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ACYLOXY NEIGHBORING-GROUP PARTICIPATION IN THE ACID-CATALYZED CLEAVAGE OF METHYL 2,3-ANHYDRO-β-D-RIBOFURANOSIDE*

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ABSTRACT

The reaction of methyl 2,3-anhydro-β-D-ribofuranoside with hydrogen bromide in an acetic acid–acetic anhydride solution leads to the formation of methyl 2,3-di-*O*-acetyl-5-bromo-5-deoxy-α,β-D-xylofuranoside. Similar treatment of methyl 2,3-anhydro-5-*O*-benzoyl-β-D-ribofuranoside provided methyl 2-*O*-acetyl-3-*O*-benzoyl-5-bromo-5-deoxy-α,β-D-xylofuranosides. The position of halogen substitution was ascertained by hydrogenolysis to the resultant 5-deoxy sugars, which were characterized by their n.m.r. spectra. Confirmation of the structural assignment for methyl 2-*O*-acetyl-3-*O*-benzoyl-5-deoxy-α,β-D-xylofuranoside was obtained by synthesis from 1,2-*O*-isopropylidene-α-D-xylofuranose. The formation of the 5-bromo derivatives under the reported conditions probably occurred through the intermediacy of the 3,5-acyloxonium ions. Similar conversions were observed when the starting compound was treated with hydrogen chloride, acetyl bromide, or acetyl chloride in acetic acid–acetic anhydride solutions.

INTRODUCTION

Neighboring-group participation in reactions of carbohydrates has been the subject of numerous investigations and reviews[1–3]. In particular, epoxide cleavage with neighboring group assistance of an acyloxy substituent is well documented in pyranosides[4]. This report deals with the serendipitous observation of an acyloxy neighboring-group participation in the cleavage of methyl 2,3-anhydro-β-D-ribofuranosides **1** and **3**. The interest in this project was prompted by our previous report[5] of the significant activity *in vitro* of 1-(3-bromo-3-deoxy-β-D-xylofuranosyl)cytosine hydrochloride against P815 leukemia cells in culture. It was planned to effect a total synthesis of this compound by condensation of a suitably protected 3-bromo-3-deoxy-D-xylofuranosyl derivative with the appropriate aglycon.

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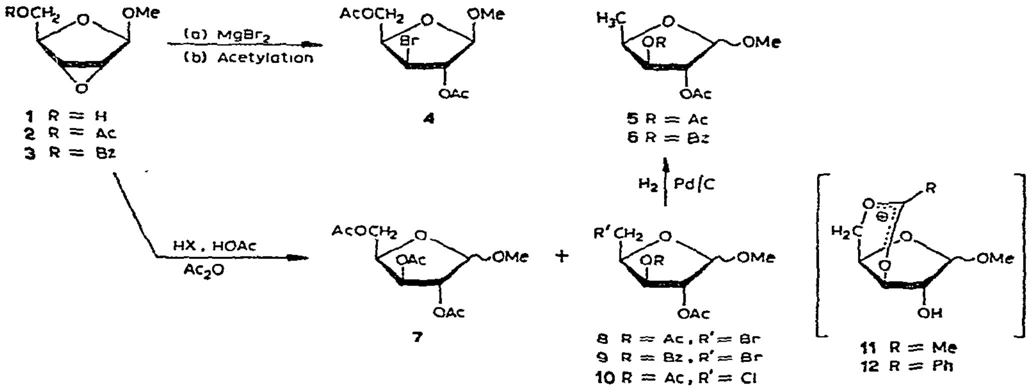
The desired sugar (as the diacetate **4**) had been synthesized (in 29% yield) by cleavage of methyl 5-*O*-acetyl-2,3-anhydro-β-D-ribofuranoside (**2**) with magnesium bromide, and subsequent acetylation[6]. During attempts to synthesize **4** in improved yield, we observed neighboring-group participation in the cleavage of pentofuranoside epoxides. This finding was unexpected in view of the numerous reports of epoxide opening of methyl 2,3-anhydro-β-D-ribofuranosides[6–10] under various conditions to yield preponderantly 3-substituted xylofuranosides. Although Reist and Holton[6] recognized the possibility of neighboring-group participation in the epoxide cleavage of **2**, they found no evidence for the presence of products resulting from such participation.



RESULTS AND DISCUSSION

In an attempt to effect a one-step synthesis of **4** from **1**, the epoxide was treated with an acetic acid–acetic anhydride–hydrogen bromide. Under these conditions, **1** provided a mixture of two compounds, as shown by t.l.c. (R_F of major component, 0.53; of minor component, 0.24). After separation by column chromatography, both the major component (I) and the minor component (II) were found to be anomeric mixtures, as shown by their n.m.r. spectra. On the basis of its n.m.r. spectrum, component II was tentatively assigned structure **7**. The n.m.r. spectrum of I, while superficially consistent with that expected for **4**, was not in accord with that reported previously[6]. The spectrum was more complicated, and the 5-proton absorption appeared at δ 3.52, whereas these protons were reported to resonate at δ 4.3. Hydrogenolysis of I resulted in the isolation of an anomeric mixture of 5-deoxyfuranosides (**5**), as shown by the appearance of two doublets in the methyl region of the n.m.r. spectrum. On this basis, I was assigned structure **8***. Similarly, treatment of **1** with

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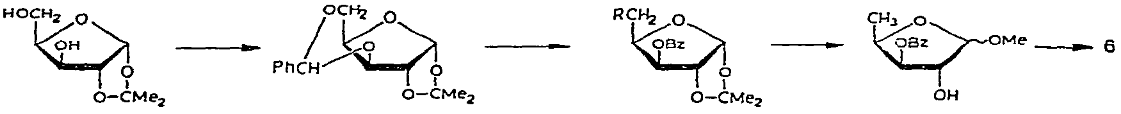
*Although less likely, the isomeric 5-bromo-5-deoxy-D-arabinofuranoside could not be excluded *a priori* as the structure of I. This product would arise from 2,5-neighboring-group participation. The independent synthesis of **6** and comparison with the products of hydrogenolysis of **9** precluded the intermediacy of the 2,5-acyloxonium ion in these reactions.

acetic acid–acetic anhydride–hydrogen chloride resulted in the formation of **7** and the analogous **10**. Both **8** and **10** must be formed by neighboring-group participation of the 5-substituent in the opening of the epoxide ring. In both instances, the products of epoxide cleavage (**7**, **8**, and **10**) were isolated as anomeric mixtures, with the β anomer predominating. Anomerization must occur under the reaction conditions, since **1** contained no α anomer, as shown by n.m.r. spectrometry. Subsequently, it was found that the ratio of **8** to **7** formed in the reaction of **1** with hydrogen bromide was at least partially dependent on the proportion of acetic acid in the reaction mixture. Lowering the initial concentration of acetic acid decreased the amount of **7** formed. In addition, the reaction of **1** with acetyl bromide in an acetic acid–acetic anhydride solution led to the exclusive isolation of **8** (see Experimental section). In the case of the reaction of **1** with hydrogen chloride, however, these same modifications did not lead to significantly higher yields of **10**. This finding might be rationalized on the basis of the relative nucleophilicity of the halide ions in relation to the acetate ion.

In order to show the possible intermediacy of an acyloxonium ion in the formation of **8** and **10**, the 5-*O*-benzoylepoxide **3** was treated with acetic acid–acetic anhydride–hydrogen bromide. An anomeric mixture (predominantly β) of **9** was obtained in nearly quantitative yield. Hydrogenolysis resulted in the isolation of an anomeric mixture of the corresponding 5-deoxy-D-xylofuranosides **6**. From these results, **8**–**10** are probably formed by nucleophilic attack of a halide ion on an intermediate acyloxonium ion (**11**, **12**). To confirm the structure of **6** (and by extrapolation, the structures of **8**–**10**), the synthesis of methyl 2-*O*-acetyl-3-*O*-benzoyl-5-deoxy-D-xylofuranosides (**6**) was undertaken.

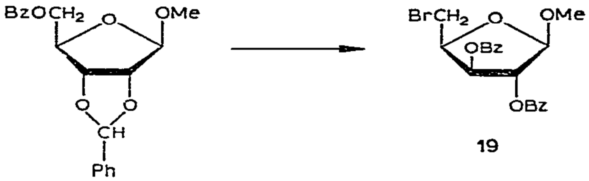
Treatment of 1,2-*O*-isopropylidene-α-D-xylofuranose (**13**) with α,α-dimethoxytoluene (benzaldehyde dimethyl acetal) in *N*,*N*-dimethylformamide in the presence of a trace of acid[11] gave 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-α-D-xylofuranose[12] (**14**) in good yield. Reaction of **14** with *N*-bromosuccinimide[13] resulted in the nearly quantitative formation of 3-*O*-benzoyl-5-bromo-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose[14] (**15**), which was further hydrogenolyzed to give 3-*O*-benzoyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose (**16**). Treatment of this compound with methanolic hydrogen chloride provided an anomeric mixture of **17**, which was partially separated on column chromatography. The early fractions were enriched in the α anomer, and the later fractions in the β anomer. Acetylation of these materials, separately, gave products that had n.m.r. spectra indentical to the products obtained by hydrogenolysis of **9**. This confirmed the structure of the products of the reaction of **3** with hydrogen bromide in acetic acid–acetic anhydride, and, by analogy, of the



13 14 15 R = Br 16 R = H 17

reaction of **1** to yield **8** and **10**. Presumably, the principal reaction pathway involves the formation of the 3,5-acyloxonium ions, **11** and **12**, followed by nucleophilic attack of the halide ion at the primary position.

Although acyloxy neighboring-group participation in cleavage of cyclopentanol epoxide esters[15] and pyranoside epoxide esters[4] has been reported, we believe this is the first instance of acyloxy group-participation in the cleavage of a pentofuranoside epoxide. A similar rearrangement has been observed by treatment of methyl 5-*O*-benzoyl-2,3-*O*-benzylidene-β-D ribofuranoside (**18**) with *N*-bromosuccinimide[13], wherein **19** was obtained by neighboring group participation of the 5-*O*-benzoyl group.



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EXPERIMENTAL

General. — Solutions were evaporated at temperatures below 45° under diminished pressure. Melting points are uncorrected. N.m.r. spectra were recorded at 60 MHz with a Varian A-60 spectrometer, on solutions in chloroform-*d* and with tetramethylsilane as internal standard; abbreviations: singlet (s), doublet (d), double doublet (dd), and broad (b). Thin-layer chromatography (t.l.c.) was performed on microscope slides (75 × 25 mm) coated with a 0.25-mm layer of silica gel PF_{254} (Brinkman Instruments, Inc.). The plates were eluted with 6:1 (v/v) benzene–ethyl acetate. Detection was accomplished by spraying the plates with methanolic sulfuric acid. Column chromatography was performed on either Woelm Silica Gel (0.063–0.2 mm) (distributed by ICN Pharmaceuticals, GmbH and Co., West Germany) or on Silica Gel G (type 60) (Brinkman Instruments, Inc.). Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

*Methyl 2,3-di-O-acetyl-5-bromo-5-deoxy-α,β-*D*-xylofuranoside* (**8**). — *Method A.* Methyl 2,3-anhydro-β-D-ribofuranoside[16] (**1**, 4.0 g) was dissolved in 2:1 acetic acid–acetic anhydride (30 ml), and a 30% solution of hydrogen bromide in acetic acid (5 ml) was added with stirring and cooling in an ice-bath. After 45 min, more acetic anhydride (5 ml) and hydrogen bromide in acetic acid (1 ml) were added, and the solution was allowed to come to room temperature. The reaction was stirred until only two spots were evident on t.l.c. (R_F of major product 0.53; R_F of minor product 0.24). Crushed ice (~30 ml) was added, and the suspension was stirred vigorously. The resulting solution was extracted with benzene (3 × 300 ml) and the extracts washed with a sodium hydrogencarbonate solution. The organic layer was dried (sodium sulfate) and evaporated, and the residual syrup applied to a silica gel column (150 g, Woelm). Elution with 6:1 (v/v) benzene–ethyl acetate provided I (6.1 g), II (1.2 g), and a mixture of I and II (0.8 g). The n.m.r. of I showed it to be an anomeric mixture of **8**, the major component being the β anomer as deduced from the following data: δ 2.09 (s, OAc), 2.11 (s, OAc), 3.39 (s, OCH_3), 3.52 (d, $J_{4,5}$ 4 Hz), 4.57 (broadened quintet, $J_{4,5}$ 6 Hz), 4.88 (s), 5.06 (s), and 5.35 (quartet, $J_{3,4}$ 6 Hz; $J_{2,3}$ ~1 Hz).

In addition, absorptions at δ 3.41 (shoulder on signal at 3.39), 5.03 (triplet, J ~3 Hz), and 5.41–5.58 (multiplet), presumably those of the α anomer, were evident. Compound **8** is unstable upon storage at room temperature, becoming very dark after two weeks.

Anal. Calc. for $C_{10}H_{15}BrO_6$: C, 38.60; H, 4.86; Br, 25.68. Found: C, 38.72; H, 4.79; Br, 25.71.

Structure **7** was tentatively assigned to Fraction II (predominantly the β anomer) on the basis of its n.m.r: δ 2.10 (broad singlet, 9 H, OAc), 3.39 (s, 3 H, OCH_3), 4.26 (d, 2 H, $J_{4,5}$ 5 Hz), 4.3–4.78 (poorly resolved multiplet, 1 H), 4.89 (broad singlet, 1 H), 5.10 (d, 1 H, $J_{2,3}$ ~1 Hz), and 5.36 (quartet, 1 H, $J_{3,4}$ 6 Hz; $J_{2,3}$ ~1 Hz). Additional minor absorptions were attributed to the anomer of **7**.

Method B. Methyl 2,3-anhydro-β-D-ribofuranoside (**1**, 1.0 g) was dissolved in acetic anhydride (4 ml). The solution was cooled in ice, and 1:1 (v/v) acetyl bromide–acetic acid (2 ml) was added over a period of 5 min. The reaction mixture was kept at 0° for 22 h, and then poured into a cold, saturated sodium hydrogencarbonate solution (100 ml) with stirring. The resulting mixture was extracted with ethyl acetate (2 × 100 ml), and the combined organic extracts were washed successively with a saturated sodium hydrogencarbonate solution, and then with water, dried (sodium sulfate), and evaporated. A light-yellow oil (**8**, 2.25 g, contaminated with a small amount of acetic anhydride) was obtained. This material was homogeneous on t.l.c. in a number of solvent systems (R_F 0.53 in benzene–ethyl acetate, 6:1, v/v). An n.m.r. spectrum of this material showed it to be a mixture of anomers of **8** with a β to α ratio of ~6:1. The absorptions of the anomers were the same as described above. This material was used in the next step without further purification.

*Methyl 2,3-di-O-acetyl-5-chloro-5-deoxy-α,β-*D*-xylofuranoside* (**10**). — A solution of **1** (4.0 g) in acetic anhydride (10 ml), was cooled in ice and a 10% solution of hydrogen chloride in acetic acid (20 ml) was added. After 1 h, acetic anhydride was added (5 ml). After 2 h, more hydrogen chloride in an acetic acid solution (5 ml) was added, and the solution was allowed to reach room temperature, before being stirred overnight. T.l.c. indicated one major product (R_F 0.40), and three minor products (R_F 0.24, 0.09, and 0.00). The mixture was poured with stirring into an ice–sodium hydrogencarbonate solution. The aqueous mixture was extracted with dichloromethane (2 × 500 ml). The combined organic fractions were washed with a sodium hydrogencarbonate solution, dried (sodium sulfate), and evaporated. The residual oil showed two products on t.l.c. (R_F of major compound 0.40; of minor compound 0.24). Chromatography on silica gel (Silica Gel G, 150 g, gradient elution with benzene–ethyl acetate 8:1 to 6:1, v/v) gave **10** (3.8 g, single spot on t.l.c.: R_F 0.40) and **7** (1.9 g). These products were identified by comparison of the n.m.r. spectra with those of the compounds obtained by treatment of **1** with hydrogen bromide–acetic acid–acetic anhydride. The n.m.r. spectrum of the anomeric mixture of **10** showed δ 2.06 (s, OAc), 3.33 (s, OCH_3), 3.59 (d, $J_{4,5}$ 6 Hz), 4.43 (broadened quintet, $J_{4,5}$ ~6 Hz), 4.80 (s), 4.97 (s), and 5.27 (quartet, $J_{3,4}$ 6 Hz; $J_{2,3}$ ~1 Hz), which were attributed to the β anomer. Additional absorptions at δ 3.52 (d, $J_{4,5}$ 6 Hz), 4.95 (triplet, J ~3 Hz), and 5.35–5.53 (poorly resolved multiplet) were ascribed to the α anomer. The ratio of β to α anomer was ~9:1.

Anal. Calc. for $C_{10}H_{15}ClO_6$: C, 45.04; H, 5.67; Cl, 13.29. Found: C, 45.39; H, 5.79; Cl, 13.48.

*Methyl 2,3-di-O-acetyl-5-deoxy-α,β-*D*-xylofuranoside* (**5**). — Crude **8** (2.25 g, obtained from the reaction of 1.0 g of **1** with 4 ml acetic anhydride, 1 ml acetic acid, and 1 ml acetyl bromide) was dissolved in absolute ethanol (100 ml) and triethylamine (10 ml) was added. The mixture was hydrogenated over 10% palladium-on-charcoal (500 mg) in a Parr apparatus (2 atm, initial pressure) for 2 h. The solution was filtered through Celite, and the filtrate evaporated. The residue was dissolved in ether, triethylamine hydrobromide was filtered off, and evaporation gave a syrup; n.m.r. spectrometry showed this to be an anomeric mixture of 5-deoxy sugars (**5**), the major product being the β anomer (ratio of β to α ~6:1); n.m.r. data (β anomer): δ 1.22 (d, $J_{4,5}$ 6 Hz), 2.06 (s, OAc), 3.34 (s, OCH_3), 4.42 (broad quintet, $J_{4,5}$ 6 Hz), 4.73 (broad singlet), 5.01 (s), and 5.07 (distorted quartet); the presence of the α anomer was evident from minor absorptions at δ 1.14 (d, $J_{4,5}$ 6 Hz), 3.32 (s, OCH_3), and a complex multiplet at δ 5.15–5.39. An analytical sample of the anomeric mixture was obtained by passage through a silica gel column [150 g, Woelm, eluted with 3:1 (v/v) petroleum ether–ethyl acetate].

Anal. Calc. for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94. Found: C, 51.44; H, 6.89.

*Methyl 2,3-anhydro-5-O-benzoyl-β-*D*-xylofuranose* (**3**). — Methyl 2,3-anhydro-β-D-ribofuranoside (**1**, 21.0 g) was dissolved in cold pyridine (100 ml) and benzoyl chloride (23 g, 19.1 ml) was added dropwise with stirring. After 1.5 h, the solution was poured into water (800 ml) with stirring. The amorphous precipitate was filtered and then dissolved in chloroform. This solution was washed with water, saturated sodium hydrogencarbonate, and water, and then dried (sodium sulfate). Upon evaporation, a colorless, mobile oil was obtained which was dissolved in boiling ethanol (300 ml), and water was added to turbidity. Upon cooling overnight at 0°, long needles were obtained (34.3 g). Recrystallization from petroleum ether provided **3**, m.p. 58°, $[\alpha]_D^{27} -112°$ (c 1.08, chloroform); n.m.r. data: δ 3.39 (s, 3 H, OCH_3), 3.73 (d, 1 H, J ~3 Hz), 3.86 (d, 1 H, J 3 Hz), 4.43 (s, 3 H, H-4, H-5, H-5′), 5.00 (s, 1 H, H-1), and 7.4–8.2 (5 H, benzoyl protons).

Anal. Calc. for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.23; H, 5.48.

*Methyl 2-O-acetyl-3-O-benzoyl-5-bromo-5-deoxy-*D*-xylofuranosides* (**9**). — Compound **3** (1.9 g) was dissolved in cold acetic anhydride (20 ml) and a 30% solution of hydrogen bromide in acetic acid (8 ml) was added with stirring. The solution was allowed to warm to room temperature (4 h) and then kept overnight at 0°. T.l.c. indicated the presence of one major product (R_F 0.56; R_F of **3** 0.51). The solution was poured into a cold, saturated sodium hydrogencarbonate solution, and solid sodium hydrogencarbonate was added to keep the solution slightly basic. The solution was extracted with ethyl acetate (200 ml), and the organic fractions were washed with saturated sodium hydrogencarbonate and then water, dried (sodium sulfate) and evaporated. An anomeric mixture of **9** was obtained as a light-yellow oil (3.1 g) R_F 0.56) contaminated with a small amount of acetic anhydride. An analytical sample of **9** was obtained by passage through a column of silica gel [75 g, Woelm, eluted with 6:1 (v/v) benzene–ethyl]; n.m.r. data of the anomeric mixture (β anomer): δ 2.09 (s, 3 H, OAc), 3.39 (s, 3 H, OCH_3), 3.51 (d, 2 H, $J_{4,5}$ 6 Hz), 4.62 (broadened quartet, 1 H, $J_{4,5}$ 6 Hz), 4.87 (s, 1 H), 5.16 (slightly split s, 1 H), 5.50 (dd, 1 H, $J_{3,4}$ 6 Hz, $J_{2,3}$ <1 Hz), and 7.3–8.1 (5 H, benzoate); the presence of the α anomer was shown by absorptions at δ 3.37 and a complex multiplet centered at δ 5.67. The ratio of β to α anomer was ~8:1, as judged by the n.m.r. spectrum; this varied from 6:1 to ~10:1 in separate preparations.

Anal. Calc. for $C_{15}H_{17}BrO_6$: C, 48.28; H, 4.59; Br, 21.41. Found: C, 48.42; H, 4.70; Br, 21.69.

*Methyl 2-O-acetyl-3-O-benzoyl-5-deoxy-*D*-xylofuranosides* (**6**). — Compound **9** (2.5 g) was dissolved in absolute ethanol (75 ml) and triethylamine (10 ml), and the mixture was hydrogenated over 10% palladium-on-charcoal (430 mg) in a Parr apparatus (2 atm, initial pressure) for 2 h. The reaction mixture was filtered through Celite and evaporated. A solution of the residue in ethyl acetate was washed with water (2 × 50 ml), dried (sodium sulfate), and evaporated to give a light-yellow oil (1.8 g, R_F 0.66); the n.m.r. spectrum showed it to be an anomeric mixture of 5-deoxy sugar (**6**) (ratio of β to α anomer: ~6:1). An analytical sample of the mixture was obtained by passage through a column of silica gel (75 g, Woelm, gradient elution with 9:1 to 3:1 benzene–dichloromethane); n.m.r. data of the mixture: (β-anomer): δ 1.30 (d, $J_{4,5}$ 6 Hz), 2.05 (s, OAc), 3.37 (s, OCH_3), 4.50 (center of broadened multiplet $J_{4,5}$ 6 Hz), 4.84 (s), 5.20 (bs), 5.35 (dd, $J_{3,4}$ 5 Hz, $J_{2,3}$ ~1 Hz), and 7.3–8.2 (benzoate); in addition, signals for the α anomer were evident at δ 1.22 (d, $J_{4,5}$ 6 Hz), 3.34 (s, OCH_3), 5.1 (distorted d, J ~2 Hz), and 5.56 (double triplet).

Anal. Calc. for $C_{15}H_{18}O_6$: C, 61.22; H, 6.17. Found: C, 61.09; H, 6.02.

*3,5-O-Benzylidene-1,2-O-isopropylidene-α-*D*-xylofuranose* (**14**). — 1,2-*O*-Isopropylidene-α-D-xylofuranose (15.0 g) was mixed with *N*,*N*-dimethylformamide (100 ml), α,α-dimethoxytoluene (13.0 g), and *p*-toluenesulfonic acid (0.15 g). The solution was evaporated on a rotary evaporator (bath temperature <65°). When evaporation was almost complete, another charge of α,α-dimethoxytoluene (5 g) and *N*,*N*-dimethylformamide (15 ml) was added, and evaporation was resumed. Crystallization occurred during evaporation. The residue was dissolved in ethyl acetate, and washed with a saturated sodium hydrogencarbonate solution (2 × 100 ml) and then water (1 × 100 ml). The organic layer was dried (sodium sulfate), evaporated, and the residual **14** was recrystallized from ethanol to give 18.8 g (81% yield), m.p. 123–123.5°, $[\alpha]_D^{27}$ $+1°$ (*c* 1.6, chloroform); additional material could be obtained from the mother liquors; n.m.r. data: δ 1.33 (s, 3 H, CH_3), 1.52 (s, 3 H, CH_3), 4.08–4.20 (complex multiplet, 2 H, H-4, H-5′), 4.41 (s, 1 H, H-3), 4.49 (d, H-5), 4.64 (d, 1 H, $J_{1,2}$ 4 Hz), 5.46 (s, 1 H, benzylic H), 6.07 (d, 1 H, $J_{1,2}$ 4 Hz), and 7.3–8.43 (5 H, aromatic). Compound **14** has been reported[12]; the synthesis, and the chemical and physical properties were not given.

Anal. Calc. for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.78; H, 6.61.

3-O-Benzoyl-5-bromo-5-deoxy-1,2-O-isopropylidene-α-D-xylofuranose (**15**). — Compound **14** (10.0 g) was mixed with carbon tetrachloride (150 ml) and barium carbonate (12.8 g). *N*-Bromosuccinimide (6.6 g) was added and the solution was boiled at reflux for 90 min, at which point t.l.c. indicated only one spot (R_F 0.65, R_F of **14** 0.54). The hot suspension was filtered, and the residue washed with hot carbon tetrachloride. The filtrate and washings were evaporated, the residual oil was dissolved in diethyl ether and washed with water (2 × 100 ml), and dried (sodium sulfate). After evaporation, a virtually quantitative yield of **15** was obtained as a colorless glass, $[\alpha]_D^{27}$ −40° (*c* 3.0, chloroform); lit.[14] $[\alpha]_D^{25}$ −46.6° (*c* 1.00, chloroform). The n.m.r. spectrum of this product was identical with that reported for **15**.

3-O-Benzoyl-5-deoxy-1,2-O-isopropylidene-α-D-xylofuranose **16**. — A solution of **15** (2.0 g) in ethanol (50 ml) and triethylamine (5 ml) was hydrogenated over 10% palladium-on-charcoal in a Parr apparatus (2 atm, initial pressure) for 3 h. Filtration through Celite and evaporation provided a light-yellow syrup which still contained **15**, as shown by t.l.c. and n.m.r. spectrometry. The syrup was redissolved in ethanol, and palladium-on-charcoal (280 mg) and triethylamine (5 ml) were added, and the hydrogenation was continued, as just described, for 3 h. The residue obtained following filtration and evaporation was dissolved in diethyl ether and washed with water. The ethereal solution was dried and evaporated to provide **16** (1.36 g, 87% yield) as a straw-colored syrup, $[\alpha]_D^{27}$ +5° (*c* 1.64, chloroform); lit.[17]: $[\alpha]_D$ +6.1° (*c* 0.9, chloroform); n.m.r. data: δ 1.31 (d, 3 H, $J_{4,5}$ 6 Hz), 1.32 (s, 3 H, CH_3), 1.54 (s, 3 H, CH_3), 4.55 (octet, 1 H, $J_{3,4}$ 3 Hz, $J_{4,5}$ 6 Hz), 4.65 (d, 1 H, $J_{1,2}$ 4 Hz), 5.37 (d, 1 H, $J_{3,4}$ 3 Hz), 6.00 (d, 1 H, $J_{1,2}$ 4 Hz), and 7.3–8.2 (5 H, benzoate). An analytical sample was obtained by chromatography on a preparative, thin-layer plate [Silica Gel PF_{254}, eluted with 6:1 (v/v) benzene–ethyl acetate].

Anal. Calc. for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 65.00; H, 6.41.

Methyl 3-O-benzoyl-5-deoxy-α,β-D-xylofuranoside (**17**). — Compound **16** (0.718 g) was dissolved in methanol (30 ml) and methanolic hydrogen chloride (1 ml, saturated at 0°) was added. The flask was sealed and kept at room temperature for 3 days. The mixture was evaporated, dissolved in chloroform, washed with saturated sodium hydrogencarbonate and water, dried, and evaporated to provide a mixture of methyl glycosides (**17**, 622 mg, 95%). A partial separation of the anomers was obtained by chromatography on a silica gel column [75 ml, Woelm, gradient elution with 8:1 to 5:1 (v/v) benzene–ethyl acetate]; n.m.r. data of the first fraction showed it to be enriched in the α anomer: δ 1.24 (d, 3 H, $J_{4,5}$ 6 Hz), 3.43 (s, 3 H, OCH_3), 4.2–4.71 (m, 2 H, H-2 superimposed on H-4, $J_{4,5}$ 6 Hz), 4.94 (d, 1 H, $J_{1,2}$ 4 Hz), 5.1–5.4 (complex multiplet, 1 H), and 7.26–8.1 (5 H, benzoyl); the later fractions were enriched in the β anomer: δ 1.34 (d, 3 H, $J_{4,5}$ 6 Hz), 3.37 (s, 3 H, OCH_3), 3.76 (bd, 1 H), 4.24 (bs, 1 H), 4.56 (broad quintet, $J_{4,5}$ 6 Hz), 4.81 (d, 1 H, $J_{1,2}$ ~1 Hz), 5.11 (dd, 1 H, $J_{2,3}$ ~2 Hz, $J_{3,4}$ ~5 Hz), and 7.3–8.2 (5 H, benzoyl).

Separate acetylation of the above fractions (compound **17**, enriched in α and β anomer, respectively) was performed in pyridine (~3 ml) with acetic anhydride (0.5 and 1 ml, respectively). When acetylation was complete (as shown by t.l.c.) a small amount of water (1 ml) was added. The solutions were evaporated, and the residues treated by additions and evaporations of toluene to remove residual pyridine and acetic acid. The n.m.r. spectra of these products were superimposable on the respective portions of the n.m.r. of the mixture obtained from hydrogenolysis of **9**; n.m.r. data of the acetylation product of **17** enriched in β anomer: δ 1.30 (d, 3 H, $J_{4,5}$ 6 Hz), 2.08 (s, 3 H, OAc), 3.38 (s, 3 H, OCH_3), 4.57 (b quintet $J_{4,5}$ ~6 Hz), 4.84 (s, 1 H, H-1), 5.18 (distorted doublet, 1 H, $J_{2,3}$ ~1 Hz), 5.35 (dd, 1 H, $J_{2,3}$ ~1 Hz, $J_{3,4}$ ~5 Hz), and 7.2–8.2 (5 H, aromatic); n.m.r. data of the acetylation product of the fraction enriched in α anomer: δ 1.23 (d, 3 H, $J_{4,5}$ 6 Hz), 2.05 (s, 3 H, OAc), 3.34 (s, 3 H, OCH_3), 4.48 (broadened quintet, 1 H, $J_{4,5}$ 6 Hz), 5.11 (d, 1 H, overlapped on signal of H-2, $J_{1,2}$ ~2 Hz), 5.15 (dd, 1 H, $J_{1,2}$ ~2 Hz, $J_{2,3}$ ~2 Hz), 5.56 (double triplet, 1 H), and 7.2–8.2 (5 H, aromatic).

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