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STEREOSPECIFIC SYNTHESIS OF METHYL D,L-HEX-2-ULOPYRANOSIDES FROM FURAN COMPOUNDS

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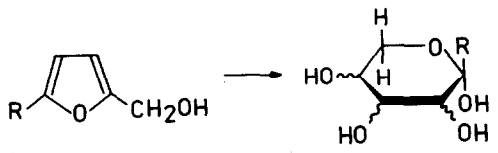
Abstract—2-Benzyloxymethyl-5-hydroxymethylfuran was converted, according to the known method, into methyl 1-O-benzyl-3,4-dideoxy-D,L-hex-3-en-2-ulopyranos-5-ulose. Reduction of the latter and hydroxylation or epoxidation, followed by the oxirane ring opening, afforded the title compounds with α-sorbo-, β-fructo-, α-tagato- and α-psico- configuration. The steric course of reduction, hydroxylation and epoxidation reactions were examined.

There have been many syntheses described for monosaccharides from non-sugar starting materials.[2] Most of the syntheses dealt with aldoses, whereas less attention has been devoted to the total synthesis of ketoses. Apart from the early work of Fischer[3a,b] only D-fructose and D-sorbose[4a,b,c] and a few relatively simple ketoses[5a,b] have been obtained from non-sugar precursors.

We have previously described the stereospecific synthesis of aldoses from furan compounds,[6] and now present the application of this approach to 2-ketohexoses, which are the most widespread and the biologically most important keto-sugars.[7]

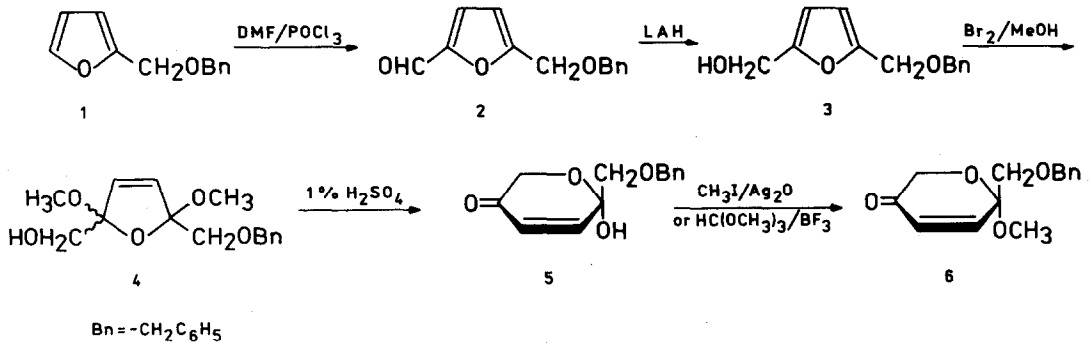
RESULTS AND DISCUSSION

The transformation of furan compounds into monosaccharides according to our method can be summarized by the following equation:

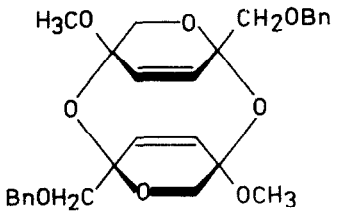


Therefore the synthesis of 2-ketohexoses requires 2,5-dihydroxymethylfuran (R = CH_2OH) as the starting compound. Its monobenzyl ether (**3**) was obtained by Vilsmeier formylation of benzyl ether **1** and subsequent LAH reduction of aldehyde **2**. Compound **3** was treated with bromine in methanol to give a mixture of *cis* and *trans* isomers (^{1}H NMR) of 2,5-dimethoxy-2,5-dihydroderivative **4**, which on mild acidic hydrolysis afforded diulose **5** in an excellent overall yield. Its structure followed unambiguously from analytical and spectral data. The IR spectrum confirmed the presence of OH (3400 cm^{-1}) and α,β-unsaturated CO group (1695 cm^{-1}), whereas ^{1}H NMR spectrum revealed the presence of two vinylic protons and methylene group (two AB systems centered at δ 6.32 and 4.17, respectively), as well as signals corresponding to the benzyloxy-Me group. Glycosidation of diulose **5** with methyl iodide–silver oxide reagent gave methyl glycoside **6**. Its IR and ^{1}H NMR spectrum confirmed replacement of the OH hydrogen in **5** by Me group. Reacting diulose **5** with trimethyl orthoformate in the presence of boron trifluoride gave the same glycoside **6**, though in a smaller yield, and a side-product **7**. Elemental analysis and parent ion, *m/e* 496, of the latter gave molecular formula $C_{28}H_{32}O_4$. Its IR spectrum showed the disappearance of the CO and OH groups, whereas in the ^{1}H NMR spectrum appeared four singlets (δ 3.24, 4.53, 5.99 and 7.26) with relative intensity 3:2:2:5 which were assigned to the protons of methoxy, methylene, vinyl and phenyl groups, respectively. Two AB systems centered at δ 3.25 (J = 10.5 Hz) and 3.88 (J = 11.5 Hz) were attributed to the geminal protons at C-1 and C-6. On the basis of the foregoing data the "dimeric" structure **7** was assigned to the side-product, which arose by methylation of the corresponding "dimeric" hemiacetal presumably present in equilibrium with diulose **5**. High symmetry of the molecule accounts for the simplicity of the ^{1}H NMR spectrum.

Since in diulose **5** and its glycoside **6** there is no hydrogen at C-2, their ^{1}H NMR spectra are lacking vicinal coupling constants which could be used to ascribe the dihydropyran ring conformation. However it could



Bn = $-CH_2C_6H_5$



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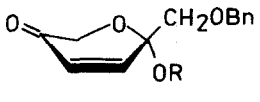
be confidently predicted from the knonw steric interactions of benzyloxymethyl group and from the anomeric effects of MeO (OH) groups in dihydropyran ring[8a,b] that conformation **8** will be preferred. Analysis based on comparison with other pyranosid-4-uloses for which conformational equilibrium have been assigned,[9] indicates that for compounds **5** and **6** conformation **8** is preferred to the extent of at least 99%.



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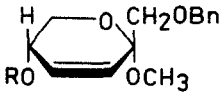
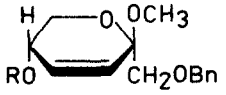
R = H, CH_3

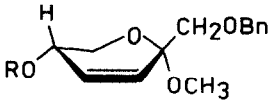
The steric course of the hydride reduction of the CO group in the dihydropyran system depends on the conformation.[10] From these studies it can be deduced that hydride reduction of **6** should lead predominantly to the α-anomer **9**.† In fact reduction of diulose **6** with sodium borohydride in THF–H_2O solution was stereoselective and led to a mixture of anomeric carbinols **9** and **11** in a ratio 14:1 (VPC).



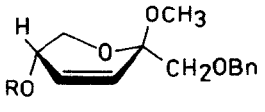
9 R = H
10 R = Ac



11 R = H
12 R = Ac
13 R = Bz



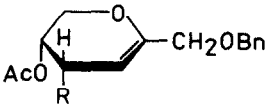
$^0H_6$



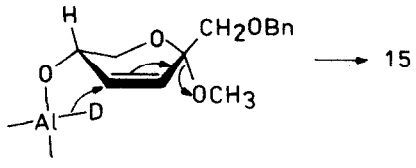
$^6H_0$

Assignment of their configuration was based on the ^1H NMR spectra of their O-acetyl derivatives **10** and **12** the conformations of which were confidently predicted to be $^0H_6$ and $^6H_0$ respectively. This prediction was also based on the known anomeric effect and steric interaction of the benzyloxymethyl group. Therefore coupling constants in the spectrum of acetate **10** $J_{5,6} = 7.5$ Hz and $J_{5,6} = 5.4$ Hz indicated that H-5 occupied a pseudoaxial position and consequently that the acetate **10** has α-configuration, whereas $J_{5,6} = 3.0$ Hz and $J_{5,6} = 1$ Hz in the spectrum of acetate **12** testified to the pseudoequatorial position of H-5 and β-configuration of the minor product.

Reduction of diulose **6** with LAH at 5° gave three products (tlc). Two of them were identified as carbinols **9** and **11**. The third was an anhydrohexenitol which was characterized as the acetate **14**. This product predominated when the reaction was carried out at room temperature with excess of LAH. Compound **14** could be also obtained by the reductive elimination of the OMe group and subsequent acetylation from carbinol **9**.



14 R = H
15 R = D



Scheme 1.

The steric course of this reaction was established by carrying out the reduction with LAD. The ^1H NMR spectrum of the deuterated acetate showed it to have configuration **15**, hence the steric pathway is that shown on the Scheme. This is analogous to previously studied cases.[11a,b]

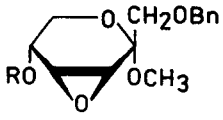
The β-anomer **10**, which is not available directly from diulose **6**, was obtained by inversion of configuration at C-5 in the α-isomer **9**. Treatment of **9** with triphenylphosphine–diethyl azodicarboxylate reagent in the presence of benzoic acid[12a,b] gave without any by-products and in good yield the benzoate **13**.

Methyl 3,4-anhydrohex-2-ulopyranosides. To date few 3,4-anhydroketoses have been synthesized[13a,b,c,d] and none of them by a direct epoxidation of a corresponding unsaturated sugar. We found that the introduction of benzyloxymethyl group at the anomeric center does not change the steric course of an epoxidation as compared with that of methyl 2,3-unsaturated aldopyranosides.[14] Thus treatment of the carbinols α (**9**) and β (**11**) with *m*-chloroperbenzoic acid gave stereoselectively compounds **16** and **18**, respectively. Their α-ribo (**16**) and β-ribo (**18**) configuration followed from the $J_{4,5}$ coupling constants in the ^1H NMR spectra of the corresponding acetates **17** and **19** which amounted to 1.9 Hz and 4.0 Hz, indicating in both cases that H-4 and H-5 are *cis*.[14] Stereoselective introduction of oxirane ring *cis* to the free OH group at C-5 is presumably due to the H-bonding of peroxy acid.

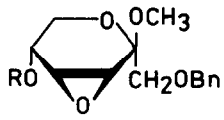
Reaction of benzoyl derivative **13** with benzonitrile and 30% hydrogen peroxide in the presence of sodium hydrogen carbonate[15] yielded anhydro compound **21** (and **20**) with oxirane ring *trans* to the bulky substituents at C-2 and C-5. β-Lyxo configuration was confirmed by *trans* relation of H-4 and H-5 indicated by $J_{4,5} \sim 0$.

α-D,L-Sorbo- and β-D,L-fructopyranoside. Basic hydrolysis of oxirane ring in the anhydro compounds **16** and **20** proceeded with high regioselectivity. In both cases a single product was obtained due to the attack of

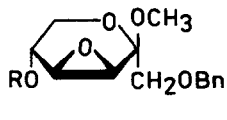
†All obtained compounds are D,L-mixtures; for the sake of simplicity formulae represent only D-compounds.



16 R=H
17 R=Ac



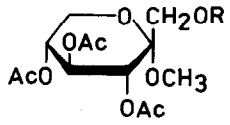
18 R=H
19 R=Ac



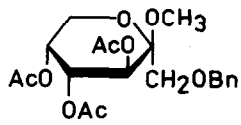
20 R=H
21 R=Bz
22 R=Ac

hydroxide at the C atom farthest from the anomeric center, i.e. C-4.[16]

The α-sorbo and β-fructo configuration of the hydrolysis products were assigned on the basis of the coupling constants of the H-3, H-4 and H-5 protons of the acetate **23** ($J_{3,4} = 10.0$, $J_{4,5} = 9.2$ Hz) and **25** ($J_{3,4} = 10$, $J_{4,5} = 3.6$ Hz) respectively. Structure **23** was confirmed by direct comparison (^{1}H NMR) of tetra-O-acetate **24** (obtained by catalytic debenzylation and subsequent acetylation of **23**) with methyl 1,3,4,5-tetra-O-acetyl-α-L-sorbopyranoside.

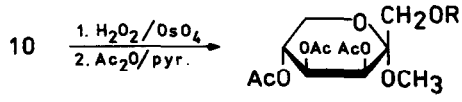


23 R=Bn
24 R=Ac



25

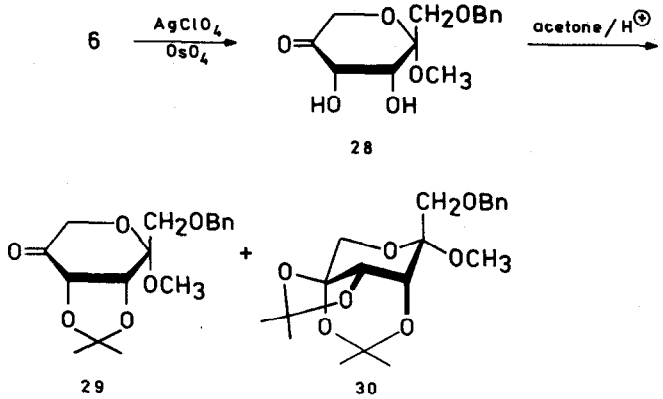
Methyl α-D,L-tagato- and α-D,L-psicopyranoside. *cis*-Hydroxylation of acetate **10** with Milas reagent (H_2O_2 in t-BuOH with catalytic amounts of OsO_4) introduced OH groups at C-3 and C-4 from the less hindered side of the dihydropyran ring.[17] α-Lyxo configuration and hence the structure of methyl 3,4,5-tri-O-acetyl-1-O-benzyl-α-D,L-tagatopyranoside (**26**) was confirmed by the *trans* relation of H-4 and H-5 which followed from their coupling constant $J_{4,5} = 10.2$ Hz.



26 R=Bn
27 R=Ac

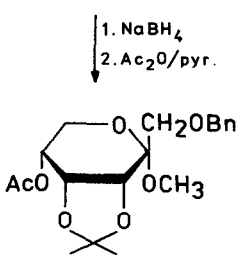
The α-ribo configuration of the tetrahydropyran ring was obtained by *cis*-hydroxylation of the diuloside **6**. The reaction was carried out with silver perchlorate–osmium tetroxide reagent[18] and the resulting diol **28** was treated with acetone in the presence of sulfuric acid to give the isoporpylidene derivative **29** and a by-product (10%) **30**.

Sodium borohydride reduction and subsequent acetylation of **29** gave the acetate **31** as a single product.



28

29 30



31

Table. ^{1}H NMR data[a]

Compound	Solvent[b]	Chemical shifts, δ (ppm, TMS = 0)											Coupling constants (Hz)					
		H-1,	H-1′	H-3	H-4	H-5	H-6,	H-6′	OCH_2	C_6H_5	OCH_3	OAc	$J_{1,1'}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
5	CCl_4	3.47		6.72	5.92	—	4.42	3.92	4.52	7.25	—	—	—	10.5	—	—	—	17.5
6	CCl_4	3.66	3.35	6.92	5.99	—	4.25	3.98	4.50	7.27	3.26	—	10.5	10.5	—	—	—	17.0
10	C_6D_6	3.60	3.35	6.02	5.85	5.18	3.98	3.74	4.30	7.19	3.20	1.67	10.2	10.4[c]	2.3	7.5	5.4	11.5
12	C_6D_6	3.74	3.40	6.35	6.00	4.90	4.02	3.82	4.36	7.30	3.18	1.68	11.0	10.7	5.2	3.0	~1	13.5
13	CCl_4	3.67	3.35	6.16	5.99	5.08	4.10	3.75	4.48[d]	e	3.22	—	10.5	10.2	4.2	3.0	0.8	12.5
14[f]	C_6D_6	3.90		4.66	2.01	4.93	3.86	3.65	4.42	7.12	—	1.60	—	3.4	5.5	5.2	2.5	11.3
15[g]	C_6D_6	3.85		4.64	2.02	4.89	3.86	3.64	4.39	7.12	—	1.60	—	3.4	5.5	5.2	2.5	11.3
16	$CDCl_3$	3.75 — 3.10				4.00	3.75 — 3.10		4.58	7.35	3.30	—	—	—	1.5	10.2	—	—
17	$CDCl_3$	3.55 — 3.05				5.12	3.55 — 3.05		4.58	7.32	3.30	2.10	—	—	1.5	10.2	6.2	—
18	CCl_4	3.75 — 3.10							3.98	7.25	3.20	—	—	—	—	—	—	—
19	CCl_4	3.39	3.51	3.56 — 3.12[h]		4.80	3.72	—	4.56[d]	7.23	3.12	2.05	10.7	—	4.0	4.0	1.9	12.5
21	$CDCl_3$	3.85 — 3.30				5.33	—	4.00	4.62[d]	i	3.32	—	—	—	—	—	1.5	12.7
22	$CDCl_3$	3.52	3.70	3.60 — 3.10		5.05	3.55	3.67	4.55[d]	7.30	3.28	2.04	10.2	—	—	3.5	1.6	13.2
23	C_6D_6	4.21		5.45	5.81	5.05	3.72	3.38	3.48	7.17	3.00	j	11.7	10.0	9.2	6.2	10.5	10.7
25	C_6D_6	4.27		5.93	5.63	5.40	3.31		3.58	7.26	3.01	j	11.5	10.6	3.6	—	—	—
26	C_6D_6	4.19		5.91	5.75	5.45	3.88	3.40	3.37	7.10	2.99	k	11.7	3.4	10.2	5.7	10.2	10.5
29[l]	$CDCl_3$	3.54		4.8 — 4.7		—	4.80 — 4.70			7.30	3.24	—	—	—	—	—	—	—
30[m]	$CDCl_3$	4.54	4.48	4.72	4.50	—	4.24	3.90	3.50[d]	7.30	3.28	—	10.7	7.8	—	—	—	10.6
31[n]	$CDCl_3$	3.50		4.31	4.55	5.40	3.75	3.66	4.57[d]	7.30	3.30	2.05	—	7.5	3.8	6.2	7.5	10.6

[a]Spectra were analysed as first-order; not reported coupling constants (–) could not be obtained from the spectrum. [b]Choice of the solvent depended on the resolution of signals. [c]$J_{3,5}$ = 1.0 Hz. [d]Center of AB system, J = 12 Hz. [e]7.95 (m, 2H), 7.20 (m, 8H). [f]δ 2.19 (H-4′) $J_{3,4'}$ = 4.0 Hz, $J_{4',5}$ = 4.7 Hz; $J_{4,6}$ = 1.5 Hz, $J_{4,6'}$ ~ 1 Hz. [g]$J_{4,6}$ = 1.5 Hz, $J_{4,6'}$ = 1.0 Hz. [h]Includes H-6′. [i]8.08–7.95 (m, 2H), 7.4–7.2 (m, 8H). [j]δ 1.69 (s, 3H), 1.70 (s, 3H), 1.77 (s, 3H). [k]δ 1.61 (s, 3H), 1.68 (s, 3H), 1.79 (s, 3H). [l]δ 1.49 (s, 3H), 1.38 (s, 3H), >C(CH$_3$)$_2$. [m]δ 1.47 (s, 3H), 1.39 (s, 3H), 1.37 (s, 3H), 1.30 (s, 3H), 2x >C(CH$_3$)$_2$. [n]δ 1.52 (s, 3H), 1.42 (s, 3H), >C(CH$_3$)$_2$.

In the hydride reduction of the CO group the attack of the reagent from the side opposite to the isopropylidene substituent should be favoured[19] assuring ribo configuration of the product. Since stereoselectivity of the *cis*-hydroxylation of **6** could not be predicted it remained to decide the configuration of the anomeric center in **31**. The ^{1}H NMR spectrum of **31** revealed coupling constants $J_{5,6} = 6.2$ and $J_{5,6} = 7.5$ Hz indicating a distortion of the tetrahydropyran ring towards smaller dihedral angles H_5–C_5–C_6–H_6 and H_5–C_5–C_6–$H_{6'}$, due to the condensation with 5-membered ring and the quasi-axial position of H-5. Coupling constant $J_{4,5} = 3.8$ Hz, even for distorted tetrahydropyran ring, excluded axial–axial relation of H-4 and H-5. These data pointed to the α-ribo configuration of acetate **31**. The exclusive formation of methyl α-psicopyranoside **31** shows that also *cis*-hydroxylation step is highly stereoselective presumably due to the larger steric hindrance of benzyloxymethyl group.

The IR spectrum of the side-product **30** lacked the CO group absorption whereas its ^{1}H NMR spectra revealed the presence of two isopropylidene groups. From these data the structure **30** was deduced consistent with elemental analysis and the mass spectrum.

EXPERIMENTAL

M.ps were determined on a Koffler bloc and are uncorrected. B.ps refer to the air bath temp. The IR spectra were obtained on Unicam SP-200 using KBr discs for solids and films for liquids. The ^{1}H NMR spectra were measured on Varian HA-60-IL or Jeol JNM-4H-100 spectrometers and chemical shifts are reported in ppm downfield from internal TMS. The UV spectra were recorded with Unicam SP-500 and mass spectra were obtained on KLB 900 spectrometer. Glc analyses were made with a Willy Giede gas chromatograph 18/3. For column chromatography silica gel Schuchardt 100–200 mesh was used. All reactions and chromatographic separations were monitored by tlc, which was done using silica gel G (Merck).

2-Benzyloxymethylfuran (**1**). A suspension of powdered NaOH (80 g, 2 mol) in dry DMSO (700 mL) was added to a soln of furfuryl alcohol (125 g, 1.27 mol) in dry DMSO and stirred for 45 min. Benzyl chloride (157 mL, 1.37 mol) was added and stirring was continued. After 5 hr when the reaction was complete (tlc) the mixture was poured on ice–water (1.5 L) and extracted with ether (3 L). The organic layer was washed with water, dried and evaporated. Distillation of the residue gave **1** (230 g, 98%) b.p. 165°/35 Torr. IR: 1502 and 888 (furan), 1459, 740 (C_6H_5–), 1210, 1145, 1020 cm^{-1} (C–O–C). (Found: C, 76.7; H, 6.6. Calc. for $C_{12}H_{12}O_2$: C, 76.6; H, 6.4%).

2-Benzyloxymethyl-5-formylfuran (**2**). $POCl_3$ (48 mL, 0.52 mol) was added dropwise with stirring to freshly distilled DMF (45 g, 0.6 mol) chilled in the ice–water bath. Then **1** (100 g, 0.53 mol) was added and the stirring was continued for 1 hr at room temp. The mixture was poured into ice–water, neutralized with NaOAc and left overnight. The product was extracted with ether, dried ($MgSO_4$) and evaporated. Distillation yielded **2** (70 g, 61%) b.p. 147°/0.4 Torr. IR: 1690 (C=O), 1460, 740, 695 (C_6H_5), 1500 (furan), 1240, 1080, 1025 cm^{-1} (C–O–C). (Found: C, 72.2; H, 5.6. Calc. for $C_{13}H_{12}O_3$: C, 72.2; H, 5.6%).

2 - Benzyloxymethyl - 5 - hydroxymethylfuran (**3**). Compound **2** (95 g) was reduced with LAH (9.0 g) in ether (1050 mL) at room temp. The usual work-up and distillation afforded **3** (89.7 g, 93.5%), b.p. 159°/0.06 Torr. IR: 3450 (OH), 1505 (furan), 1460, 740, 700 (C_6H_5), 1075, 1020 cm^{-1} (C–O–C). ^{1}H NMR (CCl_4): δ 7.22 (s, 5H, C_6H_5), 6.12 (s, 2H, H-3, H-4), 4.40 (s, 2H), 4.35 (s, 2H) and 4.28 (s, 2H) (3 × CH_2), 3.63 (s, 1H, OH). (Found: C, 71.1; H, 6.6. Calc. for $C_{13}H_{14}O_3$: C, 71.5; H, 6.5%).

2 - Benzyloxymethyl - 5 - hydroxymethyl - 2,5 - dimethoxy - 2,5 - dihydrofuran (**4**). Compound **3** (41 g, 0.19 mol) was dissolved in ether (200 mL)—MeOH (100 mL) mixture, chilled to −40° and Br_2 (13 mL, 0.32 mol) in MeOH (50 mL) was added dropwise with stirring. The mixture was stirred at −45–−35° for 30 min, neutralized with gaseous ammonia, evaporated, the residue diluted with water and extracted with benzene. After removal of the solvent distillation yielded **4** (45.3 g, 86%) b.p. 175°/0.1 Torr. IR: 3450 (OH), 1640 (C=C), 1460, 740 (C_6H_5), 1100, 1070 cm^{-1} (C–O–C). ^{1}H NMR (CCl_4): δ 7.26 (s, 5H, C_6H_5), 5.90 (d) and 5.79 (d, 2H, J = 5.7 Hz, H-3, H-4), 4.50 (m, 2H, $-CH_2-C_6H_5$), 3.61 (d, 2H, J = 11.5 Hz, C_5–CH_2), 3.59 (d, 2H, J = 10.0 Hz, C_2–CH_2), 3.30 (s, 3H, OCH_3), 3.25 (s, 3H, OCH_3), 2.93 (s, 1H, OH). (Found: C, 64.5; H, 7.2. Calc. for $C_{15}H_{20}O_5$: C, 64.3; H, 7.2%).

1 - O - Benzyl - 3,4 - dideoxy - D,L - hex - 3 - en - 2 - ulopyranos - 5 - ulose (**5**). A mixture of **4** (13 g, 0.046 mol) and 1% H_2SO_4 (25 mL) was made homogeneous with acetone and left at room temp. for 2 hr. The soln was brought to pH 5 with solid $NaHCO_3$, acetone evaporated in vacuum and the residue extracted with benzene. Removal of the solvent gave a gum **5** (10.8 g, ~100%) which was homogenous by tlc. An analytical sample was obtained by chromatography on silica gel column. IR: 3400 (OH), 1695, 1630 cm^{-1} (C=C–C=O). (Found: C, 66.2; H, 6.2. Calc. for $C_{13}H_{14}O_4$: C, 66.6; H, 6.0%).

Methyl 1 - O - benzyl - 3,4 - dideoxy - D,L-hex - 3 - en - 2 - ulopyranosid - 5 - ulose (**6**)

Method (*a*). A soln of **5** (10 g, 0.042 mol) and trimethyl orthoformate (6.5 g, 0.06 mol) in abs ether (200 mL) was chilled to 0° and BF_3–etherate (1.6 g) in abs ether (25 mL) was added slowly with stirring. After 5 hr at room temp. the reaction was quenched with Et_3N, etheral soln washed with water and dried. Partial evaporation gave a colourless ppt which was filtered off and recrystallized (MeOH) to give **7** (0.32 g, 3%) m.p. 162–163°. IR: 1500, 1460, 730 (C_6H_5), 1120, 1080, 1050 cm^{-1} (C–O–C). (Found: C, 67.5; H, 6.6. Calc. For $C_{28}H_{32}O_8$: C, 67.7; H, 6.4%).

The syrupy filtrate obtained after the removal of **7** was chromatographed on a silica gel column using a benzene–ether 9:1 eluent. The pyranoside **6** (7.2 g, 68%) b.p. 130°/0.01 Torr, was obtained as viscous oil. IR: 1695, 1630 cm^{-1} (C=C–C=O). (Found: C, 67.2; H, 6.3. Calc. for $C_{14}H_{16}O_4$: C, 67.7; H, 6.5%).

Method (*b*). Silver oxide (21 g, 0.15 mol) was added to a soln of **5** (11.7 g, 0.05 mol) and MeI (21 g, 0.15 mol) in abs ether (200 mL). The mixture was stirred for 8 hr at room temp. The inorganic material was filtered off and washed with ether. The combined ether solns were evaporated and the residue distilled to give **6** (10.5 g, 85%), b.p. 130°/0.01 Torr, identical in every respect with the sample obtained in the preceding experiment.

Methyl 1 - O - benzyl - 3,4 - dideoxy - α - D,L - glycero - hex - 3 - en - 2 - ulopyranoside (**9**). A soln of **10** (3.0 g) in MeOH (50 mL) was treated with a small lump of Na and left overnight at room temp. The mixture was neutralized with Dowex, filtered and evaporated to give **9** (2.47 g, 98%) as thick colourless oil.

Methyl 1 - O - benzyl - 3,4 - dideoxy - β - D,L - glycero - hex - 3 - en - 2 - ulopyranoside (**11**). The pyranoside **11** was obtained as a thick, colourless oil from benzoate **13** as described.

Methyl 5 - O - acetyl - 1 - O - benzyl - 3,4 - dideoxy - D,L - glycero - hex - 3 - en - 2 - ulopyranoside α (**10**) *and β* (**12**). A soln of **6** (9.9 g, 0.04 mol) in THF (30 mL) was added to a soln of $NaBH_4$ (0.76 g, 0.02 mol) in water (100 mL) and chilled in an ice-bath. The mixture was stirred for 30 min at room temp., neutralized with AcOH and extracted with EtOAc. Removal of the solvent and treatment of the resulting thick oil (9.0 g, 91%) with pyridine–Ac_2O mixture gave after the usual work up a mixture of two (tlc) acetates which were separated on a silica gel column. Elution with benzene–ether (9:1) gave **10** (8.22 g, 74.7%) b.p. 175°/0.2 Torr. IR: 1725, 1230 (OAc), 1650 cm^{-1} (C=C). (Found: C, 65.6; H, 6.8. Calc. for $C_{16}H_{20}O_5$: C, 65.7; H, 6.9%).

Further elution of the column with the same solvent gave **12** (0.58 g, 5.3%) b.p. 175°/0.2 Torr. IR: 1740, 1240 (OAc), 1660 cm^{-1} (C=C). (Found: C, 65.6; H, 7.3. Calc. for $C_{16}H_{20}O_5$: C, 65.7, H, 6.9%).

5 - O - Acetyl - 2,6 - anhydro - 1 - O - benzyl - 3,4 - dideoxy - D,L - glycero - hex - 2 - enitol (**14**). A soln of **10** (1.0 g, 3.4 mmol) in ether (40 mL) was stirred with LAH at room temp. for 3 days. The excess of hydride was decomposed with water and 15% NaOH. A ppt was filtered off and ether evaporated. The residue

on acetylation with pyridine–Ac_2O mixture, after usual work up and chromatography on silica gel, gave **12** (0.61 g, 68%) b.p. 180°/0.2 Torr. IR: 1740, 1245 (OAc), 1680, 1060 cm^{-1} (C=C–O). (Found: C, 68.7, H, 7.1. Calc. for $C_{15}H_{18}O_4$: C, 68.7, H, 6.9%).

5 - O - *Acetyl* - 2,6 - *anhydro* - 1 - O - *benzyl* - 4 - *deuterio* - 3,4 - *dideoxy* - D,L - *glycero* - *hex* - 2 - *enitol* (**15**). Compound **15** was obtained from **10** using LAD.

Methyl 5 - O - *benzoyl* - 1 - O - *benzyl* - 3,4 - *dideoxy* - β - D,L - *glycero* - *hex* - 3 - *en* - 2 - *ulopyranoside* (**13**). Benzoic acid (2.90 g, 24 mmol) and triphenylphosphine (7.70 g, 24 mmol) were added to a soln of **9** in THF (50 mL). Diethyl azodicarboxylate (4.20 g, 24 mmol) was introduced dropwise with stirring. After 1 hr the solvents were evaporated and the residue chromatographed on the silica gel column. Elution with petroleum ether–EtOAc (9:1) gave **11** (3.65 g, 86%) as a thick liquid. IR: 1800, 1270 cm^{-1} (ester). (Found: C, 71.1; H, 6.4. Calc. for $C_{21}H_{22}O_5$: C, 71.2; H, 6.2%).

Methyl 3,4 - *anhydro* - 1 - O - *benzyl* - α - D,L - *ribo* - *hex* - 2 - *ulopyranoside* (**16**). A soln of **9** (0.43 g, 1.72 mmol) in CH_2Cl_2 (10 ml) was treated with *m*-chloroperbenzoic acid (0.3 g, 1.74 mmol). After 4 days *m*-chlorobenzoic acid was filtered off, solvent evaporated and the residue chromatographed on silica gel (10 g) column. Elution with benzene–ether (4:1) gave **16** (0.327 g, 70.9%), m.p. 61–63°, b.p. 180°/0.01 Torr. IR (KBr): 3450 (OH), 880, 820 cm^{-1} (epoxide). (Found: C, 63.1; H, 6.8. Calc. for $C_{14}H_{18}O_5$: C, 63.1; H, 6.8%).

Methyl 5 - O - *acetyl* - 3,4 - *anhydro* - 1 - O - *benzyl* - α - D,L - *ribo* - *hex* - 2 - *ulopyranoside* (**17**). Acetylation of **16** with Ac_2O–pyridine mixture gave **17** (84%), m.p. 68–69° (toluene). IR: 1745, 1230 (OAc), 870, 840, 818 cm^{-1} (epoxide). (Found: C, 62.5; H, 6.6. Calc. for $C_{16}H_{20}O_6$: C, 62.3; H, 6.5%).

Methyl 3,4 - *anhydro* - 1 - O - *benzyl* - β - D,L - *ribo* - *hex* - 2 - *ulopyranoside* (**18**). Epoxidation of **11** with *m*-chloroperbenzoic acid as described gave **18** (76%) as thick oil. IR: 3500 (OH), 860, 830 cm^{-1} (epoxide). (Found: C, 62.7; H, 6.9. Calc. for $C_{14}H_{18}O_5$: C, 63.1; H, 6.8%).

Methyl 5 - O - *acetyl* - 3,4 - *anhydro* - 1 - O - *benzyl* - β - D,L - *ribo* - *hex* - 2 - *ulopyranoside* (**19**). Acetylation of **18** with Ac_2O–pyridine afforded **19**, m.p. 89°. IR: 1740, 1250 (OAc), 875, 830, 810 cm^{-1} (epoxide). (Found: C, 62.2; H, 6.6. Calc. for $C_{16}H_{20}O_6$: C, 62.3; H, 6.5%).

Methyl 3,4 - *anhydro* - 5 - O - *benzoyl* - 1 - O - *benzyl* - β - D,L - *lyxo* - *hex* - 2 - *ulopyranoside* (**21**). To a soln of **13** (1.1 g, 3.1 mmol) in MeOH (30 mL), MeCN (2 mL), 30% H_2O_2 (3 mL) and $NaHCO_3$ (0.2 g) were added. The mixture was stirred at room temp. for 14 days, then poured into water (15 mL), extracted with benzene and dried. Benzene and acetamide were removed under reduced pressure and the residue comprising three compounds (tlc) was chromatographed on silica gel column. Elution with benzene–ether (9:1) afforded **21** (0.63 g, 55%) m.p. 74–76°. IR: 1720, 1270 (ester), 900, 870, 830 cm^{-1} (epoxide). (Found: C, 68.1; H, 6.2. Calc. for $C_{21}H_{22}O_6$: C, 68.1; H, 6.0%).

Further elution of the column with the same solvent and evaporation of combined appropriate fractions (tlc) yielded anhydro **20** (0.18 g, 18%) and then unsaturated **11** (0.10 g, 10%).

Methyl 5 - O - *acetyl* - 3,4 - *anhydro* - 1 - O - *benzyl* - β - D,L - *lyxo* - *hex* - 2 - *ulopyranoside* (**22**). The pyranoside **21** was debenzoylated with NaOMe in MeOH. Subsequent acetylation with Ac_2O–pyridine gave **22** as a colourless gum. IR: 1740, 1240 (acetate), 860, 800 cm^{-1} (epoxide). (Found: C, 61.9; H, 6.6. Calc. for $C_{16}H_{20}O_6$: C, 62.3; H, 6.5%).

Methyl 3,4,5 - *tri* - O - *acetyl* - 1 - O - *benzyl* - α - D,L - *sorbopyranoside* (**23**). Compound **16** (0.347 g, 1.3 mmol) was heated for 7 days under reflux with a sat. $Ba(OH)_2$aq. in 2:1 water–dioxane mixture (30 mL). After neutralization with CO_2 the mixture was filtered. The inorganic salt was washed with water, combined solns evaporated to dryness and the residue treated with Ac_2O–pyridine. After usual work-up column chromatography on silica gel column in benzene–ether (4:1) gave **23** (0.288 g, 54%) m.p. 132–133° (hexane–ether). IR: 1750, 1240 (OAc), 1460, 760 (aromatic), 1120, 1040 cm^{-1} (C–O–C). (Found: C, 58.4; H, 6.3. Calc. for $C_{20}H_{26}O_9$: C, 58.5; H, 6.4%).

Methyl 1,3,4,5 - *tetra* - O - *acetyl* - α - D,L - *sorbopyranoside* (**24**). A soln of **23** (0.25 g, 0.61 mmol) in 80% aqueous AcOH (40 mL) was hydrogenated in the presence of palladium oxide (50 mg). When the absorption of H_2 ceased, the catalyst was filtered off and the solvent evaporated. The residue after acetylation with Ac_2O–pyridine gave **24** (0.165 g, 75%) m.p. 104–105°. IR: 1750, 1240 (OAc), 1120, 1040 cm^{-1} (C–O–C). ^1H NMR spectrum identical with that of methyl 1,3,4,5 - tetra - O - acetyl - α - L - sorbopyranoside.

Methyl 3,4,5 - *tri* - O - *acetyl* - 1 - O - *benzyl* - β - D,L - *fructopyranoside* (**25**). Hydrolysis and acetylation of **20** (133 mg) carried out as described for **16**, gave **25** (98 mg, 48%) m.p. 119–121°. IR: 1740, 1260 (OAc), 1460, 750 (aromatic), 1120, 1080 cm^{-1} (C–O–C). (Found: C, 58.5; H, 6.4. Calc. for $C_{20}H_{26}O_9$: C, 58.5; H, 6.4%).

Methyl 3,4,5 - *tri* - O - *acetyl* - 1 - O - *benzyl* - α - D,L - *tagatopyranoside* (**26**). A mixture of **10** (584 mg), osmium tetroxide (0.04 g) and 6% H_2O_2 in t-BuOH (5 mL) was left for 7 days at room temp. The solvent was evaporated and the residue acetylated with Ac_2O–pyridine. The usual work-up and chromatography gave **26** (220 mg, 28%) b.p. 144°/0.005 Torr. IR: 1750, 1230 (OAc), 1460, 740 (aromatic), 1090, 1060 cm^{-1} (C–O–C). (Found: C, 58.4, H, 6.2. Calc. for $C_{20}H_{26}O_9$: C, 58.4; H, 6.4%).

Methyl 1,3,4,5 - *tetra* - O - *acetyl* - α - D,L - *tagatopyranoside* (**27**). Debenzylation and subsequent acetylation of **26** carried out as described for **23** gave **27** (82%) m.p. 104–105°. IR: 1750, 1220 (OAc), 1160, 1100, 1060, cm^{-1} (C–O–C). (Found: C, 49.8; H, 6.1. Calc. for $C_{15}H_{22}O_{10}$: C, 49.7; H, 6.1%).

Methyl 1 - O - *benzyl* - α - D,L - *erythro* - *hex* - 2 - *ulopyranosid* - 5 - *ulose* (**28**). A soln of **6** (8.5 g, 0.034 mol), silver chlorate (6.5 g, 0.034 mol) and osmium tetroxide (40 mg) in THF–H_2O 4:1 (50 mL) was stirred at room temp. for 12 hr, filtered and evaporated. The residue was taken up into EtOAc, filtered through short silica gel column and evaporated to give **28** (6.9 g, 71%) as a thick yellowish oil. IR: 3450 (OH), 1740 (C=O), 1460, 745 (aromatic), 1120, 1040 cm^{-1} (C–O–C). (Found: C, 59.6; 6.6. Calc. for $C_{14}H_{18}O_6$: C, 59.6; H, 6.4%).

Methyl 1 - O - *benzyl* - 3,4 - O - *isopropylidene* - α - D,L - *erythro* - *hex* - 2 - *ulopyranosid* - 5 - *ulose* (**29**). A soln of **28** (3.0 g) in acetone (200 mL) with H_2SO_4 (0.1 mL) was left at room temp. for 8 hr. The mixture was neutralized with anhyd. K_2CO_3, filtered and evaporated. Chromatography of the residue on silica gel (60 g) column with benzene–EtOAc (9:1) gave **29** (2.40 g, 68%) b.p.160°/10^{-3} Torr. IR: 1760 (C=O), 1220, 1180, 1110 cm^{-1} (C–O–C). (Found: C, 63.1; H, 6.9. Calc. for $C_{17}H_{22}O_6$: C, 63.3; H, 6.9%).

Further elution of the column with the same solvent yielded **30** (0.40 g, 10%) b.p. 165°/10^{-3} Torr. IR: 1200, 1150, 1090, 1060 (C–O–C), 1500, 740 cm^{-1} (aromatic). MS: *m/e* 43(40%), 59(21%), 91(100%), 100(18%), 259(53%), 365(9%). (Found: C, 63.3; H, 7.2. Calc. for $C_{20}H_{28}O_7$: C, 63.1; H, 7.4%).

Methyl 5 - O - *acetyl* - 1 - O - *benzyl* - 3,4 - O - *isopropylidene* - α - D,L - *psicopyranoside* (**31**). $NaBH_4$ (0.07 g, 1.86 mmol) dissolved in a THF–H_2O 2:1 (30 mL) mixture was added to a soln of **29** (1.20 g, 3.72 mmol) in THF (10 mL). After 30 min the soln was neutralized with AcOH and evaporated to dryness. The residue was treated with Ac_2O–pyridine and after the usual work-up and chromatography on silica gel column gave **31** (1.03 g, 83%) as thick oil. IR: 1750, 1250 (OAc), 1220, 1100 (C–O–C), 1465, 750 cm^{-1} (aromatic). (Found: C, 62.6; H, 7.4. Calc. for $C_{19}H_{26}O_7$: C, 62.3; H, 7.2%).

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