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The Synthesis of the Four Possible Methyl 3-Amino-3-deoxy-D-xylosides. A Novel Ring Expansion of a Furanoside to a Pyranoside

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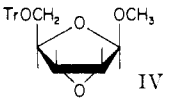
The reaction of ammonia with methyl 2,3-anhydro-5-*O*-trityl-β-D-ribofuranoside (IV), the synthesis of which is described, was unsuccessful. This reaction with methyl 2,3-anhydro-β-D-ribofuranoside (XVb) gave the desired methyl 3-amino-3-deoxy-β-D-xylofuranoside (XVIIb). In the course of the synthesis of XVb, treatment of methyl 2-*O*-benzoyl-3-*O*-mesyl-5-*O*-trityl-β-D-xylofuranoside (XIIb) with hot 80% acetic acid resulted not only in detritylation but also in a ring expansion of some of the product to the corresponding pyranoside, which, after oxide formation and ammonolysis, gave methyl 3-amino-3-deoxy-β-D-xylopyranoside (XVIIIb). The same results were obtained in the α-series. Thus all four possible methyl 3-amino-3-deoxy-D-xylosides were obtained. A mechanism is proposed for the ring expansion, which took place with retention of configuration. The selectivity of ammonia for C-3 in its reaction with 2,3-anhydropentosides is discussed as is the relative facility of the methyl 3-aminoxylosides toward glycosidic hydrolysis.

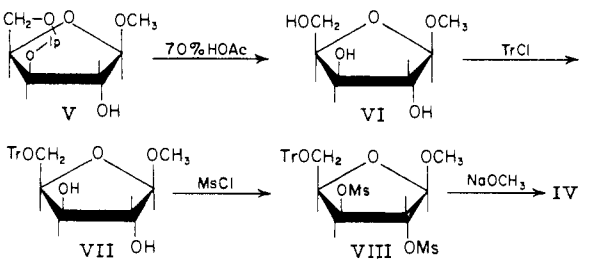
The synthesis of 9-(3-amino-3-deoxy-β-D-xylofuranosyl)-6-dimethylaminopurine (I), an analog of the aminonucleoside [9-(3-amino-3-deoxy-β-D-ribofuranosyl)-6-dimethylaminopurine, II] derived from the antibiotic puromycin, is reported in an accompanying paper.[1] The present paper describes the preparation of methyl 3-amino-3-deoxy-D-xylofuranoside (XVII), an intermediate required for the synthesis of the nucleoside analog I. In the course of the synthesis of this aminosugar, there occurred an unexpected expansion of the furanoside ring to produce the corresponding xylopyranoside of the same anomeric configuration. Since the same sequence was carried out in both the α- and β-anomeric series, all four possible methyl 3-amino-3-deoxy-D-xylosides were obtained and are described here.

The synthesis of aminosugars by the amination of anhydrosugars is a well known procedure.[2,3,4] Thus, ammonolysis of methyl 2,3-anhydrolyxofuranoside has given methyl 3-aminoarabinofuranoside.[4] Analogously, the desired 3-aminoxylofuranoside should result from the amination of a 2,3-anhydroribofuranoside. Although the reaction of ammonia with a 2,3-anhydroribofuranoside, such as IV, could conceivably take place at either C-2 or C-3, it was reasonably expected that C-3 would be the reaction site. This expectation was based upon the fact that the C-3 substituted product results from the reaction of 9-(2,3-anhydro-5-*O*-trityl-β-D-ribofuranosyl)-theophylline with sodium ethyl mercaptide.[5]



IV

The required methyl 2,3-anhydro-5-*O*-trityl-β-D-ribofuranoside (IV) was prepared from methyl 3,5-*O*-isopropylidene-β-D-xylofuranoside (V)[4,6] by two pathways. The sequence *via* the 2,3-di-*O*-mesylate VIII involved four steps and proceeded in 9–18% over-all yield, whereas the second and more satisfactory procedure *via* the 2-*O*-benzoyl-3-*O*-mesylate (XII) required an additional step but gave an over-all yield of 51%. The synthesis based on dimesylate VIII proceeded as follows. Deacetonation of the isopropylidene derivative V with 70% acetic acid gave methyl β-D-xylofuranoside (VI) as a glass in quantitative yield. Methyl D-xylofuranoside has been reported previously as a mixture of α- and β-anomers contaminated with small amounts of free xylose and methyl xylopyranosides.[4,7] Treatment of VI with triphenylmethyl (trityl) chloride in pyridine gave the sirupy 5-*O*-tritylxyloside VII in quantitative yield. The crystalline 2,3-di-*O*-mesylate VIII was then obtained in 49% yield on reaction with a pyridine solution of methanesulfonyl (mesyl) chloride. Heating of dimesylate VIII with sodium methoxide in refluxing methanol for two hours afforded the desired methyl 2,3-anhydro-5-*O*-trityl-β-D-ribofuranoside (IV) as a crystalline product in 36% yield, but on repetition in only 18% yield.[5,8,9] The relatively low yields probably are attributable to a subsequent reaction of the anhydro sugar with methoxide ion.[8,10]



However, the conversion of a 2-*O*-benzoyl-3-*O*-mesyl derivative to an anhydrosugar can be smoothly effected with relatively mild methanolic methoxide conditions (5°, three days).[1] This proved to be the basis of a more satisfactory synthetic sequence which is described as follows. Treatment of methyl 3,5-*O*-isopropylidene-β-D-xylofuranoside (Vb)[4,6] with benzoyl chloride in

(1) R. E. Schaub, M. J. Weiss and B. R. Baker, THIS JOURNAL, **80**, 4692 (1958).

(2) N. K. Richtmyer, *Adv. in Carbohydrate Chem.*, **1**, 57 (1945); A. B. Foster and M. Stacey, *ibid.*, **7**, 253 (1952).

(3) B. R. Baker and R. E. Schaub, *J. Org. Chem.*, **19**, 646 (1954).

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

(5) J. Davoll, B. Lythgoe and S. Trippett, *J. Chem. Soc.*, 2230 (1951).

(6) J. M. Anderson and E. Percival, *ibid.*, 819 (1956).

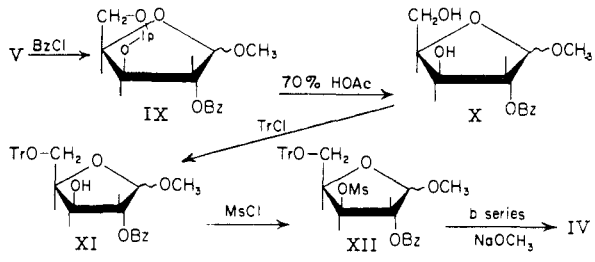
(7) P. A. Levene, A. L. Raymond and R. T. Dillon, *J. Biol. Chem.*, **95**, 699 (1932).

(8) G. J. Robertson and C. F. Griffith, *J. Chem. Soc.*, 1193 (1935).

(9) N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **63**, 1727 (1941).

(10) See footnote 9 in ref. 1.

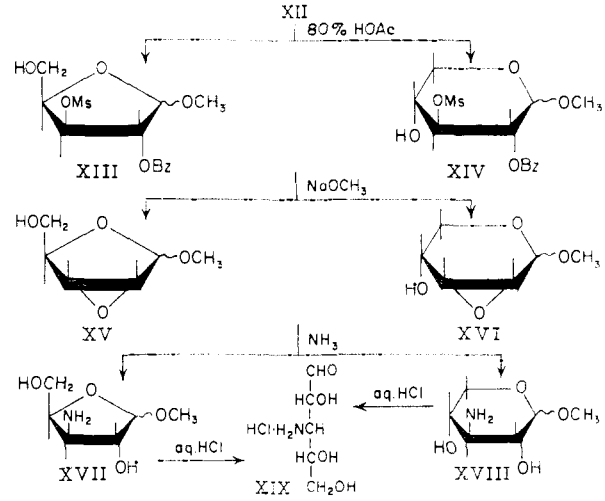
pyridine solution produced the 2-*O*-benzoate IXb as a glass in quantitative yield. Deacetonation of IXb with 70% acetic acid quantitatively gave sirupy methyl 2-*O*-benzoyl-β-D-xylofuranoside (Xb) which on tritylation afforded, in 96% yield, the 5-*O*-trityl derivative XIb also as a sirup. Mesylation of XIb produced the crystalline 2-*O*-benzoyl-3-*O*-mesyl-5-*O*-tritylxyloside (XIIb) in 60% overall yield for the four steps from Vb, the previous crystalline intermediate. Finally, methanolic methoxide treatment (5°, three days) of XIIb gave crystalline methyl 2,3-anhydro-5-*O*-trityl-β-D-ribofuranoside (IV) in 88% yield. This product was identical with the product obtained *via* the dimesylate VIII.



a series, α-configuration
b series, β-configuration

Attempts to aminate anhydroglycoside IV gave inconclusive results. Alcoholic ammonia treatment at 100° for two hours resulted in a 95% recovery of IV. It is noteworthy that under these same conditions 9-(2,3-anhydro-β-D-lyxofuranosyl)-6-dimethylamino-2-methylmercaptopurine gave the corresponding 3′-aminonucleoside in 79% yield.[11] More vigorous conditions resulted in decreased recoveries of IV and increased amounts of nitrogen-containing, amorphous product. Although this nitrogenous material may have contained the desired aminosugar, it was not possible to obtain a crystalline derivative or to isolate material with good analytical values. The failure to satisfactorily aminate the 2,3-anhydro-5-*O*-tritylriboside (IV) recalled the unreactivity of ammonia with the anhydroribofuranosyl nucleosides, 9-(2,3-anhydro-β-D-ribofuranosyl)-6-dimethylamino-2-methylmercaptopurine (III) and the 5′-*O*-trityl derivative of III.[1] These failures were interpreted as due to a steric inhibition of reaction and led to an attempt at ammonolysis of the non-tritylated methyl 2,3-anhydro-β-D-ribofuranoside (X-Vb), since it was anticipated that this anhydroriboside would present a minimum of steric hindrance to the approach of an ammonia molecule.

Methyl 2,3-anhydro-β-D-ribofuranoside (XVb), which was required for this approach, was prepared as follows. Crystalline methyl 2-*O*-benzoyl-3-*O*-mesyl-5-*O*-trityl-β-D-xylofuranoside (XIIb) was detritylated by heating with 80% aqueous acetic acid on the steam-bath for one hour. This procedure gave an amorphous product in 98% yield which, as will be shown below, probably contained at least two isomeric compounds—the desired methyl 2-*O*-benzoyl-3-*O*-mesyl-β-D-xylofuranoside (XIIIb) and also a product of ring expansion, methyl 2-*O*-benzoyl-3-*O*-mesyl-β-D-xylopyranoside (XIVb). Methanolic sodium methoxide treatment (5°, three to five days) of this presumed mixture gave a distillable oil (61%) which was probably a mixture of the desired methyl 2,3-anhydro-β-D-ribofuranoside (XVb) and methyl 2,3-anhydro-β-D-ribopyranoside (XVIb) and/or methyl 3,4-anhydro-β-D-ribopyranoside.[12] Treatment of the distilled oil with aqueous ammonia for eighteen hours at 100° gave a mixture which was separated into a crystalline product (A) (13% yield) and a gum (B) (86% yield). Both crystalline A and gum B analyzed satisfactorily for a methyl aminodeoxypentoside.



a series, α-configuration; b series, β-configuration

Consumption by A of 2.0 equivalents of periodate within five minutes indicated a pyranoside configuration.[13] This, coupled with the failure of the N-acetyl derivative of A to consume any periodate, required an amino group at C-3 and, therefore, A was considered to be a methyl 3-amino-3-deoxypentopyranoside. More specifically, it was postulated that A was a 3-aminoxylopyranoside for the following reasons. The formation of a pyranoside from crystalline XIIb, which is undoubtedly a furanoside, must have involved a ring enlargement in the course of one of the three intervening reactions—detritylation with 80% aqueous acetic acid, epoxide formation on methanolic methoxide treatment or amination with methanolic ammonia.

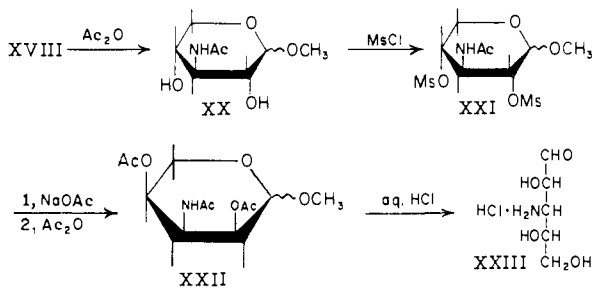
(11) B. R. Baker and R. E. Schaub, THIS JOURNAL, **77**, 5900 (1955).

(12) Epoxide formation requires a hydroxy or acyloxy group adjacent and *trans* to a mesyloxy group. Since this requirement is fulfilled at positions 2 and 4 of XIV, both the 2,3-anhydro- and the 3,4-anhydroribopyranosides are possible.

(13) Periodate oxidations of aminosugars must be interpreted with caution. Work carried out in this Laboratory indicates that 3-aminopentofuranosides consume two rather than the theoretically anticipated one equivalent of periodate. In some cases (for example, methyl 3-amino-3-deoxy-β-D-ribofuranoside) this uptake of two equivalents by an aminofuranoside is very rapid. More often, however, the uptake curve for an aminofuranoside will show a break between one and two equivalents and, in our experience, no aminofuranoside has reacted so rapidly with sodium metaperiodate that the two equivalents are consumed within five minutes. In contrast to the aminofuranosides, 3-aminopyranosides react normally with periodate consuming the expected two equivalents of oxidant. The reaction of aminosugars with periodate and other glycol cleavage reagents will be the subject of a future communication (M. J. Weiss, J. P. Joseph, H. M. Kissman, A. M. Small, R. E. Schaub and F. J. McEvoy).

Mechanistically, it would seem most reasonable that ring expansion should have occurred under acidic conditions, that is, during the detritylation step to give pyranoside XIV. As mentioned above, epoxide formation from XIV could give a 2,3-anhydroribopyranoside XVI or a 3,4-anhydroribopyranoside.[12] However, reaction of ammonia with either of these anhydroribopyranosides at C-3 (as required by the periodate data) would give a xylose derivative, namely, a methyl 3-amino-3-deoxy-D-xylopyranoside (XVIII). That A was indeed a methyl 3-amino-3-deoxy-D-xylopyranoside and furthermore was the β-anomer of this sugar was demonstrated by comparison of A and several of its derivatives with the known[3] methyl 3-amino-3-deoxy-β-L-xylopyranoside and its corresponding derivatives. Thus, A and its crystalline *N*-acetyl, *N*-acetyl-2,4-di-*O*-acetyl and *N*-acetyl-2,4-di-*O*-mesyl derivatives gave specific optical rotations equal in magnitude but opposite in sign to the rotations of methyl 3-amino-3-deoxy-β-L-xylopyranoside and its corresponding derivatives. Moreover, the infrared spectrum of A was identical to that of the L-xylopyranoside, and the spectrum of each of the above-mentioned derivatives of A was identical to that of the corresponding derivative in the L-series. Therefore, A must be the enantiomorph of methyl 3-amino-3-deoxy-β-L-xylopyranoside and, hence, is unequivocally methyl 3-amino-3-deoxy-β-D-xylopyranoside (XVIIIb).

Additionally, the *N*-acetyl-2,4-di-*O*-mesyl derivative (XXIb) of A, on treatment with sodium acetate in refluxing 95% aqueous 2-methoxyethanol solution, underwent inversion of configuration at C-2 and C-4 to give, after acetylation, a crystalline product (66%) which was shown to be methyl 3-acetamido-3-deoxy-2,4-di-*O*-acetyl-α-L-ribopyranoside (XXIIa) by a comparison of its specific optical rotation and infrared spectrum with that of its enantiomorph, methyl 3-acetamido-3-deoxy-2,4-di-*O*-acetyl-α-D-ribopyranoside, a previously reported compound.[3] Aqueous 1% hydrochloric acid hydrolysis of the triacetyl L-riboside (XXIIa) then gave crystalline 3-amino-3-deoxy-L-ribose hydrochloride (XXIII).

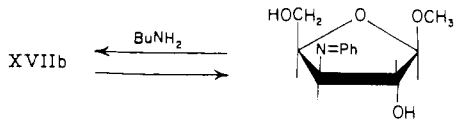


a series, α-configuration; b series, β-configuration

Baker and Schaub[3] have reported an analogous double inversion with methyl 3-acetamido-3-deoxy-2,4-di-*O*-mesyl-β-L-xylopyranoside to give methyl 3-acetamido-3-deoxy-2,4-di-*O*-acetyl-α-D-ribopyranoside. These inversions involve successive displacement of the mesyloxy groups at positions 2 and 4, presumably by participation of the neighboring acetamido group *via* an intermediate oxazoline derivative which is hydrolyzed by the water present.[3]

Residual gum B, obtained after isolation of the crystalline aminopyranoside (A, XVIIIb) from the ammonolysis product, was shown to contain at least a substantial amount of the desired methyl 3-amino-3-deoxy-β-D-xylofuranoside (XVIIb). From this gum crystalline N-phthaloyl (C) and N-acetyl derivatives were obtained in yields of 43 and 45%, respectively. These substances, which analyzed for methyl aminopentoside derivatives, represented new compounds, different from the corresponding derivatives of the aminopyranoside XVIIIb. Also, gum B, on hydrolysis with 1% hydrochloric acid, gave in 65% yield a crystalline aminosugar hydrochloride which was identical with the 3-amino-3-deoxy-D-xylose hydrochloride (XIX) obtained on hydrolysis of aminoxylopyranoside XVIIIb. Since the 43 and 45% yields of the N-phthaloyl (C) and N-acetyl derivatives overlap with this 65% yield, C must also be a 3-amino-D-xyloside.

Dephthaloylation of C with methanolic butylamine[14] gave a sirupy aminoxyloside, presumably free of any methyl 3-amino-β-D-xylopyranoside (XVIIIb). Consumption by this product of 1.3 equivalents of periodate[13] (one hour) with a break in the uptake curve at approximately 1.1 equivalents indicated a furanoside configuration. The sirup, therefore, was provisionally considered to be crude methyl 3-amino-3-deoxy-β-D-xylofuranoside (XVIIb), C being the N-phthaloyl derivative (XXIV) thereof. Conclusive evidence for these structures is presented below. The N-phthaloyl derivative XXIV proved to be a satisfactory intermediate for the synthesis of the desired nucleoside I.[1,15]



Ph = phthaloyl XXIV

In the α-series, ring expansion to an aminoxylopyranoside also was observed. Thus, detritylation of methyl 2-*O*-benzoyl-3-*O*-mesyl-5-*O*-trityl-α-D-xylofuranoside (XIIa)—prepared as described above for the β-series from methyl 3,5-*O*-isopropylidene-α-D-xylofuranoside (Va)[4] *via* benzoylation (IXa), deacetonation (Xa), tritylation (XIa) and mesylation (XIIa)—followed by epoxide ring formation and ammonolysis produced a glass from which a crystalline product (D) could be isolated in 18% yield. Both D and the residual gum (65% yield) gave combustion values in satisfactory agreement for a methyl aminodeoxypentoside.

The skeletal structure of D was established as 3-amino-D-xylose, since dilute acid hydrolysis gave the above-described hydrochloride salt XIX of this sugar. A pyranoside configuration for D was indi-

(14) L. Goldman, J. W. Marsico and R. B. Angier, THIS JOURNAL, **78**, 4173 (1956).

(15) Further evidence for the methyl 3-amino-3-deoxy-β-D-xylofuranoside structure was available from crystalline uucleoside II, thus prepared. Periodate titration data again indicated a furanoside configuration and aqueous hydrochloric acid hydrolysis of II gave 3-amino-D-xylose hydrochloride in 66% yield.

cated by the consumption within five minutes of two equivalents of periodate,[13] and was unequivocally demonstrated in the following manner. Compound D was converted in 72% yield to a crystalline *N*-acetyl derivative, mesylation of which gave a crystalline *N*-acetyl-di-*O*-mesyl derivative in 79% yield. Treatment of this latter product with sodium acetate in refluxing 95% aqueous 2-methoxyethanol solution ("inversion" conditions)[3] gave, after acetylation, a 72% yield of a crystalline 3-acetamido-di-*O*-acetylpentoside. This product, on hydrolysis with 1% hydrochloric acid, afforded in 70% yield the above-described 3-amino-3-deoxy-L-ribose hydrochloride (XXIII). The transformation of D, already proven to be a 3-amino-D-xyloside, to a 3-amino-L-riboside requires inversion of configuration at C-2 and at C-4. Thus, the hydroxyl group at C-4 in the N-acetyl derivative of D had to be free to form a mesyloxy derivative (*i.e.*, to give XXIa) and, therefore, D must be a pyranoside and, more specifically, a methyl 3-amino-3-deoxy-D-xylopyranoside (XVIII). Since D is different from the unequivocally established β-anomer of XVIII, it must be the α-anomer XVIIIa. The N-acetyl derivative is, therefore, represented by XXa, the *N*-acetyl-di-*O*-mesyl derivative by XXIa, and the inversion product is methyl 3-acetamido-3-deoxy-2,4-di-*O*-acetyl-β-L-ribopyranoside (XXIIb).

With the characterization of the two anomeric methyl 3-amino-3-deoxy-D-xylopyranosides (XVIII), conclusive evidence was at hand for the postulated furanoside structure XXIV of the N-phthaloyl derivative C. It may be recalled that this derivative had been obtained from gum B and was to be used for the synthesis of nucleoside II.[1] Examination of compound C showed it to be different from the N-phthaloyl derivatives of either the anomeric 3-aminoxylopyranosides. Inasmuch as C had already been shown to be a 3-amino-D-xylose derivative, it had to be a furanoside by elimination of other possibilities. Since it is reasonable to assume that in the conversion of XIIb to XVII anomeric configuration was retained, C was considered to be methyl 3-phthalimido-3-deoxy-β-D-xylofuranoside (XXIV). This structure for C was fully confirmed by isolation and identification of the corresponding α-anomer.

Thus, in the α-series, when the sequence—detritylation of XIIa, epoxide formation and ammonolysis—was effected in the same manner as previously described, except that the detritylation treatment with 80% acetic acid was allowed to proceed for only twenty minutes instead of sixty minutes, there was isolated from the amination mixture in 10% yield a new compound having m.p. 122–123°. This product gave satisfactory analytical values for a methyl aminopentoside, and hydrolysis with 1% hydrochloric acid gave 3-amino-3-deoxy-D-xylose hydrochloride (XIX). On phthaloylation, there was obtained a crystalline product which was different from the N-phthaloyl derivatives of the two anomeric aminoxylopyranosides and from that of the assumed β-furanoside. Therefore, this new N-phthaloyl derivative must be presumed to represent the α-furanoside as the only remaining possibility. A comparison of the optical rotation value for this derivative ($[\alpha]^{25}D$ +231°) with that for the N-phthaloyl derivative of the assumed β-anomer ($[\alpha]^{25}D$ +95°) substantiates these assignments of anomeric configuration. The product with m.p. 122–123° is, therefore, methyl 3-amino-3-deoxy-α-D-xylofuranoside (XVIIa). Hence, each of the four possible methyl 3-amino-3-deoxy-D-xylofuranosides has been unequivocally characterized.

Thus, as expected, ammonia reacts with the 2,3-anhydroribofuranoside anomers at C-3, the same position at which the 2,3-anhydrolyxofuranoside anomers react with ammonia[4] and at which 9-(2,3-anhydro-5-*O*-trityl-β-D-ribofuranosyl)-theophylline and 9-(2,3-anhydro-α-D-lyxofuranosyl) theophylline react with sodium ethyl mercaptide.[5] This is an interesting observation. The electronic situation at C-2 and C-3 is presumably influenced by inductive effects from C-1 and C-4, respectively. The bis-oxygen substituted C-1 would be expected to have a greater electron-attracting capacity than the mono-oxygen substituted C-4. Therefore, C-2 should be more electrophilic than C-3 and, on this basis, would be expected to react preferentially with a nucleophilic reagent such as ammonia. On the other hand, the C_3–oxygen bond should be easier to split ionically than the C_2–oxygen bond, and on this basis, reaction of the anhydro-sugar with ammonia would be expected to favor C-3. The fact that ammonia reacts with these anhydrosugars with what is apparently a great selectivity[16] for C-3 indicates the importance of this latter consideration.[17] That the relative facility of the two carbon–oxygen bonds of an epoxide ring to split ionically is an important factor in governing the course of reaction with nucleophilic reagents has already been demonstrated by VanderWerf and coworkers.[18] In their studies with the unsymmetrically substituted stilbene oxides, they obtained 60–40 ratios of the two possible products. These workers suggested that the more than usual contribution of the bond-splitting factor to the course of this displacement reaction was due to the strained nature of the epoxide ring.[18] It may be noted that the bicyclic character of the anhydro sugars should further enhance this strain; and indeed with these epoxides, rather than 60–40 ratios, only the C-3 product has been observed.

It is also of interest that ammonia reacts with methyl 2,3-anhydro-β-L-ribopyranoside, where a

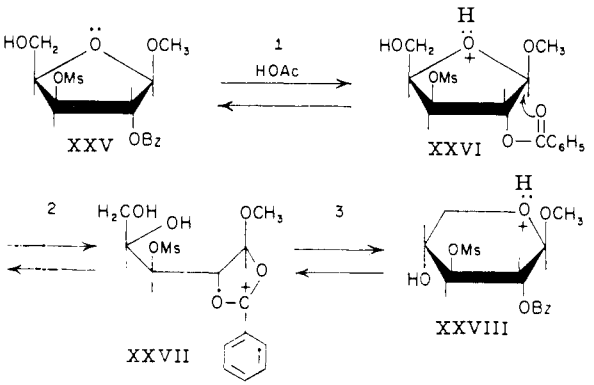
(16) Although the yield of isolated methyl 3-amino-3-deoxy-α-D-xylofuranoside was only 8%, the yield of the β-anomer, as indicated by the yield of crystalline N-phthaloyl derivative, was at least 47% and actually was probably considerably higher. The reported yields of the anomeric methyl 3-amino-3-deoxyarabinofuranosides obtained from the corresponding anomeric 2,3-anhydrolyxofuranosides were in the range 47 to 52% based on isolated crystalline N-isopropylidene derivatives, and in actuality were also probably somewhat higher.[4] The yield reported for the reaction of the anhydroribofuranosyl theophylline derivative with sodium ethyl mercaptide was 90%.[5] In none of these examples was there any evidence for the formation of any significant amount of C-2 substituted product.

(17) The directive effect of steric factors is unknown, but should be given consideration. Note the apparent effect of steric factors on reactivity.

(18) A. Feldstein and C. A. VanderWerf, THIS JOURNAL, **76**, 1626 (1954); R. Fuchs and C. A. VanderWerf, *ibid.*, **76**, 1631 (1954).

similar electronic situation prevails,[19] to give a 3-aminopentoside,[3] and that certain 2,3-anhydroribopyranosides have been reported to undergo ring scission with various nucleophilic reagents to give in each instance as the major product the one resulting from attack at C-3.[22,24-27] However, methyl 2,3-anhydro-4-*O*-acetyl-β-L-lyxopyranoside on alkaline hydrolysis gives a mixture containing approximately 65% xyloside and 35% arabinoside, indicating preferential reaction at C-2.[24]

A mechanism for the ring expansion to give pyranoside derivatives is of interest. As discussed above, an assumption that ring expansion occurs under the conditions of the acid-catalyzed detritylation step seems most reasonable, since it is well understood that the two C_1–oxygen bonds of an alkyl glycoside are usually labile to acid and stable to base. Any rationalization must account for the observed retention of anomeric configuration in the course of furanoside to pyranoside conversion. This eliminates a C-1 carbonium ion intermediate from consideration, since presumably the same intermediate would be obtained from either anomer with resulting loss of anomeric identity. We suggest the mechanism schematically illustrated as



Thus, the first step is considered to be the protonation of the ring oxygen of XXV to give XXVI (equation 1).[28] Proton attack at the methoxyl oxygen is also conceivable, but this should ultimately lead to elimination of methanol. It is difficult to conceive of any appreciable return reaction of methanol with a subsequent species in the presence of a large excess of aqueous acetic acid solvent. Since the product is a methyl glycoside, it must be assumed that the C_1-methoxyl bond is not broken. Protonation is then followed by displacement of the oxonium group of XXVI, *i.e.*, rupture of the ring oxygen–C_1 bond, by an attack at the opposite face of C-1 by the carbonyl oxygen of the 2-benzoyloxy group to form cyclic carbonium ion XXVII (equation 2).[29] Finally, C-1 of cation XXVII may be intramolecularly attacked at the original face by the newly formed C-4 hydroxyl to reproduce the β-furanoside XXVI (reverse of equation 2) or by the C-5 hydroxyl to give a pyranoside XXVIII of the same anomeric configuration as the original furanoside XXV (equation 3).[30]

This sequence amounts to a double Walden inversion at C-1. Thus, the original anomeric configuration is not disturbed, and since each postulated intermediate is a rigid structure (*i.e.*, free rotation about the C_1–C_2 bond is not possible) there is no opportunity for anomeric equilibration. This mechanism would apply as well to the α-anomeric series. An examination of Catalin molecular models[31] appears to confirm its steric feasibility for both the α- and β-series. The carbonium ion XXVII, which presumably has only transitory existence, should have a more than usual stability since it is monocyclic and should, therefore, encounter no difficulty in assuming the planar configuration required for maximum resonance stabilization. Furthermore, in contrast to the cyclic carbonium ions formed by participation of an acetoxy group, cation XXVII is afforded additional stabilization by the distribution of positive charge to the *o*- and *p*-positions of the benzene ring.

Although a detailed study was not undertaken, it is apparent that the methyl aminoxylopyranoside α- and β-anomers (XVIIIa and b) underwent hydrolysis with 1% aqueous hydrochloric acid at 100° at appreciably different rates. Thus, the β-anomer gave crystalline 3-aminoxylose hydrochloride (XIX) in 72% yield after eighteen hours reflux; whereas the α-anomer gave only a 35% yield of this aminosugar hydrochloride after eighteen hours, and even after heating for thirty-six hours the yield was only 44%. The increased susceptibility to glycosidic hydrolysis of the β-anomer parallels the results reported for the methyl α- and β-xylopyranosides.[32] Also, the hydrolysis of the methyl 3-aminoxylopyranoside anomers appears to proceed with greater facility than the hydrolysis of either of the methyl 2-aminoglucoside anomers.[33-35]

(19) This electronic situation has been cited as an explanation for the direction of ring opening of monocyclic anhydropyranosides.[20] This view, however, has been disputed[21] and in general, with anhydropyranosides, the conformational aspects of the ring-scission reaction have been considered more important.[21-23]

(20) R. C. Cookson, *Chemistry & Industry*, 223 (1954); 1512 (1954).

(21) S. J. Angyal, *ibid.*, 1230 (1954).

(22) W. G. Overend and G. Vaughan, *ibid.*, 995 (1955).

(23) A. K. Bose, D. K. R. Chaudhuri and A. K. Bhattacharyya, *ibid.*, 869 (1953).

(24) J. Honeyman, *J. Chem. Soc.*, 990 (1946).

(25) S. Mukherjee and A. R. Todd, *ibid.*, 969 (1947).

(26) R. Allerton and W. G. Overend, *ibid.*, 1480 (1951).

(27) P. W. Kent, M. Stacey and L. F. Wiggins, *ibid.*, 1232 (1949).

(28) F. Shafizadeh and A. Thompson [*J. Org. Chem.*, **21**, 1059 (1956)] *inter alia* have suggested that the acid-catalyzed glycosidic hydrolysis of alkyl aldopyranosides and aldofuranosides most probably involves an initial protonation of the ring oxygen.

(29) See R. U. Lemieux [*Adv. in Carbohydrate Chem.*, **9**, 1 (1954)], for a discussion of the cyclic carbonium ion concept as applied to carbohydrate chemistry.

(30) Prolonged heating periods with 80% acetic acid for the detritylation step did not ultimately produce increased yields of methyl aminoxylopyranoside. Shorter heating periods, however, resulted in decreased yields. These observations would appear to suggest an equilibrium situation.

(31) These models, which are produced by Catalin Ltd., Waltham Abbey, Essex, England, are similar to the Fisher–Taylor–Hirschfelder models.

(32) See W. W. Pigman and R. M. Goepp, Jr., "Chemistry of the Carbohydrates," Academic Press, Inc., New York, N. Y., 1948, p. 204.

(33) R. C. G. Moggridge and A. Neuberger, *J. Chem. Soc.*, 745 (1938).

(34) A. Neuberger and R. Pitt-Rivers, *ibid.*, 122 (1939).

(35) The conformational and other factors which govern the rate of hydrolysis of the non-amino α- and β-xylopyranosides[28] probably also apply to the hydrolysis of the aminoxylopyranosides. However, with the aminoglycosides another and perhaps predominating factor is the ability of the N-protonated derivative to assume a second proton at the ring or alkoxyl oxygen. This second protonation, which is a prerequisite for hydrolysis, is resisted by coulombic repulsion forces

Treatment of gum B, which probably consisted mainly of methyl 3-amino-3-deoxy-β-D-xylofuranoside (XVIIb), with 1% hydrochloric acid at reflux temperature for three hours gave 3-aminoxylose hydrochloride (XIX) in 56% yield. In contrast, the β-pyranoside XVIIIb after heating for three hours gave XIX in only 13% yield. The increased reactivity of the furanoside is in agreement with the usual observations concerning the relative rates of glycosidic hydrolysis of furanosides and pyranosides.[36]

It is interesting to note that, in the two instances where a comparison is available, replacement of a hydroxy or acetoxy group in a xylopyranoside with an amino or acetamido group, respectively, in the 3-position results in no significant change in the specific optical rotation value.[37] Thus the $\alpha^{26}D$ for methyl 3-amino-3-deoxy-β-D-xylopyranoside is −62° (2.0%, water), whereas the $\alpha^{20}D$ for methyl β-D-xylopyranoside is reported[38,39] to be −65.6 (0.3%, water). The $\alpha^{25}D$ for methyl 3-acetamido-3-deoxy-2,4-di-*O*-acetyl-β-D-xylopyranoside is −61° (2%, chloroform) and the $\alpha^{20}D$ value for methyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside is reported[40,41] to be −60.8° (2%, chloroform).

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Experimental

Note: With the exception of compound IV, the preparation of which follows that of compound VIII, the experiments are listed in the order indicated by the Roman numerals. Melting points and boiling points are uncorrected.

Methyl β-D-Xylofuranoside (VI).—A solution of 20 g. of methyl 3,5-*O*-isopropylidene-β-D-xylofuranoside (V)[4,6] in 200 cc. of 70% aqueous acetic acid was heated in a water-bath at 50° for 2 hours, then evaporated to dryness *in vacuo* (bath temperature 50°). The sirupy residue was dissolved in toluene by the addition of sufficient absolute alcohol to cause a solution, which was then evaporated to dryness *in vacuo*. This evaporation was repeated two additional times to give a sirup; yield 16 g. (99%). In a pilot run the yield was 1.54 g. (94%), $[\alpha]^{24}D$ −15° (2% in $CHCl_3$).

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.9; H, 7.37. Found: C, 43.5; H, 7.71.

Methyl 5-*O*-Trityl-β-D-xylofuranoside (VII).—A solution of 16 g. of methyl β-D-xylofuranoside (VI) and 29.9 g. of triphenylmethyl chloride in 160 cc. of reagent pyridine was heated in an oil-bath at 50° for 72 hours. The cooled solution was diluted with 250 cc. of chloroform, then 800 cc. of water. Solid sodium bicarbonate was added until the mixture was slightly basic. The separated organic phase was washed with water, dried with magnesium sulfate and evaporated to dryness *in vacuo*. The residue was dissolved in toluene and the evaporation repeated leaving 43 g. (108%) of product as a sirup which was contaminated with triphenylcarbinol.

Methyl 2,3-Di-*O*-mesyl-5-*O*-trityl-β-D-xylofuranoside (VIII).—To a solution of 43 g. of methyl 5-*O*-trityl-β-D-xylofuranoside (VII) in 800 cc. of reagent pyridine, cooled in an ice-bath to 5°, was added 43 cc. of methanesulfonyl chloride at such a rate that the temperature was maintained at 5–12°. The solution was then allowed to stand in a stoppered flask at room temperature for four days. The cooled solution was diluted with 250 cc. of chloroform, then 3 liters of water. The separated aqueous phase was extracted with 200 cc. of chloroform. The combined chloroform extracts were washed with saturated aqueous sodium bicarbonate, dried over magnesium sulfate and evaporated to dryness *in vacuo*. The residue was twice evaporated with toluene leaving 57 g. (96%) of sirup. Crystallization from absolute alcohol gave 29.2 g. (49%) of product, m.p. 136–138°. In a pilot run the yield was 2.2 g. (47%), m.p. 136–137°. Recrystallization from absolute alcohol afforded white crystals, m.p. 139–140°, $[\alpha]^{25}D$ −18.8° (2% in $CHCl_3$).

Anal. Calcd. for $C_{27}H_{30}O_9S_2$: C, 57.6; H, 5.37; S, 11.4. Found: C, 57.6; H, 5.61; S, 11.7.

Methyl 2,3-Anhydro-5-*O*-trityl-β-D-ribofuranoside (IV) (A).—A mixture of 500 mg. of methyl 2,3-di-*O*-mesyl-5-*O*-trityl-β-D-xylofuranoside (VIII), 5 cc. of absolute methanol and 3.56 cc. of 1 *N* methanolic sodium methoxide was brought into solution by heating to the boil. Refluxing was then continued on the steam-bath for 2 hours. The cooled solution was acidified with 0.2 cc. of acetic acid and evaporated to dryness *in vacuo*. The residue was dissolved in 5 cc. of water and extracted with two 10-cc. portions of chloroform. The combined extracts were dried with magnesium sulfate and evaporated to dryness *in vacuo* to give 340 mg. (94%) of a glass. Slow crystallization of the residue from ether at 0° gave 100 mg. (20% recovery) of starting material VIII, m.p. and mixed m.p. with VIII 139–140°. The mother liquor deposited 100 mg. (36% based on unrecovered VIII) of product in several crops, m.p. 121–126°. Recrystallization from ether gave white crystals, m.p. 127°, $[\alpha]^{24}D$ −59° (1% in $CHCl_3$); λ_{max}^{KBr} 9.10, 9.25 μ (C–O–C) 14.1, 14.3 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{25}H_{24}O_4$: C, 77.4; H, 6.23. Found: C, 77.8; H, 6.53.

In a subsequent preparation from 20 g. of VIII there was obtained 1.34 g. (7% recovery) of starting material and 2.14 g. (18% based on unrecovered VIII) of product in several crops, m.p. 120–127°.

(B).—To a hot mixture of 2.0 g. of methyl 2-*O*-benzoyl-3-*O*-mesyl-5-*O*-trityl-β-D-xylofuranoside (XIIb) (see below) in 50 cc. of absolute methanol, was added 10.2 cc. of 1 *N* methanolic sodium methoxide. Solution was complete in about two minutes. After standing at 3° for 72 hours, the separated product was collected, washed with absolute methanol and then with water; yield 945 mg., m.p. and mixed m.p. with preparation A 126–127°. The mother liquor was acidified with 0.7 cc. of acetic acid and evaporated to dryness *in vacuo*. The residue was twice evaporated with water to remove methyl benzoate, leaving a sirup. Crystallization from absolute methanol afforded an additional 215 mg. (total yield, 88%) of product, m.p. 126–127°.

Attempts to combine the anhydro glycoside IV with alcoholic ammonia under various conditions of time and temperature gave inconclusive results (see Discussion).

Methyl 2-*O*-Benzoyl-3,5-*O*-isopropylidene-β-D-xylofuranoside (IXb).—To a solution of 25 g. of methyl 3,5-*O*-isopropylidene-β-D-xylofuranoside (Vb)[4,6] in 250 cc. of reagent pyridine cooled in an ice-bath to 5° was added 17.8 cc. of benzoyl chloride at such a rate that the temperature was maintained at 5 to 10°. After 24 hours at room temperature in a stoppered flask, the solution was poured into 1250 cc. of iced water and the resulting mixture was extracted with three 200-cc. portions of methylene chloride. The combined extracts were washed with aqueous sodium bicarbonate, dried with magnesium sulfate and evaporated to dryness *in vacuo*. The residue was twice dissolved in toluene and the evaporation repeated leaving 37.6 g. (99%) of a glass. In a pilot run the yield was 2.8 g. (93%); λ_{max}^{KBr} 5.80, 7.90 μ (ester); 7.3 μ (C-methyl); 9.00, 9.30 μ (C–O–C); 14.1 μ (monosubstituted phenyl).

stemming from the already positively charged nitrogen atom.[38] Presumably the hydrolysis rate differences between the various aminosugars may, to a large extent, be ascribed to differences in the distance between the protonated nitrogen and oxygen atoms in conformationally feasible structures. With increasing distance there should be a decreasing resistance to the formation of the required diprotonated structure and a resulting increased ease of hydrolysis.

(36) Reference 32, p. 206.

(37) This phenomenon with aminosugars has also been observed by E. E. van Tamelen and co-workers, THIS JOURNAL, **78**, 4817 (1956); also see ref. 34.

(38) E. Fischer, *Ber.*, **28**, 1145 (1895).

(39) C. S. Hudson, THIS JOURNAL, **47**, 265 (1925).

(40) C. S. Hudson and J. M. Johnson, *ibid.*, **37**, 2748 (1915).

(41) J. K. Dale, *ibid.*, **37**, 2745 (1915).

Anal. Calcd. for $C_{16}H_{20}O_6$: C, 62.4; H, 6.54. Found: C, 62.9; H, 6.54.

Methyl 2-*O*-Benzoyl-3,5-*O*-isopropylidene-α-D-xylofuranoside (IXa).—Benzoylation of 50 g. of methyl 3,5-*O*-isopropylidene-α-D-xylofuranoside (Va)[4,5] as described for IXb gave 77 g. of a sirup which was crystallized from petroleum ether (b.p. 30–60°); yield 52.8 g. (70%), m.p. 84–87°. Recrystallization of a pilot run (66% yield) from petroleum ether (b.p. 30–60°) afforded white crystals, m.p. 92–93°, $[\alpha]^{25}D$ +127° (2% in $CHCl_3$); λ_{max}^{KBr} 5.83, 7.80 μ (ester); 7.30 μ (C-methyl); 9.00, 9.40, 9.80 μ (C-O-C); 13.95 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{16}H_{20}O_6$: C, 62.4; H, 6.54. Found: C, 62.6; H, 6.67.

Methyl 2-*O*-Benzoyl-β-D-xylofuranoside (Xb).—A solution of 37.6 g. of methyl 2-*O*-benzoyl-3,5-*O*-isopropylidene-β-D-xylofuranoside (IXb) in 376 cc. of 70% aqueous acetic acid was heated in a bath at 50° for 2 hours, then evaporated to dryness *in vacuo*. The residue was dissolved in toluene on the addition of sufficient absolute alcohol to cause solution, then evaporated to dryness *in vacuo* leaving 32.7 g. (100%) of a sirup. In a pilot run the yield was 2.35 g. (100%); λ_{max}^{KBr} 2.92 μ (OH); 5.80, 7.90 μ (ester); 9.00, 9.34 μ (OH and C-O-C); 14.1 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{13}H_{16}O_6$: C, 58.2; H, 6.01. Found: C, 58.8; H, 6.28.

Methyl 2-*O*-Benzoyl-α-D-xylofuranoside (Xa).—From 24.3 g. of methyl 2-*O*-benzoyl-3,5-*O*-isopropylidene-α-D-xylofuranoside (IXa) there was obtained as described for Xb, a sirup which was crystallized by trituration with heptane; yield 20.7 g. (98%), m.p. 83–85°. Recrystallization from ethyl acetate–heptane gave white crystals, m.p. 89–90°, $[\alpha]^{25}D$ +142° (2% in $CHCl_3$); λ_{max}^{KBr} 2.91 μ (OH); 5.80, 7.81 μ (ester); 9.25, 9.50 μ (OH and C-O-C); 14.1 μ (monosubstituted phenyl). This compound failed to consume any periodate in aqueous sodium bicarbonate after 24 hours.

Anal. Calcd. for $C_{13}H_{16}O_6$: C, 58.2; H, 6.01. Found: C, 58.1; H, 5.89.

Methyl 2-*O*-Benzoyl-5-*O*-trityl-β-D-xylofuranoside (XIb).—A solution of 38 g. of methyl 2-*O*-benzoyl-β-D-xylofuranoside (Xb) and 40 g. of triphenylmethyl chloride in 380 cc. of reagent pyridine (protected by a drying tube) was heated in an oil-bath at 50° for 96 hours. The cooled solution was diluted with 250 cc. of chloroform, then 1 l. of water. Solid sodium bicarbonate was added portionwise with swirling until the mixture was slightly basic. The organic phase was separated, washed with water, dried with magnesium sulfate and evaporated to dryness *in vacuo*. The residue was twice evaporated with toluene leaving 72 g. (100%) of sirupy product. In a pilot run the yield was 4.2 g. (95%); λ_{max}^{KBr} 2.87 μ (OH); 5.79, 7.92 μ (ester); 9.10, 9.31 μ (OH and C-O-C); 14.2 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{32}H_{30}O_6$: C, 75.4; H, 5.92. Found: C, 75.8; H, 6.51.

Methyl 2-*O*-Benzoyl-5-*O*-trityl-α-D-xylofuranoside (XIa).—Tritylation of 20 g. of methyl 2-*O*-benzoyl-α-D-xylofuranoside (Xa) as described for the preparation of XIb gave 38 g. (100%) of product as a sirup.

Anal. Calcd. for $C_{32}H_{30}O_6$: C, 75.4; H, 5.92. Found: C, 75.8; H, 6.15.

Methyl 2-*O*-Benzoyl-3-*O*-mesyl-5-*O*-trityl-β-D-xylofuranoside (XIIb).—A solution of 72 g. of methyl 2-*O*-benzoyl-5-*O*-trityl-β-D-xylofuranoside (XIb) in 500 cc. of reagent pyridine was cooled in an ice-bath to 7° and 23 cc. of methanesulfonyl chloride was added, with swirling, at such a rate that the temperature was maintained at 7–12°. The mixture was kept in a stoppered flask at room temperature for 72 hours. The solution was diluted with 500 cc. of chloroform and then with 2 l. of iced water. The separated aqueous phase was further extracted with two 200-cc. portions of chloroform. The combined chloroform extracts were washed with excess saturated aqueous sodium bicarbonate, then with water, dried with magnesium sulfate and evaporated to dryness *in vacuo*. The residue was twice evaporated to dryness *in vacuo* with toluene; yield 81 g. (98%) of a sirup. Crystallization from absolute methanol afforded 43.4 g. (60% based on Vb) of product, m.p. 133–134°. In a previous preparation the yield was 32 g. (60% based on Vb), m.p. 130–132°. Recrystallization from absolute alcohol afforded white crystals, m.p. 135–136°, $[\alpha]^{25}D$ −9.1° (2% in $CHCl_3$); λ_{max}^{KBr} 5.80, 7.90 μ (ester); 7.41, 8.50 μ (sulfonate); 9.00, 9.31 μ (C-O-C); 14.1 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{33}H_{32}O_8S$: C, 67.4; H, 5.49; S, 5.45. Found: C, 67.3; H, 5.82; S, 5.76.

Methyl 2-*O*-Benzoyl-3-*O*-mesyl-5-*O*-trityl-α-D-xylofuranoside (XIIa).—Mesylation of 68 g. of methyl 2-*O*-benzoyl-5-*O*-trityl-α-D-xylofuranoside (XIa) as described for the preparation of XIIb gave 76.5 g. (97%) of a semi-solid. Recrystallization from absolute alcohol gave 62 g. (79% or 52% from Va), m.p. 151–153°. Recrystallization of the product from a pilot run (65% yield) from absolute alcohol afforded white crystals, m.p. 151–153°, $[\alpha]^{26}D$ +102° (2% in $CHCl_3$); λ_{max}^{KBr} 5.81, 7.92μ (ester); 7.32, 8.50 μ (sulfonate); 8.95, 9.20 μ (C-O-C); 14.0 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{33}H_{32}O_8S$: C, 67.4; H, 5.49; S, 5.45. Found: C, 67.6; H, 5.81; S, 5.68.

Methyl 2-*O*-Benzoyl-3-*O*-mesyl-β-D-xylofuranoside (XIIIb) and Probably Methyl 2-*O*-Benzoyl-3-*O*-mesyl-β-D-xylopyranoside (XIVb).—A mixture of 85 g. of methyl 2-*O*-benzoyl-3-*O*-mesyl-5-*O*-trityl-β-D-xylofuranoside (XIIb) and 850 cc. of 80% aqueous acetic acid was heated, with stirring, on the steam-bath for 25 minutes; solution was complete within 5 minutes. Dilution of the cooled solution with 3500 cc. of water and filtration gave 37.5 g. (100%) of triphenylcarbinol (m.p. and mixed m.p. with an authentic sample, 160–163°). The filtrate was saturated with sodium chloride and extracted with three 500-cc. portions of chloroform. After drying over magnesium sulfate, the combined extracts were evaporated to dryness *in vacuo*. The residue was twice evaporated with toluene *in vacuo* leaving 49.1 g. (98%) of a sirup. In a pilot run the yield of triphenylcarbinol was 99% (8.8 g.), m.p. 160–163°, and the yield of product was 98% (11.5 g.).

Anal. Calcd. for $C_{14}H_{18}O_8S$: C, 48.5; H, 5.24; S, 9.25. Found: C, 49.7; H, 5.44; S, 8.94.

Methyl 2-*O*-Benzoyl-3-*O*-mesyl-α-D-xylofuranoside (XIIIa) and Probably Methyl 2-*O*-Benzoyl-3-*O*-mesyl-α-D-xylopyranoside (XIVa).—By heating 43.5 g. of methyl 2-*O*-benzoyl-3-*O*-mesyl-5-*O*-trityl-α-D-xylofuranoside (XIIa) with 400 cc. of 80% aqueous acetic acid on the steam-bath for 75 minutes as described for the preparation of XIIIb and XIVb there was obtained 21 g. (109%) of triphenylcarbinol (m.p. 150–154°) and 15 g. (59%) of a glass-like product, which did not give satisfactory analytical data. In another experiment, where the reaction time was decreased to 35 minutes, there was obtained 13.3 g. (100%) of triphenylcarbinol (m.p. 161–163°) and 17.3 g. (98%) of a glass-like product.

Anal. Calcd. for $C_{14}H_{18}O_8S$: C, 48.5; H, 5.24; S, 9.25. Found: C, 50.3; H, 5.80; S, 8.58.

Methyl 2,3-Anhydro-β-D-ribofuranoside (XVb) and Probably Methyl 2,3-Anhydro-β-D-ribopyranoside (XVIb) and/or Methyl 3,4-Anhydro-β-D-ribopyranoside.[12]—To a solution of 49.1 g. of the preceding detritylated mixture (XIIIb and XIVb) in 191 cc. of absolute methanol, cooled in an ice-bath to 10°, was added portionwise a solution of 23 g. of sodium methoxide (Mathieson) in 300 cc. of absolute methanol. The resulting solution was kept at 0–3° for 4 days. After acidification with 14 cc. of acetic acid, the solution was evaporated to dryness *in vacuo*. The residue was twice evaporated with water to remove methyl benzoate and was then dissolved in 35 cc. of water and extracted with five 50-cc. portions of chloroform. The combined extracts, after drying over magnesium sulfate, were evaporated to dryness *in vacuo*. Distillation of the residue (15.5 g.) gave 12.7 g. (61%) of product, b.p. 70–75° at 0.1–0.2 mm. In a similar preparation there was obtained 2.9 g. (60%) of product, b.p. 70° at 0.1 mm., $[\alpha]^{24}D$ −129° (2% in $CHCl_3$); λ_{max}^{KBr} 2.9 μ (OH); 9.10, 9.60 μ (C-O-C and C-OH).

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.3; H, 6.90. Found: C, 49.0; H, 7.25.

Methyl 2,3-Anhydro-α-D-ribofuranoside (XVa) and Probably Methyl 2,3-Anhydro-α-D-ribopyranoside (XVIa) and/or Methyl 3,4-Anhydro-α-D-ribopyranoside.[12]—From 14.7 g. of the probable mixture of XIIIa and XIVa there was obtained, in the manner described for the separation of XVb and XVIb, 3.25 g. of crude product. Distillation

afforded 2 g. (32%) of an oil, b.p. 98–101° at 0.1 mm., $[\alpha]^{25}D$ +77.4° (2% in $CHCl_3$).

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.3; H, 6.90. Found: C, 49.1; H, 7.06.

In another experiment from 17.2 g. of product which had been isolated from the 35-minute detritylation step, there was obtained 3.2 g. (44%) of product, b.p. 102–105° (0.1 mm.), $[\alpha]^{25}D$ +46.1° (2% $CHCl_3$).

Methyl 3-Amino-3-deoxy-β-D-xylofuranoside (XVIIb) and Methyl 3-Amino-3-deoxy-β-D-xylopyranoside (A, XVIIIb).—A solution of 5 g. of the presumed mixture of anhydroribosides (XVb and XVIb) in 45 cc. of concentrated aqueous ammonium hydroxide was heated in a steel bomb at 100° for 18 hours. The solution was clarified by filtration through Celite (diatomaceous earth). Evaporation to dryness *in vacuo* gave 5.5 g. of a partially crystalline sirup which on trituration with 50% absolute alcohol–ether and filtration gave 700 mg. (13%) of the aminoxylopyranoside (A, XVIIIb), m.p. 195–196°. Recrystallization from absolute alcohol gave white crystals, m.p. 196–197°; $[\alpha]^{26}D$ −62° (2% in H_2O). The enantiomorph, methyl 3-amino-3-deoxy-β-L-xylopyranoside,[3] exhibited an optical rotation of +61.4° (1% in water). Both compounds had identical infrared spectra. This compound consumed 2.0 equivalents of periodate in aqueous sodium bicarbonate within 5 minutes; no additional oxidant was consumed after one hour.[13]

Anal. Calcd. for $C_6H_{13}O_4N$: C, 44.2; H, 8.03; N, 8.58. Found: C, 43.9; H, 8.10; N, 8.44.

Evaporation of the filtrate obtained after isolation of the 700 mg. of aminopyranoside afforded 4.6 g. (86%) of crude methyl 3-amino-xylofuranoside (XVIIb) as a gum (B) $[\alpha]^{25}D$ −92° (2% in $CHCl_3$). Hydrolysis of gum B with 1% aqueous hydrochloric acid gave 3-amino-3-deoxy-D-xylose·HCl (XIX) (see below).

Anal. Calcd. for $C_6H_{13}O_4N$: C, 44.2; H, 8.03; N, 8.58. Found: C, 44.2; H, 8.42; N, 8.46.

Methyl 3-Amino-3-deoxy-β-D-xylofuranoside (XVIIb) *via* the N-Phthaloyl Derivative XXIV.—A solution of 310 mg. of methyl 3-phthalimido-3-deoxy-β-D-xylofuranoside (XXIV) (see below), 1.05 cc. of butylamine[14] and 7 cc. of methanol was refluxed on the steam-bath for 18 hours, and then evaporated to dryness *in vacuo*. Trituration with water and filtration gave 232 mg. (80%) of N,N-dibutylphthalamide, m.p. and mixed m.p. with an authentic sample[42] 118–119°. The filtrate was extracted twice with ether and evaporated to dryness *in vacuo* leaving a sirup; yield 131 mg. (76%). Satisfactory analytical values could not be obtained for this product. The product consumed 1.3 equivalents of periodate in 1 hour with a break in the uptake curve at 1.1 equivalents.[13]

Methyl 3-Amino-3-deoxy-α-D-xylofuranoside (XVIIa) and Methyl 3-Amino-3-deoxy-α-D-xylopyranoside (D, XVIIIa). A.—From 1.85 g. of the presumed mixture of anhydro sugars (XVa and XVIa) there was obtained (as described for the preparation of XVIIb and XVIIIb), by crystallization of the partially crystalline, sirupy, reaction product, 360 mg. (18%) of the aminoxylopyranoside (D, XVIIIa), m.p. 195–196°. Recrystallization from absolute alcohol did not alter the melting point; $[\alpha]^{26}D$ +155° (1% in pyridine). Admixture of this product with methyl 3-amino-3-deoxy-β-D-xylopyranoside (XVIIIb) of m.p. 195–196° gave a 25° depression in melting point. Hydrolysis of this product with 1% aqueous hydrochloric acid gave 3-amino-3-deoxy-D-xylose·HCl (XIX) (see below). This compound consumed 2.1 equivalents of periodate in aqueous sodium bicarbonate in 5 minutes, then consumed no additional oxidant in 40 minutes.[13]

Anal. Calcd. for $C_6H_{13}O_4N$: C, 44.2; H, 8.03; N, 8.58. Found: C, 44.6; H, 7.92; N, 8.44.

Evaporation of the filtrate obtained after isolation of the 360 mg. of aminopyranoside afforded 1.35 g. (65%) of the presumed crude aminoxylofuranoside XVIIa as a sirup.

Anal. Calcd. for $C_6H_{13}O_4N$: C, 44.2; H, 8.03; N, 8.58. Found: C, 43.5; H, 8.13; N, 7.63.

B. Isolation of Crystalline Methyl 3-Amino-3-deoxy-α-D-xylofuranoside (XVIIa).—In another experiment, using the presumed mixture of anhydro sugars XVa and XVIa which had been obtained from the sequence in which the reaction time for detritylation was 35 minutes, there was obtained 3.3 g. of sirup. Crystallization from absolute alcohol gave 325 mg. (10%) of 3-amino-3-deoxy-α-D-xylofuranoside (XVIIa), m.p. 116–118°. Recrystallization from absolute alcohol–heptane afforded white crystals, m.p. 122–123°. $[\alpha]^{25}D$ +236° (0.4% in $CHCl_3$). Hydrolysis of this product with 1% aqueous hydrochloric acid gave 3-amino-3-deoxy-D-xylose·HCl (XIX) (see below).

Anal. Calcd. for $C_6H_{13}O_4N$: C, 44.2; H, 8.03; N, 8.58. Found: C, 44.5; H, 8.36; N, 8.83.

Evaporation of the filtrate from the 325 mg. afforded 2.7 g. (78%) of sirup.

Anal. Calcd. for $C_6H_{13}O_4N$: C, 44.2; H, 8.03; N, 8.58. Found: C, 45.1; H, 7.97; N, 8.25.

3-Amino-3-deoxy-D-xylose Hydrochloride (XIX). A. **From Methyl 3-Amino-3-deoxy-β-D-xylopyranoside (A, XVIIIb).**—A solution of 500 mg. of XVIIIb in 10 cc. of 1% aqueous hydrochloric acid, to which had been added 0.26 cc. of concentrated hydrochloric acid, was refluxed for 18 hours, then evaporated to a sirup *in vacuo* (bath temperature 50°). The sirup crystallized on cooling. Trituration with 5 cc. of acetic acid gave 408 mg. (72%) of product, m.p. 167° dec. Recrystallization from 0.5 cc. of water by addition of 6 cc. of acetic acid gave white crystals, m.p. 169° dec., $[\alpha]^{25}D$ +29° (2% in H_2O). The product gave a positive test with Benedict reagent. When the hydrolysis time was 3 hours the yield of product was 13%, m.p. 169° dec.

Anal. Calcd. for $C_5H_{11}O_4N·HCl$: C, 32.4; H, 6.52; N, 7.55. Found: C, 32.7; H, 6.57; N, 7.78.

B. **From Crude Methyl 3-Amino-3-deoxy-β-D-xylofuranoside (XVIIb) (Gum B).**—Hydrolysis of 316 mg. of gum B (XVIIb) carried out as described in preparation A above afforded 235 mg. (65%) of product, m.p. 164° dec. When the reaction time was 3 hours instead of 18 hours the yield was 310 mg. (56%), m.p. 162° dec. Recrystallization as in preparation A afforded white crystals, m.p. 165° dec. The compound gave an infrared spectrum identical with that of the product obtained from preparation A.

Anal. Calcd. for $C_5H_{11}O_4N·HCl$: C, 32.4; H, 6.52; N, 7.55. Found: C, 32.8; H, 6.67; N, 7.64.

C. **From Methyl 3-Amino-3-deoxy-α-D-xylopyranoside (XVIIIa, D).**—By refluxing for 36 hours a solution of 100 mg. of XVIIIa (D) in 3.5 cc. of 1% hydrochloric acid, to which had been added 0.052 cc. of concentrated hydrochloric acid, as described in preparation A, there was obtained 50 mg. (44%) of product, m.p. 169° dec. The compound gave an infrared spectrum identical with that of the product obtained from preparation A. When the reaction time was 18 hours instead of 36 hours the yield was 40 mg. (35%), m.p. 168–169° dec., $[\alpha]^{25}D$ +29.5° (2% in H_2O).

D. **From Crystalline Methyl 3-Amino-3-deoxy-α-D-xylofuranoside (XVIIa).**—By refluxing for 3 hours and 40 minutes a solution of 73 mg. of crystalline XVIIa in 4 cc. of 1% hydrochloric acid, to which had been added 0.038 cc. of concentrated hydrochloric acid as described in preparation A, there was obtained 63 mg. (76%) of product, m.p. 169° dec. Recrystallization as in preparation A gave white crystals, m.p. 169° dec., $[\alpha]^{25}D$ +27.3° (1% in H_2O). The compound gave an infrared spectrum identical with that of the product obtained by procedure A.

Anal. Calcd. for $C_5H_{11}O_4N·HCl$: C, 32.4; H, 6.52; N, 7.55. Found: C, 32.7; H, 6.74; N, 7.75.

Methyl 3-Phthalimido-3-deoxy-β-D-xylopyranoside.—A solution of 300 mg. of methyl 3-amino-3-deoxy-β-D-xylopyranoside (XVIIIb) and 300 mg. of phthalic anhydride in 3 cc. of dimethylformamide was refluxed for 90 minutes. Solvent was removed *in vacuo* and the residue was crystallized by trituration with ethyl acetate; yield 461 mg. obtained in several crops (85%), m.p. 232–234°. Recrystallization from ethyl acetate afforded white crystals, m.p. 237–238°, $[\alpha]^{25}D$ −27° (2% in EtOH); λ_{max}^{KBr} 2.92 μ (OH); 5.64, 5.90 μ (C=O of phthalimido).

Anal. Calcd. for $C_{14}H_{15}O_6N$: C, 57.4; H, 5.15; N, 4.78. Found: C, 57.7; H, 5.20; N, 4.67.

Methyl 3-Phthalimido-3-deoxy-α-D-xylopyranoside.—A solution of 100 mg. of methyl 3-amino-3-deoxy-α-D-xylopyranoside (XVIIIa) and 100 mg. of phthalic anhydride in 3

(42) Private communication from L. Goldman, J. W. Marsico and R. B. Angier of these laboratories.

cc. of dimethylformamide was refluxed for 90 minutes, and then evaporated to dryness *in vacuo*. The residue was dissolved in 3 cc. of water and the resulting solution was extracted with three 5-cc. portions of chloroform. The combined extracts were washed with aqueous sodium bicarbonate solution and then dried over magnesium sulfate. After evaporation to dryness *in vacuo*, there was obtained 146 mg. (81%) of a glass. Crystallization from ethyl acetate–heptane afforded 90 mg. (50%) of product, m.p. 184–185°. Recrystallization from ethyl acetate–heptane gave white crystals, m.p. 185–186°, $[\alpha]^{25}D$ +98.5° (2% in EtOH); λ_{max}^{KBr} 2.95 μ (OH); 5.65, 5.88 μ (C=O of phthalimido).

Anal. Calcd. for $C_{14}H_{15}O_6N$: C, 57.4; H, 5.15; N, 4.78. Found: C, 56.9; H, 5.19; N, 4.85.

Methyl 3-Acetamido-3-deoxy-2,4-di-*O*-acetyl-β-D-xylopyranoside.—To a mixture of methyl 3-amino-3-deoxy-β-D-xylopyranoside (XVIIIb) and 2 cc. of reagent pyridine was added 1 cc. of acetic anhydride; complete solution was obtained in a few minutes on swirling. After 18 hours at room temperature in a stoppered flask, the solution was diluted with 10 cc. of ice water and then extracted with three 10-cc. portions of chloroform. The combined extracts, dried with magnesium sulfate, were evaporated to dryness *in vacuo*. Crystallization of the semi-solid residue from ethyl acetate–heptane gave 290 mg. (82%) of product, m.p. 174–176°. Recrystallization from ethyl acetate–heptane afforded white needles, m.p. 175–176°, $[\alpha]^{25}D$ −61° (2% in $CHCl_3$). The known[3] enantiomorph, methyl 2,4-di-*O*-acetyl-3-acetamido-3-deoxy-β-L-xylopyranoside, showed an optical rotation of +60.7° (2% in $CHCl_3$). Both compounds had identical infrared spectra.

Anal. Calcd. for $C_{12}H_{19}O_7N$: C, 49.8; H, 6.62; N, 4.85. Found: C, 50.1; H, 6.67; N, 4.86.

Methyl 3-Acetamido-3-deoxy-α-D-xylopyranoside (XXa).—Acetylation of 50 mg. of methyl 3-amino-3-deoxy-α-D-xylopyranoside (XVIIIa) with 0.05 cc. of acetic anhydride and 2 cc. of water as described below for the preparation of XXb gave 45 mg. (72%) of product, m.p. 198–200°. Recrystallization from ethyl acetate afforded white needles, m.p. 205–206°, $[\alpha]^{25}D$ +121° (0.9% in H_2O); λ_{max}^{KBr} 3.05 μ (OH, amide NH); 6.05, 6.40 μ (amide C=O).

Anal. Calcd. for $C_8H_{15}O_5N$: C, 46.8; H, 7.36; N, 6.83. Found: C, 46.7; H, 7.61; N, 7.19.

Methyl 3-Acetamido-3-deoxy-β-D-xylopyranoside (XXb).—To a solution of 1.5 g. of methyl 3-amino-3-deoxy-β-D-xylopyranoside (XVIIIb) in 10 cc. of water was added 1.5 cc. of acetic anhydride. The mixture was shaken for 6 minutes, then evaporated to dryness *in vacuo*. Trituration of the residual solid with ethyl acetate and filtration afforded 1.82 g. (96%) of product, m.p. 195–197°.

In a pilot run the yield was 340 mg. (90%), m.p. 200–201°. Recrystallization from ethyl acetate–absolute alcohol gave white crystals, m.p. 201–202°, $[\alpha]^{25}D$ −66.2° (2% in H_2O). The known[3] enantiomorph, methyl 3-acetamido-3-deoxy-β-L-xylopyranoside, showed an optical rotation of +64.4° (2% in H_2O). Both compounds had identical infrared spectra. This compound failed to consume any periodate in aqueous sodium bicarbonate after 1 hour.

Anal. Calcd. for $C_8H_{15}O_5N$: C, 46.8; H, 7.36; N, 6.83. Found: C, 46.7; H, 7.32; N, 6.91.

Methyl 3-Acetamido-3-deoxy-2,4-di-*O*-mesyl-β-D-xylopyranoside (XXIb).—To a solution of 1.82 g. of methyl 3-acetamido-3-deoxy-β-D-xylopyranoside (XXb) in 35 cc. of reagent pyridine, cooled in an ice-bath to 5°, was added 1.82 cc. of methanesulfonyl chloride at such a rate that the temperature was maintained at 5–10°. When the reaction mixture was no longer exothermic, it was kept in a stoppered flask at room temperature for 72 hours. Sufficient water was added to dissolve the pyridine hydrochloride, then the solution was concentrated *in vacuo* (water-bath temperature 50–55°) to about 5 cc. Dilution with 25 cc. of water and cooling to ice-bath temperature gave a buff solid which was collected and washed with water to afford 2.2 g. (69%) of product, m.p. 155–156°.

In a pilot run the yield was 235 mg. (67%), m.p. 151–153°. Recrystallization from absolute alcohol afforded white crystals, m.p. 155–156°, $[\alpha]^{25}D$ −45° (2% in pyridine); λ_{max}^{KBr} 2.96 μ (NH); 6.00, 6.50 μ (amide C=O); 7.40, 8.56 μ (sulfonate); 9.30 μ (COC). The known[3] enantiomorph, methyl 2,4-di-*O*-mesyl-3-acetamido-β-L-xylopyranoside, had an optical rotation of +41.2° (2% in pyridine). Both compounds had identical infrared spectra.

Anal. Calcd. for $C_{10}H_{19}O_9NS_2$: C, 33.2; H, 5.30; N, 3.88; S, 17.7. Found: C, 33.5; H, 5.23; N, 3.83; S, 17.8.

Methyl 3-Acetamido-3-deoxy-2,4-di-*O*-mesyl-α-D-xylopyranoside (XXIa).—Mesylation of 309 mg. of methyl 3-acetamido-3-deoxy-α-D-xylopyranoside (XXa), as described above for the preparation of XXIb, gave 430 mg. (79%), m.p. 163–164°. Recrystallization from absolute alcohol afforded white crystals, m.p. 164–166°. $[\alpha]^{25}D$ +135° (0.3% in pyridine); λ_{max}^{KBr} 3.04 μ (NH); 6.05, 6.42 μ (amide C=O); 7.35, 8.48 μ (sulfonate); 9.55 (C-O-C).

Anal. Calcd. for $C_{10}H_{19}O_9NS_2$: C, 33.2; H, 5.30; N, 3.88; S, 17.7. Found: C, 33.8; H, 5.46; N, 3.94; S, 17.8.

Methyl 3-Acetamido-3-deoxy-2,4-di-*O*-acetyl-α-L-ribopyranoside (XXIIa).—A solution of 1 g. of methyl 3-acetamido-3-deoxy-2,4-di-*O*-mesyl-β-D-xylopyranoside (XXIb), 1.14 g. of anhydrous sodium acetate and 15 cc. of 95% aqueous 2-methoxyethanol was refluxed for 24 hours. The cooled solution was filtered from 380 mg. (116%) of sodium methanesulfonate, m.p. >250°, and then evaporated to dryness *in vacuo*. The residue was heated on the steam-bath with 10 cc. of reagent pyridine and 10 cc. of acetic anhydride for one hour. After dilution with 60 cc. of ice water, the solution was extracted with five 25-cc. portions of chloroform. The combined chloroform extracts, dried with magnesium sulfate, were evaporated to dryness *in vacuo*. The residue was twice dissolved in toluene and evaporated to dryness *in vacuo* to remove pyridine. Crystallization of the final glass-like residue (800 mg.) from ethyl acetate–heptane afforded 530 mg. (66%) of product, m.p. 116–118°.

In a pilot run the yield was 413 mg. (52%), m.p. 117–119°. Recrystallization from ethyl acetate–heptane gave white crystals, m.p. 119–120°, $[\alpha]^{25}D$ −92.5° (2% in $CHCl_3$); λ_{max}^{KBr} 3.05 μ (amide NH); 5.80 μ (ester C=O); 6.00, 6.57 μ (amide C=O); 9.18, 9.50, 9.70 μ (C-O-C). The known[3] enantiomorph, methyl 3-acetamido-3-deoxy-2,4-di-*O*-acetyl-α-D-ribopyranoside, had an optical rotation of +93.7° (1.6% in $CHCl_3$). Both compounds had identical infrared spectra.

Anal. Calcd. for $C_{12}H_{19}O_7N$; C, 49.8; H. 6.62; N, 4.85. Found: C, 50.2; H, 6.48; N, 4.81.

Methyl 3-Acetamido-3-deoxy-2,4-di-*O*-acetyl-β-L-ribopyranoside (XXIIb).—From 378 mg. of methyl 3-acetamido-3-deoxy-2,4-di-*O*-mesyl-α-D-xylopyranoside (XXIa) there was obtained 216 mg. (72%) of product, m.p. 148–150°, as described above for the preparation of XXIIa. Recrystallization from ethyl acetate–heptane gave white crystals, m.p. 148–150°, $[\alpha]^{25}D$ +116° (0.8% in $CHCl_3$); λ_{max}^{KBr} 3.00 μ (amide NH); 5.74 μ (ester C=O); 5.96, 6.54 μ (amide C=O); 8.80, 9.30 μ (C-O-C). Hydrolysis of this compound with 1% aqueous hydrochloric acid solution gave 3-amino-3-deoxy-L-ribose·HCl (XXIII) (see below).

Anal. Calcd. for $C_{12}H_{19}O_7N$: C, 49.8; H, 6.62; N, 4.85. Found: C, 49.5; H, 6.45; N, 4.66.

3-Amino-3-deoxy-L-ribose Hydrochloride (XXIII). A. From Methyl 3-Acetamido-3-deoxy-2,4-di-*O*-acetyl-α-L-ribopyranoside (XXIIa).—A solution of 530 mg. of XXIIa in 10 cc. of 1% hydrochloric acid, to which had been added 0.15 cc. of concentrated hydrochloric acid, was refluxed for 22 hours. The solution was clarified with Norit and was evaporated to a sirup *in vacuo* (water-bath temperature 50–55°). The sirup crystallized on cooling. Trituration with 10 cc. of acetic acid gave 210 mg. (62%) of product, m.p. 168° dec. Recrystallization from 0.3 cc. of water by addition of 5 cc. of acetic acid gave white crystals, m.p. 169° dec., $[\alpha]^{25}D$ +18.6° (2% in H_2O). The product gave a positive test with Benedict reagent.

Anal. Calcd. for $C_5H_{11}O_4N$·HCl: C, 32.4; H, 6.52; N, 7.55. Found: C, 32.5; H, 6.48; N, 7.86.

B. From Methyl 3-Acetamido-3-deoxy-2,4-di-*O*-acetyl-β-L-ribopyranoside (XXIIb).—Hydrolysis of 166 mg. of XXIIb as described above in preparation A afforded 75 mg. (70%) of product, m.p. 166° dec. Recrystallization as in preparation A gave white crystals, m.p. 169° dec., $[\alpha]^{25}D$ +21° (1% in H_2O). The compound gave an infrared spectrum identical with that of the product obtained by procedure A.

Anal. Calcd. for $C_6H_{11}O_4N\cdot HCl$: C, 32.4; H, 6.52; N, 7.55. Found: C, 32.4; H, 6.52; N, 7.80.

Methyl 3-Phthalimido-3-deoxy-β-D-xylofuranoside (XXIV, C).—A solution of 4.33 g. of residual gum B (mainly methyl 3-amino-3-deoxy-β-D-xylofuranoside, XVIIb) and 4.33 g. of phthalic anhydride in 43 cc. of dimethylformamide was refluxed for 3 hours and then evaporated to dryness *in vacuo*. The residue was dissolved in 20 cc. of water and the solution saturated with sodium chloride and extracted with three 20-cc. portions of chloroform. The combined chloroform extracts were washed with excess saturated aqueous sodium bicarbonate, dried with magnesium sulfate and evaporated to dryness *in vacuo* to give 6 g. of a sirup. Crystallization from ethyl acetate–heptane afforded 3.35 g. (43%) of product which was obtained in two crops, m.p. 139–142°. When the reaction time was 90 minutes instead of 3 hours as above, the yield was 41% (300 mg.), m.p. 140–142°. In a pilot run, when the reaction time was 45 minutes, the yield was 20% (100 mg.), m.p. 140–142°. Recrystallization from ethyl acetate–heptane afforded white crystals, m.p. 140–142°, $[\alpha]^{25}D$ +90° (2% in $CHCl_3$); λ_{max}^{KBr} 2.92 μ (OH); 5.67, 5.85 μ (C=O of phthalimido).

Anal. Calcd. for $C_{14}H_{15}O_6N$: C, 57.4; H, 5.15; N, 4.78. Found: C, 57.2; H, 5.53; N, 5.05.

Methyl 3-Phthalimido-3-deoxy-α-D-xylofuranoside.—By refluxing a solution of 75 mg. of crystalline methyl 3-amino-3-deoxy-α-D-xylofuranoside (XVIIa) and 75 mg. of phthalic anhydride in 3 cc. of dimethylformamide for 90 minutes, there was obtained, as described above for the preparation of XXIV, 37 mg. (27%) of product, m.p. 126–128°. Recrystallization from ethyl acetate–heptane afforded white crystals, m.p. 128–129°, $[\alpha]^{25}D$ +231° (0.4% in $CHCl_3$); λ_{max}^{KBr} 2.92 μ (OH); 5.63, 5.84 μ (C=O of phthalimido).

Anal. Calcd. for $C_{14}H_{15}O_6N$: C, 57.4; H, 5.15; N, 4.78. Found: C, 57.1; H, 5.39; N, 4.95.

Methyl 3-Acetamido-3-deoxy-β-D-xylofuranoside.—To a solution of 323 mg. of gum B (mainly methyl 3-amino-3-deoxy-β-D-xylofuranoside, XVIIb) in 2 cc. of water was added 0.3 cc. of acetic anhydride. The mixture was shaken for 7 minutes, then evaporated to dryness *in vacuo*. Crystallization of the residual sirup from ethyl acetate–absolute alcohol afforded 183 mg. (45%) of product which was obtained in two crops, m.p. 107–109°. Recrystallization from ethyl acetate–absolute alcohol gave white crystals, m.p. 109–110°, $[\alpha]^{25}D$ −30.7° (2% in H_2O); λ_{max}^{KBr} 3.05, 3.41 μ (OH and NH); 6.07, 6.48 μ (secondary amide); 8.81, 9.1, 9.5 μ (C–O–C and C–OH). This compound failed to consume any periodate in aqueous sodium bicarbonate after 30 minutes.

Anal. Calcd. for $C_8H_{15}O_5N$: C, 46.8; H, 7.36; N, 6.83. Found: C, 46.9; H, 7.61; N, 6.88.

PEARL RIVER, N. Y.

[CONTRIBUTION FROM THE ORGANIC CHEMICAL RESEARCH SECTION, PEARL RIVER LABORATORIES, RESEARCH DIVISION, AMERICAN CYANAMID CO.]

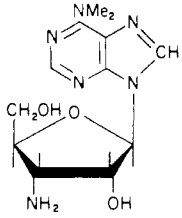
The Synthesis of 9-(3-Amino-3-deoxy-β-D-xylofuranosyl)-6-dimethylaminopurine, an Analog of the Aminonucleoside Derived from Puromycin

BY ROBERT E. SCHAUB, MARTIN J. WEISS AND B. R. BAKER

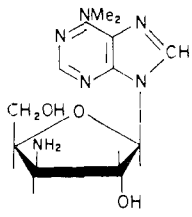
RECEIVED MARCH 6, 1958

The subject nucleoside II was prepared by condensation of 2,5-di-*O*-benzoyl-3-phthalimido-3-deoxy-D-xylofuranosyl chloride (XVIII) with 6-chloropurine-mercuri chloride followed by dimethylamine and butylamine treatment. Halogenose XVIII was prepared from methyl 3-phthalimido-3-deoxy-β-D-xylofuranoside (XV) by 2,5-di-*O*-benzoylation, acetolysis of the glycosidic linkage and, finally, ethereal hydrogen chloride treatment. Attempts to prepare II *via* the reaction of ammonia with 9-(2,3-anhydro-β-D-ribofuranosyl)-6-dimethylamino-2-methylmercaptopurine (VIII) or with the corresponding 5′-*O*-trityl derivative III failed. The synthesis of the 2,3-anhydroribofuranosyl nucleosides III and VIII are described.

A pertinent analog of the aminonucleoside I derived from the antibiotic puromycin[1] is 9-(3-amino-3-deoxy-β-D-xylofuranosyl)-6-dimethylaminopurine (II). Analogs of I are of interest because of the carcinostatic[2] and trypanocidal[3] activities in experimental animals which this compound exhibits. This paper describes the synthesis of analog II.

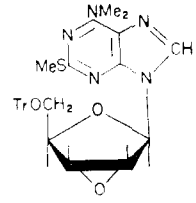


I



II

Previous work from this Laboratory has shown that aminonucleosides can be prepared by the amination of anhydronucleosides. Thus, a 3-aminoarabinoside was prepared by reaction of the corresponding 2,3-anhydrolyxofuranosylpurine with ammonia.[4] By analogy, it was expected that the synthesis of II would proceed from the reaction of ammonia with a 2,3-anhydroribofuranosylpurine, such as III. The reaction of ammonia with the epoxide group of III could conceivably take place at C-2 as well as at the required position, C-3. However, inasmuch as the related anhydronucleoside 7-(2,3-anhydro-5-*O*-trityl-β-D-ribofuranosyl)-theophylline already had been shown[5] to react in high yield with sodium ethyl mercaptide at C-3, it was reasonable to expect that III would react with ammonia also at C-3 to give the desired 3′-aminoxyloside.



III

(1) For the chemistry of puromycin see B. R. Baker and co-workers, THIS JOURNAL, **77**, 12 (1955), and preceding papers.

(2) P. L. Bennett, S. L. Halliday, J. J. Oleson and J. H. Williams, "Antibiotics Annual 1954–1955," Medical Encyclopedia, Inc., New York, N. Y., 1954, pp. 766–769.

(3) R. I. Hewitt, A. R. Gumble, W. S. Wallace and J. H. Williams, *Antibiotics & Chemotherapy*, **4**, 1222 (1954).

(4) B. R. Baker and R. E. Schaub, THIS JOURNAL, **77**, 5900 (1955).

(5) J. Davoll, B. Lythgoe and S. Trippett, *J. Chem. Soc.*, 2230 (1951).