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The Reaction of Derivatives of D-Xylal and D-Arabinal with Hydrogen Chloride and Hydrogen Bromide

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Treatment of di-*O*-acetyl-D-xylal with hydrogen chloride or hydrogen bromide in benzene gives only small amounts of the expected 3,4-di-*O*-acetyl-2-deoxy-D-*threo*-pentopyranosyl halides. The main products are 3-halo-4-*O*-acetyl-2,3-dideoxy-D-*threo*-pentopyranosyl halides and small amounts of the corresponding D-*erythro*-derivatives. The reaction of di-*O*-acetyl-D-arabinal with hydrogen chloride or hydrogen bromide gives, on the other hand, largely the 3,4-di-*O*-acetyl-2-deoxy-D-*erythro*-pentopyranosyl halides and only small amounts of 3-halo-3-deoxy-compounds. Both di-*O*-benzoyl-D-xylal and di-*O*-benzoyl-D-arabinal give almost exclusively 3,4-di-*O*-benzoyl-2-deoxy-pentopyranosyl halides when treated with hydrogen halide. All the glycosyl halides were converted into 1-*O*-benzoyl-derivatives by treatment with silver benzoate prior to purification. A reaction mechanism is proposed, substantiated by studies of the reaction with deuterium bromide. The reaction of methyl 3,4-di-*O*-acetyl-2-deoxy-D-*threo*-pentopyranoside with hydrogen bromide gives, in addition to the expected 3,4-di-*O*-acetyl-2-deoxy-D-*threo*-pentopyranosyl bromide, a small amount of a 3-bromo-4-*O*-acetyl-2,3-dideoxy-D-*threo*-pentopyranosyl bromide. The structure of all products were determined by NMR spectroscopy.

The reaction of acetylated glycals with hydrogen chloride or hydrogen bromide in benzene solution leads to the formation of 2-deoxy-glycosyl halides.[1,2] These products are unstable and cannot be purified, but have, in the crude state, in many cases been used for the synthesis of nucleosides.[1,3] However, the yields are often low and byproducts are formed, indicating that the reaction between glycals and hydrogen halides gives other products than the 2-deoxy-glycosyl halides.[3] This has been confirmed recently by Maki and Tejima [4] who found that treatment of tri-*O*-acetyl-D-glucal with hydrogen bromide in glacial acetic acid gave, besides the expected 3,4,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranosyl bromide, an equal amount of 4,6-di-*O*-acetyl-3-bromo-2,3-dideoxy-D-*arabino*-hexopyranosyl bromide.

The reaction of di-*O*-acetyl-D-xylal and -D-arabinal with hydrogen chloride and hydrogen bromide has now been studied and results similar to those of Maki and Tejima [4] have been obtained.

Treatment of di-*O*-acyl-D-xylal (II) or di-*O*-acyl-D-arabinal (XI) with hydrogen chloride or hydrogen bromide in dry benzene gave crude products which were unstable. These were immediately treated with silver benzoate in dry acetonitrile without previous concentration of the benzene solution. By this procedure, mixtures of stable 1-*O*-benzoyl-derivatives were obtained which could be separated and purified by preparative thin layer chromatography.

Reaction between di-*O*-acetyl-D-xylal (II, R=Ac) and hydrogen chloride in benzene, followed by treatment with silver benzoate as described above, gave, after chromatography, the anomeric 1-*O*-benzoyl-3-chloro-4-*O*-acetyl-2,3-dideoxy-D-*threo*-pentopyranoses (IX, R=Ac, X=Cl) together with 1-*O*-benzoyl-3,4-di-*O*-acetyl-2-deoxy-α- and β-D-*threo*-pentopyranose (IV, R=Ac) (Table 1). When di-*O*-acetyl-D-xylal (II, R=Ac) was treated with hydrogen bromide as described above similar products, (IX, R=Ac, X=Br) and (IV, R=Ac), were isolated. In addition, some of the C_3-epimeric bromo-compounds (α- and β-X, R=Ac, X=Br) were formed. As seen from the product distribution (Table 1) little addition has occurred, the principal reaction being one leading to the 3-halo-2,3-dideoxy-compounds. Di-*O*-acetyl-D-arabinal (XI, R=Ac), on the other hand gave primarily the normal addition products (α- and β-XIII, R=Ac), accompanied by small amounts of the 3-halo-2,3-dideoxy-compounds (α- and β-IX, R=Ac, X=Cl or Br).

Table 1. Yields of products formed in the reaction of glycals or 2-deoxy-pentoses with hydrogen halide followed by treatment of the crude glycosyl halide with silver benzoate.

		Yield %							
	Hydrogen halide	IX		X		IV		XIII	
		α	β	α	β	α	β	α	β
II, R=Ac	HCl	6	54	t	t	6	13		
II, R=Ac	HBr	7	33	8	2	2	6		
XI, R=Ac	HCl	2	9	t	t			21	21
XI, R=Ac	HBr	3	9	t	t			19	18
II, R=Bz	HCl	3	8			22	25		
II, R=Bz	HBr	1	4			28	32		
XI, R=Bz	HCl							32	32
XI, R=Bz	HBr							32	32
V	HCl	9	45	5	2				
V	HBr	13	31	5	3				
I	HCl	t	t	t	t	16	32		
I	HBr	4	9	t	t	13	13		
XIII, R=Ac	HBr	1	2	t	t			15	15
IX, R=Ac	HBr	11	44	4	3				
II, R=Ac	DBr	10	27	6	4	t	t		
V	DBr	12	26	6	5				
I	DBr	1	6			12	15		

(t): traces are seen on TLC.

Di-*O*-benzoyl-D-xylal (II, R=Bz) and -D-arabinal (XI, R=Bz) under the same conditions both gave the simple 2-deoxy-compounds (IV and XIII, R=Bz); only from the xylal-derivative (II, R=Bz) was a small amount of the 3-halo-2,3-dideoxy-product (IX) observed (Table 1).

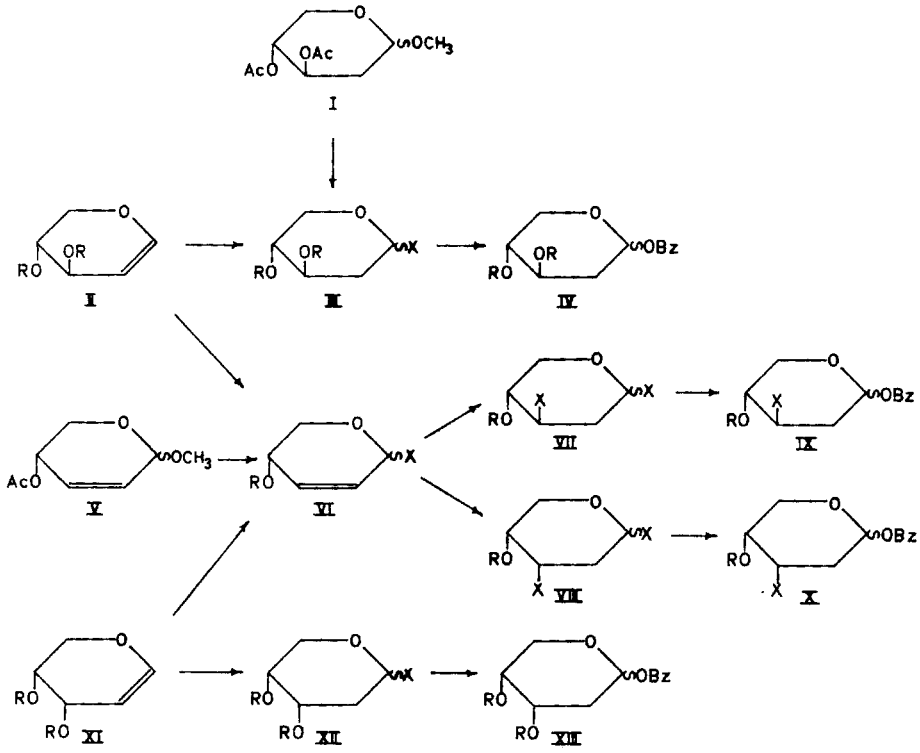

Fig. 1.

The configurations and conformations of the above products were determined by NMR spectroscopy. The conformation of all the products shown in Table 1 were determined from the H_4-H_{5a} and H_4-H_{5e} coupling constants (Table 2). When both of these are small, H_4 must be *gauche* to both the H_5-protons; consequently the conformation is predominantly *1C* (Fig. 2). If the H_4-H_{5a} coupling constant is large then H_4 must be axially oriented and the molecule is in the *C1* conformation.[5,6]

The anomeric configuration was easily determined from the pattern of H_1, which in all cases was found to be a triplet with a small spacing. This indicates that H_1 is *gauche* to two H_2-protons and thus equatorially oriented. The 1-*O*-benzoyl-group must therefore be axially oriented in all of the products discussed, probably conditioned by the anomeric effect.[5,7]

The tri-*O*-benzoyl-2-deoxy-D-*erythro*-pentopyranoses (XIII, R=Bz) have been described previously [8] and their spectra discussed.[9] The spectra of the

Table 2. Chemical shifts (δ-values) and coupling

Compound	Anomer	H_1	H_{2e}	H_{2a}	H_3	H_4	H_{5e}	H_{5a}
I	α	4.77(t)	2.21(m)	1.77(m)	5.27(m)	4.89(m)	3.81(q)	3.67(q)
	β	4.53(q)	2.21(m)	1.74(m)	4.9	4.8	3.38(q)	4.07(q)
XIII, R=Ac	α	6.23(t)	2.10 — 2.60		5.40	5.16(m)	3.82(q)	4.20(q)
	β	6.57(t)	2.10 — 2.60		5.56	5.36	4.15(q)	3.98(q)
IV, R=Ac	α	6.42(t)	2.00 — 2.70		5.44(m)	5.02(m)	4.00(q)	3.80(q)
	β	6.35(t)	2.44(m)	2.24	5.11	4.91	3.80(q)	4.33(q)
IX, R=Ac	α	6.34(t)	2.30—3.00		4.45(m)	5.12(m)	4.00(q)	3.72(q)
X=Br	β	6.34(t)	2.90(m)	2.56(m)	4.36(m)	5.17(m)	3.77(q)	4.57(q)
IX, R=Ac X=Br 2-deuterio	α	6.30(d)	2.30 — 2.70		4.43(q)	5.10(m)	4.03(q)	3.73(q)
	β	6.34(d)	2.20 — 2.60		4.35(t)	5.17(m)	3.77(q)	4.57(q)
X, R=Ac	α	6.24(t)	2.50	2.50	4.64	5.10(m)	3.85(q)	4.35(q)
X=Br	β	6.40(t)	2.30 — 2.90		4.72(m)	5.22	4.12(q)	3.95(q)
X, R=Ac X=Br 2-deuterio	β	6.40(d)	2.30 — 3.00		4.70(q)	5.22	4.14(q)	3.99(q)
IX, R=Ac	α	6.34(t)	2.55(m)	2.25(m)	4.35(m)	5.00(m)	4.02(q)	3.71(q)
X=Cl	β	6.28(t)	2.64(m)	2.25(m)	4.20(m)	4.98(m)	3.68(q)	4.42(q)
IV, R=Bz	α	6.55(t)	2.66(m)	2.25(m)	5.89(m)	5.48(m)	4.28(q)	4.08(q)
	β	6.47(t)	2.66(m)	2.43(m)	5.50	5.33	4.03(q)	4.57(q)
IX, R=Bz X=Cl	β	6.32(t)	2.70(m)	2.30(m)	4.37	5.21	3.80(q)	4.54(q)
II, R=Bz		6.81(d)	5.25(m)		5.41—5.61		4.50(m)	4.31(q)
IX, R=Bz		6.70(d)	5.16(q)		5.92	5.65(m)	4.20 — 4.50	
V		4.90(d)	5.90 —		6.20	4.97	4.15(q)	3.85

(d)=doublet, (q)=quartet, (m)=multiplet, (t)=triplet.

constants (cps) of compounds shown in Fig. 1.

J_{12e}	J_{12a}	J_{2e3}	J_{2a3}	J_{34}	J_{45e}	J_{45a}	J_{5a5e}	J_{2a2e}	J_{13}	Conformation derived from spectrum
2.8	3.2	5.0	10.0	9.0	5.2	9.2	11.0	13.0		*C1*
3.2	6.0	4.5	7.0		6.2	4.0	12.2	13.5	~1	*1C*
4.0				3.5	3.8	7.0	12.0			*C1*
2.6					1.8	2.8	13.0			*1C*
3.2		5.0	9.0	9.0	5.0	9.0	11.5	14.0		*C1*
3.5		3.5	3.5	3.5	2.5	3.5	13.0	14.5	~1	*1C*
2.7		5.5	9.5	9.0	5.0	9.5	11.5			*C1*
4.0		5.0	6.0	5.0	5.0	3.1	12.5	14.5	~1	*1C*
3.0			11.5	9.5	5.0	9.5	11.0			*C1*
5.0				5.0	5.0	3.0	12.5		~1	*1C*
4.5		6.0	6.0	6.0	3.0	7.0	12.5		~1	*C1*
2.8		6.0	11.5	3.0	2.0	2.7	12.5			*1C*
3.0			12.5	3.5	2.0	2.5	12.5			*1C*
3.0		5.0	10.0	9.5	5.0	9.5	11.5	14.0		*C1*
4.0		5.0	5.5	5.0	5.5	2.8	12.5	15.0	~1	*1C*
3.0	3.5	5.0	10.5	9.0	5.0	9.0	11.5	13.5		*C1*
4.0		4.0	4.0	4.0	3.0	2.2	13.0	15.5	~1	*1C*
3.2				5.0	5.0	4.0	13.0	15.0	~1	*1C*
6.0		5.0			3.0	1.8	12.5			
6.0		5.0		4.0						
2.0		11.2		1.4	2.8	1.0	12.5			

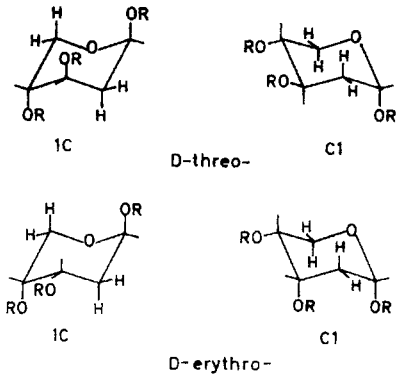

Fig. 2.

corresponding 3,4-di-*O*-acetates (XIII, R=Ac) are very similar. The configurations of the tri-*O*-acyl-2-deoxy-D-*threo*-pentopyranoses (IV, R=Ac or Bz) were established from the coupling of the H_3-proton with the neighbouring protons (Table 2). Thus the compound which is an α-anomer in the *C1* conformation (see above) and has $J_{3,4}=9.0$ cps, $J_{2e,3}=5.0$ cps, and $J_{2a,3}=9.0$ cps (Table 2) must have the *threo*-configuration (see Fig. 2) (α-IV, R=Ac). In the NMR spectra of the halogen-containing compounds (IX and X) the signal of the H_3-proton was shifted approximately 1 δ-unit upfield relative to that of H_3 in the tri-*O*-acyl-compounds (IV and XIII) indicating that the compounds have the halogen positioned at C_3. The configuration at this centre was established from the coupling constants $J_{2,3}$ and $J_{3,4}$ as illustrated above.

Lemieux *et al.*[10,11] observed that equatorial ring protons absorb at lower field than their axial counterparts. This was found to be the case for the H_{5e}-protons in compounds with the α-D-*threo*-configuration (*C1* conformation), namely the α-anomers of (I), (IV), and (IX). For the α-D-*erythro*-compounds (*C1* conformation) (X and XIII), H_{5a} absorbs at lower field than H_{5e}, probably because of the deshielding effect of the *syn*-diaxial substituents at C_1 and C_3.[11] A similar deshielding of the H_{5a}-proton was observed for the β-D-*threo*-compounds (*1C* conformation) (IV and IX).

The assignment of signals to H_{5a} and H_{5e} is unambiguous for compounds with the *C1* conformation because of the large difference between the *cis*- and *trans*-coupling constants $H_{4,5e}$ and $H_{4,5a}$. These cannot be used, however, to assign signals to the H_{5a}- and H_{5e}-protons for compounds in the *1C* conformation because H_4 is *gauche* to both H_5-protons. For compounds with the β-D-*threo*-configuration (*1C* conformation) H_3 is equatorially oriented and long range coupling to H_{5e} is therefore possible.[12] Such coupling ($J_{3,5e}=1$ cps) has indeed been found in all compounds possessing this structure (Table 2) and on this basis signals were assigned to the two H_5-protons. An unambiguous assignment to the H_5-protons of the β-D-*erythro*-compounds (*1C* conformation) was not possible on the basis of the coupling constants. In these cases (*e.g.* β-XIII, R=Ac), the low-field absorption was assigned to H_{5e}.[10]

The di-*O*-acyl-2-deoxy-derivatives (III and XII) are probably formed by direct addition of hydrogen halide to the 1,2-double bond in the glycals (II and XI). The formation of the 3-halo-2,3-dideoxy-derivatives (VII and VIII) is assumed to proceed *via* the 2,3-unsaturated glycosyl halide (VI). An analogous reaction has been observed when tri-*O*-acyl-D-glucal is treated with hydrogen fluoride in benzene.[13] In agreement herewith the 2,3-unsaturated methyl glycoside (V), when treated with hydrogen halide followed by reaction with silver benzoate, gave the 3-halo-compounds (IX and X, R=Ac) (Table 1) in the same relative proportions as those obtained from the glycals (II and XI). A similar experiment performed with deuterium bromide led to the 3-bromo-2,3-dideoxy-compounds (IX and X, R=Ac) containing one deuterium atom at C_2. The same products were obtained (Table 1) when di-*O*-acetyl-D-xylal (II, R=Ac) was treated with deuterium bromide. Attempts to prepare compounds derived from the 2,3-unsaturated intermediate (VI) by treating di-*O*-acetyl-D-xylal (II, R=Ac) with one equivalent of hydrogen bromide followed by silver benzoate gave a mixture of the 3-bromo-2,3-dideoxy-compound (IX, R=Ac, X=Br) and unreacted glycal (II, R=Ac).

It was found by Zorbach and Payne [14] that treatment of 1,3,4-tri-*O*-benzoyl-2,6-dideoxy-*β*-D-*ribo*-hexopyranose with hydrogen bromide in acetic acid gave a 31 % yield of a bromo-compound which was not a glycosyl bromide. The structure of this product was not investigated. Therefore, the reaction of methyl 3,4-di-*O*-acetyl-2-deoxy-D-*threo*-pentopyranoside (I) with hydrogen bromide in benzene followed by treatment with silver benzoate was studied. Besides the expected products (IV, R=Ac), small amounts (13 %) of the 3-bromo-compounds (IX, R=Ac, X=Br) were formed. Similar results were obtained when (XIII, R=Ac) was treated with hydrogen bromide (Table 1). When (I) was treated with deuterium bromide in the same way, small amounts of the 3-bromo-2-deuterio-2,3-dideoxy-compound (IX, R=Ac, X=Br) were formed along with the non-labelled 2-deoxy-tri-*O*-acyl compounds (IV, R=Ac). The incorporation of deuterium into (IX, R=Ac) shows that this compound is formed from (I) by addition of deuterium bromide to a double bond and not by direct replacement of the 3-*O*-acyl group. It is therefore assumed that the glycosyl bromide (III, R=Ac, X=Br), the initial product formed from (I) and hydrogen bromide, can eliminate hydrogen bromide to a certain extent and afford the glycal (II, R=Ac). The reaction of the latter with hydrogen bromide according to the mechanism suggested above would then explain the formation of the 2-deuterio-compound (IX, R=Ac, X=Br) from (I). Alternatively, acetic acid could be eliminated from (III, R=Ac, X=Br) to (VI, R=Ac, X=Br) which would then add deuterium bromide.

The present results indicate that the xylal derivatives give more of the 3-halo-compounds than the arabinal derivatives. This may be explained by assuming that the 4-*O*-acyl-group in the xylal derivatives assists in abstracting the 3-*O*-acyl-group in the first step of the reaction when the 2,3-unsaturated compound (VI) is formed. In the arabinal derivatives, with their two *cis*-oriented acyl-groups, such an assistance is not possible and the reaction is therefore more likely to give the normal addition product (XII). Similar results have been found by Ferrier [15,16] in studies of D-glucal and D-galactal derivatives.

EXPERIMENTAL

Thin layer chromatography (TLC) was performed on silica gel PF_{254} ("Merck"); for preparative work 1 mm layers were used. Spots were visualized by spraying with 10 % sulfuric acid followed by heating to 120° or by viewing under UV-light. NMR spectra were taken in deuteriochloroform on Varian A-60 or HA-100 instruments using tetramethyl silane as an internal standard. Positions of signals are given in δ-values. All evaporations were carried out *in vacuo* at 40°. Melting points are uncorrected.

Di-O-benzoyl-D-xylal (II, R=Bz). Di-*O*-acetyl-D-xylal (12.32 g) was dissolved in methanolic sodium methoxide (100 ml methanol, 150 mg Na). The solution was allowed to stand overnight at room temperature after which it was neutralized with dry ice, and the solvent was removed. The residue was extracted with ethyl acetate (3×50 ml). Evaporation gave a syrup (6.7 g) which was dissolved in pyridine (15 ml) at −15°, and a cold solution of benzoyl chloride (31 ml) in pyridine (100 ml) was added slowly with stirring. The mixture was allowed to stand overnight at +5° after which 1 g of ice was added. After 1 h, the reaction mixture was diluted with chloroform (300 ml) and washed successively with 3 N sulfuric acid, saturated sodium hydrogen carbonate and water, and dried. After evaporation, the product crystallized and was recrystallized from ether-pentane to give 15.46 g (78 %) of (II, R=Bz), m.p. 105−107°. After several recrystallizations from ether-pentane the m.p. was 110°. $[\alpha]_D^{23} = -369°$ (*c* 0.94, $CHCl_3$). (Found: C 70.15; H 5.05. Calc. for $C_{19}H_{16}O_5$: C 70.43; H 4.98).

Di-O-benzoyl-D-arabinal (XI, R=Bz). This product was prepared as described above. From di-*O*-acetyl-D-arabinal (5.0 g), 7.2 g (89 %) of crude di-*O*-benzoyl-D-arabinal was obtained. Crystallization from ether-pentane gave 4.6 g (57.5 %) of a product with m.p. 42−47°. The material in the mother liquor (1.9 g) was chromatographed on a column of silica gel (200 g) using ether-pentane 1:1 as eluent. This gave an additional 1.2 g (15 %) of product bringing the total yield to 5.8 g (72.5 %). Five recrystallizations gave a product with m.p. 47−48°. $[\alpha]_D^{23} = +260°$ (*c* 2.57, $CHCl_3$). (Found: C 70.36; H 4.78. Calc. for $C_{19}H_{16}O_5$: C 70.43; H 4.98).

Methyl 3,4-di-O-acetyl-2-deoxy-D-threo-pentopyranoside (I) was prepared by the method of Lemieux and Fraser-Reid.[17,18] Di-*O*-acetyl-D-xylal (7.5 g) was dissolved in methanol (250 ml). Silver acetate (8.76 g) was added and the mixture was cooled to 0°. Bromine (2.75 ml) was then added over a period of 10 min with stirring and cooling. After an additional period of 30 min the silver salts were removed by filtration through activated carbon and the solvent was evaporated. The crude syrup was dissolved in methylene chloride and washed twice with aqueous sodium hydrogen carbonate and twice with a 5 % solution of sodium thiosulfate and dried. Evaporation of the solvent left 10.55 g (91 %) of a syrup, which was shown by NMR to contain several isomeric products. The syrup was dissolved in 200 ml of a mixture of methanol, water and triethylamine (10:9:1) and palladium on carbon (600 mg) was added. Hydrogenation was performed by atmospheric pressure at room temperature for 12 h after which the catalyst was removed by filtration and the solvent was evaporated. Benzene (2×50 ml) was added and evaporated, leaving a semi-crystalline product to which pyridine (20 ml) was added. The crystalline triethylammonium bromide was filtered off and washed once with pyridine (20 ml). The combined pyridine solutions were cooled to 0° and acetylated with acetic anhydride (22 ml) giving 6.47 g (75 %) of a syrup which consisted mainly of a mixture of the anomeric methyl glycosides. A sample was separated into two fractions by preparative TLC, developing twice with ether-pentane (1:2). The fastest running component was a syrup, $[\alpha]_D^{23} = +86.5°$ (*c* 1.9, $CHCl_3$). (Found: C 51.57; H 6.83. Calc. for $C_{10}H_{16}O_6$: C 51.73; H 6.95). The second component was also a syrup, $[\alpha]_D^{23} = -103°$ (*c* 3.0, $CHCl_3$). (Found: C 51.76; H 6.61). The optical rotation and the NMR spectra (Table 2) showed that the first component was the α-anomer and the slower moving component the β-anomer.

Methyl 4-O-acetyl-2,3-didehydro-2,3-dideoxy-α and β-D-glycero-pentopyranoside (V). The procedure used was that described by Ferrier.[19] Di-*O*-acetyl-D-xylal (986 mg) was dissolved in methylene chloride (5 ml) and a mixture of methanol (0.2 ml) and boron trifluoride etherate (0.1 ml) in methylene chloride (0.3 ml) was added. The reaction was followed by NMR spectroscopy and after 30 min at room temperature the glycal absorption at 6.6 δ had disappeared. The dark coloured solution was poured into saturated aqueous sodium hydrogen carbonate. The organic layer was washed with sodium hydrogen

carbonate and water and dried. Evaporation of the solvent left 836 mg (98 %) of a syrup which contained two main components as apparent from TLC. A sample was purified by preparative TLC using ether-pentane (1:1) as an eluent. The fastest moving component was a syrup with $[\alpha]_D^{23} = +138°$ (*c* 2.53, $CHCl_3$). The product contained a small amount of the other anomer. The slower moving component had $[\alpha]_D^{23} = +158°$ (*c* 0.58, $CHCl_3$). (Found: C 55.97; H 6.97. Calc. for $C_8H_{12}O_4$: C 55.81; H 7.03). NMR spectra showed that the two components were the anomeric methyl glycosides, but the anomeric configuration has not yet been unequivocally determined.

Reaction between di-*O*-acyl-glycals and hydrogen halides

The following general procedure was used in all experiments: the glycal (2.5 mequiv.) was dissolved in benzene (10 ml) and the hydrogen halide was passed through the solution with ice-cooling. After 20 min, the solution was poured into dry acetonitrile (35 ml) containing 6 g of silver benzoate and the suspension was stirred for 2 h at room temperature. The silver salts were removed by filtration through activated carbon and the solvent was evaporated leaving a residue which was dissolved in methylene chloride (50 ml) and filtered. The filtrate was washed with saturated aqueous sodium hydrogen carbonate, dried and evaporated, leaving a crude product.

*Di-*O*-acetyl-*D*-xylal (II, R=Ac) and hydrogen chloride.* Treatment of (II, R=Ac) (736 mg) with hydrogen chloride in benzene as described above gave 1070 mg of crude product. Crystallization from ether-pentane gave 515 mg (47 %) of the 3-chloro-3-deoxy-compound (β-IX, R=Ac, X=Cl), m.p. 128–130°. $[\alpha]_D^{23} = -98.4°$ (*c* 0.94, $CHCl_3$). (Found: C 56.15; H 5.01; Cl 11.95. Calc. for $C_{14}H_{15}O_5Cl$: C 56.31; H 5.03; Cl 11.87). The material in the mother liquor was separated into 4 fractions by preparative TLC using ether-pentane (1:1) as eluent. The fastest moving fraction gave 63 mg (6 %) of the 3-chloro-3-deoxy-compound (α-IX, R=Ac, X=Cl), which was recrystallized from ether-pentane, m.p. 93–95°, $[\alpha]_D^{23} = +33.3$ (*c* 1.0, $CHCl_3$). (Found: C 55.95; H 4.94; Cl 11.81). The second fraction gave an additional 72 mg (7 %) of (β-IX, R=Ac, X=Cl). The third fraction gave 66 mg (6 %) of the normal addition product (α-IV, R=Ac), which was recrystallized from ether-pentane, m.p. 126–127°, $[\alpha]_D^{23} = 67.0$ (*c* 1.4, $CHCl_3$). (Found: C 59.70; H 5.53. Calc. for $C_{16}H_{18}O_7$: C 59.64; H 5.63). The corresponding β-anomer was found in the fourth fraction. The product was further purified by preparative TLC giving 119 mg (13 %) of (β-IV, R=Ac) as a syrupy product, $[\alpha]_D^{23} = -125°$ (*c* 4.8, $CHCl_3$). (Found: C 59.62; H 5.75).

*Di-*O*-acetyl-*D*-xylal and hydrogen bromide.* From (II, R=Ac) (571 mg) 859 mg of crude product was obtained. Crystallization from ether-pentane gave 276 mg (27 %) of the 3-bromo-3-deoxy-compound (β-IX, R=Ac, X=Br), m.p. 108–109°. The remaining material was separated into 6 fractions by preparative TLC using ether-pentane (1:1) as eluent. One of the fractions gave an additional amount (52 mg, 6 %) of (β-IX, R=Ac, X=Br). Recrystallization from ether-pentane gave pure (β-IX, R=Ac, X=Br), m.p. 115–116°. $[\alpha]_D^{23} = -85.4°$ (*c* 1.3, $CHCl_3$). (Found: C 48.95; H 4.48; Br 23.00. Calc. for $C_{14}H_{15}O_5Br$: C 49.01; H 4.38; Br 23.29). In addition, 64 mg (7 %) of the corresponding α-anomer (α-IX, R=Ac, X=Br) was isolated. The product was recrystallized from ether-pentane, m.p. 96–98°. $[\alpha]_D^{23} = +43.1°$ (*c* 1.6, $CHCl_3$). (Found: C 48.90; H 4.48; Br 23.19). Small amounts of the C_3-epimeric bromo-compounds were also obtained. The β-anomer (β-X, R=Ac, X=Br), 19 mg (2 %) were recrystallized from ether-pentane, m.p. 119–120°, $[\alpha]_D^{23} = -120°$ (*c* 1.2, $CHCl_3$). (Found: C 50.05; H 4.42; Br 22.58). The α-anomer (α-X, R=Ac, X=Br), 78 mg (8 %), had m.p. 88–90°, $[\alpha]_D^{23} = -8.1°$ (*c* 1.0, $CHCl_3$). (Found: C 50.95; H 4.47; Br 22.81). The NMR spectrum indicated that it contained a small amount of (β-IX, R=Ac, X=Br). Finally, the normal addition products (β-IV, R=Ac) (52 mg, 6 %) and (α-IV, R=Ac) (21 mg, 2 %) were also isolated. They were identical with the products described above.

*Di-*O*-acetyl-*D*-arabinal (XI, R=Ac) and hydrogen chloride.* (XI, R=Ac) (525 mg) gave 763 mg of crude product which was separated into 4 fractions by preparative TLC using ether-pentane (1:1) as an eluent. The main compounds were the normal addition products. The β-anomer (β-XIII, R=Ac) (177 mg, 21 %) was recrystallized twice from

ether-pentane, m.p. 103–104°. $[\alpha]_D^{23} = -138°$ (*c* 1.3, $CHCl_3$). (Found: C 59.50; H 5.61. Calc. for $C_{16}H_{18}O_7$: C 59.64; H 5.63). The α-anomer (α-XIII, R=Ac) (178 mg, 21 %) was also recrystallized from ether-pentane, m.p. 108.5–110°. $[\alpha]_D^{23} = +68.8$, (*c* 1.6, $CHCl_3$). (Found: C 59.79; H 5.12). In addition 15 mg (2 %) of (α-IX, R=Ac, X=Cl) and 73 mg (9 %) of (β-IX, R=Ac, X=Cl) was isolated. NMR spectra proved the identity with the compounds described above.

Di-O-*acetyl*-D-*arabinal (XI, R=Ac) and hydrogen bromide.* The products were isolated by the procedure described above and the results are given in Table 1. The identity of the products was established by NMR spectroscopy.

Di-O-*benzoyl*-D-*xylal (II, R=Bz) and hydrogen chloride.* Treatment of (II, R=Bz) (597 mg) with hydrogen chloride followed by reaction with silver benzoate as described for the acetylated compounds gave 782 mg of crude product. By preparative TLC using acetone-pentane (1:2) as an eluent the product was separated into two fractions.

The largest fraction (372 mg, 47 %) was a mixture of the anomeric tribenzoates (IV, R=Bz). The relative amounts of the two anomers were determined by NMR spectroscopy and the yields calculated on this basis are given in Table 1. Crystallization from methylene chloride-pentane gave the pure β-anomer (β-IV, R=Bz), m.p. 160–162°. $[\alpha]_D^{23} = -104°$ (*c* 1.2, $CHCl_3$). (Found: C 69.75; H 5.10. Calc. for $C_{26}H_{22}O_7$: C 69.80; H 4.95). The α-anomer was isolated from the mother liquor by preparative TLC using ether-pentane (1:2) as eluent. The product was a syrup, $[\alpha]_D^{23} = +12.2$ (*c* 3.5, $CHCl_3$). (Found: C 69.88; H 4.80).

The second fraction (73 mg, 11 %) was crystallized from ether-pentane to give the pure β-3-chloro-3-deoxy-compound (β-IX, R=Bz, X=Cl), m.p. 114–115°. $[\alpha]_D^{23} = -95.3°$ (*c* 0.6, $CHCl_3$). (Found: C 63.50; H 4.80; Cl 9.80. Calc. for $C_{19}H_{17}O_5Cl$: C 63.24; H 4.75; Cl 9.83). The NMR spectrum of the material in the mother liquor showed that a small amount of the α-anomer was present.

Di-O-*benzoyl*-D-*xylal and hydrogen bromide.* The crude product was separated into two fractions by preparative TLC using acetone-pentane (1:2) as an eluent. The main fraction contained the anomeric tribenzoates (IV, R=Bz) and a small fraction consisted of a mixture of the anomeric 3-bromo-3-deoxy-compound (IX, R=Bz, X=Br). The yields given in Table 1 are calculated from the NMR spectra of the two fractions.

Di-O-*benzoyl*-D-*arabinal (XI, R=Bz) and hydrogen chloride.* (XI, R=Bz) (2.18 g) gave 2.39 g of a crude product. Crystallization from ether-pentane gave 1.73 g (57 %) of a mixture of the anomeric tribenzoates (XIII, R=Bz), m.p. 119–126°. Preparative TLC using ether-pentane (1:1) as an eluent gave an additional amount (200 mg, 7 %) of this mixture, m.p. 120–126°. The two anomers were separated by preparative TLC using ether-pentane (1:2) as an eluent. The α-anomer (α-XIII, R=Bz) was recrystallized from ether-pentane, m.p. 148–149°. $[\alpha]_D^{23} = +34.2°$ (*c* 0.77, $CHCl_3$) (lit.[8] m.p. 151–152°, $[\alpha]_D = +41.6°$). The β-anomer (β-XIII, R=Bz) was recrystallized from ether-pentane, m.p. 156–157°. $[\alpha]_D^{23} = -189°$ (*c* 1.2, $CHCl_3$) (lit.[8] m.p. 159–161°, $[\alpha]_D = -195°$).

Di-O-*benzoyl*-D-*arabinal (XI, R=Bz) and hydrogen bromide.* This reaction gave the same products (XIII, R=Bz) as those obtained from the reaction with hydrogen chloride (Table 1).

Methyl 4-O-*acetyl*-*2,3-didehydro*-*2,3-dideoxy*-D-glycero-*pentopyranoside (V) and (a) hydrogen chloride.* The mixture of the anomeric methyl glycosides (V) (478 mg) was treated with hydrogen chloride in benzene followed by reaction with silver benzoate as described above. Crystallization of the crude product (720 mg) from ether-pentane gave 313 mg (38 %) of the β-3-chloro-3-deoxy-D-*threo*-compound (β-IX, R=Ac, X=Cl), m.p. 123–130°. Preparative TLC using ether-pentane (1:1) as an eluent gave the products indicated in Table 1. The two 3-chloro-3-deoxy-D-*erythro*-compounds (X, R=Ac, X=Cl) were only characterized through their NMR spectra which were very similar to those of the corresponding bromo-compounds (X, R=Ac, X=Br). *(b) hydrogen bromide.* Analogously, (V) (276 mg) gave a crude product (467 mg) by treatment with hydrogen bromide. Crystallization from ether-pentane gave 150 mg (26 %) of the 3-bromo-3-deoxy-D-*threo*-compound (β-IX, R=Ac, X=Br), m.p. 107–110°. After chromatography the products shown in Table 1 were obtained. They were characterized through their NMR spectra.

Reaction of methyl 3,4-di-O-*acetyl*-*2-deoxy*-D-threo-*pentopyranoside (I) with hydrogen chloride and hydrogen bromide.* The reactions were carried out as described above. The

products which are indicated in Table 1 were isolated by chromatography and characterized through their m.p. and NMR spectra.

The corresponding reaction was performed with (XIII, R=Ac) and (IX, R=Ac) and hydrogen bromide. The results are given in Table 1.

Reactions with deuterium bromide

Deuterium bromide was prepared from phosphorus tribromide (4 ml) and deuterium oxide (1 ml) at 50–60°.[20] The deuterium bromide formed was passed directly into the benzene solution containing the sugar.

*Di-*O*-acetyl-*D*-xylal (II, R=Ac)* was reacted with deuterium bromide and the resulting benzene solution was directly treated with silver benzoate as described above. From the crude product 160 mg (21 %) of (*β*-IX, R=Ac, X=Br, 2-deuterio) was crystallized, m.p. 113–115°. The mother liquor was subjected to preparative TLC using ether-pentane (1:1) as an eluent and a further amount of (*β*-IX, R=Ac, X=Br, 2-deuterio) (48 mg, 6 %) was isolated. After recrystallization from ether-pentane the m.p. was 114–115°. $[\alpha]_D^{23} = -87.6°$ (*c* 2.6, $CHCl_3$). (Found: C 48.80; H+D 4.49; Br 22.98. Calc. for $C_{14}H_{14}BrDO_5$: C 48.85; H+D 4.69; Br 23.21). The chromatographic separation also gave 80 mg (10 %) of the α-anomer (α-IX, R=Ac, X=Br, 2-deuterio) which after recrystallization from ether-pentane melted at 97–98°. $[\alpha]_D^{23} = +42.7°$ (*c* 2.3, $CHCl_3$). (Found: C 48.90; H+D 4.49; Br 23.13). Besides, the C_3-epimeric bromo-compounds were obtained. The *β*-anomer (*β*-X, R=Ac, X=Br, 2-deuterio) (34 mg, 4 %) was recrystallized from ether-pentane, m.p. 118.5–119.5°. $[\alpha]_D^{23} = -131°$. (Found: C 48.55; H+D 4.49; Br 23.00). The α-anomer (α-X, R=Ac, X=Br, 2-deuterio) (48 mg, 6 %) was only identified by comparing the NMR spectrum with that of the corresponding non-deuterated product (α-X, R=Ac, X=Br). The NMR spectra of all the products showed that only one proton was present at C_2.

*Methyl 4-*O*-acetyl-2,3-didehydro-2,3-dideoxy-*D*-*glycero*-pentopyranoside (V)* gave essentially the same products as those obtained from (II, R=Ac) (Table 1).

*Methyl 3,4-di-*O*-acetyl-2-deoxy-*D*-*threo*-pentopyranoside (I).* From (I) (437 mg) a crude product (350 mg) was obtained. This was separated into 4 components by preparative TLC using ether-pentane (1:1) as an eluent. The major products were the anomeric 2-deoxy-compounds (α-IV, R=Ac) (70 mg, 12 %) and (*β*-IV, R=Ac) (89 mg, 15 %). The two products did not contain deuterium. The two other products were the anomeric 3-bromo-2-deuterio-compounds (α-IX, R=Ac, X=Br, 2-deuterio) (8 mg, 1 %) and (*β*-IX, R=Ac, X=Br, 2-deuterio) (43 mg, 6 %). All the products were identified through their NMR spectra.

Microanalyses were carried out by Dr. A. Bernhardt.

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