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Reaction of Tetra-*O*-acyl-1-deoxy-D-*arabino*-hex-1-enopyranose with Hydrogen Fluoride. Preparation of Methyl-3,4-dideoxy-D-hexopyranosides

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Treatment of tetra-*O*-acyl-1-deoxy-D-*arabino*-hex-1-enopyranose (I) with anhydrous hydrogen fluoride gives a high yield of 6-*O*-acyl-3,4-dideoxy-D-*glycero*-hex-3-enopyranosylulose fluoride (IX). The latter, on reaction with methanol and boron trifluoride, forms a mixture of the anomeric methyl 6-*O*-acyl-3,4-dideoxy-D-*glycero*-hex-3-enopyranosiduloses (VI) and (X). Reduction of (VI) and (X) with lithium aluminiumhydride gives, after acylation, the methyl 2,6-di-*O*-acyl-3,4-dideoxy-D-hex-3-enopyranosides (III) and (XV), respectively. Catalytic hydrogenation of (VI) and (X) gives the anomeric methyl 6-*O*-acyl-3,4-dideoxy-D-hexopyranosiduloses (VII) and (XI). Reduction of the latter two compounds with sodium borohydride, or catalytic reduction of (III) and (XV), gives methyl 2,6-di-*O*-acyl-3,4-dideoxy-β-D-*threo*-hexopyranosides (VIII) and the corresponding α-D-*erythro*-compound (XII).

In a preliminary publication[1] it was described that treatment of tetra-*O*-acyl-1-deoxy-D-*arabino*-hex-1-enopyranose (I) with anhydrous hydrogen fluoride at −70° gave the 2,3-unsaturated fluoride (V). The latter, on further reaction with hydrogen fluoride at −30°, gave a high yield of the 3,4-unsaturated keto-fluoride (IX). Compounds analogous to (V) and (IX) were obtained in the pentose series by treating acylated 2-hydroxy-glycals with hydrogen chloride or hydrogen bromide.[2] In the present paper a more detailed description of the reaction with hydrogen fluoride is given.

The reaction of the tetraacetate (Ia) with anhydrous hydrogen fluoride has now been studied by NMR spectroscopy. A spectrum of (Ia) in hydrogen fluoride solution at −70° showed that the 2,3-unsaturated fluoride (Va) was formed almost immediately, together with one molar equivalent of acetic acid. At −70° the further reaction of (Va) with hydrogen fluoride was slow. However, when the temperature was raised to −30°, (Va) was completely converted into the 6-*O*-acetyl 3,4-dideoxy-D-*glycero*-hex-3-enopyranosylulose fluorides (IXa) in the course of 2 h. At the same time, one additional equivalent

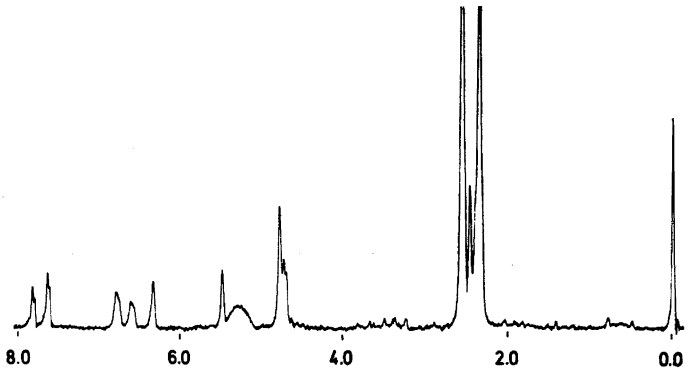
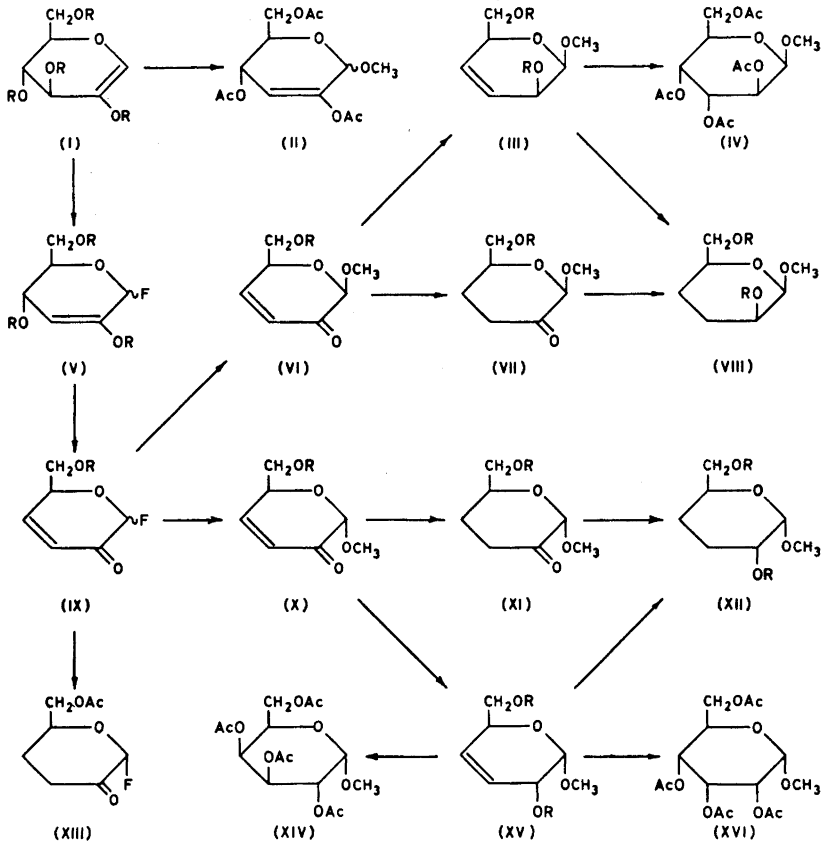


Fig. 1. NMR spectrum of tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose in anhydrous hydrogen fluoride after 2 h at −30°.

of acetic acid was formed together with one equivalent of acetyl fluoride (Fig. 1). The latter was easily detected, since it gave a characteristic doublet centered at 2.45 δ with a spacing of 8.2 cps. The unsaturated ketone (IXa) was stable in hydrogen fluoride at −30° for several days, as seen from the NMR spectra, and it was isolated in 95 % yield as a mixture of the two anomers when the hydrogen fluoride solution was worked up. Similar results were obtained when the corresponding tetrabenzoate (Ib) was treated with hydrogen fluoride, and (IXb) could be prepared in 93 % yield as a mixture of anomers. Treatment of (Ia or b) with hydrogen fluoride in benzene solution gave the 2,3-unsaturated fluorides (Va or b) which could be isolated in good yields. The products did not react further with hydrogen fluoride in benzene, however, treatment of (Va) with anhydrous hydrogen fluoride gave an almost quantitative yield of (IXa), as expected on the basis of the results described above.

Treatment of the fluorides (IXa or b) with methanol in the presence of catalytic amounts of boron trifluoride gave a mixture of the anomeric methyl glycosides, (VIa or b) and (Xa or b). Alternatively, (VIa) and (Xa) could be obtained directly, although in lower yield, from (Ia) by reaction with methanol and boron trifluoride. This reaction proceeds *via* the 2,3-unsaturated glycoside (II).[3] The methyl glycosides (VI) and (X) could be separated by chromatography.

Reduction of the β-glycosides (VIa or b) with lithium aluminium hydride was stereospecific, giving, after acylation, methyl 2,6-di-*O*-acyl-3,4-dideoxy-β-D-*threo*-hex-3-enopyranoside (IIIa or b) as the only detectable product. The structure of (III) was proved through its conversion to methyl tetra-*O*-acetyl-β-D-altropyranoside (IV) with osmium tetraoxide and hydrogen peroxide. This also proves the anomeric configuration of (VIa or b). In a similar manner, reduction of (Xa or b) gave the *erythro*-compounds (XVa or b), which, by hydroxylation, were converted into a mixture of methyl tetra-*O*-acetyl-α-D-galactopyranoside (XIV) and the corresponding D-allose derivative (XVI).



Reduction of the 3,4-unsaturated methyl glycosides (IIIa) and (XVa) with hydrogen and palladium on carbon gave the acetylated methyl 3,4-dideoxy-hexopyranosides, (VIIIa) and (XIIa), respectively. It was also possible to reduce selectively the double bonds of (VIa) and (Xa) using palladium on barium sulfate as catalyst. This gave the anomeric methyl 6-*O*-acetyl-3,4-dideoxy-D-*glycero*-hexopyranosid-2-uloses, (VIIa) and (XIa), respectively. Further reduction of the latter two compounds with sodium borohydride was stereospecific, giving (VIIIa) and (XIIa), respectively, after acetylation. Finally, it may be mentioned that reduction of the α-anomer of (IXa) with hydrogen and palladium on barium sulfate gave 6-*O*-acetyl-3,4-dideoxy-α-D-*glycero*-hexopyranosyl-2-ulose fluoride (XIII) as a rather unstable syrup, which was characterized through its NMR spectrum.

The preparation of the 3,4-dideoxy-glycosides (VIII) and (XII) could be carried out directly from (Ia) *via* (IXa), (VIa)+(Xa), and (VIIa)+(XIa)

Table 1. NMR-data of 3,4-unsaturated compounds.

Substance	Solvent	δ-Values							Coupling constants												
		H_1	H_2	H_3	H_4	H_5	H_6	H_6'	J_{12}	J_{13}	J_{14}	J_{23}	J_{24}	J_{25}	J_{34}	J_{35}	J_{45}	J_{56}	J_{56}	J_{66}'	J_{1F}
α IXa	[a]	5.57		6.29	7.10	4.97	4.40	4.32		0.7					10.4	2.4	1.7	5.0	5.0	11.8	51.2
α IXb	[a]	5.57		6.28	7.12	5.05	4.61	4.55		0.8					10.4	2.0	1.6	4.8	4.8	12.0	51.0
β IXa	[a]	5.58		6.35	7.18	4.83	4.1	−4.6							10.7	2.0	3.2				52.0
β IXb	[a]	5.58		6.36	7.13	4.90	4.0	−4.5							10.5		3.0				52.0
Xa	[a]	4.80		6.17	6.97	4.76	4.35	4.29		0.8					10.7	2.5	1.8	5.0	5.0	11.6	
Xb	[a]	4.81		6.20	7.05	4.85	4.60	4.51		0.7					10.7	2.6	1.5	5.0	5.0	11.4	
VIa	[a]	4.82		6.22	7.03	4.70	4.40	4.32		0.4					10.7	2.0	3.0	ca. 6	ca. 6	ca. 11	
VIb	[a]	4.84		6.23	7.08	4.85	4.63	4.55		0.3					10.3	2.0	2.9				
XVa	[a]	5.10	5.30	5.72	5.85	4.37	4.05	−4.30	4.2	1.5	0.6	1.6	1.7	3.1	10.2	1.5	1.3				
XVa	[c]	5.01	5.19	5.67	5.85	4.34	4.10	4.14	4.2	1.4	0.5	2.0	1.7	3.0	10.2	1.6	1.5	5.2	5.0	11.4	
XVb	[c]	5.25	5.53	5.91	6.06	4.59	4.35	−4.55	4.2	1.4	0.6	1.7	1.8	3.0	10.4	1.4	1.2				
XVb	[a]	5.29	5.60	5.93	6.01	4.4	——	4.7	4.1												
IIIa	[b]	4.48	5.20	5.71	5.58	*3.9*	——	4.4	2.9			3.6	0.6	1.6	10.1	1.5	1.2				
IIIa	[a]	4.76	5.25	5.85	6.05	4.46	4.20	4.24	2.8						10.0			6.0	5.8	11.0	
IIIb	[b]	4.60	5.47	5.84	5.65	4.4	——	4.7	2.8			3.9	0.8	2.0	10.0	1.7	1.2				
IIIb	[a]	4.91	5.52	5.98	6.18	4.4	——	4.7	2.8												

[a] $CDCl_3$. [b] $CDCl_3+C_6D_6$ 1 : 1. [c] $(CD_3)_2CO$.

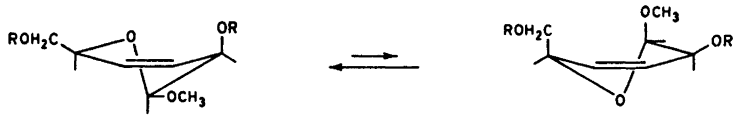
Note added in proof: ^{19}F-spectra have been measured on the following compounds (position of signals are given in ppm relative to methyl trifluoroacetate): (α IXa) −67.4 ppm, J_{5F}=5.9 cps; (α IXb) −61.0 ppm, J_{5F}= 5.9 cps; (β IXa) −44.4 ppm, J_{5F}= 4.8 cps; (β IXb) −44.0 ppm, J_{5F}= 4.6 cps.

without isolation of any intermediates. This gave an 80 % yield of a mixture of (VIIIa) and (XIIa). The latter two products could be separated by column chromatography to give 48 % of (XIIa) and 11 % of (VIIIa).

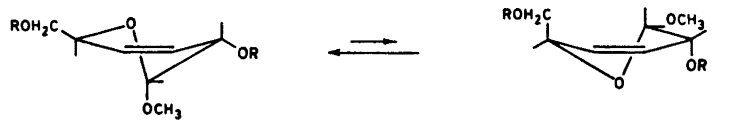
NMR spectra were recorded of all the compounds described above. The δ-values and the observed first order coupling constants are given in Table 1. Some spectral data were published previously.[1]

The anomeric hex-enopyranosiduloses (VI) and (X) are apparently predominantly in the conformation proposed by Anet [4] for the corresponding 6-*O*-methyl-derivatives, as seen from the coupling constants $J_{3,5}$ and $J_{4,5}$ (Table 1). The anomeric structure of the fluorides (IX) has not been proved, but it would be reasonable to expect that the product formed in largest amount from the reaction of (I) with hydrogen fluoride is the α-anomer, since this would be expected to be the most stable of the two anomers. This assignment is supported by the NMR spectra (Table 1), which show that J_{45} is small (1.5 – 1.8 cps) for both the α-fluorides (IXa and b) and the α-glycosides (Xa and b), whereas a value of 2.9 – 3.2 cps is found for the β-anomers of (IXa and b) and (VIa and b).

The configuration of the 3,4-unsaturated acetates or benzoates (III) and (XV) was proved as described above. As far as it could be deduced from the NMR spectra (Table 1), both compounds seem to be predominantly in the $^{O}H_{1}$ conformation, (XVII) and (XVIII), respectively. As the spectra were rather complex, they were run in different solvents in order to separate the signals. The fact that the signal of H-1 is found at higher field in (IIIa or b) than in (XVa or b) is in agreement with the proposed conformations, (XVII) having H-1 axial and (XVIII) equatorial. Furthermore, the equatorial H-1 of (XVIII) shows a long range coupling with the vinylic protons at both C-3 and C-4, whereas the axial H-1 of (XVII) only couples with H-2 in agreement with the well-known angular dependence of long range coupling constants.[5] None of these data would agree with the alternative conformations (XIX) and (XX). In addition, a homoallylic coupling of $J_{2,5}=3.0$ cps in (XVIII) indicates a diaxial orientation of H-2 and H-5.[5–7] The conformations are further confirmed by the vicinal and allylic coupling constants.



(XVII) (XIX)



(XVIII) (XX)

The NMR spectra of (VIII), (XI), and (XII) were rather complex. However, the δ-values and coupling constants that could be obtained (Table 2) indicate that all the compounds adopt the expected conformation, in which C-6 is equatorially oriented.

Table 2. NMR data of 3,4-dideoxy-hexosides.

Substance	Solvent	δ-Values and coupling constants						
		H_1	H_{3a}	H_{3e}	H_4	H_5	H_6	H_6'
XIa	$CDCl_3$	4.39	2.63	2.37	1.6–2.1	3.9——4.2		
		$J_{1,3e}=1.0$	$J_{3a,4e}=3.4$	$J_{3a,4a}=12.0$	$J_{3e,4e}=2.8$	$J_{3e,4a}=4.8$		$J_{3a,3e}=14,8$
XIb	$CDCl_3$	4.57	2.82	2.45	1.8–2.2	4.3——4.7		
		$J_{1,3e}=1.0$	$J_{3a,4e}=7.0$	$J_{3a,4a}=12.0$	$J_{3e,4e}=3.0$	$J_{3e,4a}=4.0$		$J_{3a,3e}=14.6$
VIIa	$CDCl_3$	4.62	2.3——2.8		2.0–2.3	4.0——4.4		
		H_1	H_2	H_3	H_4	H_5	H_6	H_6'
XIIa	$CDCl_3$	4.80	4.78	1.4——2.0		3.95	4.0——4.2	
XIIa	C_6D_6	4.78	4.72	1.0——2.0		3.75	3.89	3.97
		$J_{1,2}=3.5$	$J_{2,3}=11.0$	$J_{2,3}'=5.0$	$J_{5,6}=6.5$	$J_{5,6}'=3.5$		$J_{6,6}'=11.0$
XIIb	$CDCl_3$	4.97	5.06	1.6–2.4	4.13	4.2——4.5		
		$J_{1,2}=3.4$	$J_{2,3}=10.0$	$J_{2,3}'=5.4$				
VIIIa	$CDCl_3$	4.44	4.99	1.4——2.2		3.80	4.14	4.22
		$J_{1,2}=1.5$	$J_{2,3}=4.0$	$J_{2,3}'=2.8$	$J_{5,6}=6.0$	$J_{5,6}'=5.0$		$J_{6,6}'=11.0$
VIIIb	$CDCl_3$	4.68	5.25	1.5——2.4		4.02	4.3——4.7	
		$J_{1,2}=1.5$	$J_{2,3}=3.4$	$J_{2,3}'=2.4$				

EXPERIMENTAL

Melting points are uncorrected. Chromatography was performed as described previously.[8] NMR spectra were obtained on Varian A-60 or HA-100 instruments using tetramethylsilane as internal standard.

Reactions with hydrogen fluoride in benzene. Tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (Ia)[9] (620 mg) was dissolved in a saturated solution of hydrogen fluoride in benzene (15 ml) and kept in ice for 3 h. The solution was then diluted with methylene chloride, poured unto ice, washed with aqueous sodium hydrogen carbonate, and dried. Evaporation gave 550 mg (93 %) of (Va) as a mixture of anomers with an $\alpha:\beta$ ratio of 85 : 15, as seen from the NMR spectrum. The two anomers could not be separated by TLC. NMR data[1] of the α-anomer were obtained from the spectrum of the mixture.

By a similar treatment the tetrabenzoate (1b)[9] gave 98 % of a syrupy mixture of the 2,3-unsaturated fluorides (Vb) in an $\alpha:\beta$ ratio of 85:15.

Reactions with anhydrous hydrogen fluoride. The tetraacetate (Ia) (1.10 g) was dissolved in anhydrous hydrogen fluoride (2.5 ml) at $-78°$, and the solution was kept at $-30°$ for 3 h. It was then diluted with methylene chloride and poured on ice; the organic phase was washed with aqueous sodium hydrogen carbonate and dried. Evaporation gave 600 mg (98 %) of (IXa) in an α to β ratio of 7 : 1, as seen from the NMR spectrum. The two anomers could be separated by preparative TLC, using ether-pentane (2 : 1) as eluent. The fastest moving fraction gave 400 mg of the α-anomer (α-IXa) as a syrup, $[\alpha]_D^{23}=-127°$ (*c* 8.2, $CHCl_3$). An IR spectrum showed bands at 1702 and 1710 cm^{-1} (conjugated ketone) and at 1740 cm^{-1} (ester carbonyl). The slower moving fraction gave 48 mg of (β-IXa) as a syrup with $[\alpha]_D^{23}=-55.6°$ (*c* 2.2, $CHCl_3$). Correct elementary analyses could not be obtained due to instability of the products.

Treatment of tetra-*O*-benzoyl-1-deoxy-D-*arabino*-hex-1-enopyranose (1b) (1.40 g) with anhydrous hydrogen fluoride (2.5 ml) at −30° for 18 h and work up as described above gave 554 mg (93 %) of (IXb) in an α:β ratio of 7:1. The two anomers were separated by preparative TLC, using ether-pentane (2:1), as eluent. The fast moving fraction consisted of the α-anomer (α-IXb) as a syrup, yield 250 mg, $[\alpha]_D^{23} = -116°$ (*c* 3.7, $CHCl_3$). An IR spectrum showed bands at 1705 and 1720 cm^{-1}. The slower moving fraction gave 48 mg of (β-IXb) as an unstable syrup, showing IR bands at 1705 and 1725 cm^{-1}.

Preparation of methyl 6-*O*-acyl-3,4-dideoxy-α- and β-D-*glycero*-hex-3-enopyranosid-2-uloses (VI) and (X)

The acetates (VIa) and (Xa). The tetraacetate (Ia) (2.0 g) was treated with hydrogen fluoride, as described above, to give 1.1 g of (IXa). This product was dissolved in methylene chloride (10 ml) and 3 ml of a mixture of methanol, boron trifluoride-etherate, and methylene chloride (1 : 1 : 8) was added. The resulting solution was kept at room temperature for 20 min. It was then diluted with methylene chloride (30 ml), washed with aqueous sodium hydrogen carbonate, dried and evaporated, leaving 1.2 g (99 %) of crude product. Preparative TLC, using ether-pentane (2 : 1), as eluent, separated this into two fractions. The fast moving fraction gave 950 mg (78 %) of the α-glycoside (Xa) as a syrup, $[\alpha]_D^{23} = -7.9°$ (*c* 3.2, $CHCl_3$). An IR spectrum showed bands at 1622, 1702, and 1740 cm^{-1}. The slow moving fraction gave 130 mg (14 %) of the β-glycoside (VIa) as a syrup, $[\alpha]_D^{23} = -133°$ (*c* 2.1, $CHCl_3$), IR bands at 1702 and 1742 cm^{-1}. The two products are unstable and become coloured on standing; correct analyses could therefore not be obtained. (A sample of (Xa) gave the following values: C 53.30; H 5.98. Calc. for $C_9H_{12}O_5$: C 54.00; H 6.04.)

The same preparation was carried out starting with a mixture of the anomeric tetra-*O*-acetyl-3-deoxy-D-*erythro*-hex-2-enopyranoses instead of (Ia). This gave 50 % of (Xa) and 14 % of (VIa).

By treatment of (Ia) with methanol and boron trifluoride. To a solution of (Ia) (825 mg) in methylene chloride (8 ml) was added 2 ml of a 1 : 1 : 8 mixture of methanol, boron trifluoride-etherate, and methylene chloride. The solution was kept at room temperature while the reaction was followed by NMR spectroscopy. After 48 h the reaction was completed; the mixture had then become dark coloured. It was worked up as described above, yielding 153 mg (31 %) of (Xa) and 46 mg (10 %) of (VIa).

The benzoates (VIb) and (Xb). The tetrabenzoate (Ib) (2.13 g) was treated with hydrogen fluoride to give (IXb). This was dissolved in methylene chloride (10 ml) and 2.5 ml of a 1 : 1 : 8 mixture of methanol, boron trifluoride-etherate, and methylene chloride was added. The solution was kept for 30 min at room temperature and worked up as described above. The crude product (930 mg) crystallized from ether to give 220 mg (23 %) of (Xb), m.p. 80 – 83°. Recrystallization from ether gave the pure product, m.p. 85 – 86°, $[\alpha]_D^{23} = -39.6°$ (*c* 4.8, $CHCl_3$), IR bands at 1705 and 1720 cm^{-1}. (Found: C 64.20; H 5.37. Calc. for $C_{14}H_{14}O_5$: C 63.98; H 5.50.)

The material in the mother liquors was separated into two fractions by preparative TLC, using ether-pentane (1 : 1) as eluent. The fast moving fraction gave an additional 338 mg (35 %) of (Xb), m.p. 83 – 84°. The slow moving fraction gave 133 mg (14.5 %) of the β-anomer (VIb) as a syrup, $[\alpha]_D^{23} = -112$ (*c* 3.6 $CHCl_3$). IR bands were observed at 1705 and 1720 cm^{-1}.

Reduction of (VI) and (X) with $LiAlH_4$. Preparation of (XVa and b). A solution of (Xa) (277 mg) in ether (4 ml) was added with stirring to a suspension of $LiAlH_4$ (60 mg) in ether (5 ml) in the course of 10 min. The stirring was continued for 10 min, and excess $LiAlH_4$ was then destroyed by careful addition of water. The mixture was diluted with methanol, filtered through activated carbon, and evaporated. The residue was dried and benzoylated in the usual manner with benzoyl chloride (0.5 ml) in pyridine (1 ml), yielding 400 mg of crude (XVb). This product was purified by preparative TLC, using ether-pentane (1 : 1) as eluent, to give 220 mg (44 %) of methyl 2,6-di-*O*-benzoyl-3,4-dideoxy-α-D-*erythro*-hex-3-enopyranoside (XVb) as a syrup, $[\alpha]_D^{23} = -39.4°$ (*c* 5.0, $CHCl_3$). (Found: C 68.25; H 5.64. Calc. for $C_{21}H_{20}O_6$: C 68.48; H 5.44.)

In a separate experiment, (Xa) (624 mg) was reduced, as described above, followed by acetylation with acetic anhydride in pyridine. The product thus obtained (570 mg)

was purified by preparative TLC, using ether-pentane (2 : 1) as eluent to give 350 mg (48 %) of methyl 2,6-di-*O*-acetyl-3,4-dideoxy-α-D-*erythro*-hex-3-enopyranoside (XVa) as a syrup, $[\alpha]_D^{23} = -26.8°$ (*c* 6.2, $CHCl_3$). (Found: C 53.85; H 6.64. Calc. for $C_{11}H_{16}O_6$: C 54.09; H 6.60.)

Reduction of the 6-*O*-benzoate (Xb) (500 mg) with $LiAlH_4$ (150 mg) in ether (10 ml), followed by benzoylation and purification by chromatography as described above, gave 350 mg (50 %) of (XVb).

Preparation of (IIIa and b). Reduction of (VIa) (360 mg) with $LiAlH_4$, as described above, followed by acetylation gave 300 mg of the product, which was purified by preparative TLC (ether-pentane (1 : 1)). The main fraction thus obtained gave 150 mg (33 %) of methyl 2,6-di-*O*-acetyl-3,4-dideoxy-β-D-*threo*-hex-3-enopyranoside (IIIa) as a syrup, $[\alpha]_D^{23} = -11.7°$ (*c* 1.2, $CHCl_3$). (Found: C 53.92; H 6.35.)

Reduction of (VIa) (280 mg) followed by benzoylation and purification by preparative TLC (ether-pentane (1 : 1)) gave, as the main product, 200 mg (40 %) of methyl 2,6-di-*O*-benzoyl-3,4-dideoxy-β-D-*threo*-hex-3-enopyranoside (IIIb), m.p. 75 – 78°. Recrystallization from methanol gave the pure product, m.p. 77 – 78°, $[\alpha]_D^{23} = +0.1°$ (*c* 2.1, $CHCl_3$). (Found: C 68.40; H 5.57.)

The benzoate (VIb), by reduction and benzoylation, gave a 39 % yield of (IIIb), m.p. 76 – 78°.

Hydroxylation of (III) and (XV). A solution of (IIIb) (341 mg) in methanol (5 ml), containing a small amount of sodium, was kept over night. The base was then removed with an ion exchange resin (Amberlite IR-120), and the methanol was evaporated. The residue was dissolved in *t*-butanol (3 ml), and 0.5 ml of a solution of osmium tetraoxide (100 mg) in *t*-butanol (10 ml) was added, together with 1 ml of a solution of hydrogen peroxide in t-butanol.[10] The solution was kept a room remperature for 3 days, after which time the reaction was completed, as seen by TLC. The solvent was then removed, and the residue was acetylated with acetic anhydride in pyridine. The crude product (150 mg) thus obtained was subjected to preparative TLC (benzene-ether (1 : 1)). The main fraction was crystallized from ethanol and gave 46 mg of methyl tetra-*O*-acetyl-β-D-altropyranoside (IV), m.p. 93 – 94°, $[\alpha]_D^{23} = -60°$ (*c* 1.5, $CHCl_3$), in agreement with the reported values.[11] Its NMR spectrum was identical with that of an authentic sample.

Debenzoylation of (XVb) (350 mg), followed by hydroxylation and acetylation as described above, gave a crude product, which was separated into two fractions by preparative TLC, using benzene-ether (1 : 1) as eluent. The fastest moving fraction was crystallized from ethanol and gave 40 mg of methyl tetra-*O*-acetyl-α-D-allopyranoside (XVI), m.p. 115 – 116°, $[\alpha]_D^{23} = +103°$ (*c* 2.0, $CHCl_3$), in agreement with reported values.[12] The slow moving fraction gave, by crystallization from hexane, 20 mg of methyl tetra-*O*-acetyl-α-D-galactopyranoside (XIV), m.p. 84 – 85°, $[\alpha]_D^{23} = +130°$ (*c* 1.3, $CHCl_3$).[13] Both compounds gave NMR spectra which were identical with those of authentic products.

Catalytic reduction of X and VI. A solution of (Xa) (202 mg) in ethyl acetate (25 ml) was hydrogenated at room temperature and 1 atm. pressure for 18 h, using 400 mg of 5 % palladium on barium sulfate as catalyst. Filtration and evaporation gave 200 mg of crude product, which was purified by preparative TLC (benzene-ether (1 : 1)) to give methyl 6-*O*-acetyl-3,4-dideoxy-α-D-*glycero*-hexopyranosid-2-ulose (XIa) as a rather unstable syrup, $[\alpha]_D^{23} = +78.9°$ (*c* 3.1, $CHCl_3$). (Found: C 53.17; H 6.98. Calc. for $C_9H_{14}O_5$: C 53.46; H 6.93.)

The β-glycoside (VIa) was reduced by the same procedure, and the product was purified by chromatography to give methyl 6-*O*-acetyl-3,4-dideoxy-β-D-*glycero*-hexopyranosid-2-ulose (VIIa) as a syrup which was less stable than (XIa), and correct analysis could not be obtained. $[\alpha]_D^{23} = -4.3°$ (*c* 4.2, $CHCl_3$). NMR data are given in Table 2.

Preparation of methyl 3,4-dideoxy-hexopyranosides (VIII) and (XII)

The acetate (XIIa). To a solution of (XIa) (92 mg) in methanol (5 ml), sodium borohydride (100 mg) was added in three portions in the course of 20 min. The solution was then neutralized with acetic acid and evaporated to dryness. The residue was acetylated with acetic anhydride (0.5 ml) in pyridine (1 ml). Work up in the usual manner gave

108 mg (99 %) of almost pure methyl 2,6-di-*O*-acetyl-3,4-dideoxy-α-D-*erythro*-hexopyranoside (XIIa) as a syrup. Preparative TLC (ether-pentane (1 : 2)) gave the pure product, $[\alpha]_D^{23} = +109°$ (*c* 6.8, $CHCl_3$). (Found: C 53.25; H 7.28. Calc. for $C_{11}H_{18}O_6$: C 53.65; H 7.37.)

Alternatively, (XVa) (200 mg) in ethyl acetate (25 ml) was hydrogenated over night at room temperature in the presence of 500 mg of 5 % palladium on carbon. Filtration and evaporation gave 200 mg of (XIIa), identical with the product described above.

The benzoate (XIIb). Deacetylation of (XIIa) with methanolic sodium methoxide, followed by benzoylation with benzoyl chloride in pyridine, gave methyl 2,6-di-*O*-benzoyl-3,4-dideoxy-α-D-*erythro*-hexopyranoside (XIIb). The product was crystallized from ethanol, m.p. 70 – 71°, $[\alpha]_D^{23} = +55.6°$ (*c* 1.1, $CHCl_3$). (Found: C 68.20; H 6.06. Calc. for $C_{21}H_{20}O_6$: C 68.11; H 6.00.)

The acetate (VIIIa). A solution of (IIIa) (120 mg) in ethyl acetate was hydrogenated with palladium on carbon as described above to give 100 mg of methyl 2,6-di-*O*-acetyl-3,4-dideoxy-β-D-*threo*-hexopyranoside (VIIIa). Preparative TLC (ether-pentane (1 : 1)) gave the pure product as a syrup. $[\alpha]_D^{23} = -26.2°$ (*c* 1.8, $CHCl_3$). (Found: C 53.25; H 7.44.)

The benzoate (VIIIb). Deacetylation of (VIIIa) with methanolic sodium methoxide, followed by benzoylation with benzoyl chloride in pyridine, gave the corresponding dibenzoate (VIIIb). The product was crystallized from ethanol, m.p. 92 – 93°, $[\alpha]_D^{23} = -30.1°$ (*c* 0.8, $CHCl_3$). (Found: C 67.95; H 6.00.)

Direct preparation of (VIII) and (XII) from (I). Tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (Ia) (5.88 g) was dissolved in anhydrous hydrogen fluoride (10 ml) at −78°, and the solution was kept at −20° for 4 h. Methylene chloride was then added and the mixture was poured on ice. The organic layer was washed with aqueous sodium hydrogen carbonate, dried, and evaporated, leaving 3.1 g of a mixture of the anomeric fluorides (IXa). Methylene chloride (30 ml) was then added together with 10 ml of a mixture of methanol, boron trifluoride-etherate, and methylene chloride (1 : 1 : 8). The solution was kept for 20 – 30 min at room temperature. It was then washed with aqueous sodium hydrogen carbonate, dried and evaporated to give 3.19 g of a mixture of (VIa) and (Xa). This product was dissolved in ethyl acetate (10 ml), and the solution was added to a suspension of 1.5 g of 5 % palladium on barium sulfate in ethyl acetate (50 ml), which was previously saturated with hydrogen. The mixture was hydrogenated at 1 atm. and room temperature until 515 ml (1.05 mequiv.) of hydrogen was absorbed (34 h). The catalyst was filtered off, and the solvent was evaporated, leaving 3.3 g of a mixture of (VIIa) and (XIa). This mixture was dissolved in methanol (50 ml), and sodium borohydride (1.4 g) was added in three portions during 1 h. The solution was then neutralized with acetic acid and evaporated to dryness. The residue was dissolved in pyridine (10 ml) and acetic acid anhydride (10 ml), and the solution was kept over night at room temperature. Water was then added, followed by methylene chloride, and the solution was washed with 3 N sulfuric acid and aqueous sodium hydrogen carbonate, and dried. Evaporation of the solvent left 3.5 g of a mixture, which contained largely (VIIIa) and (XIIa) in the proportion 1 : 6. The two isomers may be separated by preparative TLC or by column chromatography, using ether-pentane (1 : 1) as an eluent.

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