optical rotation data. The authors are indebted to the late Dr. Samuel A. Fuqua for most of the n.m.r. interpretations, and are indebted to Mr. O. P. Crews and staff for large-scale preparation of intermediates.

[CONTRIBUTION FROM LIFE SCIENCES RESEARCH, STANFORD RESEARCH INSTITUTE, MENLO PARK, CALIF.]

Synthesis of Homoribose (5-Deoxy-D-allose) and Homoadenosine[1]

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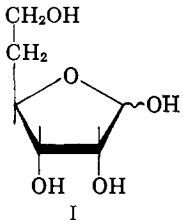
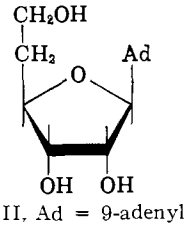
5-Deoxy-D-allose (XIV) has been synthesized by two independent routes. Hydroboration–oxidation of the olefin XXIV, obtained by pyrolysis of the 6-deoxy-D-allose xanthate (XXII), afforded a mixture of all three possible hydration products; gas chromatography separated the 5-deoxy-D-allose derivative XXI. The more practical synthesis was from a 5-deoxy-D-glucose derivative XV by configurational inversion at C-3 with sodium benzoate–dimethylformamide. A suitable derivative (XVII) of 5-deoxy-D-allose was coupled with chloromercuri-6-benzamidopurine and the initial blocked nucleoside deacylated to form 9-(5′-deoxy-β-D-allofuranosyl)adenine (II).

Reasons for interest in the synthesis of 5-deoxy-D-allose (I) and the 5′-deoxyalloside of adenine (II) as homologs of ribose and adenosine, respectively, were discussed in a previous paper[3] in this series. This



I

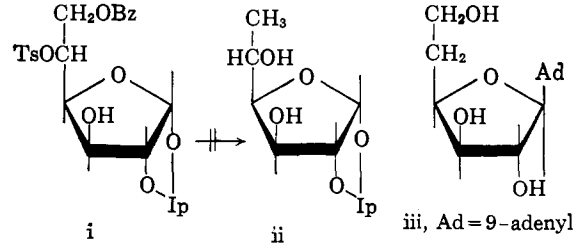


II, Ad = 9-adenyl

paper reports the synthesis of 5-deoxy-D-allose by two independent methods and its conversion to "homoadenosine" (II, 9-(5′-deoxy-β-D-allofuranosyl)adenine).

Of the two syntheses of I, the one (shown in Scheme I) practical in a preparative sense involved the conversion at C-3 of a 5-deoxy-D-glucose derivative (XV) by the method of configurational inversion with anchimeric assistance, recently reported[4] for converting 5-deoxy-D-xylose to 5-deoxy-D-ribose. The known olefin mesylate[5] III, obtained from glucose in several steps, was subjected to the general hydroboration–oxidation reaction,[6] using externally generated diborane as reagent. The product, as expected,[7] was the 3-mesylate acetonide VI of 5-deoxy-D-glucose. This material could be purified as the *p*-nitrobenzoate VII. The identity of VI was confirmed by saponification of the 3-mesylate to form the free acetonide VIII of 5-deoxy-D-glucose, a solid of known melting point,[7,8] and n.m.r. spectrum.[7] An authentic sample of VIII was obtained from 3,6-di-O-acetyl-5-deoxy-1,2-O-isopropylidene-5-thioacetyl-L-idofuranose[9] (A, Scheme II) by sponge nickel desulfurization and deacetylation of the resultant mixture of 5-deoxy- and 5,6-dideoxy-D-glucose[10] derivatives (B and C); finally, VIII was separated from the dideoxy sugar D by extraction and crystallization.[11] The samples of VIII were identical. Free 5-deoxy-D-glucose (IV) was obtained[7] from VIII and converted to the phenylosazone[7,13] V.

In continuation of the synthetic sequence, acid-catalyzed methanolysis of the mesylate VI afforded the methyl α,β-furanoside X. There is no question as to the ring size in X, since 5-deoxyhexoses cannot form pyranosides. Benzoylation of sirupy X afforded the dibenzoate α,β-XV, which required alumina chromatography to separate polymeric material that apparently originated by a "reversion" process[14] in the methanolysis step. Purified XV was heated for 6 hr. with sodium benzoate in boiling dimethylformamide, according to the general procedure.[15] Spectral evidence that the product was (largely) the monohydroxybenzoate XI is indicative[4] of participation of the neighboring 2-O-benzoate in the displacement of the 3-O-mesylate, through a bridged cation, as occurred[4] with an analo-



i ii iii, Ad = 9-adenyl

entirely VIII. This was disclosed from the n.m.r. spectrum and confirmed by nondepression of the mixture melting point with VIII. Consequently, the nucleosides reported in ref. 12 are derivatives of 5-deoxy-D-glucose (*e.g.*, iii) and not of 6-deoxy-L-idose.

(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. PH43-64-500. The opinions expressed in this paper are those of the authors and not necessarily those of the Cancer Chemotherapy National Service Center.

(2) To whom reprint requests should be sent.

(3) H. Arzoumanian, E. M. Acton, and L. Goodman, *J. Am. Chem. Soc.*, **86**, 74 (1964).

(4) K. J. Ryan, H. Arzoumanian, E. M. Acton, and L. Goodman, *ibid.*, **86**, 2497 (1964).

(5) J. K. N. Jones and J. L. Thompson, *Can. J. Chem.*, **35**, 955 (1957).

(6) (a) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962; (b) G. Zweifel and H. C. Brown, *Org. Reactions*, **13**, 1 (1963).

(7) Hydroboration of the (more difficulty obtained) 3-hydroxyl olefin III (Ms = H) afforded the acetonide VIII of 5-deoxy-D-glucose: M. L. Wolfrom, K. Matsuda, F. Komitsky, Jr., and T. E. Whiteley, *J. Org. Chem.*, **28**, 3551 (1963).

(8) E. J. Hedgeley, O. Meresz, W. G. Overend, and R. Rennie, *Chem. Ind.* (London), 938 (1960).

(9) T. J. Adley and L. N. Owen, *Proc. Chem. Soc.*, 418 (1961); we are indebted to Professor Owen for an authentic reference sample of A.

(10) The dideoxy sugar C is believed to have resulted from saponification of the thioacetate in A by base present in the nickel to form a mercaptide ion, expulsion of the 6-O-acetate with formation of a 5,6-episulfide, and subsequent desulfurization.

(11) Another source of VIII was revealed when it was found that in previous work from this laboratory (ref. 12) the sugar obtained from lithium aluminum hydride reduction of the 6-O-benzoyl-5-O-tosylate i was not the 6-deoxy-L-idofuranose ii as was supposed,[12] but rather surprisingly was

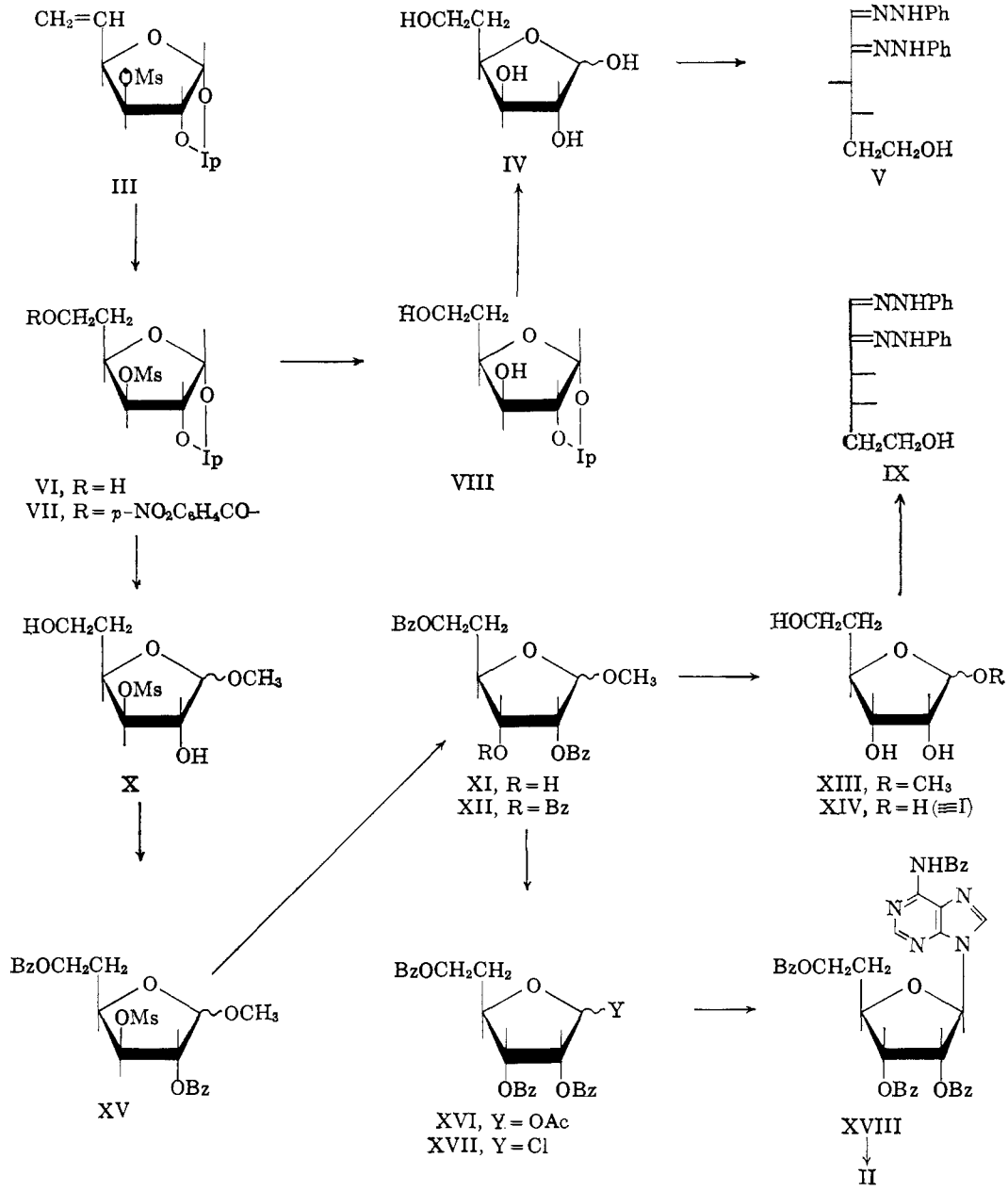
(12) E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, **23**, 1757 (1958).

(13) P. P. Regna, *J. Am. Chem. Soc.*, **69**, 246 (1947).

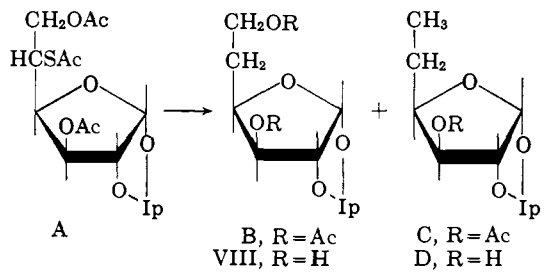
(14) W. Pigman, "The Carbohydrates," Academic Press, Inc., New York, N. Y., 1957, pp. 59–60, 486; *cf.* ref. 4.

(15) E. J. Reist, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **80**, 5775 (1958).

SCHEME I



SCHEME II



gous 5-deoxy-D-xylose derivative. That example was used to demonstrate the unambiguity of inversions at C-3 in such furanose derivatives. Free 5-deoxy-D-allose (XIV, = I) was obtained from XI upon saponification of the benzoate groups and hydrolysis of the resultant methyl furanoside XIII in 0.04 *M* hydrochloric acid. The sugar XIV was a hygroscopic sirup, but could be distinguished from 5-deoxy-D-glucose (IV) by zone electrophoresis with basic lead acetate[16] as electrolyte. Also, the phenylosazone IX of 5-deoxy-D allose was distinct in optical rotation from the osazone V of 5-deoxy-D-glucose, and the two exhibited mixture melting point depression.

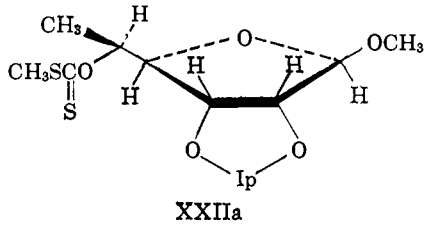
For use in the nucleoside synthesis, the inversion product XI was benzoylated to form the tribenzoate XII, a sirup. This was converted to an adenine nucleoside by the general sequence, previously used for nucleosides of related 6-deoxyhexoses.[15,17] The sirupy 1-O-acetate XVI was obtained by acetolysis of XII and afforded the chloro sugar XVII, also a sirup, on treatment with ethereal hydrogen chloride. Condensation of XVII with chloromercuri-6-benzamidopurine in refluxing xylene formed the crude tetrabenzoyl nucleoside XVIII as a sirup. Debenzoylation of XVIII in refluxing sodium methoxide afforded the crude homoadenosine II, isolated as the picrate. Regeneration with Dowex 2 resin (CO_3) converted the picrate to II in 9%

(16) J. L. Frahn and J. A. Mills, *Australian J. Chem.*, **12**, 65 (1959).

(17) E. J. Reist, L. Goodman, R. R. Spencer, and B. R. Baker, *J. Am. Chem. Soc.*, **80**, 3962 (1958).

yield[18] (based on XVI); a trace of adenine, disclosed by paper chromatography as the only impurity, was removed by water recrystallization. The sharp-melting homoadenosine II was characterized as a 5′-deoxynucleoside by the presence in the n.m.r. spectrum of a quartet centered at *ca.* 8.15 τ which was assigned to the methylene group at C-5′. A quartet of identical chemical shift was present in the related nucleoside[12] now found to be 9-(5′-deoxy-β-D-glucofuranosyl)adenine (iii, footnote 11).

In an independent synthesis (Scheme III), 5-deoxy-D-allose XIV was obtained from a 6-deoxy-D-allose derivative, the methyl 2,3-O-isopropylidenefuranoside XIX.[17,19] The 5-S-methylxanthate XXII of XIX was prepared and was pyrolyzed by the Chugaev procedure[20] to form the terminal olefin XXIV. Redistillation of the olefin XXIV removed sulfur-containing impurities along with some high-boiling residue, which had codistilled during the pyrolysis and gave rise to low optical rotation values. Dimethyl trithiocarbonate, originating in some xanthate preparations, was carried along with XXIV and could be removed only by preparative gas chromatography of XXIV or by prior alumina chromatography of XXII. The absence, in the allylic olefin XXIV, of any isomeric vinyl ether[3] XXV was apparent from the n.m.r. spectrum, upon noting the absence, in even crude XXIV, of any signal near 8.31 τ attributable to the C-6-methyl doublet of XXV. Comparison of infrared spectra provided supporting evidence for this conclusion most significantly in the absence, in the spectrum of XXIV, of the C=C stretching band at 5.87 μ characteristic of XXV. The vinyl ether XXV had been obtained[3,21] from a base-catalyzed elimination of the 6-deoxyallose 5-tosylate XXIII; deliberate treatment of XXIV verified previous indications[3] that XXIV was not isomerized to XXV under these conditions of elimination. The selectivity of the Chugaev reaction in favor of XXIV over XXV was unexpected in view of the rather general



XXIIa

experience in xanthate pyrolyses that mixtures of the possible olefins are formed.[20] Steric hindrance exists in the transition state required for the formation of XXV, due to eclipsing between the C-6 methyl and the C-3 hydrogen in the requisite *cis* orientation XXIIa; this factor may be sufficient to exclude the formation of XXV.

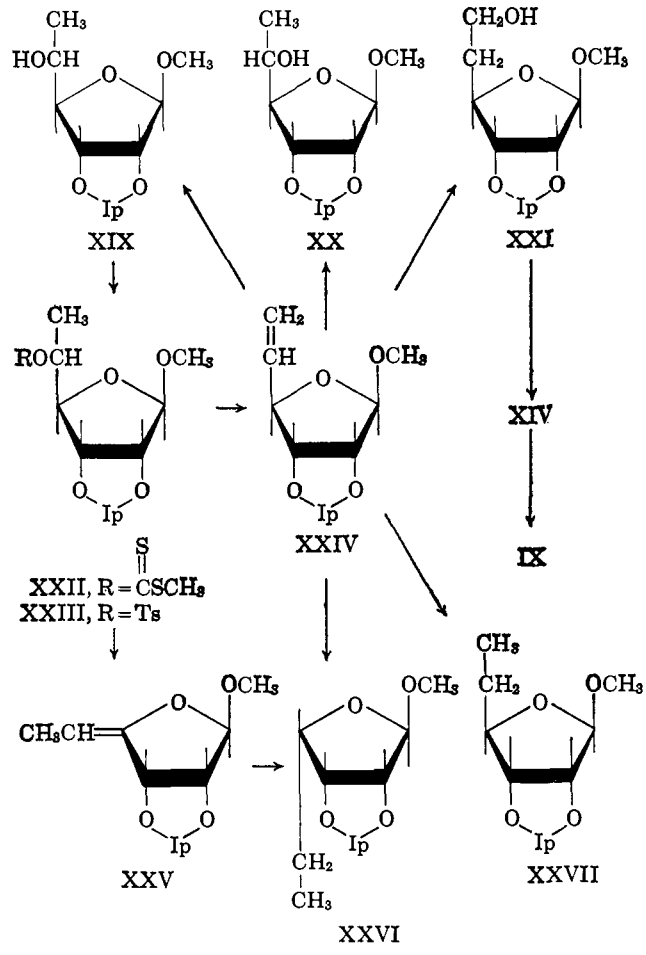
(18) Yields are often low in the coupling of 1-chlorohexoses with chloromercuripurines. The yield of 9-(5′-deoxy-β-D-glucofuranosyl)adenine (iii, footnote 11) was 15% (ref. 12); the yield of 9-β-D-glucofuranosyladenine was 24%; E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, **23**, 1958 (1958).

(19) P. A. Levene and J. Compton, *J. Biol. Chem.*, **116**, 169 (1936).

(20) H. R. Nace, *Org. Reactions*, **12**, 57 (1962).

(21) Use of 1,2-dimethoxyethane as solvent instead of *t*-butyl alcohol in the preparation of XXV afforded an improved sample, $[\alpha]^{25}D$ +65.9° (chloroform), free of traces of XIX; the material then, when stored at 5° under nitrogen for 2 months, did not undergo autoxidative polymerization, as did material previously purified from traces of XIX by alumina chromatography.[2]

SCHEME III



Partial isomerization of the allyl ether XXIV to the vinyl ether XXV apparently did occur under hydrogenation conditions using palladium–charcoal catalyst. Gas chromatography of the hydrogenation product of XXIV unexpectedly disclosed the presence, in approximately equal amounts, of two components; the retention times were identical to those of methyl 5,6-dideoxy-2,3-O-isopropylidene-β-D-gulofuranoside (XXVI) and an unidentified accompanying isomer obtained previously[3] upon hydrogenation of XXV. The two hydrogenation products from XXIV were collected separately from the gas chromatograph. The first component was identical with XXVI in both infrared and n.m.r. spectra. The second component was identical in infrared spectrum with the previously obtained isomer of XXVI; comparison of n.m.r. spectra confirmed the reasonable assumption that it must be methyl 5,6-dideoxy-2,3-O-isopropylidene-β-D-allofuranoside (XXVII), epimeric with XXVI at C-4 and the only substance to have been expected from simple hydrogenation of XXIV. In XXVII the C-4 proton was split into a triplet by the $-CH_2-$ at C-5; the coupling with the *trans*-oriented proton on C-3 was <0.5 c.p.s. In XXVI, the C-4 proton is *cis* to the C-3 proton and the triplet formed by coupling with the C-5 protons was further split into a triplet of doublets, as was previously found.[3] The n.m.r. spectra were otherwise strikingly similar.

Hydroboration of the terminal olefin XXIV was expected to afford the 5-deoxy-D-allose derivative XXI as the single product, since predominant formation of primary alcohols from terminal olefins seemed to be a

general rule.[6] Such indeed was the case with III, and with the 3-hydroxyl compound[7] parent to III. Gas chromatographic analysis of the hydroboration product of XXIV, however, surprisingly revealed the presence of three components. Samples of these were collected from the gas chromatogram and identified as the three possible hydration products of XXIV, the 6-deoxy-D-allose (XIX, 25%), the 6-deoxy-L-talose (XX, 15%), and the desired 5-deoxy-D-allose derivative XXI (60%). The crystalline tosylate[17,19] XXIII of XIX and the crystalline 5-O-benzoate[15] of XX were identical with authentic samples. The n.m.r. spectra (as in the structure proof[7] of VIII) readily distinguished XXI, the only possible 5-deoxy sugar (C-5 methylene quartet centered at 8.20 τ) from the two 6-deoxy sugars XIX and XX (C-6 methyl doublets in each at 8.78 τ). The spectrum of XXI exhibited a triplet (C-6, $-CH_2O-$) centered at 6.25 τ; it showed no signal above 8.7 τ, and the spectra of XIX and XX were free of signals near 6.2 and 8.2 τ.

The hydroboration of XXIV was repeated with bis-(3-methyl-2-butyl)borane[22] in an attempt to increase the selectivity of the reaction, by increasing the steric requirements of the reagent, to favor formation of XXI exclusively. Gas chromatographic analysis then disclosed that the product still contained about 65% of the desired XXI but that the only other component was the 6-deoxy-L-taloside XX. That XX should be favored to the exclusion of XIX, when the yield of XXI was not appreciably increased, seems even more surprising.

From either hydroboration, isolation of the 5-deoxy-D-allofuranoside XXI was achieved by preparative gas chromatography. This pure substance upon heating in very dilute hydrochloric acid was converted to 5-deoxy-D-allose (XIV), identical with XIV from the configurational inversion route. The phenylosazones IX of XIV from both routes were, as expected, identical in melting point and showed no melting point depression on admixture.

Experimental[23]

5,6-Dideoxy-1,2-O-isopropylidene-3-O-methylsulfonyl-α-D-xylo-5-hexosene (III) was prepared[5] from 1,2-O-isopropylidene-3,5,6-tri-O-methylsulfonyl-α-D-glucofuranose[24] in refluxing acetone for 24 hr. instead of briefly at 100°.[5] The product III was negative to olefin tests with bromine in carbon tetrachloride and tetranitromethane in chloroform, and a C=C stretching band at 6.01 μ in the infrared was unexpectedly weak; however, it did decolorize potassium permanganate; n.m.r. data: τ 4.00 d (C_1–H), 4.0–4.8 m (CH_2=CH—), 5.02 d (C_3–H), 5.19 d (C_2–H), 6.96 (OMs), and 8.48 and 8.67 (Ip).

5-Deoxy-1,2-O-isopropylidene-3-O-mesyl-D-glucofuranose (VI).—Diborane, generated by adding dropwise a diglyme[25] solution (200 ml.) of 5.0 g. of sodium borohydride onto 36 g. of boron trifluoride etherate,[26] was bubbled into a solution of 19 g. of the mesyl olefin III in 200 ml. of tetrahydrofuran[25] while the temperature rose to 35–40°. Nitrogen was used as carrier gas and, after addition of diborane was complete, the tetrahydrofuran solution was stirred at room temperature for 1.5 hr. Water (70 ml.) was added with stirring, dropwise at first, then slowly, to hydrolyze excess diborane; considerable foaming ensued. Sodium hydroxide (17 g.) in 35 ml. of water was added, followed by 50 ml. of 30% aqueous hydrogen peroxide, which resulted in moderate evolution of heat. Finally, the mixture was stirred for 2 hr. at room temperature, and the tetrahydrofuran was removed *in vacuo*. The product was extracted with two 200-ml. portions of ether. The dried ether extracts were concentrated to form 15 g. (74%) of a residual sirup, $[\alpha]^{24}D$ −10.6° (chloroform). A strong mesyl band remained in the infrared at 8.48 μ, but a band at 12.8 μ characteristic of III was missing and hydroxyl absorption appeared at 2.8 μ. The multiplet due to the vinyl protons in III was missing from the n.m.r. spectrum.

The sirup was purified by conversion to the crystalline ***p*-nitrobenzoate VII** upon treatment in pyridine solution at 0° with *p*-nitrobenzoyl chloride. Solid VII was obtained from a chloroform extract of the reaction mixture, hydrolyzed after 4 hr. at room temperature. Recrystallization from 95% ethanol afforded a 63% yield, m.p. 122–123°, $[\alpha]^{25}D$ −3.0° (chloroform); n.m.r. data: τ 1.78 (Ar–H), 4.06 d (C_1–H), 4.99 d (C_3–H), 5.22 d (C_2–H), 5.47 m (C_4–H plus CH_2 at C-6), 6.87 (OCH_3), 7.82 q (CH_2 at C-5), 8.52 and 8.68 (Ip).

Anal. Calcd. for $C_{17}H_{21}NO_{10}S$: C, 47.3; H, 4.91; S, 7.43. Found: C, 47.3; H, 4.61; S, 7.76.

Pure VI was regenerated by treating 15.5 g. of VII in 500 ml. of methanol with 2.0 g. of sodium hydroxide in 500 ml. of water at room temperature and stirring the suspension until a nearly complete solution was attained (4 hr.). Methanol was removed *in vacuo*, and the residual aqueous mixture was extracted with two 200-ml. portions of chloroform. The chloroform extracts were washed with water, dried, and concentrated *in vacuo* to form a residual oil (10.0 g., 98%), $[\alpha]^{24}D$ −2.1° (chloroform); n.m.r. data: τ 4.06 d (C_1–H), 5.02 d (C_3–H), 5.23 d (C_2–H), 5.55 triplet of doublets (C_4-H), 6.21 q (CH_2O at C-6), 6.89 (OMs), 7.33 t (OH), 8.07 q (CH_2 at C.5), 8.49 and 8.67 (Ip); c.p.s. $J_{1,2}$ = 4.0, $J_{2,3}$ < 0.5, $J_{3,4}$ = 3.0, $J_{4,5}$ = $J_{5,6}$ = *ca.* 6.2.

Anal. Calcd. for $C_{10}H_{18}O_7S$: C, 42.6; H, 6.42; S, 11.4. Found: C, 42.7; H, 6.50; S, 11.3.

Methyl 3-O-mesyl-5-deoxy-α,β-D-glucofuranoside (X) was obtained from VI in refluxing 2% methanolic hydrogen chloride by the procedure[4] for the analogous xyloside. The yield was 72% of a sirup, mol. wt. found 295 (theory 255).

Methyl 2,6-Di-O-benzoyl-5-deoxy-3-O-mesyl-α,β-D-glucofuranoside (XV).—To a stirred solution of 6.5 g. (0.024 mole) of X in 30 ml. of pyridine at 5° was added dropwise 13 g. (0.092 mole) of benzoyl chloride. After 16 hr. at room temperature, the stirred mixture was diluted with 100 ml. of benzene and washed with 200 ml. each of 1 *M* hydrochloric acid, saturated aqueous sodium bicarbonate, and water. The benzene layer was dried and evaporated *in vacuo*. The residual sirup, free of hydroxyl absorption at 2.8 μ, was applied in 5 ml. of benzene to a chromatographic column of neutral alumina[26] (16 × 1.75 in.) in benzene. No material was eluted by the addition of benzene and ether (450 ml. each) or of ether (200 ml.) containing methanol gradually increased in amount from 1 to 4%. Elution was continued with 4% methanol in ether. The next two (50-ml.) fractions contained 4.2 g. (42% from X) of product, obtained as a sirup after removal of solvent; mol. wt. found 478 (theory 464). Infrared benzoate absorption was at 5.80, 7.82, and 14.05 μ; both mesyl and some benzoate absorption was at 8.5 μ. When the n.m.r. spectrum was integrated, a slight deficiency in the methoxyl (6.58, 6.69 τ; α,β) and mesylate (6.78, 6.92 τ; α,β) signals relative to the benzoate (*ca.* τ 1.9 m, 2.5 m) signals suggested the material XIV may have been only 85% pure.

(22) Reference 6a, Chapter 13; ref. 6b, p. 9.

(23) Melting points were determined on a Fisher–Johns block and are corrected. Optical rotations were determined on 1% (except as noted with II) solutions in 1-dm. tubes with a Rudolph photoelectric polarimeter (instrument error at this concentration is ±1.2°). Molecular weights were determined on a Mechrolab vapor pressure osmometer. Magnesium sulfate was used to dry organic solutions. Infrared spectra were determined for all compounds described, as liquid films or in Nujol mull. Analytical and preparative gas–liquid partition chromatography (g.l.p.c.) was performed on a 1.5-m. aluminum column, $^3/_8$ in. diam., packed with 20% butanediol succinate supported on acid-washed, 80–100 mesh Chromosorb W in an Autoprep A-700 from Wilkens Instrument and Research, Inc., with an injection temperature of 210° and helium as carrier gas. The temperature was 200° and flow rate 200 ml./min. unless otherwise designated; retention times are abbreviated r.t.

Nuclear magnetic resonance spectra were determined with a Varian A-60 spectrometer, using chloroform-*d* solutions containing 1% tetramethylsilane as internal standard (except where dimethyl sulfoxide-d_6 was used with II). Signals reported are singlets unless otherwise designated as doublet (d), triplet (t), or quartet (q). Chemical shifts were measured from multiplet centers.

(24) W. P. Shyluk, J. Honeyman, and T. E. Timell, *Can. J. Chem.*, **33**, 1202 (1955).

(25) Diglyme, bis(2-methoxyethyl) ether (Matheson Coleman and Bell, practical grade), was used without further purification. Boron trifluoride etherate was always freshly distilled. Tetrahydrofuran was distilled from lithium aluminum hydride.

(26) BioRad Laboratories, Richmond, Calif., pH 6.9–7.1, 100–200 mesh, Brockmann Activity grade I.

Further addition to the alumina column of 4% methanol in ether (500 ml.) slowly eluted trimeric material (in amounts gradually decreasing from 200 to 50 mg. per 50-ml. fraction) as a fluffed glass (*ca.* 1.3 g.), mol. wt. found 1370 (theory 464).

Methyl 2(3),6-Di-O-benzoyl-5-deoxy-α,β-D-allofuranoside (XI).—A mixture of 4.2 g. (9.1 mmoles) of XV and 9.0 g. of sodium benzoate in 300 ml. of refluxing dimethylformamide was treated according to the general procedure.[15] The product was a brown oil, weighing 3.0 g. (86%, calcd. as the monohydroxy compound XI). Removal of the mesyl group was suggested in the infrared spectrum by nearly complete loss of a medium band at 7.3 μ and loss of most of a strong band at 8.5 μ (bands assigned to OMs in XV); the medium band remaining at 8.5 μ was attributed to benzoate. Other benzoate bands at 5.7, 7.8, and 14.05 μ remained; a single hydroxyl was suggested by a weak band at 2.85 μ.

Methyl 2,3,6-Tri-O-benzoyl-5-deoxy-α,β-D-allofuranoside (XII).—A stirred solution at 0° of 10.5 g. (0.0297 mole) of XI in 50 ml. of pyridine was treated dropwise with 7.0 ml. of benzoyl chloride. After 18 hr. at room temperature, the stirred mixture was treated with 3 ml. of water, and 30 min. later was poured into 150 ml. of benzene. The benzene solution was washed with 250 ml. each of 1 *M* hydrochloric acid, saturated aqueous sodium bicarbonate, and water, then was dried and concentrated *in vacuo*. The residual product weighed 12.0 g. (82%), $[\alpha]^{25}D$ +37.0° (chloroform), and was free of hydroxyl absorption *ca.* 2.8–3.0 μ in the infrared. Absence of any O-mesyl signals in the n.m.r. spectrum (*cf.* that of XV) confirmed that the precursor XI contained no uninverted XV.

1-O-Acetyl 2,3,6-tri-O-benzoyl-5-deoxy-D-allofuranoside (XVI) was obtained as a sirup, $[\alpha]^{25}D$ +13.4° (chloroform), in 97% yield from XII, by the method[15] for the analogous 6-deoxy-L-taloside. Acetate bands (medium) appeared at 7.28 and 8.13 μ in the infrared.

2,3,6-Tri-O-benzoyl-5-deoxy-D-allofuranosyl chloride (XVII) was likewise obtained as described[15] for the analogous 6-deoxy-L-taloside; the infrared spectrum showed loss of the acetate bands in XVI.

6-Benzamido-9-(2',3',6'-tri-O-benzoyl-5'-deoxy-β-D-allofuranosyl)purine (XVIII) was obtained in 78% yield (based on XVI) upon treating XVII with chloromercuri-6-benzamidopurine, using the procedure in ref. 15 and 17.

9-(5'-Deoxy-β-D-allofuranosyl)adenine (II) was obtained by debenzoylation[15,16] of XVIII and was isolated by precipitation of the picrate, which was regenerated with Dowex 2 (CO_3) as for the analogous 6-deoxy-L-taloside.[15] The product (12% yield from XVIII) was crystallized from water, R_{Ad} 0.92, 1.54, and 0.68 in paper chromatographic[27] solvent systems A, B, and C, respectively (a partial resolution from the D-*gluco* analog, compound iii in footnote 11, was achieved, R_{Ad} 1.00 and 1.45 in systems A and B). The only impurity disclosed, a trace of adenine, was removed by water–dimethyl sulfoxide recrystallization, m.p. 231.5–232.5°, $[\alpha]^{25}D$ −16.4° (*c* 0.4 in methanol), $\lambda_{max(m\mu)}^{pH\ 7.14}$ 260 (ε 15,400 in H_2O, 15,000 in 0.1 *N* NaOH), $\lambda_{max(m\mu)}^{pH\ 1}$ 257 (ε 14,600); n.m.r. data in dimethyl sulfoxide-d_6: τ 1.71 and 1.81 (purine C_2–H and C_8–H), 1.75 (NH_2), 4.03 d (sugar C_1'–H), 6.58 q (CH_2 at C-6'), 8.17 q (CH_2 at C-5').

Anal. Calcd. for $C_{11}H_{15}N_5O_4$: C, 47.0; H, 5.38; N, 24.9. Found: C, 46.7; H, 5.26; N, 25.0.

Methyl 6-Deoxy-2,3-O-isopropylidene-β-D-allofuranoside 5-S-methylxanthate (XXII) was prepared from XIX[17,19] by the procedure of O'Connor and Nace.[28] Upon addition of carbon disulfide to the sodium alcoholate, the sodium xanthate formed as a gel, which prevented stirring until the methyl iodide was added and the S-methyl xanthate formed with gradual dissipation of the gel. The crude xanthate was obtained as a reddish brown oil (110–120%) after concentrating the dried benzene extracts at 25–35° *in vacuo*. The presence of dimethyl trithiocarbonate in some preparations could be discerned in the infrared spectrum by bands at 7.03 (medium, CH_3) and 12.25 μ (strong, C–S[29]) where the xanthate exhibited little or no absorption; a strong band at 8.2 μ was characteristic of the xanthate moiety. The xanthate methyl gave rise to a singlet at 7.42 τ in the n.m.r. spectrum; dimethyl trithiocarbonate showed a singlet at 7.32 τ. The dimethyl trithiocarbonate and other highly colored impurities could be removed by alumina chromatography (120 g./3 g. of xanthate). The thiocarbonate containing only a little XXII was eluted with 170 ml. of benzene; 200 ml. more eluted the xanthate, $[\alpha]^{26}D$ −30.4° (chloroform). No impurity could then be detected in infrared or n.m.r. spectra: τ *ca.* 4.25 m (C_5–H), 5.00 (C_1–H), 5.28 d (C_2–H), 5.42 d (C_3–H), 5.76 q (C_4–H), 6.64 (OCH_3), 7.42 ($OCSSCH_3$), 8.57 d (CH_3 at C_6), 8.57 and 8.68 (Ip); c.p.s. $J_{3,4}$ *ca.* 1, $J_{4,5}$ *ca.* 8.6, $J_{5,6}$ 6.5.

Methyl 5,6-Dideoxy-2,3-O-isopropylidene-β-D-allofuranosid-5-ene (XXIV).—Crude xanthate VII (*ca.* 50 g.) was simultaneously pyrolyzed and distilled at 17 mm. with stirring in a 200-ml. flask to minimize bumping. A forerun (9.90 g., *ca.* 40% product by g.l.p.c., plus several sulfur-containing impurities) was collected at 160–180° (bath temp.). Pyrolysis occurred at 190–200° (bath temp.) to form (*ca.* 2 g./hr.) 14.7 g. of yellow product, 95–97% of purity by g.l.p.c., $[\alpha]D$ −47 to −50° (chloroform). The r.t., 1.8 min., was the same as for XXV. An additional 1.6 g. (56% total yield based on IV) of identical purity was obtained from the forerun by silica gel chromatography with benzene as eluent. Redistillation of the product at 17 mm., b.p. 104–105°, removed 22% of nonvolatile residue and afforded pale yellow olefin of greater than 99% purity by g.l.p.c., $[\alpha]^{24}D$ −56.3° (chloroform). A colorless sample obtained by preparative g.l.p.c., $[\alpha]^{24}D$ −57.9° (chloroform), was identical in n.m.r. and infrared spectra (product containing dimethyl trithiocarbonate carried through from preparation of XXII could be freed of this impurity only by preparative g.l.p.c.). Weak infrared bands at 3.23, 6.07, 7.01 μ, and medium ones at 10.1 and 10.75 μ tentatively were assigned to the terminal olefin; n.m.r. data: τ 4.0–5.0 m (CH_2=CH—), 5.03 (C_1–H), *ca.* 5.4 m (C_2–H plus C_3–H, singlet; C_4–H, m), 6.67 (OCH_3), 8.52 and 8.69 (Ip).

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 60.0; H, 8.05. Found: C, 60.2; H, 8.12.

Methyl 5-Deoxy-2,3-O-isopropylidene-β-D-allofuranoside (XXI).—(1) The olefin XXIV (4.37 g., 21.8 mmoles) was hydroborated as described in the preparation of VI. The product (2.50 g., 53% yield), $[\alpha]^{24}D$ −42.1° (chloroform), lacked the olefinic infrared bands cited for XXIV and showed strong –OH absorption at 2.9 μ. According to g.l.p.c., it consisted of three components: methyl 6-deoxy-2,3-O-isopropylidene-α-L-talofuranoside (XX, 15%, r.t. 3.25 min.), methyl 6-deoxy-2,3-O-isopropylidene-β-D-allofuranoside (XIX, 25%, r.t 3.75 min.), and the desired product XXI (60%, r.t. 9.50 min.). These materials were separated by preparative g.l.p.c. with temperature programming from 160–210°, and 1.00 g. (20%) of XXI was obtained. The infrared spectrum of XXI was distinguished from that of XIX only in the absence of bands at 9.78 and 10.28 μ; n.m.r. data: τ 5.06 (C_1–H), 5.40 (C-2 plus C-3 protons combined), 5.66 t (C_4–H), 6.25 t (CH_2O at C_6), 6.67 (OCH_3), *ca.* 7.01 (OH), 8.20 q (CH_2 at C-5), 8.53 and 8.69 (Ip).

(2) The olefin XXIV was hydroborated with bis(3-methyl-2-butyl)borane (disiamylborane) as described for some 3-methylcycloalkenes.[30] The oxidation step and isolation of alcohol were done as described for VI. The product (*ca.* 10% yield) consisted of 2 components according to g.l.p.c. analysis, XX (35%, r.t. 3.25 min.) and XXI (65%, r.t. 9.50 min.).

Methyl 6-deoxy-2,3-O-isopropylidene-β-D-allofuranoside (XIX) obtained from XXIV was identical in infrared and n.m.r.[3] spectra with an authentic sample (regenerated from the 5-O-tosylate with sodium in liquid ammonia[31] rather than with sodium amalgam[19]), and formed a 5-O-tosylate XXIII identical with authentic XXIII[17,19] by melting point comparison and nondepression on admixture.

Methyl 6-deoxy-2,3-O-isopropylidene-α-D-talofuranoside (XX) obtained from XXIV showed n.m.r. data: τ 5.03 (C_1–H), 5.22 d and 5.44 d (C_2–H and C_3–H), 6.57 (OCH_3), 8.52 and 8.68 (Ip), 8.78 d (CH_3 at C-6). It formed a benzoate identical with authentic 5-O-benzoate[15] by melting point comparison and nondepression on admixture.

Methyl 5-Deoxy-α,β-D-allofuranoside (XIII).—A solution of 8.5 g. of the inversion product XI and 129 mg. of sodium meth-

(27) Paper chromatography by the descending technique was done with Whatman No. 1 paper and the spots detected visually under ultraviolet light. Solvent systems were A, 1-butanol–acetic acid–water (5:2:3); B, 5% aqueous disodium hydrogen phosphate (R_f's same as for distilled water); C, water-saturated 1-butanol. Adenine was the standard of comparison, R_{Ad} = R_f compound/R_f adenine.

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(29) R. Mecke, R. Mecke, and A. Lüttringhaus, *Chem. Ber.*, **90**, 985 (1957).

(30) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **33**, 2550 (1961).

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oxide in 250 ml. of methanol was refluxed for 2 hr. and then concentrated to dryness. A solution of the residue in 50 ml. of water was neutralized with IR 120 resin (H), filtered, and washed with benzene. The water layer upon concentration afforded 2.9 g. (71%) of a residual sirup, free of benzoate bands at 5.7, 7.8, and 14.05 μ in the infrared.

5-Deoxy-D-allose (XIV). (1) **From XIII.**—A solution of 2 g. of XIII in 120 ml. of 0.04 *M* hydrochloric acid was heated at 95° for 2 hr., neutralized with Dowex 2 resin (CO_3), filtered, and concentrated *in vacuo*. Methanol was twice added to the resultant residue and removed *in vacuo*. The residual product (1.7 g., 92%) was a hygroscopic sirup, $[\alpha]^{23}D$ +19.4° (water). The electrophoretic[32] mobility, M_T, was 0.54, using basic lead acetate[16] as electrolyte. No contamination could be detected when 300 μg. of XIV was run; at the same time, it was shown that 10 μg. of 5-deoxy-D-glucose IV, M_T 0.00, could very easily have been detected.

Anal. Calcd. for $C_6H_{12}O_5 \cdot 0.5H_2O$: C, 41.6; H, 7.56. Found: C, 41.7; H, 7.07.

(2) **From XXI.**—A mixture of 0.25 g. of methyl 5-deoxy-2,3-O-isopropylidene-β-D-allofuranoside (XXI) and 10 ml. of 0.04 *M* hydrochloric acid was converted as in (1) to 80% of XIV, of identical zone electrophoretic mobility and purity.

5-Deoxy-D-allose phenylosazone (IX) was prepared from XIV as for the 6-deoxy[19] sugar, in 30 (XIV from XIII) and 58% (XIV from XXI) yields, and recrystallized from methanol–water and from benzene; m.p. 137–139°, $[\alpha]^{24}D$ +15.1° (methanol). The melting point was not depressed on admixture of samples of osazone (*i.e.*, IX from XIV obtained from XIII and from XXI), but admixture with 5-deoxy-D-glucose phenylosazone V (*vide infra*) produced m.p. 108–132°. A sample of IX for analysis was prepared by chromatography of 200 mg. on a column of silica gel (1.2 × 10.2 cm.) in chloroform. Elution with 500 ml. of chloroform removed some dark gum. The eluent (250 ml.) was then gradually changed to ethyl acetate. Finally, IX was eluted with 800 ml. of ethyl acetate, m.p. unchanged, $[\alpha]^{23}D$ +17.8° (methanol).

Anal. Calcd. for $C_{18}H_{22}N_4O_3 \cdot 0.5H_2O$: C, 61.5; H, 6.59; N, 15.9. Found: C, 61.9; H, 6.37; N, 16.2.

5-Deoxy-1,2-O-isopropylidene-D-glucofuranose (VIII). (1) **From VI.**—A solution of the 3-O-mesylate VI (2.0 g.) in 70 ml. of methanol mixed with 6.0 g. of potassium hydroxide in 60 ml. of water was refluxed overnight, neutralized with carbon dioxide, and concentrated to dryness *in vacuo*. Extraction of the residue with ether afforded 1.0 g. (68%), m.p. 88–90°, free of mesyl absorption at 8.48 μ in the infrared. The m.p. after recrystallization from carbon tetrachloride–petroleum ether was 90–91° (lit.[7,8] 94–96°, 89–90°), undepressed on admixture with a sample from (2).

(2) **From Compound A.**—An ethanol solution (200 ml.) of 3.30 g. of 3,6-di-O-acetyl-5-deoxy-1,2-O-isopropylidene-5-thioacetyl-L-idofuranose (A, Scheme II) containing *ca.* 70 g. of suspended sponge nickel catalyst[33] was refluxed for 1 hr. and filtered through Celite. The filtrate upon concentration *in vacuo* afforded 2.00 g. of an oil, presumably a mixture of B and C. Deacetylation occurred with 0.190 g. of sodium methoxide in 10 ml. of methanol solution at reflux for 2 hr. The methanol was removed *in vacuo*, and the residue was treated with water (15 ml.) and extracted with two 10-ml. portions of dichloromethane.

The dried organic layer was concentrated *in vacuo* to form a residual oil that crystallized on standing, m.p. 72–75°; recrystallization from carbon tetrachloride–hexane afforded 0.749 g. (57%), m.p. 73–75°, of 5,6-dideoxy-1,2-O-isopropylidene-D-glucose (D, lit.[34] m.p. 77–79°); n.m.r. data: τ 4.11 d (C_1–H), 5.49 d (C_2–H), *ca.* 5.9 m (C_3-H and C_4-H), 7.72 d (OH), 8.29 quintet (CH_2 at C-5), 8.50 and 8.69 (Ip), 8.99 (CH_3 at C-6).

The aqueous layer was neutralized to a pH of 7 with IRC 50 resin (H) and concentrated *in vacuo* to dryness; extraction of the residual solid with dichloromethane and concentration of the dichloromethane solution afforded a residual sirup which crystallized on standing. Recrystallization from carbon tetrachloride–hexane afforded 0.127 g. (9%) of VIII, m.p. 90–91°. The n.m.r. spectrum was the same as that recorded in ref. 7.

The mixture melting point between D and VIII was 65–68°. If dioxane was used as solvent in the desulfurization, the ratio of D to VIII was 1 to 1. The compounds could be distinguished in the infrared by two bands at 2.97 and 3.11 μ (OH) for VIII *vs.* one band at 2.92 μ (OH) for D; a band at 11.25 μ, strong in VIII, weak in D; absence in VIII of strong bands at 10.75 and 12.66 μ present in D.

5-Deoxy-D-glucose[7] (IV) was obtained from VIII by the procedure for XIV. Determined simultaneously with that of XIV, the M_R was 0.00, $[\alpha]^{23}D$ +16.6° (water; lit.[7] +38° at *c* 2, +24° footnote 1a in ref. 7).

5-Deoxy-D-glucose phenylosazone[7,13] (V) was obtained from IV and purified by the procedure for IX, m.p. 155–157° (lit.[7,13] m.p. 151°, 153°), $[\alpha]^{24}D$ −31.5° (methanol; lit.[13] −34.5°).

Hydrogenation of the 5,6-olefin XXIV as described[3] for the 4,5-olefin XXV, but for 5 hr., afforded 81% of an oil composed of two components (50:50), according to g.l.p.c., and identical with the isomers (90:8) obtained[3] from XXV, upon comparison of the samples.

As before,[3] the faster moving component, isolated by preparative g.l.p.c., was **methyl 5,6-dideoxy-2,3-O-isopropylidene-β-D-gulofuranoside (XXVI)**, identical in infrared and n.m.r. spectra.

The other substance was **methyl 5,6-dideoxy-2,3-O-isopropylidene-β-D-allofuranoside (XXVII)**, identical in infrared spectrum with the previously unidentified[3] isomer; n.m.r. data: τ 5.13 (C_1–H), 5.49 m (C_2–H plus C_3–H), 6.01 t (C_4–H), 6.72 (OCH_3), *ca.* 8.4 m (CH_2 at C-5), 8.57 and 8.70 (Ip), 9.2 m (CH_3 at C-6); c.p.s. $J_{1,2}$ = <0.5, $J_{2,3}$ = 6.2, $J_{3,4}$ = <0.5, $J_{4,5}$ = 7.5, $J_{5,6}$ = 6.8.

Anal. Calcd. for $C_{10}H_{18}O_4$: C, 59.4; H, 8.97. Found: C, 58.8; H, 8.72.

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(32) Zone electrophoresis was done with Schleicher and Schuell no. 2043A paper, and the sugars were detected with the potassium periodatocuprate reagent: T. G. Bonner, *Chem. Ind.* (London), 345 (1960). The mobility, M_T, was determined relative to ribose.

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