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

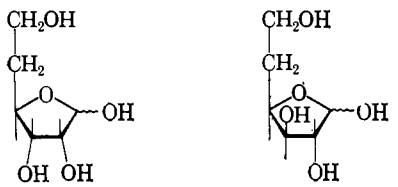
Configurational Inversion within a Furanoside Ring by Anchimerically Assisted Displacement: 5-Deoxy-D-ribose from 5-Deoxy-D-xylose[1]

BY KENNETH J. RYAN, HENRI ARZOUMANIAN, EDWARD M. ACTON,[2] AND LEON GOODMAN

RECEIVED JANUARY 10, 1964

Treatment with sodium benzoate in boiling dimethylformamide easily displaced the mesyl group in methyl 2-O-benzoyl-5-deoxy-3-O-mesyl-α,β-D-xylofuranoside (VIII) with inversion at C-3, forming a derivative of 5-deoxy-D-ribose as the only sugar detected in the product. The presence of 5-deoxy-D-ribose and absence of 5-deoxy-D-xylose and 5-deoxy-D-arabinose were determined from a gas chromatographic comparison of bis-O-(trimethylsilyl) derivatives of the methyl furanosides. Since methyl 2-O-benzyl-5-deoxy-3-O-mesyl-α-D-xylofuranoside (α-XXIV), an analog of VIII lacking a participating group, was found more resistant to this type of displacement, it is therefore concluded that the inversion observed with VIII occurs *via* participation of the neighboring benzoyl group. Furthermore, the more drastic conditions necessary for the conversion of α-XXIV to a derivative of 5-deoxy-D-ribose led to the formation of by-products, notably the 3,4-olefin XXVII.

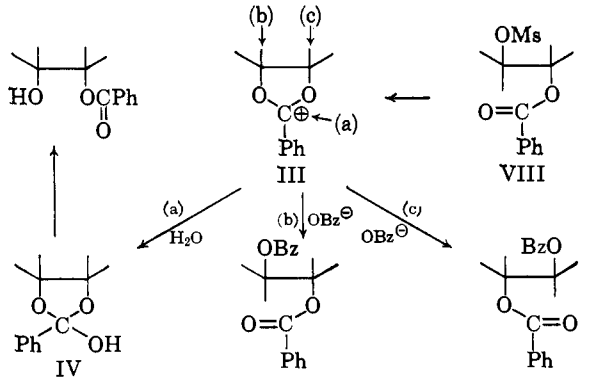
In a continuing series of studies[3] on the synthesis of 5-deoxy-D-allose (I), desired as a precursor for the preparation of "homoadenosine," a scheme was considered which involved the conversion of 5-deoxy-D-glucose (II) to I by inversion of the C-3 hydroxyl in an appropriate derivative of II. A considerable amount of work has been done on the nucleophilic displacements of secondary sugar sulfonate esters, but most of this has involved sulfonates in open-chain sugar derivatives or the exocyclic secondary sulfonates in ring sugars. In particular, in the case where the over-all result of the displacement is simple epimerization of a secondary sugar hydroxyl (*i.e.*, the sulfonate ester is displaced by an oxygen of the nucleophile), only one example is recorded where a secondary sulfonate ester in a sugar ring was involved. In this example,[4] the conversion of methyl 3-O-mesyl-2,5-di-O-methyl-α-L-rhamnofuranoside to methyl 3-O-benzoyl-6-deoxy-2,5-di-O-methyl-α-L-altrofuranoside with sodium benzoate in dimethylformamide (DMF) occurred with relative ease, in a reaction that would appear to be SN2 in character. The sodium benzoate–DMF reagent[5] has been widely exploited in such epimerizations. It is known that secondary sulfonates are much less readily displaced than primary, and that the presence of the sulfonate in a sugar ring increases the difficulty of displacement.[6] The fact that the sulfonate ester of 1,2:5,6-di-O-isopropylidene-3-O-tosyl-D-glucose was not displaced by[7] sodium benzoate–DMF, a displacement that is successful with hydrazine,[8] however, makes it clear that the successful transformation of II to I *via* sulfonate displacement could not be predicted from the work of the Birmingham group.[4] Furthermore, it seemed desirable to investigate facilitation of the displacement by a substituent capable of neighboring group participation, since recent studies in open-chain sugars[9,10] pointed out the ease of displacement of secondary sulfonate esters with anchimeric assistance using the sodium benzoate–DMF reagent. It was also important to clarify any doubts posed by the fact that attempts[11] (with a less favorable solvent) to utilize such neighboring group participation in solvolyses of ring sulfonates failed to convert a D-glucopyranoside or a D-altropyranoside to a D-allopyranoside.



I II

In the initial work on the conversion of II to I, a simple model system was sought which would minimize the blocking and deblocking problems necessary in such an investigation. This paper reports the facile displacement of a secondary ring sulfonate ester, assisted by a neighboring benzoate, in the model compound methyl 2-O-benzoyl-5-deoxy-3-O-mesyl-α,β-D-xylofuranoside (VIII); and it provides a procedure for the preparation of 5-deoxy-D-allose from II, which will be described in a separate paper.

In the model compound VIII, it was seen that inversion could occur either by neighboring group participation or by direct displacement at C-3, if that was easy.



III VIII IV

Direct SN2 displacement could afford a derivative only of 5-deoxy-D-ribose. Participation, through the inter-

(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 addressed.

(3) For the first paper in this series, see H. Arzoumanian, E. M. Acton, and L. Goodman, *J. Am. Chem. Soc.*, **86**, 74 (1964).

(4) A. B. Foster, J. Lehmann, and M. Stacey, *J. Chem. Soc.*, 4649 (1961).

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

(6) R. S. Tipson, *Advan. Carbohydrate Chem.*, **8**, 180, 212 (1953); J. M. Sugihara, *ibid.*, **8**, 26 (1953).

(7) E. J. Reist and R. Spencer, unpublished results from these laboratories.

(8) M. L. Wolfrom, J. Bernsmann, and D. Horton, *J. Org. Chem.*, **27**, 4505 (1962).

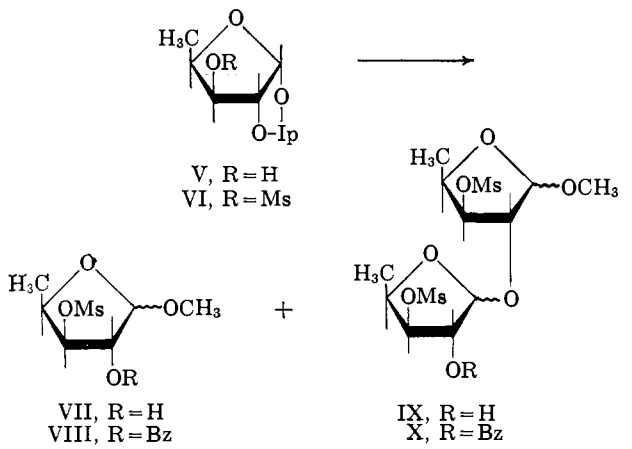
(9) B. R. Baker and A. H. Haines, *ibid.*, **28**, 438 (1963).

(10) M. A. Bukhari, A. B. Foster, J. Lehmann, M. H. Randall, and J. M. Webber, *J. Chem. Soc.*, 4167 (1963).

(11) R. W. Jeanloz and D. A. Jeanloz, *J. Am. Chem. Soc.*, **80**, 5692 (1958).

mediate acylonium ion III, could afford this and two additional possibilities, depending on how III subsequently reacts. Attachment of water, from moisture present during the reaction or from the work-up, to the benzoyl carbon (path a) and opening of the resultant ortho ester IV results in the *ribo* configuration. Attack on III at C-3 (path b) or C-2 (path c) by benzoate anion or other nucleophile present could give the *xylo* (*i.e.*, starting material) or the *arabino* configuration, respectively. These alternatives needed to be studied and, hopefully, paths b and c excluded before the inversion method could be applied to the glucose–allose transformation.

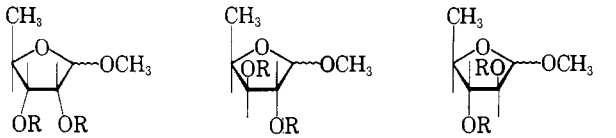
In the preparation of VIII, the known 5-deoxy-1,2-O-isopropylidene-D-xylofuranose[12,13] (V) was first converted to the 3-O-mesylate[14] VI. This material, analytically pure but noncrystalline in our hands, was converted to the α,β-methyl furanoside VII upon removal of the isopropylidene group in boiling 2% methanolic hydrogen chloride. The resultant sirup was benzoylated to form VIII, which was purified by chromatography on alumina. Benzene elution afforded analytically pure α,β-VIII in several fractions. The n.m.r. spectrum indicated the proportion of anomers was *ca.* 2α/β; this was verified by comparison with a sample of pure α-VIII, later obtained by another route (see Experimental).



Further elution of the original chromatogram with methanol unexpectedly afforded a fraction of nearly double the molecular weight of VIII, and in which the ratio of sulfonate to carbonyl absorption in the infrared was qualitatively higher than that in VIII. These facts, along with the elemental analyses, suggested structure X for this material. We suspect dimerization occurred in the methanolysis step by a process akin to that called "reversion,"[15,16] and that the resultant IX was benzoylated to form X along with VIII.

Treatment of α,β-VIII with sodium benzoate in refluxing dimethylformamide for 6 hr., the general procedure,[5,17] caused complete ejection of the mesyl group, as shown by n.m.r. and infrared spectra. Evidence from these spectra that the product existed largely as a monohydroxybenzoate suggested that it was formed by path a. Direct displacement or either of paths b and c should form, at least initially, a dibenzoate, and it was quite unlikely that very extensive saponification of a benzoate to a hydroxyl had taken place subsequently during the reaction. The product was investigated further after removal of protecting groups. Debenzoylation afforded a water-soluble methyl 5-deoxypentofuranoside which was potentially a mixture of the D-*ribo* (XI), D-*xylo* (XII), and D-*arabino* (XIII) compounds.

The most definitive evidence for the nature of the material came from a gas chromatographic study of the 2,3-bis-O-(trimethylsilyl) derivative. The trimethylsilyl derivatives[18] (XIV, XV, and XVI) of authentic samples of the methyl α,β-D-furanosides (XI, XII, and XIII) of 5-deoxy-D-ribose,[19] 5-deoxy-D-xylose, and 5-deoxy-D-arabinose, respectively, were prepared for comparison. Compounds XII and XIII were obtained by acidic methanolysis of the corresponding *xylo* and *arabino* 1,2-isopropylidene derivatives, and, as was the case with VII, molecular weight determinations indicated the presence of appreciable amounts of dimeric or trimeric material. This did not, however, interfere with the utility of the monomeric, volatile silyl derivatives as gas chromatographic standards.



XI, R = H
XIV, R = $Si(CH_3)_3$
XII, R = H
XV, R = $Si(CH_3)_3$
XIII, R = H
XVI, R = $Si(CH_3)_3$

It was found that for each α,β-sugar (XIV, XV, and XVI) the anomers were resolved, giving rise to two peaks as shown in Table I. Although α,β-XV and α,β-XVI (the undesired *xylo* and *arabino* sugars) were indistinguishable, the 5-deoxyriboside α,β-XIV was characterized by the chromatographic peak at 5.2 min. and by the absence of the peak at 3.9 min. If α,β-XIV was mixed with either α,β-XV or α,β-XVI, or with both, three symmetrical peaks were obtained of which the one at 4.5 min. was the strongest. A correlation between retention times and the appropriate anomers could be rationalized from the *cis–trans* relationship of the oxygen-linked substituents on C-1, C-2, and C-3. That is, since the α-deoxyriboside α-XIV is the only 1,2-*cis*-2,3-*cis* isomer, it was assigned to the unique peak at 5.2 min. There are two 1,2-*trans*-2,3-*trans* sugars, the β-xyloside β-XV and the α-arabinoside α-XVI, and these were assigned the peaks at 3.9 min. For each of the three sugars there is a *cis–trans* isomer, and these (β-XIV, α-XV, and β-XVI) were assigned the intermediate retention times of 4.5 min. These assignments could be verified for the *xylo* and *ribo* sugars. When the pure α-anomer of methyl 5-deoxy-D-xylofuranoside (α-XII) was prepared (*vide infra*), the corresponding silane α-XV did show a single gas chromatographic peak at 4.5 min. Furthermore, examination of the n.m.r. spectrum of the

(12) P. A. Levene and J. Compton, *J. Biol. Chem.*, **111**, 325 (1935).
(13) P. A. Levene and A. L. Raymond, *ibid.*, **102**, 317 (1933).
(14) H. Kuzuhara and S. Emoto, *Agr. Biol. Chem.* (Tokyo), **27**, 689 (1963).
(15) W. Pigman, "The Carbohydrates," Academic Press, Inc., New York, N. Y., 1957, pp. 59–60, 486.
(16) This was, apparently, largely or completely avoided in ref. 14 by preparing VII from VI by an acetolysis–mild methanolysis sequence.
(17) When α,β-VIII was heated in DMF for 6 hr. in the *absence* of sodium benzoate, the mixture darkened badly and there was spectral evidence for degradative side reactions; the presence of appreciable (10–30%) unreacted mesylate suggested that sodium benzoate functions not merely as an acid acceptor, but is essential to the displacement.
(18) C. C. Sweeley, R. Bentley, M. Makita, and W. W. Wells, *J. Am. Chem. Soc.*, **85**, 2497 (1963).
(19) C. H. Shunk, J. B. Lavigne, and K. Folkers, *ibid.*, **77**, 2210 (1955).

authentic methyl 5-deoxy-D-riboside[19] α,β-XI disclosed that the β-anomer was predominant (60–70%; 30–40% α-XI); if one makes the reasonable assumption that the anomeric distribution in XI was not disturbed by silylation to form α,β-XIV, this verifies the assignment of β-configuration to the predominent (70%) *ribo*-silane peak at 4.5 min. (and 30% α-XIV at 5.2 min.) in the gas chromatograph. Thus retention times were successfully shown to depend on the *cis–cis*, *cis–trans*, or *trans–trans* orientations of substituents on the ring oxygens; generalizations of this sort were apparently more difficult with some pyranosides recently studied.[18]

TABLE I

GAS CHROMATOGRAPHY OF BIS-O-(TRIMETHYLSILYL) DERIVATIVES[a]

Compound (parent sugar, methyl)	Retention times, min. (rel. peak areas, %)		
α,β-XIV[b] (α,β-D-ribofuranoside)		4.5 (70)	5.2 (30)
α,β-XV[b] (α,β-D-xylofuranoside)	3.9 (50)	4.5 (50)	
α-XV[b] (α-D-xylofuranoside)		4.5 (100)	
α,β-XVI[b] (α,β-D-arabinofuranoside)	3.9 (65)	4.5 (35)	
α,β-XIV[c] (α,β-D-ribofuranoside)		4.5 (55)	5.2 (45)
α-XIV + α-XV[d] (α-D-ribofuranoside + α-D-xylofuranoside)		4.5 (50)[e]	5.2 (50)[e]

[a] A 1.5-m. column, 3/8 in. diam., packed with 20% butanediol succinate supported on acid-washed, 80–100 mesh Chromosorb W, was used at 145° with helium as carrier gas, at 120 ml./min. in an Autoprep A-700, from Wilkens Instrument and Research, Inc. [b] From the authentic sugar. [c] From inversion of VIII. [d] From inversion of XXIV. [e] In another run under drastic conditions, the ratio of peaks at 4.5 and 5.2 min. was 10 to 90.

Attention was then shifted to identification of the methyl furanoside (potentially a mixture of α,β-XI, α,β-XII. and α,β-XIII) from the inversion of α,β-VIII. When converted to a bis-O-(trimethylsilyl) derivative, this sugar exhibited only gas chromatographic peaks identical with those from the authentic *ribo* derivative α,β-XIV; when the sample was mixed with authentic XIV, only the same two peaks were observed. Three peaks were observed when the sample was mixed with either authentic *xylo*-silane XV or *arabino*-silane XVI, with the peak at 4.5 min. increased in intensity just as in mixtures of XV or XVI with authentic XIV. From the absence of the peak at 3.9 min. in the silane from the inversion product, it was concluded that no xyloside or arabinoside was present. It was estimated that 5% or more of those sugars could have been detected. Any alternative conclusion requires the presence of 5-deoxyxylose as the α-anomer only, or of 5-deoxyarabinose as the β-anomer only, two highly remote possibilities. It will be noted in Table I that the anomeric composition of α,β-XIV from the inversion is essentially identical with the anomeric composition of the xyloside α,β-XV; both have apparently maintained the anomeric distribution which results from the methanolysis of a 1,2-O-isopropylidene xylofuranoside, and this indicates the anomeric distribution is not affected during the inversion or subsequent steps. The methyl furanoside from the inversion of VIII was finally converted to the free sugar and thence to an osazone identical with the osazone[19,20] from 5-deoxy-D-ribose. Depression of the melting point on admixture with an authentic sample of 5-deoxy-D-xylose phenylosazone[21] independently distinguished the sugar from 5-deoxy-D-xylose; furthermore, the two osazones had optical rotations of equal magnitudes and opposite signs.[22]

To distinguish better between the possibilities of direct displacement or of neighboring group participation in the inversion of VIII, a closely related model was sought in which the possibility of participation to form a 2,3-*cis* sugar would be excluded. The 2-O-benzyl ether XXIV was chosen for study, since the benzyloxy group in XXIV should approximate the steric requirements of the benzoyloxy group in VIII. It is reasonable to assume that the O-benzyl group in XXIV would not participate in the displacement of the O-mesyl; nonparticipation of neighboring O-methyl groups has been recorded with open-chain sugar derivatives[9,10] and in the cyclohexane series.[23] Furthermore, it seems unlikely that, upon replacing a benzoate with a benzyl ether, the electron density on C-3 would be changed so as to hinder SN2 displacement. From XXIV, then, with the possibility of participation excluded, only a D-*ribo* sugar could be formed, by direct displacement, and only derivatives of 5-deoxy-D-ribose or 5-deoxy-D-xylose (unreacted XXIV) would have to be sought in the product. The method of synthesis of XXIV made it possible to study this compound as a single anomer. Sirupy methyl 3,5-O-isopropylidene-α-D-xylofuranoside[24] (XVII) was obtained pure from the crystalline 2-O-benzoate[25,26] XVIII. Benzylation[27] of α-XVII gave the ether XIX that was deacetonated with 80% acetic acid.[24] The sirupy diol XX afforded a crystalline ditosylate XXI that was first reduced with lithium aluminum hydride to give the 5-deoxy sugar XXII, which, by saponification, yielded the crystalline hydroxy sugar XXIII. The desired mesylate XXIV, then, was obtained as an analytically pure oil.

The reaction of α-XXIV with sodium benzoate in dimethylformamide was markedly sluggish as compared with the similar reaction of α,β-VIII. A reaction period of 6 hr. as used for VIII caused displacement of only 5–10% of the 3-mesylate of XXIV. After 16 hr., roughly 60% of the mesylate was retained and the product formed was benzoate ester with a small amount of a hydroxy sugar. A reaction period of 40 hr. was required to remove a major part of the mesylate. The integrated n.m.r. spectrum of the product indicated that 18% of the mesylate (*i.e.*, XXIV) remained and that the major component of the mixture was a benzoate (XXV, 36%) along with 14% of a hydroxyl-containing sugar (possibly XXVI formed by the slow hydrolysis of XXV). A fourth component (about 32%) was assigned the olefinic structure XXVII by the presence of an infrared band at 5.95 μ (C=C) and a C-5 methyl multiplet in the n.m.r. spectrum at 8.20 τ; presumably the prolonged heating in dimethylformamide is responsible for the elimination reaction giving XXVII. In an apparently identical run, after 40 hr., less elimination unaccountably occurred and

(20) F. Micheel, *Ber.*, **63**, 347 (1930).

(21) P. A. J. Gorin, L. Hough, and J. K. N. Jones, *J. Chem. Soc.*, 2140 (1953).

(22) Since 5-deoxy-D-ribose and 5-deoxy-D-arabinose form the same phenylosazone, this derivative could not supply additional evidence about the presence or absence of deoxyarabinose in the inversion product.

(23) A. B. Foster, R. Harrison, J. Lehmann, and J. M. Webber, *J. Chem. Soc.*, 4471 (1963), footnote 10.

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

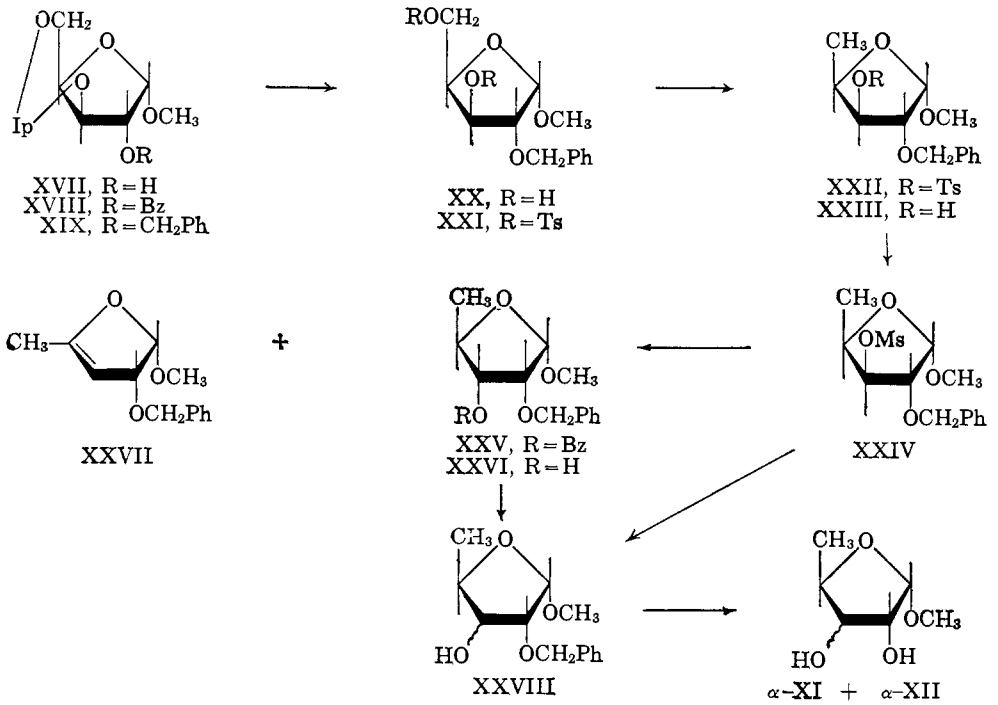
(25) E. E. Percival and R. Zobrist, *J. Chem. Soc.*, 4306 (1952).

(26) R. E. Schaub and M. J. Weiss, *J. Am. Chem. Soc.*, **80**, 4683 (1958).

(27) C. M. McCloskey, *Advan. Carbohydrate Chem.*, **12**, 142 (1957).

more mesylate survived to be inverted to XXV; nevertheless, the amount of mesylate XXIV unreacted and the hydroxyl sugar XXVI formed remained nearly the same. The predominant formation of benzoate XXV over hydroxy sugar XXVI, compared to the predominant formation of hydroxy sugar in the inversion product from VIII, is in accord with the occurrence of direct displacement in the former case and of participation in the latter.

In order to establish the nature of the sugars in the product from XXIV, lengthy treatment with a hot potassium hydroxide solution was used to remove benzoyl and mesyl esters. It was established that this treatment did not cause any significant change in the



olefin XXVII content. Alumina chromatography removed the olefin from the epimers XXVIII which were then catalytically debenzylated to the mixture of methyl 5-deoxypentofuranosides (α-XI plus α-XII). Gas chromatography of the 2,3-bis-O-(trimethylsilyl) derivatives (α-XIV plus α-XV; see Table I) showed two peaks. That at 5.2 min. was previously established as the characteristic peak (α-anomer) of the ribose derivative α,β-XIV and resulted from the inversion of XXIV. The peak at 4.5 min. was identical with that of an authentic sample of the α-anomer of methyl 5-deoxy-D-xylofuranoside as the silyl derivative α-XV and is indicative of unreacted XXIV.

Thus under the reaction conditions that serve to give complete reaction of VIII, only 5–10% of the 3-mesylate of XXIV was displaced. Since the product from VIII contained 88% of monohydroxymonobenzoate and 12% of 2,3-dibenzoate, it appears reasonable from the results with XXIV to suggest that the 12% of dibenzoate arises by the direct displacement while the 88% of hydroxybenzoate is the result of the neighboring benzoate displacement.

Application of this anchimerically-assisted configurational inversion for the preparation of L-ribose is actively under investigation.

Experimental[28]

5-Deoxy-1,2-O-isopropylidene-D-xylofuranose (V).—5-Deoxy-5-iodo-1,2-O-isopropylidene-α-D-xylofuranoside[12,13] in methanol solution was hydrogenated with platinum oxide catalyst as described[19] for a 5-deoxyribose derivative, but with excess triethylamine[30] as acid acceptor. Hydrogen consumption was complete overnight, and a 94% yield of triethylamine hydriodide was recovered. The residual product from ether solution (95% yield) crystallized on standing, m.p. 65–66° (lit.[12] m.p. 69–70°).

5-Deoxy-1,2-O-isopropylidene-3-O-mesyl-D-xylofuranose (VI) was obtained[13] as a light tan sirup (98%), which was not crystallized (lit.[14] m.p. 49–51°); it displayed strong sulfonate bands at 7.35 and 8.50 μ in the infrared. A sample prepared on a small scale and decolorized in solution with charcoal was analyzed. The negligible amount of chlorine indicated little if any of the corresponding alkyl chloride was present as by-product.

Anal. Calcd. for $C_9H_{16}O_6S$: C, 42.8; H, 6.39; S, 12.7. Found: C, 43.0; H, 6.40; S, 12.5; Cl, 0.14.

Methyl 5-Deoxy-3-O-mesyl-α,β-D-xylofuranoside (VII).—A solution of 10 g. of VI in 250 ml. of anhydrous 2% methanolic hydrogen chloride was refluxed for 24 hr. and then concentrated *in vacuo*. The residual sirup was dissolved in 50% aqueous methanol and the solution neutralized to pH 7 with an anion exchange resin (Dowex 2, CO_3^{-2}). The filtrate after removal of the resin was concentrated *in vacuo* to form a light brown sirup (7.03 g.,

(28) Melting points were determined on a Fisher-Johns block and are corrected. Optical rotations were determined on 1% solutions in 1-dm. tubes with a Rudolph photoelectric polarimeter; chloroform was the solvent unless otherwise noted. Molecular weights were determined on a Mechrolab vapor pressure osmometer. Magnesium sulfate was used to dry organic solutions. Infrared spectra were determined on all compounds described, as liquid films or in Nujol mull for solids (except for XXI, which could not be mulled and was cast from chloroform). Gas chromatograms other than those in Table I were performed under the same conditions, except at 200° and 200 ml./min.; 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. Signals reported are singlets, unless otherwise designated as doublets (d), triplets (t), or multiplets (m). Chemical shifts were measured from multiplet centers. Names of functional groups are abbreviated, *e.g.*, isopropylidene (Ip), benzoyl (Bz). For the D-ribose and D-xylose derivatives measured, α-anomers were characterized by C-1 proton doublets, and β-anomers by singlets.[29] Both types of signals were distinguished in the anomeric mixture α,β-XI.

(29) K. L. Rinehart, Jr., W. S. Chilton, and M. Hichens, *J. Am. Chem. Soc.*, **84**, 3216 (1962); L. D. Hall, *Chem. Ind.* (London), 950 (1963); L. Goldman and S. W. Marsico, *J. Med. Chem.*, **6**, 413 (1963).

(30) H. M. Kissman and B. R. Baker, *J. Am. Chem. Soc.*, **79**, 5534 (1957).

78% yield). A new infrared band appeared in the hydroxyl region at 2.87 μ.

Anal. Calcd. for $C_7H_{14}O_6S$: C, 37.2; H, 6.24; S, 14.2. Found: C, 36.8; H, 5.99; S, 13.9.

Methyl 2-O-Benzoyl-5-deoxy-3-O-mesyl-α,β-D-xylofuranoside (VIII).—A stirred solution of 6.84 g. (0.0302 mole) of VII in 110 ml. of dry pyridine at 0–5° was treated with 5.70 ml. (0.0485 mole) of benzoyl chloride. The mixture was stirred at 0–5° for 1 hr. and at 25° for 90 hr. to ensure complete reaction; 5 ml. of water was added and, after additional stirring for 30 min., 100 ml. of saturated aqueous sodium bicarbonate. The product was extracted with two 50-ml. portions of dichloromethane, and the extracts were washed with water and dried. Removal of solvent afforded a light brown sirup, which was free of hydroxyl absorption (2.8–3.1 μ) in the infrared. A chromatographic column (43 × 2.5 cm.) of neutral alumina[31] was treated with a benzene solution (4 ml.) of the sirup, and the column was eluted with benzene. The initial 3.2 l. (8 fractions) of eluate contained, after removal of solvent, 5.29 g. (53%) of product α,β-VIII, which partly crystallized on standing; in several runs, molecular weights for these fractions varied from 325 to 345 (330, theory), $[\alpha]^{25}D$ from +80 to +110°. If the chromatogram was repeated, 91% of this material could be recovered in the benzene eluate. Integration of the n.m.r. spectrum indicated the anomeric composition was $^2/_3$ α, $^1/_3$ β: τ 6.58 (β-OCH_3), 6.66 (α-OCH_3); 6.82 (OMs, β), 6.96 (OMs, α); 8.58 d (C-5 methyl, β), 8.64 (C-5 methyl, α).

Anal. Calcd. for $C_{14}H_{18}O_7S$: C, 50.9; H, 5.49; S, 9.71. Found: C, 50.6; H, 5.39; S, 9.40.

Further elution with 1.2 l. of benzene afforded 0.23 g. of similar material; 400 ml. of ether afforded 0.14 g. of sirup which was discarded. Finally, 400 ml. of methanol eluted 2.85 g. of dimeric material X, $[\alpha]D$ from +60 to +75°. The ratio of sulfonate (8.50 μ) to carbonyl (5.79 μ) absorption in the infrared was qualitatively higher than in the monomer VIII.

Anal. Calcd. for $C_{20}H_{28}O_{12}S_2$: C, 45.8; H, 5.38; S, 12.2. Found: C, 47.0; H, 5.52; S, 12.1.

Upon rechromatography in the system described, 74% of this material was recovered by elution with 5% methanol in ether; $[\alpha]^{25}D$ +104.4°, molecular weight 542 (524, theory for X).

Inversion of Methyl 2-O-Benzoyl-5-deoxy-3-O-mesyl-α,β-D-xylofuranoside (VIII).—In a typical experiment, 2.85 g. of sodium benzoate suspended in a dimethylformamide solution (100 ml.) containing 1.30 g. of α,β-VIII was treated by the procedure[5] for converting a 6-deoxyalloside to a taloside. Yields of 55–80% were obtained, the product (extracted with dichloromethane) calculated as a hydroxybenzoate (*i.e.*, as from path a). An n.m.r. spectrum showed that the mesylate was completely ejected (no signal at 6.8–7.0 τ) and, upon integration, that the product contained about 12% of dibenzoate and 88% of hydroxybenzoate: τ *ca.* 2.5 m (Bz), 6.55 and 6.61 (α- and β-OCH_3), 8.63 d and 8.70 d (C-5 methyl, α- and β-). Qualitative evidence for these facts was seen in the infrared spectrum: μ 2.85 (OH), 5.78 (C=O, OBz); loss of strong sulfonate absorption in VIII left only a shoulder at 7.3 μ and a medium band at 8.5 μ (OBz).

Methyl 5-Deoxy-α,β-D-ribofuranoside (XI).—The product from inversion of VIII (0.450 g., 1.78 mmoles calcd. as hydroxybenzoate) was dissolved in 25 ml. of absolute methanol containing 0.035 g. (0.64 mmole) of sodium methoxide and the solution was refluxed for 2 hr. The methanol was removed *in vacuo* and the residue was dissolved in 15 ml. of water. Methyl benzoate was removed by two extractions with 5-ml. portions of dichloromethane. Concentration of the aqueous layer to dryness afforded a brown residue, which was triturated with ethyl acetate. The ethyl acetate solution, upon concentration, afforded 0.147 g. (56%) of a yellow oil. Complete cleavage of benzoate esters was disclosed by absence of the characteristic infrared absorption band for benzoate at 14.0 μ, and by the increase in intensity of hydroxyl absorption at *ca.* 2.9 μ; bands at 5.75 and 8.1 μ in some runs were attributed to unremoved ethyl acetate solvent.

An authentic sample prepared by a known method[19] was very nearly identical in infrared spectrum. The molecular weight, 199 found, 148 theory, suggested the presence of $^2/_3$ monomer and $^1/_3$ dimer analogous to IX (Ms = H). Apparently because the chemical shifts were not altered, the dimer was not detected in the n.m.r. spectrum; integration indicated 30–40% of α-XI and 60-70% of β-XI were present: τ 5.16 d (C-1 proton, α), 5.26 (C-1 proton, β), 5.70 (C-2 + C-3 protons); 6.58 (α-OCH_3); 6.68 (β-OCH_3); 8.68 d (C-5 methyl, β-), 8.72 d (C-5 methyl, α).

5-Deoxy-D-ribose Phenylosazone.—5-Deoxy-D-ribose was obtained from XI (from the inverse of VIII) in 1% sulfuric acid by the procedure for 5-deoxy-D-xylose.[12] The acid was neutralized with an anion exchange resin (IR 45, CO_3^{-2}) and the free sugar converted[20] to the phenylosazone (36% yield), m.p. 171–173° (lit. 173–174 and 172–174°,[20] 175–177°[19]), $[\alpha]^{24}D$ −58.9° (pyridine–ethanol, 2/1, after 3 min. in solution; lit. $[\alpha]^{23}D$ −63.2 and −65°,[20] −61°[19]). On admixture with the phenylosazone, m.p. 173–174° (15% yield; lit. m.p. 179–180°,[12] 174–175°[21]; lit. $[\alpha]D$ +66.6°,[12] +67°[21] with slow mutarotation to 0°), obtained from an authentic sample of 5-deoxy-D-xylose,[12] the mixture melting point was 150–160°.

Methyl 3,5-O-isopropylidene-α-D-xylofuranoside (XVII) was prepared, $[\alpha]^{25}D$ +17° (water), by a known procedure.[24] Gas chromatography revealed the presence of *ca.* 19% of 1,2:3,5-di-O-isopropylidene xylose (r.t. 4.4 min.) in α-XVII (r.t. 6.2 min.); some β-anomer of XVII (estd. 8%, r.t. 5.7 min.) was incompletely resolved from α-XVII.

Treatment with benzoyl chloride in pyridine afforded the crystalline **α-D-2-O-benzoate XVIII** in 45% yield after recrystallization from aqueous methanol; m.p. 86–87°, $[\alpha]^{24}D$ +125.8° (lit.[26] m.p. 92–93°, $[\alpha]^{25}D$ +127°. The infrared spectrum exhibited strong benzoate absorption bands at 5.81 and 13.95 μ and was free of hydroxyl absorptions at 2.85 μ; n.m.r. data: τ *ca.* 2.5 m (Bz), 6.62 (OCH_3), 8.37 (Ip; singlet, both methyls).

Pure α-XVII was regenerated by saponification of the benzoate (25 g.) with potassium hydroxide (188 g.) in 500 ml. of methanol and 100 ml. of water at reflux for 4 hr. The methanol was removed *in vacuo* and the residue diluted to 300 ml. with water. Two dichloromethane extracts (300-ml. portions) of the aqueous solution were combined, washed twice with water (200-ml. portions), and dried. Concentration of the filtrate *in vacuo* afforded 12 g. (71%) of a clear residual oil, $[\alpha]^{25}D$ +76.1° (water), +89.8° (chloroform) (lit., $[\alpha]^{24}D$ +42° in water,[32] $[\alpha]D$ +75° in chloroform[33]); infrared data: μ 2.85 strong (–OH), benzoate bands absent; n.m.r. data: τ 4.88 d (C-1 proton, α), 6.51 (α-OCH_3), 8.61 and 8.66 (Ip).

Methyl 2-O-Benzyl-3,5-O-isopropylidene-α-D-xylofuranoside (XIX).—A stirred mixture of 41 g. of α-XVII, 30 g. of powdered potassium hydroxide, and 250 ml. of benzyl chloride was heated at 90–100° for 6 hr. The cooled mixture was treated with 200 ml. of water. The organic layer was separated, diluted with 800 ml. of chloroform, washed with three 400-ml. portions of water, dried over magnesium sulfate, and filtered. The filtrate was concentrated *in vacuo* to remove chloroform and then (at 80° and 0.5 mm. for 6 hr.) to remove unreacted benzyl chloride. The yield of residual yellow oil was 54 g. (92%). The infrared spectrum was free of hydroxyl absorption at 2.8–2.9 μ and exhibited benzyl bands at 13.55 and 14.35 μ. Gas chromatography disclosed the presence of *ca.* 15–20% of dibenzyl ether (r.t. 5.6 min.) in XIX (r.t. 42 min.). This was also disclosed in the n.m.r. spectrum: τ 2.53 (Ph), 2.91 d (C-1 proton, α), 5.29 (OCH_2Ph), 5.41 (OCH_2Ph in dibenzyl ether), 6.54 (α-OCH_3), 8.66 and 8.68 (Ip).

Methyl 2-O-benzyl-α-D-xylofuranoside (XX) was obtained as an oil in 94% yield from α-XIX by the procedure for the 2-O-mesyl analog.[24] An infrared absorption band at 11.8 μ for the isopropylidene group in α-XIX was absent; bands at 13.55 and 14.32 μ (CH_2Ph) were still present; n.m.r. data: τ 2.72 (Ph), 5.27 d (C-1 proton, α), 5.42 (OCH_2Ph), 6.70 (α-OCH_3), no Ip bands *ca.* 8.67; some dibenzyl ether was detected, τ 5.53 (OCH_2Ph).

Methyl 2-O-Benzyl-3,5-di-O-tosyl-α-D-xylofuranoside (XXI).—A stirred solution at 5° of 34.0 g. (0.134 mole) in 340 ml. of pyridine was treated with a solution of 67.0 g. (0.351 mole) of *p*-toluenesulfonyl chloride dissolved in 150 ml. of pyridine. After being stirred at room temperature for 2 days, the mixture was treated with 3–5 ml. of water, stirred briefly, then poured into 1.5 l. of ice–water. The product only partly precipitated and was isolated by extraction with three 250-ml. portions of chloroform. The combined chloroform solutions were washed with 6 *M* hydrochloric acid (250 ml. required) until the washes were acidic, then with 150 ml. of saturated aqueous sodium bicarbonate, and 150 ml. of water. The organic layer, dried and concentrated *in vacuo*, afforded a solid residual product, m.p. 126–127°, which was recrystallized from methanol; 30.2 g. (46%), m.p. 131.5°–132.5°, $[\alpha]^{24}D$ +59.2°. The infrared spectrum (cast in $CHCl_3$)

(31) Brockman Activity grade I, pH 6.9–7.1, Bio-Rad Laboratories, Richmond, Calif.

(32) R. Kuhn and G. Baschang, *Ann.*, **628**, 193 (1959).

(33) J. M. Anderson and E. Percival, *J. Chem. Soc.*, 819 (1956).

exhibited a strong new band at 8.48 μ ($-SO_2O-$), increased intensity at 7.3 μ ($-SO_2O-$), and absence of hydroxyl absorption at 2.9 μ; n.m.r. data: τ 5.38 d (C-1 proton, α), 5.63 (OCH_2Ph), 6.70 (α-OCH_3), 7.57 and 7.61 (OTs, OTs).

Anal. Calcd. for $C_{27}H_{30}O_9S_2$: C, 57.6; H, 5.37; S, 11.4. Found: C, 57.5; H, 5.27; S, 11.3.

Methyl 2-O-Benzyl-5-deoxy-3-O-tosyl-α-D-xylofuranoside (XXII).—Forty grams (0.0712 mole) of XXI in 500 ml. of anhydrous tetrahydrofuran (distilled from calcium hydride) was reduced with 9 g. of lithium aluminum hydride powder during 1 hr. at reflux. Excess hydride was decomposed by treating the cooled mixture dropwise with moist (5–10% water) tetrahydrofuran. Water (600 ml.) was added, and then 200 g. of sodium potassium tartrate. The mixture was stirred for 10 min., allowed to stand for 1 hr., and the supernatant was decanted and extracted twice with chloroform (250-ml. portions). The undecanted solids were stirred with 500 ml. of chloroform and removed by filtration. The chloroform filtrate and extracts were combined, dried, and concentrated to form a crystalline residue (28 g., 100%), m.p. 99.5–100°, identical with that of an analytical sample, $[\alpha]^{24}D$ +73.2°, recrystallized from aqueous methanol; n.m.r. data: τ 5.18 d (C-1 proton, α), 5.51 (OCH_2Ph), 6.57 (α-OCH_3), 7.55 (OTs methyl), 8.73 d (C-5 methyl).

Anal. Calcd. for $C_{20}H_{14}O_6S$: C, 61.2; H, 6.17; S, 8.15. Found: C, 61.2; H, 6.51; S, 8.29.

Methyl 2-O-benzyl-5-deoxy-α-D-xylofuranoside (XXIII) was obtained by alkaline hydrolysis of XXII according to the procedure[12] for the 1,2-O-isopropylidene analog. The crystalline product as extracted with ether (Soxhlet, 17 hr.), 16 g. (95%), m.p. 87–88°, $[\alpha]^{24}D$ +108.1°, was identical with an analytical sample obtained by sublimation. The infrared spectrum exhibited a strong, sharp hydroxyl band at 2.91 μ and was free of any sulfonate absorption at 8.5 μ due to XXII; n.m.r. data: τ 2.70 (Ph), 5.26 d (C-1 proton, α), 5.40 (OCH_2Ph), 6.65 (α-OCH_3), 8.85 (C-5 methyl).

Methyl 2-O-Benzyl-5-deoxy-3-O-mesyl-α-D-xylofuranoside (XXIV).—A stirred solution of 12.5 g. (0.0524 mole) of XXIII in 125 ml. of pyridine was treated at 0–5° with 14.0 g. (0.133 mole) of mesyl chloride added in portions. After 1 hr. at 5°, the mixture was stirred for 18 hr. at room temperature. Water (3 ml.) was added and, after 10 min. stirring, the mixture was poured into 250 ml. of saturated aqueous sodium bicarbonate and ice. The product was extracted with two 200-ml. portions of chloroform, and the extracts were washed with water (200 ml.), dried, and concentrated *in vacuo*. The residual brown oil, $[\alpha]^{24}D$ +115.9°, weighed 15.0 g. (91%), was free of hydroxyl absorption at 2.8–3.0 μ in the infrared, and exhibited sulfonate bands at 7.35 and 8.5 μ; n.m.r. data: τ 2.69 (Ph), 5.25 d (C-1 proton, α), 5.39 (OCH_2Ph), 6.64 (α-OCH_3), 7.04 ($-OSO_2CH_3$), 8.73 d (C-5 methyl).

Anal. Calcd. for $C_{14}H_{20}O_6S$: C, 53.1; H, 6.37; S, 10.1. Found: C, 52.8; H, 6.44; S, 10.3.

Inversion of Methyl 2-O-Benzyl-5-deoxy-3-O-mesyl-α-D-xylofuranoside (XXIV).—The procedure as described for inversion of VIII, but with a reflux time of 40 hr., afforded 53% (calcd. as 3-O-benzoate) of a brown oil; infrared data: μ 2.85 (OH), 5.78 strong (C=O, Bz), 5.95 (C=C), 7.28 (partly $-OSO_2-$), 7.79 (OBz), 8.45 ($-OSO_2-$ plus OBz), 13.5 (CH_2Ph), 13.95 (OBz), 14.3 (CH_2Ph). Since the material was a mixture of several components, many of the n.m.r. signals were unresolved multiplets: τ *ca.* 1.9 m (OBz), *ca.* 2.55 m (OBz), *ca.* 2.7 m (Ph, benzyl), 5.42, 5.53 (2 CH_2Ph's), *ca.* 6.6 m ($-OCH_3$), 7.10 (OSO_2CH_3), 8.18 m (CH_3COO), *ca.* 8.7 m (C-5 methyl). The relative areas under these signals, obtained upon integration, were used to estimate amounts present of the various components.

Methyl 2-O-Benzyl-5-deoxy-α-D-ribofuranoside (XXVIII), Containing XXIII and XXVII.—A solution of 4 g. of the inversion product from XXIV in 100 ml. of methanol and 90 ml. of water containing 11 g. of potassium hydroxide was refluxed for 18 hr. The base was neutralized with a stream of carbon dioxide and the methanol was removed *in vacuo*. The residue was treated with 150 ml. of water and extracted with two 150-ml. portions of chloroform. The extracts, dried and concentrated *in vacuo*, afforded 1.8 g. (60%, calcd. as XXVIII) of residual product. The infrared spectrum was free of the benzoate and mesylate bands present in the inversion product from XXIV: μ 2.88 (OH), 6.00 (C=C), 13.6 and 14.3 (CH_2Ph). The n.m.r. spectrum was also free of benzoate and mesylate signals: τ 5.41, 5.47, 5.54 (OCH_2Ph, 3 kinds); 6.61, 6.67 (OCH_3, 2 kinds); 8.19 m (CH_3COO); 8.76 d, 8.83 d (C-5 methyl, 2 kinds).

A portion (1 g.) of the product in 3 ml. of benzene solution was added to a chromatographic column (32 × 2 cm.) of alumina and the column was washed with 125 ml. of benzene. The olefin XXVII was eluted with a second 125-ml. portion of benzene (110 mg. obtained) and with 400 ml. of benzene containing 2% ether (80 mg. obtained). The substance was identified from the infrared spectrum: μ 5.97 (C=C), 13.6 and 14.32 (CH_2Ph), no —OH *ca.* 2.9, no $=CH_2$ *ca.* 11.3; and from the n.m.r. spectrum: τ 2.70 (Ph), 4.82 d (C=CH), 5.17 m (C-1 proton), 5.51 (OCH_2-Ph), 6.58 (OCH_3), 8.17 t (CH_3COO). No other n.m.r. signals were detected.

The alumina column was further washed with 800 ml. of benzene–ether mixtures while the ether was gradually increased from 2 to 100%, and then washed with 100 ml. of ether mixed with from 1 to 4% methanol. No more material was obtained until 100 ml. of 5% methanol in ether was used and 580 mg. of XXVIII was obtained, a mixture of epimers. The infrared spectrum was free of the olefinic band at 5.97 μ: μ 2.86 strong (OH), 13.55 and 14.3 (CH_2Ph). The n.m.r. spectrum was free of the olefinic signals at 4.82 and 8.17 τ: τ *ca.* 2.7 m (Ph), 5.23 d (C-1 proton), *ca.* 5.4 d (OCH_2Ph, 2 kinds), *ca.* 4.65 d (OCH_3, 2 kinds), *ca.* 8.8 m (C-5 methyl).

Methyl 5-Deoxy-α-D-ribofuranoside (α-XI) Containing α-XII. Method A.—The epimeric mixture of 3-hydroxy-2-benzyl ether XXVIII (0.560 g., 2.35 mmoles) in 25 ml. of ethanol containing 0.2 g. of 10% palladium–carbon catalyst was hydrogenated at 1 atm. for 1 hr., when hydrogen consumption had ceased. The mixture was filtered through Celite to remove the catalyst, and the filtrate was evaporated *in vacuo*. The residual product weighed 0.210 g. (60%), and was free of benzyl absorption at 13.5 and 14.3 μ in the infrared.[34]

Methyl 5-deoxy-α-D-xylofuranoside (α-XII) was prepared by method A from the 2-benzyl ether α-XXIII. The product was obtained as a residual solid and was recrystallized from ethyl acetate–petroleum ether, affording 0.80 g. (54%), m.p. 83–85°, $[\alpha]^{24}D$ +149.1°. The infrared spectrum compared to that of α-XXIII suffered loss of strong benzyl absorption at 14.23 μ and marked decrease in intensity at 13.23 μ. Similarly, the n.m.r. spectrum lacked aromatic signals: τ 5.09 d (C-1 proton, α), 6.55 (α-OCH_3), 8.78 d (C-5 methyl).

Anal. Calcd. for $C_6H_{12}O_4$: C, 48.6; H, 8.16; O, 43.2. Found: C, 48.7; H, 7.95; O, 43.2.

Methyl 5-deoxy-α,β-D-xylofuranoside (α,β-XII) was prepared as a sirup (78% yield) from the acetonide V by the procedure used for VII, but with twice the volume of methanolic hydrogen chloride; molecular weight 265 (found), 148 (theory).

Methyl 5-deoxy-α,β-D-arabinofuranoside (α,β-XIII) was prepared as a sirup (69%) from methyl 5-deoxy-1,2-O-isopropylidene-D-arabinofuranoside[35] as described for XII; molecular weight 230 (found), 148 (theory) (preparation of solid α,β-XIII has been described from the mercaptal[36]); n.m.r. data: τ 6.60, 6.64 (OCH_3, 2 kinds); 8.61, 8.71 (C-5 methyl, 2 kinds).

Methyl 5-Deoxy-3-O-mesyl-α-D-xylofuranoside (α-VII).—Hydrogenolysis of the benzyl ether α-XXIV by method A for 2 days afforded 83% of a sirup, which exhibited hydroxyl absorption at 2.89 μ in the infrared, and only weak absorption in the benzyl region (*ca.* 13.5 and 14.25 μ).

Methyl 2-O-benzoyl-3-O-mesyl-5-deoxy-α-D-xylofuranoside (α-VIII) was obtained from α-VII by the procedure for α,β-VIII. After 18 hr., the product was obtained as a residual solid and recrystallized from aqueous methanol; (23% yield), m.p. 85–86°, $[\alpha]^{24}D$ +152.5°. The infrared spectrum closely resembled that α,β-VIII; n.m.r. data: τ 6.65 (α-OCH_3), 6.96 (OMs, α), 8.63 d (C-5 methyl, α).

Anal. Calcd. for $C_{14}H_{18}O_7S$: C, 50.9; H, 5.49; S, 9.71. Found: C, 51.2; H, 5.57; S, 9.78.

Acknowledgment.—The authors are indebted to Dr. Peter Lim for infrared interpretations, and to his staff for collecting the spectral, paper chromatographic, and

(34) The presence of weak benzyl bands remaining in one experiment suggested that debenzylation was not quite complete, apparently because the catalyst was poisoned by an impurity. This did not interfere with subsequent conversion of the diols α-XI and α-XII to bis-O-(trimethylsilyl) derivatives and their analysis by gas chromatography.

(35) A. K. Mitra and P. Karrer, *Helv. Chim. Acta*, **38**, 1 (1955); the 5-O-tosylacetonide as starting material was converted by the procedure of P. A. Levene and J. Compton, *J. Biol. Chem.*, **116**, 189 (1936), for the L-isomers.

(36) H. Zinner, K. Wessely, and H. Kristen, *Chem. Ber.*, **92**, 1618 (1959);

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.]

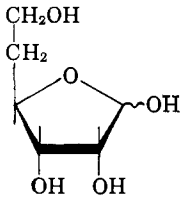
Synthesis of Homoribose (5-Deoxy-D-allose) and Homoadenosine[1]

BY KENNETH J. RYAN, HENRI ARZOUMANIAN, EDWARD M. ACTON,[2] AND LEON GOODMAN

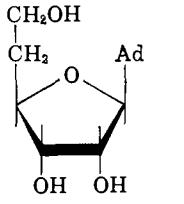
RECEIVED FEBRUARY 10, 1964

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

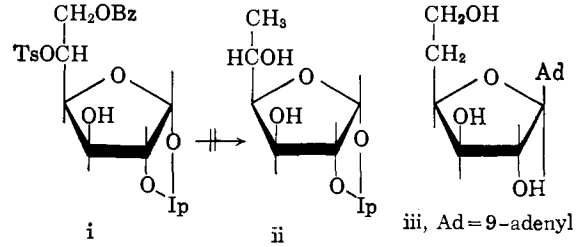


II, Ad = 9-adenyl

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).