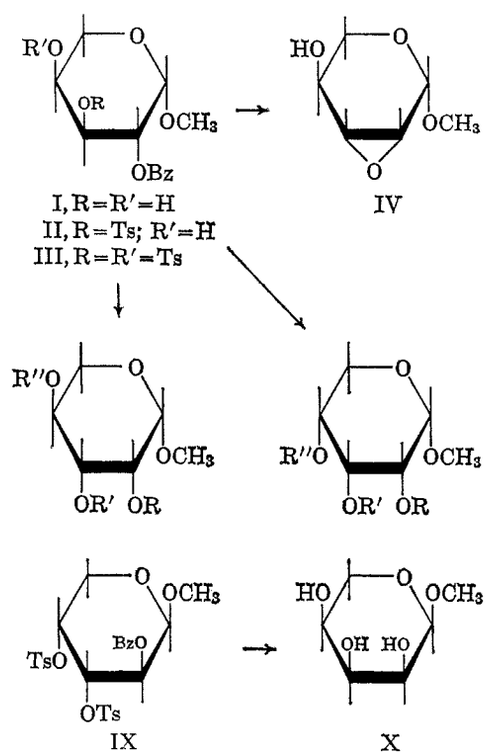
Reist, *et al.*,[5] in describing the synthesis of 9-(β-D-lyxofuranosyl)adenine, observed that the latter reagent appeared to give a significantly higher proportion of *cis* products from the intermediate ortho ester ion than did the sodium benzoate–DMF reagent. The further use of the sodium fluoride–DMF reagent as a potential means of preparing difficultly available sugars is described herein.

A recent communication from these laboratories[8] described the selective benzoylation of equatorial secondary hydroxyls in the presence of axial secondary hydroxyls in the preparation of methyl 2,3,6-tri-O-benzoyl-α-D-galactopyranoside. It might be expected that a similar selective esterification could be effected with methyl 2-O-benzoyl-β-L-arabinopyranoside (I) since the presence of the 2-O-benzoyl group on I should favor the 1C conformation in which the C-2 and C-3 functional groups are equatorial. This assumption was borne out in fact and a selective tosylation of I gave a 44% yield of methyl 2-O-benzoyl-3-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (II). That the sulfonate group of II was on C-3 rather than C-4 was



V, R, R′ = H, Bz; R″ = H
VI, R, R′, R″ = H

VII, R, R′, R″ = Bz, H, H
VIII, R, R′, R″ = H

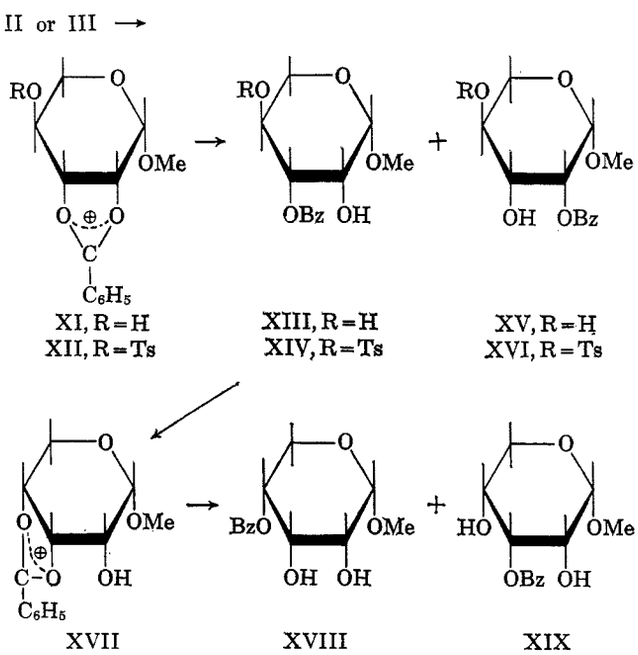
demonstrated by the facile conversion of II to an epoxide, presumably methyl 2,3-anhydro-β-L-lyxopyranoside (IV). The isomeric 4-O-tosylate could not form an epoxide and methyl 4-O-(*p*-tolylsulfonyl-β-L-arabinopyranoside would be the expected product from such treatment.

The reaction of II with sodium fluoride in DMF[4] gave a crude product which appeared to contain two components according to thin layer chromatography—probably methyl 2-O-benzoyl-β-L-lyxopyranoside and its 3-O-benzoyl isomer V. Deacylation of the crude mixture with methanolic sodium methoxide gave a 30% yield of crystalline methyl β-L-lyxopyranoside (VI). No detectable amounts of either methyl β-L-xylopyranoside or methyl β-L-arabinopyranoside, isomers which would be formed by the *trans* opening of the intermediate ortho ester ion, were observed—a finding in agreement with other participation reactions which involved a 3-O-sulfonate.[5]

At this time quantities of methyl 2-O-benzoyl-3,4-di-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (III)[9] were available. It seemed of interest to investigate the participation reaction of this compound using sodium fluoride in DMF. Displacement of both tosylates of III would give a D-ribose derivative, whereas the displacement of only the 3-tosylate would give a 4-tosylate of L-lyxose. The *trans* opening of the ortho ester ions would give derivatives of xylose, arabinose, and/or lyxose. Reaction of III with sodium fluoride in DMF gave product (VII) which contained no sulfonate absorption in the infrared; hence both tosylates had been displaced. Debenzoylation of VII with methanolic sodium methoxide gave a syrup which showed a trace amount of methyl β-L-lyxopyranoside along with the major component, presumably methyl α-D-ribopyranoside (VIII), according to thin layer chromatography. Hydrolysis of VIII with 1 *N* aqueous hydrochloric acid gave D-ribose along with a trace amount (<5%) of a contaminant which appeared to be lyxose, according to paper and thin layer chromatography.

A similar sequence of reactions was performed on methyl 2-O-benzoyl-3,4-di-O-(*p*-tolylsulfonyl)-β-D-arabinopyranoside (IX) to give L-ribose.

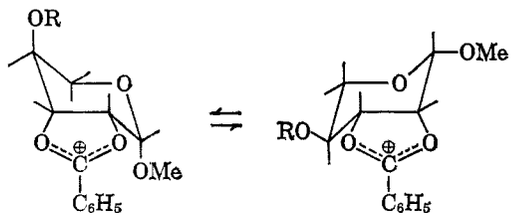
The complete elimination of both tosylates in the reaction of sodium fluoride in DMF with the ditosylate III is somewhat surprising from a mechanistic standpoint. The initial reaction undoubtedly involves the participation by the 2-O-benzoate of III to give the intermediate ortho ester ion XII. This ion might be expected to hydrolyze to give a mixture of the L-lyxoside benzoates XIV and XVI. The benzoate XIV would displace the remaining tosylate to give a second ortho ester ion XVII which would be hydrolyzed to a



(8) E. J. Reist, R. R. Spencer, D. F. Calkins, B. R. Baker, and L. Goodman, *J. Org. Chem.*, **30**, 2312 (1965).

(9) E. J. Reist, D. E. Gueffroy, and L. Goodman, *J. Am. Chem. Soc.*, **87**, 677 (1965).

mixture of the D-riboside benzoates, XVIII and XIX. Under the conditions of the reaction, the 2-O-benzoyl-4-O-(*p*-tolylsulfonyl)lyxoside (XVI) should be stable, and covalent tosylate should be observed in the product prior to the sodium methoxide treatment. The absence of covalent tosylate at this point indicates that the hydrolysis of the ortho ester ion XII gives only the 3-O-benzoate XIV. This behavior contrasts significantly with that of II in which the product prior to deacylation apparently contained both possible monobenzoates XIII and XV. It appears that the presence of the tosylate group on C-4 has a significant effect on the direction of collapse of the 2,3 ortho ester ion. This can be rationalized on a steric basis. Of the two possible conformations of XII, the C1 conformation



XIa, R = H
XIIa, R = Ts
XIb, R = H
XIIb, R = Ts

(XIIb) in which the 4-O-tosylate is equatorial is probably the favored one. Hydrolysis to a 3-O-benzoate permits the benzoate to assume an equatorial position as well, whereas hydrolysis of Xb to a 2-O-benzoate forces the benzoate to be axial.[10]

In the case of 4-hydroxy series (XIa and XIb) there is much less steric advantage in one conformer over the other and the ortho ester ion can hydrolyze either way to give an equatorial benzoate.

The formation of small amounts of methyl β-L-lyxopyranoside in the reaction of III with sodium fluoride probably occurs through the opening of ortho ester ion XVII in a *trans* manner by attack at C-4. It would be expected that any lyxoside arising from the 2-O-benzoate XVI would still bear the 4-O-tosyl group. Although a xylose derivative would also be expected through attack of this ion (XVII) at C-3, none was observed.

Experimental Section[11]

Methyl 2-O-Benzoyl-3-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (II).—A solution of 30 g. (0.112 moles) of methyl 2-O-benzoyl-β-L-arabinopyranoside[12] (I) in 180 ml. of dry pyridine was cooled to 0°, then 22.6 g. (0.118 moles) of *p*-toluenesulfonyl chloride in 120 ml. of pyridine was added in portions with stirring and continued cooling. After the addition was complete, the reaction was stored at 0° for 8 days, then was decomposed by the addition of 300 ml. of ice water. The aqueous suspension was extracted with three 100-ml. portions of ether. The ether extracts were washed with two 50-ml. portions of saturated aqueous sodium bicarbonate and three 50-ml. portions of water, dried, and evaporated to dryness *in vacuo*. The residue was triturated with two 300-ml. portions of cyclohexane and then 20 ml. of ether. The resulting crystalline product weighed 17.3 g. (37%) and had m.p. 112–115°.

The ether and cyclohexane solutions were combined and evaporated to dryness *in vacuo*. The residue was partitioned in 800 ml. of a system benzene–hexane–methanol–water (1:1:1:1). The organic phase was evaporated to dryness and the residue was triturated with a small amount of ether to give an additional 3.4 g. of product for a total yield of 20.7 g. (44%). Recrystallization from 2-propanol gave material with m.p. 114–16°.

The analytical sample from a previous reaction was recrystallized from methanol and had m.p. 111–113°; $[\alpha]^{20}D$ +219° (*c* 1, chloroform); λ_{max}^{Nujol} 2.85 (OH), 5.75 benzoate (C=O), 8.5 (SO_2) μ.

Anal. Calcd. for $C_{20}H_{22}O_8S$: C, 56.9; H, 5.25; S, 7.59. Found: C, 56.8; H, 5.17; S, 7.29.

Methyl 2,3-Anhydro-β-L-lyxopyranoside (IV).—A solution of 1.0 g. of methyl 2-O-benzoyl-3-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (II) in 40 ml. of methanol which contained 5 ml. of 1 *N* methanolic sodium methoxide was kept at room temperature for 18 hr., then was neutralized with IRC 50 (H) and evaporated to dryness *in vacuo*. The residue was partitioned between petroleum ether (b.p. 62–70°) and water. The aqueous fraction was evaporated to dryness and the residue was dissolved in 5 ml. of hot ethanol and filtered to remove some inorganic material. Addition of 10 ml. of ether caused more inorganic material to precipitate. After filtration, the filtrate was evaporated to dryness *in vacuo* to give 275 mg. (80%) of product as a semicrystalline solid.

Recrystallization from ethyl acetate–petroleum ether gave white needles, m.p. 70.0–70.5°.

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.3; H, 6.90. Found: C, 49.1; H, 6.87.

Methyl β-L-Lyxopyranoside (VI).—A mixture of 2.11 g. (5 mmoles) of methyl 2-O-benzoyl-3-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (II) and 2.1 g. (50 mmoles) of sodium fluoride in 200 ml. of DMF was heated at reflux for 2 days. The reaction was cooled to room temperature, then 3 ml. of water was added and the mixture was stirred for 4 hr. The DMF was evaporated to dryness *in vacuo* and the residue was partitioned between 30 ml. each of water and chloroform. The chloroform fraction was dried and evaporated to dryness *in vacuo*. The oily residue was triturated with 25 ml. of petroleum ether (b.p. 30–60°) to give 0.92 g. of an insoluble oil, presumably V: λ_{max}^{film} 2.90 (OH), 5.78 (benzoate C=O) μ. There was no sulfonate absorption at 8.5 μ. Thin layer chromatography using chloroform–ethyl acetate (1:1) as the developing agent showed two spots at R_f 0.37 and 0.28.

Methanolysis of V with 0.5 ml. of 1 *N* methanolic sodium methoxide in 7 ml. of methanol in the standard fashion gave 0.45 g. (55%) of crude methyl β-L-lyxopyranoside (VI) as an oil. Crystallization first from 2-propanol, then from ethyl acetate, gave 0.25 g. of crystals, m.p. 116.5–117.5°, $[\alpha]^{20}D$ +128° (*c* 0.974, 60% methanol).

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.9; H, 7.37. Found: C, 43.8; H, 7.15.

Methyl β-D-lyxopyranoside[13] has m.p. 118° and $[\alpha]^{20}D$ −128° (water).

Methyl 2-O-Benzoyl-3,4-di-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside[9] **(III).**—A soution of 19.0 g. (0.07 mole) of methyl 2-O-benzoyl-β-L-arabinopyranoside[12] (I) in 200 ml. of dry pyridine was treated with 54 g. (0.28 mole) of *p*-toluenesulfonyl chloride at room temperature for 5 days. The reaction was decomposed by pouring slowly with stirring into 500 ml. of saturated aqueous sodium bicarbonate solution. The aqueous suspension was extracted with two 50-ml. portions of chloroform. The chloroform layers were washed with water, then dried and evaporated to dryness to give a quantitative yield of crude product. Recrystallization from 1 l. of benzene–petroleum ether (b.p. 62–70°) gave 40.2 g. (98%) of product as white needles, m.p. 162–163°.

The analytical sample prepared from a previous reaction had m.p. 159–162°, $[\alpha]^{21}D$ +207° (*c* 0.997, chloroform).

(10) An alternative explanation for the displacement of both sulfonates of III to give a riboside is possible if an equilibrium is established between the ortho ester ion XII and the two monobenzoates XIV and XVI. The 3-benzoate XIV can react or return to XII. The 2-benzoate XVI can return only to XII but would be ultimately consumed by this route.

(11) Melting points were determined with the Fisher-Johns apparatus and are corrected. Rotations were determined with a Rudolph photoelectric polarimeter. Thin layer chromatograms were run on silica gel HF (E. Merck A.-G., Darmstadt). Spots were detected by spraying with sulfuric acid, then developing at *ca.* 100° for a few minutes. Vapor phase chromatograms were obtained in a Wilkens A-700 gas chromatograph using a 5-ft. column which contained 15% PDEAS on acid-washed Chromosorb W. The column temperature was 190°. Paper chromatograms were run by the descending technique on Whatman No. 1 paper using 65% aqueous 2-propanol–ethyl acetate (35:65) as the developing solvent unless otherwise specified. Spots were detected by means of an aniline citrate spray for reducing sugars. Organic solutions were dried over anhydrous magnesium sulfate.

(12) M. A. Oldham and J. Honeyman, *J. Chem. Soc.*, 986 (1946).

(13) O. Kjølberg and O. J. Tjeltveit, *Acta Chem. Scand.*, **17**, 1641 (1963).

Anal. Calcd. for $C_{27}H_{28}O_{10}S_2$: C, 56.3; H, 4.90; S, 11.2. Found: C, 56.5; H, 5.03; S, 11.0.

Methyl 2-O-benzoyl-3,4-di-O-(*p*-tolylsulfonyl)-β-D-arabinopyranoside (IX) prepared by the same procedure had m.p. 160–161.5°, $[\alpha]^{21}D$ −201° (*c* 0.981, chloroform).

Anal. Calcd. for $C_{27}H_{28}O_{10}S_2$: C, 56.3; H, 4.90; S, 11.2. Found: C, 56.2; H, 4.75; S, 11.2.

Methyl α-D-Ribopyranoside (VIII).—A solution of 2.88 g. (5 mmoles) of methyl 2-O-benzoyl-3,4-di-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (III) and 2.1 g. (50 mmoles) of sodium fluoride in 200 ml. of dry DMF was heated at reflux for 2 days. The reaction mixture was cooled to room temperature and then was stirred with 3 ml. of water for 4 hr. After evaporation to dryness *in vacuo*, the residue was partitioned between 40 ml. each of water and chloroform. The chloroform extract was evaporated to dryness *in vacuo* to give 1.9 g. of crude methyl 3(4)-O-benzoyl-α-D-ribopyranoside (VII) as a syrup which was free of sulfonate absorption at 8.5 and 12.3 μ in the infrared. Thin layer chromatography using chloroform–ethyl acetate (1:1) as the developing solvent showed two spots of equal intensities with R_f values of 0.34 and 0.28, probably the 3-O-benzoate and 4-O-benzoate (VII).

Treatment of crude VII with 0.5 ml. of 1 *N* methanolic sodium methoxide in 7 ml. of methanol at reflux for 1 hr. gave, after the usual work-up, 0.68 g. (83%) of methyl α-D-ribopyranoside (VIII) as a syrup: $[\alpha]D$ +86° (*c* 1, water). Vapor phase chromatography[11] of the trimethylsilyl ether[14] of VIII showed a single peak with a retention time of 1.0 min.

Thin layer chromatography using 1-propanol–ethyl acetate–water (3:2:1) as the eluent, showed one main spot at R_f 0.42 assignable to VIII along with a trace of methyl β-L-lyxopyranoside at R_f 0.49.

(14) R. Bentley, C. C. Sweeley, M. Makita, and W. W. Wells, *Biochem. Biophys. Res. Commun.*, **11**, 14 (1963).

Methyl α-D-ribopyranoside has $[\alpha]D$ +103° (water).[15]

A solution of 100 mg. of methyl α-D-ribopyranoside (VIII) in 3 ml. of water which contained 0.7 ml. of 1 *N* aqueous hydrochloric acid was heated at reflux for 1.5 hr. The solution was cooled, neutralized with IR 45 (OH),[16] then evaporated to dryness to give 80 mg. of crude D-ribose as a yellow syrup. Paper chromatography of the crude product showed D-ribose as the predominant component, with a trace of lyxose as the only contaminant.

The phenylosazone[17] of the above material had m.p. 163–165° and was identical in all respects with the phenylosazone of authentic D-ribose.

Methyl α-L-ribopyranoside (X) was prepared from methyl 2-O-benzoyl-3,4-di-O-(*p*-tolylsulfonyl)-β-D-arabinopyranoside (IX) by an identical series of reactions and had $[\alpha]D$ −83° (*c* 1, water). Hydrolysis of X in the manner described for D-ribose gave L-ribose as the predominant component contaminated with a trace of lyxose. The phenylosazone of L-ribose was identical spectrally with that of D-ribose and had m.p. 161–165°.

Acknowledgment.—The authors are indebted to Mr. O. P. Crews and his group for the preparation of quantities of certain of the intermediates and to Dr. Peter Lim and his staff for the infrared spectra, optical rotations, and paper chromatography. They also wish to thank Dr. Leon Goodman for his advice and encouragement throughout the course of this work.

(15) C. T. Bishop and F. P. Cooper, *Can. J. Chem.*, **41**, 2743 (1963).

(16) A weak base anion-exchange resin manufactured by the Rohm and Haas Company, Philadelphia, Pa.

(17) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 132.

A Novel Cyclization of 4-Acetyl-1-methoxy-1-cyclohexene to 4-Alkoxybicyclo[2.2.2]octan-2-ones[1]

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An acid-catalyzed cyclization of 4-acetyl-1-methoxy-1-cyclohexene (**1**) in aprotic solvents such as benzene or tetrahydrofuran gave 4-methoxybicyclo[2.2.2]octan-2-one (**2**) in over 90% yields, whereas the analogous cyclization of **1** in alcoholic solvents furnished 4-alkoxybicyclo[2.2.2]octan-2-ones (**2**–**11**). Reaction of a methanol solution of 4-acetyl-1-cyclohexanones (**17**, **19**, and **22**) with trimethyl orthoformate in the presence of hydrochloric acid furnished 4-methoxybicyclo[2.2.2]octan-2-ones (**2**, **21**, and **23**), respectively.

It was demonstrated in previous papers[1,2] that acid-catalyzed cyclizations of 1-methoxy-4-(1-methoxyvinyl)-4-methyl-1-cyclohexene and 1-methoxy-4-methyl-4-vinyl-1-cyclohexene furnished 1,3-dimethoxy-4-methylbicyclo[2.2.2]oct-2-ene and 5-methoxy-2-methylbicyclo[3.2.1]oct-2-ene, respectively. The present paper describes the novel cyclization[3] of 4-acetyl-1-methoxy-1-cyclohexene (**1**) leading to 4-alkoxybicyclo-[2.2.2]octan-2-ones (**2**–**11**).

Reaction of a tetrahydrofuran solution of 4-acetyl-1-methoxy-1-cyclohexene (**1**) with anhydrous ferric chloride or a benzene solution of **1** with anhydrous *p*-toluenesulfonic acid gave 4-methoxybicyclo[2.2.2]octan-2-one (**2**) in over 90% yields. The structure for **2** was established by the independent synthesis[4] of **2** from 1-methoxy-4-(1-methoxyvinyl)-1-cyclohexene (**12**)[5] utilizing the method already described[2] and by n.m.r. and infrared spectra. The n.m.r. spectrum confirmed the existence of a tertiary methoxyl group, τ 6.84, an isolated methylene group adjacent to a carbonyl group, τ 7.74, and a bridgehead hydrogen, τ 7.88. The infrared spectrum of **2** was also entirely consistent with the assigned structure. Bands for a methoxyl group were found at 2832 and 1112 cm.$^{-1}$, and that for a carbonyl group at 1729 cm.$^{-1}$.

When the cyclization of **1** was carried out in alcoholic solvents in the presence of hydrogen chloride or *p*-toluenesulfonic acid, alcohols were incorporated in the products and there were obtained 4-alkoxybicyclo-[2.2.2]octan-2-ones (**2**–**11**). Treatment of a propyl alcohol solution of **1** with hydrogen chloride gave 4-propoxybicyclo[2.2.2]octan-2-one (**4**), whereas an analogous reaction of a methanol solution of 4-acetyl-1-propoxy-1-cyclohexene (**13**), derived from 2-propoxy-1,3-butadiene and methyl vinyl ketone, furnished 4-

(1) Bridged Ring Compounds. IV. Paper III: K. Morita, M. Nishimura, and H. Hirose, *J. Org. Chem.*, **30**, 3011 (1965).

(2) (a) K. Morita, M. Nishimura, and Z. Suzuki, *ibid.*, **30**, 533 (1965); (b) K. Morita and Z. Suzuki, *Tetrahedron Letters*, **No. 6**, 263 (1964).

(3) The reaction is formally analogous to aldol condensation.

(4) K. Morita and Z. Suzuki, *J. Org. Chem.*, **31**, 233 (1966).

(5) I. N. Nazarov, G. P. Verkholetova, and L. D. Bergel'son, *Akad. Nauk SSSR, Otdl. Khim. Nauk*, 511 (1948); *Chem. Abstr.*, **43**, 2576*i* (1949).