Branched-chain Sugars. XXII. Synthesis of Benzyl 2,3-Di-*O*-benzyl- and 2,3-*O*-Methylene-β-L-*threo*-pentopyranosid-4-uloses, and the Corresponding 6-Deoxy-α-D-*xylo*-hexopyranosid-4-uloses[1]

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The title compounds were synthesized from L-arabinose and D-glucose as intermediates to a few naturally occuring branched-chain sugars. Oxidation conditions of precursors to the corresponding 4-uloses were examined.

In previous papers of this series, stereoselectivities in nucleophilic reactions of hexopyranosid-2-uloses[2] and 3-uloses[3] have been extensively examined, from the views of non-bonded interactions, electrostatic interaction in the transition state,[4] and kinetic or thermodynamic control in reversible reactions.[5] In order to examine the stereoselectivities in similar reactions of 4-uloses and to utilize the results for the stereoselective synthesis of 2,3-*O*-methylene-4-*C*-substituted aldono-1,5-lactones found in everninomicins,[6] flambamycin,[7] and avilamycins,[8] benzyl 2,3-*O*-benzyl-(**1**) and 2,3-*O*-methylene-β-L-*threo*-pentopyranosid-4-uloses (**2**), benzyl 2,3-*O*-benzyl-6-deoxy-(**3**) and 6-deoxy-2,3-*O*-methylene-α-D-*xylo*-hexopyranosid-4-uloses (**4**), together with benzyl 2,3-di-*O*-benzyl-6-*O*-trityl-α-D-*xylo*-hexopyranosid-4-ulose (**5**) and methyl 6-deoxy-2,3-*O*-methylene-α-D-*ribo*-hexopyranosid-4-ulose (**6**), were synthesized in this paper.

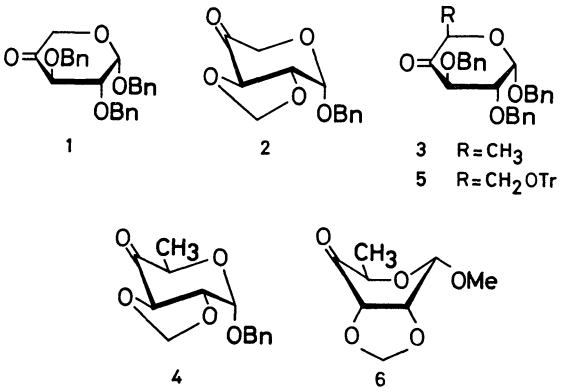

Fig. 1.

Results and Discussion

Treatment of benzyl 2,3-di-*O*-benzoyl-α-L-arabinopyranoside[9] in acetic acid with dimethyl sulfoxide and acetic anhydride[10] at room temperature for 2 days gave the corresponding 4-*O*-methylthiomethyl derivative (**7**) in 88% yield, which was converted into de-*O*-benzoylated derivative (**8**) by treatment with sodium methoxide in 57% yield. Treatment of **8** in *N*,*N*-dimethylformamide with sodium hydride and benzyl chloride or dichloromethane[11] gave the corresponding 2,3-di-*O*-benzyl (**9**) and 2,3-*O*-methylene derivatives (**10**) in 81% and 46% yields, respectively. In the case of **10**, a small amount of dimers were formed, however, they could not be characterized. Treatment of **9** and **10** in aqueous acetonitrile with mercury(II) chloride and calcium carbonate gave the corresponding de-*O*-methylthiomethyl derivatives (**11** and **12**) in quantitative and 62% yields, respectively.

On the other hand, treatment of benzyl 4,6-*O*-benzylidene-α-D-glucopyranoside[12] in *N*,*N*-dimethylformamide with sodium hydride and dichloromethane gave the corresponding 2,3-*O*-methylene derivative (**13**)[11] and two dimers (**14** and **15**) in 43%, 6.2%, 7.2% yields, respectively. The dimers showed no absorption of a hydroxyl group in IR spectra, and the parent ion peak of *m*/*e* 741 in MS spectra. Configurations of 2,3′:2′,3-bis-*O*-methylenedi(benzyl 4,6-*O*-benzylidene-α-D-glucopyranoside) (**14**) and the corresponding 2,2′:3,3′-bis-*O*-methylene isomer (**15**) were assigned from the *O*-methylene proton signals in NMR spectra. Compound **14** showed AB quartet indicating two magnetically nonequivalent protons in equivalent two methylene groups, whereas **15** two singlets indicating each two equivalent protons in non-equivalent two methylene groups. Analogous two dimers were also obtained by the reaction of the corresponding methyl glucoside with dibromomethane in each 22% yield, together with 2,3-*O*-methylene derivative (**16**),[11,13] but their structures were not assigned. While, similar reaction of methyl 4,6-*O*-benzylidene-α-D-allopyranoside[14] gave the corresponding 2,3-*O*-methylene derivative (**17**) in 65% yield.

For the deoxygenation of *C*-6 position, **13** was treated with 80% acetic acid at room temperature for one day to give de-*O*-benzylidenated product (**18**) in 64% yield. Selective tosylation of **18** in pyridine at 0 °C with 1.4 equivalent *p*-toluenesulfonyl chloride gave 6-*O*-tosyl (**19**) and 4,6-di-*O*-tosyl (**20**) derivatives in 80% and 8% yields, respectively. Reduction of **19** in *N*,*N*-dimethylformamide with lithium aluminium hydride gave the corresponding 6-deoxy derivative (**21**) in 81% yield. For the preparation of **21**, oxidative ring-opening of the 4,6-*O*-benzylidene group of **13** with *N*-bromosuccinimide was unsuccessful, probably due to the reaction of the strained 2,3-*O*-methylene group. By the same route, **16** and **17** were also converted into methyl 6-deoxy-2,3-*O*-methylene-α-D-glucopyranoside (**22**) and -allopyranoside (**23**), respectively. While, monotosylation of benzyl 2,3-di-*O*-ben-

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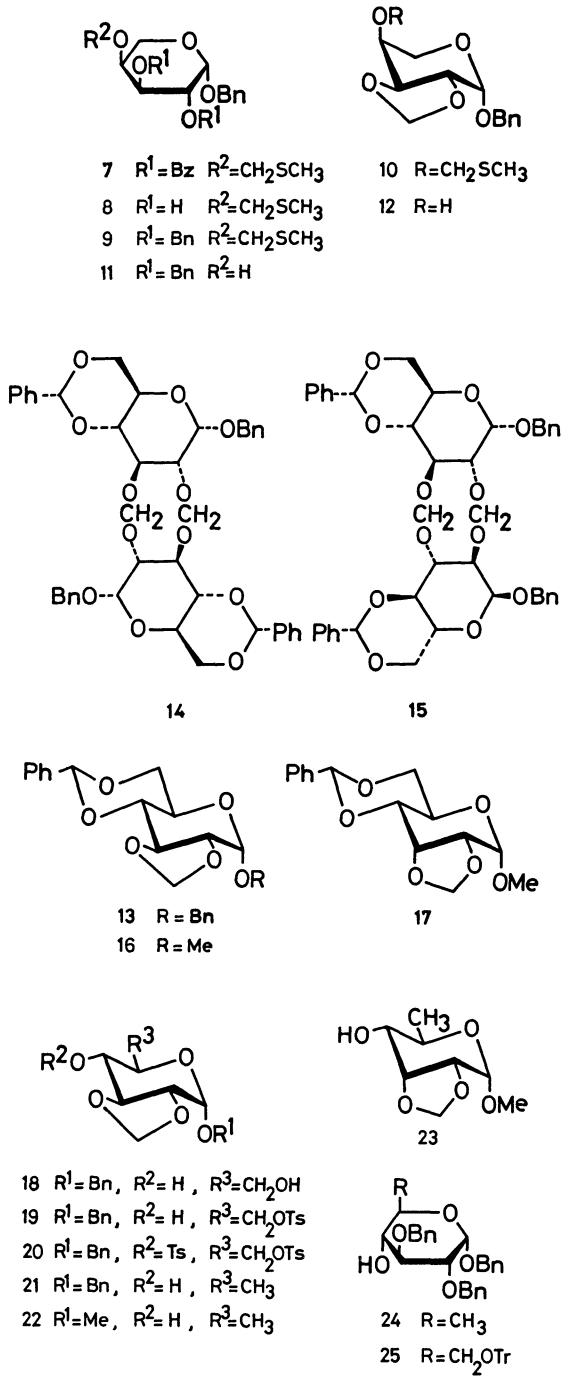

Fig. 2.

zyl-α-D-glucopyranoside[10] and successive reduction of the product with lithium aluminium hydride gave benzyl 2,3-di-*O*-benzyl-6-deoxy-α-D-glucopyranoside (**24**) in 38% overall yield.

Oxidation of **11**, **12**, **21**—**24**, and benzyl 2,3-di-*O*-benzyl-6-*O*-trityl-α-D-glucopyranoside (**25**)[12] into the corresponding 4-uloses was examined by a few methods, and the results were summarized in Table 1. The chromium trioxide-pyridine oxidation of 2,3-di-*O*-benzyl derivatives, (**11**, **24**, and **25**) was unsuccessful, probably due to the oxidation of the benzyl groups as was reported by Stevens and Czernecki[15] in the case of oxidation of methyl 6-deoxy-2,3-di-*O*-benzyl-α-D-galactopyranoside with ruthenium tetraoxide. A similar oxidation of **22** was accompanied by the epimerisation at *C*-3 position to give **6** in 45% yield. The epimerization of equatorial C–O bond to axial configuration implies that the 2,3-*O*-methylene ring from *trans*-diequatorial hydroxyl groups contains a fairly large steric strain. Configuration of 6 obtained above was confirmed by the comparison with that obtained by the oxidation of **23** with chromium trioxide in 63% yield. Oxidation of **11** with dimethyl sulfoxide (DMSO)–acetic anhydride gave the corresponding 4-ulose in 60% yield, together with a small amount of 4-*O*-methylthiomethyl derivative (**9**), however, similar oxidation of 2,3-*O*-methylene derivatives (**12** and **22**) gave only a small amount of 4-*O*-methylthiomethyl derivative. Although DMSO–acetic anhydride oxidation of the corresponding methyl glucoside of **24** was reported to be unsuccessful,[15] DMSO–trifluoroacetic anhydride oxidation[16] gave commonly good results. Thus 4-uloses, **1**—**6**, could be obtained from **11**, **12**, **24**, **21**, **25**, and **23**, respectively.

Table 1. Preparation of 4-uloses

Substrates	Oxidation methods[a]	Products (%) 4-Uloses	Products (%) 4-*O*-Methylthiomethyl derivatives
11	B	**1** (60)	**9** (7.8)
	C	**1** (82)	
24	C	**3** (72)	
25	C	**5** (98)	
12	B		**10** (10)
	C	**2** (quant)	
21	C	**4** (quant)	
22	B		(10)
	A	**6** (45)	
23	A	**6** (63)	

a) Method A, B, and C indicate the oxidation with CrO_3–pyridine, DMSO–Ac_2O, and DMSO–$(CF_3CO)_2O$, respectively.

^{1}H NMR parameters of 4-uloses thus obtained were shown in Table 2. The results indicate that **1**—**5** exist in *C*l conformation, and **6** in ^{1,4}B. Because **23** takes *C*l conformation (see Experimental), the conformational difference between **6** and **23** will be attributed to the larger bond angle of sp^2-carbon than that of sp^3-carbon at *C*-4, and the trend of coplanarity of 2,3-*O*-methylene ring.

Experimental

General Methods. Melting points were determined with a Mel-Temp melting point apparatus and not corrected. Optical rotations were measured with Carl Zeiss LEP-Al or JASCO DIP-4 polarimeter, using a 0.5 dm tube. IR spectra were recorded with a Hitachi EPI-G2 grating spectrometer. NMR spectra were recorded with a JEOL JNM PS-100 spectrometer in chloroform-*d* containing tetramethylsilane as the internal reference. Chemical shifts and coupling constants were recorded in δ(ppm) and Hz units, and IR frequencies in cm^{-1}. Evaporations were conducted under diminished pressure.

*Benzyl 2,3-Di-*O*-benzoyl-4-O-methylthiomethyl-β-L-arabinopyranoside (7).* A solution of benzyl 2,3-di-*O*-benzoyl-β-L-

Table 2. ^{1}H NMR parameters of 4-uloses

4-Uloses	Chemical shifts (δ) and coupling constants (Hz)							Other protons
	H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3 ($J_{3,5e}$)	H-5e ($J_{5e,5a}$)	H-5a ($J_{5,6}$)	H-6 ($J_{5.6'}$)	H-6′ ($J_{6,6'}$)	
1	4.96 d (3.0)	3.74 dd (10.0)	4.46 d	4.14 d (15.0)	3.86 d			5.04—4.44 (3×CH_2Ph; m)
2	5.50 d (3.0)	3.67 dd (10.8)	4.72 dd (1.0)	4.02 dd (15.0)	3.92 d			7.52—7.21 (Ph; m), 5.20 and 5.10 (OCH_2O; ABq, J=0.8), 4.86 and 4.76 (CH_2Ph; ABq, J=11.6)
3	4.92 d (4.0)	3.73 dd (10.5)	4.49 d		4.21 q (7.0)	1.22 d		7.14—7.50 (Ph; m), 4.48—5.00 (3×CH_2Ph; m)
4	5.47 d (3.0)	3.67 dd (10.5)	4.70 dd (1.0)		4.12 q (3.5)	1.35 d		ca. 7.38 (Ph; m), 5.19 and 5.10 (OCH_2O; ABq, J=0.8), 4.82 (CH_2Ph; s)
5	5.03 d (3.8)	3.78 dd (10.0)	4.44 d		4.34 dd (3.3)	3.56 dd (7.5)	3.40 dd (10.5)	7.60—7.10 (Ph; m), 4.98—4.55 (3×CH_2Ph; m)
6[a]	5.02 d (4.2)	4.8—4.6m (8.8)			4.13 q (7.0)	1.38 d		3.46 (OMe), 4.95 and 5.04 (OCH_2O, each s)

a) $J_{1,2}$ and $J_{2,3}$ were observed by the use of a shift reagent, Pr(FOD)$_3$.

arabinopyranoside[9] (50 g, 0.109 mol) in dimethyl sulfoxide (DMSO, 400 ml), acetic anhydride (240 ml) and acetic acid (80 ml) was kept at room temperature for 2 d, then poured into saturated sodium hydrogencarbonate, and the resulting solution was extracted with ether. The extract was evaporated and the residue was purified on a silica gel column to give **7** (50 g, 88%) as a syrup. $[\alpha]_D$ +176.8° (*c* 1.24, $CHCl_3$), NMR: 8.2—7.94 and 7.60—7.10 (Ph; m), 5.82 (H-3; q, $J_{2,3}$=10.8, $J_{3,4}$=2.0), 5.71 H-2; q, $J_{1,2}$=3.0), 5.31 (H-1; d), 4.74 (SCH_2O; s), 4.68 ($PhCH_2$; ABq, J=13.0), 4.46 (H-4; m, $J_{4,5e}$=1.8, $J_{4,5a}$=2.0), 4.00 (H-5e; q, $J_{5e,5a}$=13.2), 3.84 (H-5e; q), 1.98 (CH_3S, s). Found: C, 65.59; H, 5.66; S, 6.98%. Calcd for $C_{28}H_{28}O_7S$: C, 66.12; H, 5.55; S, 6.31%.

Benzyl 4-O-Methylthiomethyl-β-L-arabinopyranoside (8). A solution of **7** (600 mg, 1.18 mmol) in methanol (8 ml) containing sodium (60 mg, 2.6 mmol) was kept at room temperature for 6 h, evaporated, and the residue was purified on a silica gel column (benzene–ethyl acetate–ethanol 6:1:1) to give pure crystals in 57% (200 mg) yield. Mp 72—73 °C ($CHCl_3$–hexane), $[\alpha]_D$ +193.9° (*c* 0.72, $CHCl_3$), NMR: 7.34 (Ph; s), 5.00 (H-1; d, $J_{1,2}$=3.0), 4.73 and 4.85 (SCH_2O, ABq, J=11.3), 4.52 and 4.75 ($PhCH_2$; ABq, J=12.0), 4.02 (H-4; m, $J_{3,4}$=2.0), 3.84—3.70 (H-2, H-3, H-5e, and H-5a; m), 2.18 (CH_3S, s). Found: C, 55.53; H, 6.69; S, 10.73%. Calcd for $C_{14}H_{20}O_5S$: C, 55.98; H, 6.71; S, 10.68%.

Benzyl 2,3-Di-O-benzyl-4-O-methylthiomethyl-β-L-arabinopyranoside (9). To a solution of **8** (1 g, 3.3 mmol) in *N*,*N*-dimethylformamide (DMF, 10 ml) was added with stirring sodium hydride (0.35 g, 14.5 mmol) washed with hexane and then benzyl chloride (1.01 g, 7.9 mmol). After stirring one day at room temperature, the reaction mixture was poured into water, and the resulting solution was extracted with chloroform. The extract was evaporated, and the residue was purified on a silica gel column (hexane–ethyl acetate 10:1) to give a syrup (1.3 g) in 81.3% yield. $[\alpha]_D$ +91.4° (*c* 1.1, $CHCl_3$), NMR: 7.6—7.2 (Ph; m), 4.96—4.47 (4×$PhCH_2$, m), 4.91 (H-1; d, $J_{1,2}$=3.0), 4.18 (H-4; m, $J_{4,5e}$=1.6, $J_{4,5a}$=2.8), 4.01 (H-3; dd, $J_{2,3}$=10.3, $J_{3,4}$=2.5), 3.90 (H-2; dd), 3.80 (H-5e; dd, $J_{5e,5a}$=13.0), 3.66 (H-5a; dd), 2.13 (CH_3S; s). Found: C, 69.65; H, 6.81; S, 6.34%. Calcd for $C_{28}H_{32}O_5S$: C, 69.97; H, 6.71; S, 6.67%.

Benzyl 2,3-O-Methylene-4-O-methylthiomethyl-β-L-arabinopyranoside (10). To a solution of **8** (0.5 g, 1.66 mmol) in DMSO (30 ml) was added with stirring sodium hydride (170 mg, 7.1 mmol) washed with hexane, and then excess dichloromethane (1 ml). The usual work-up of the reaction mixture as **13** gave a syrup (0.4 g) which was purified on a silica gel column (benzene–acetone 4:1) to give pure **10** (240 mg, 46%). $[\alpha]_D$ +110.1° (*c* 1.0, $CHCl_3$), NMR: 7.33 (Ph, s), 5.36 (H-1; d, $J_{1,2}$=2.8), 5.06 and 5.09 (OCH_2O; ABq, J=1.0), 4.82 (SCH_2O; s), 4.66 and 4.73 ($PhCH_2$; ABq, J=13.0), 4.48 (H-4; m), 3.95 (H-3; dd, $J_{3,4}$=2.0), 3.87 (H-2; dd, $J_{2,3}$=10.0), 3.78 (H-5e; dd, $J_{4,5e}$=1.5, $J_{5e,5a}$=13.0), 3.65 (H-5a; dd, $J_{4,5a}$=1.0), 2.16 (CH_3S). Found: C, 57.47; H, 6.62; S, 9.97%. Calcd for $C_{15}H_{20}O_5S$: C, 57.67; H, 6.45; S, 10.27%.

Benzyl 2,3-Di-O-benzyl-β-L-arabinopyranoside (11). A supension of **9** (1.2 g, 2.5 mmol), mercury(II) chloride (1.36 g, 5.0 mmol), and calcium carbonate (0.75 g, 7.5 mmol) in aqueous acetonitrile (75%, 30 ml) was refluxed for 7 h, filtered, and the filtrate was evaporated. A dichloromethane solution of the residue was washed twice with aqueous sodium iodide (10%), and then evaporated to give a syrup (1.0 g) quantitatively. $[\alpha]_D$ +105.9° (*c* 3.2, $CHCl_3$). Found: C, 74.28; H, 6.37%. Calcd for $C_{26}H_{28}O_5$: C, 74.26; H, 6.71%.

Benzyl 2,3-O-Methylene-β-L-arabinopyranoside (12). A similar work up of **10** (240 mg, 0.77 mmol) as above and purification of syrupy product on a silica gel column (benzene–acetone 4:1) gave pure **12** (120 mg, 62%). $[\alpha]_D$ +212.2° (*c* 1.6, $CHCl_3$); NMR: 7.28—7.40 (Ph; m), 5.36 (H-1; d, $J_{1,2}$=1.0), 5.04 and 5.11 (OCH_2O, ABq, J=1.0), 4.64 and 4.75 (CH_2Ph; ABq, J=12.5), 4.30 (H-4; m), 3.89 (H-3; dd, $J_{3,4}$=1.0), 3.79 (H-2; dd, $J_{2,3}$=10.0), 3.73 (H-5e; dd, $J_{4,5e}$=2.0), 3.58 (H-5a; dd, $J_{4,5a}$=1.8, $J_{5e,5a}$=13.2). Found: C, 61.83; H, 6.39%. Calcd for $C_{13}H_{16}O_5$: C, 61.89; H, 6.39%.

Benzyl 4,6-O-Benzylidene-2,3-O-methylene-α-D-glucopyranoside (13). To a solution of benzyl 4,6-*O*-benzylidene-α-D-glucopyranoside[11] (50 g, 150 mmol) in DMF (500 ml) was added with stirring sodium hydride (21.6 g, 450 mmol) and then dichloromethane (28.6 ml, 450 mmol) dropwise, and the resulting suspension was stirred overnight at room temperature. A mixture of ethyl acetate and water was added to the reaction mixture, and the resulting solution was extracted with chloroform. The extract was washed

with water, dried, and evaporated. The residue was separated on a silica gel column (hexane–ethyl acetate 8:1) to give **13** (22.4 g, 43.3%) and a mixture of two dimers (7.2 g, 13.9%). The dimers were separated on a preparative TLC (developed three times with hexane–ethyl acetate 3:1) to give 2,3′:2′,3-bis-*O*-methylenedi(benzyl 4,6-*O*-benzylidene-α-D-glucopyranoside) (**14**) and the corresponding 2,2′:3,3′-bis-*O*-methylene isomer (**15**) in 6.2% and 7.2% yields, respectively.

13: Mp 107—108 °C, $[\alpha]_D$ +123° (*c* 1.0, $CHCl_3$); NMR: 7.6—7.2 (Ph; m), 5.58 (PhCH; s), 5.35 (H-1; d, $J_{1,2}=3.5$), 5.17 (OCH_2O, s), 4.64 and 4.67 (CH_2Ph, ABq, $J=12.8$), 3.45 (H-2; dd, $J_{2,3}=9.0$), 3.68—4.30 (H-3, H-4, H-5, H-6, and H-6′, m). Found: C, 67.99; H, 5.86%. Calcd for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99%.

14: Mp 111—113 °C, $[\alpha]_D$ +171° (*c* 0.98, $CHCl_3$); NMR: 7.14—7.53 (Ph; m), 4.75 and 4.96 (OCH_2O, ABq, $J=7.0$), 4.90 (H-1; d, $J_{1,2}=4.0$), 4.63 and 4.74 ($PhCH_2$; ABq, $J=12.0$), 4.18 (H-6e; dd, $J_{6e,6a}=9.5$, $J_{5,6a}=4.0$), 4.12 (H-3; t, $J_{2,3}=J_{3,4}=9.0$), 3.87 (H-5; dd, $J_{4,5}=9.0$), 3.71 (H-6e; d), 3.49 (H-4; t), 2.57 (H-2; dd); MS (70 eV): *m/e* 741. Found: C, 68.00; H, 5.87%. Calcd for $C_{42}H_{44}O_{12}$: C, 68.09; H, 5.99%.

15: Mp 114—116 °C, $[\alpha]_D$ +196° (*c* 0.8, $CHCl_3$); NMR: 7.10—7.60 (Ph; m), 4.92 (H-1; d, $J_{1,2}=3.5$), 3.71 and 4.90 (OCH_2O; each s), 5.49 (PhCH, s), 4.58 and 4.76 ($PhCH_2$; ABq, $J=12.0$), 4.17 (H-6e; dd, $J_{5,6e}=4.0$, $J_{6e,6a}=9.5$), 4.00 (H-3; t, $J_{2,3}=J_{3,4}=9.5$), 3.80 (H-5; dt, $J_{4,5}=J_{5,6a}=9.5$), 3.68 (H-6a; t), 3.66 (H-2; dd), 3.49 (H-4; t); MS (70 eV): *m/e* 740. Found: C, 68.47; H, 6.21%. Calcd for $C_{42}H_{44}O_{12}$: C, 68.09; H, 5.99%.

Methyl 4,6-O-Benzylidene-2,3-O-methylene-α-D-glucopyranoside (**16**) *and -α-D-allopyranoside* (**17**). *(A)*: Reaction of 4,6-*O*-benzylidene-α-D-glucopyranoside (1 g, 3.5 mmol) in DMF (50 ml) with sodium hydride (0.27 g, 10.6 mmol) and dibromomethane (1.85 g, 10.6 mmol) as above, and the usual work up of the reaction mixture gave **16** [mp 103—104 °C, $[\alpha]_D$ +124.1° (*c* 1.0, $CHCl_3$); MS: *m/e* 294; lit,[11] mp 104—105 °C, $[\alpha]_D$ +122.9° (*c* 0.21, $CHCl_3$); Found: C, 61.03; H, 6.07%. Calcd for $C_{15}H_{18}O_6$: C, 61.21; H, 6.17%], and two dimers [mp 209—212 °C and 225—229 °C; each MS: *m/e* 588. Found: C, 61.69; H, 6.20%. Calcd for $C_{30}H_{36}O_{12}$: C, 61.21; H, 6.17%] in 28% (290 mg), 22% (230 mg), and 13% (140 mg) yields, respectively.

(B): A similar reaction of methyl 4,6-*O*-benzylidene-α-D-allopyranoside[14] (3.7 g, 13.1 mmol) gave the corresponding 2,3-*O*-methylene derivative (**17**) in 50% (1.93 g) yield. Mp 162—164 °C, $[\alpha]_D$ +102.8° (*c* 1.0, $CHCl_3$); NMR: 7.5—7.2 (Ph; m), 5.54 (PhCH; s), 5.32 and 5.06 (OCH_2O; ABq, $J=1.8$), 4.74 (H-1; dd, $J_{1,2}=4.0$, $J_{1,3}=1.6$), 4.44—4.20 (H-2, H-5, H-6e; m, $J_{5,6e}=5.2$, $J_{6e,6a}=10.5$), 4.12 (H-4; dd, $J_{4,5}=10.0$, $J_{3,4}=5.0$), 3.80 (H-3; m, $J_{2,3}=8.4$), 3.68 (H-6a; t, $J_{5,6a}=10.0$), 3.40 (OMe).

Benzyl 2,3-O-Methylene-α-D-glucopyranoside (**18**). A solution of **13** (22.4 g, 60.5 mmol) in 80% acetic acid (400 ml) was stirred 1 d at room temperature. The solution was extracted with petroleum ether to remove benzaldehyde, and the water layer was evaporated to give crystals which were recrystallized from ethanol–hexane. From the mother liquor, the second crop was obtained by separation on a silica gel column (hexane–ethyl acetate 3:1). The combined yield was 63.7% (10.8 g). Mp 108—110 °C, $[\alpha]_D$ +176° (*c* 1.0, $CHCl_3$). Found: C, 59.17; H, 6.38%. Calcd for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43%.

Benzyl 2,3-O-Methylene-6-O-(p-tolylsulfonyl)-α-D-glucopyranoside (**19**). To an ice-cooled solutions of **18** (10 g, 35.4 mmol) in pyridine (150 ml) was added portionwise with stirring *p*-toluenesulfonyl chloride (9.9 g, 50 mmol). After keeping at room temperature overnight, the reaction mixture was poured into ice–water and extracted with chloroform. Evaporation of the chloroform solution gave a syrup which was separated on a silica gel column (hexane–ethyl acetate 8:1) to give **19** (12.3 g, 80%) and the corresponding di-*O*-tosylate (**20**: 1.7 g, 8%).

19: Mp 80—82 °C, $[\alpha]_D$ +78.9° (*c* 1.2, $CHCl_3$), NMR: 7.84—6.70 (Ph; m), 5.02 (H-1; d, $J_{1,2}=3.0$), 4.90 and 4.88 (OCH_2O; ABq, $J=0.8$), 4.81 (H-4; t, $J_{4,5}=9.0$), 4.50 and 4.48 (CH_2Ph; ABq, $J=12.0$), *ca.* 4.32 (H-6a and H-6e; m), 4.00 (H-3; t, $J_{3,4}=9.0$), 3.62 (H-5; m), 3.10 (H-2; dd, $J_{2,3}=9.0$), 2.94 (OH; s), 2.44 (CH_3Ph; s). Found: C, 58.14; H, 5.60; S, 7.59%. Calcd for $C_{21}H_{24}O_8S$; C, 57.79; H, 5.54; S, 7.35%.

20: Mp 144—145 °C, $[\alpha]_D$ +87.6° (*c* 1.1, $CHCl_3$), NMR: 7.15—7.85 (Ph; m), 5.21 (H-1; d, $J_{1,2}=3.0$), 5.04 (OCH_2O; s), 4.72 (H-4; t, $J_{3,4}=J_{4,5}=10.0$), 4.57 and 4.70 (CH_2Ph; ABq, $J=11.0$), 4.25 (H-6e; dd, $J_{5,6e}=2.5$, $J_{6e,6a}=11.0$), 4.03 (H-6a; dd, $J_{5,6a}=5.5$), 3.95 (H-3; t, $J_{2,3}=10.0$), 3.70 (H-5; sex), 3.30 (H-2; dd), 2.45 ($2\times CH_3Ph$). Found: C, 57.54; H, 5.16; S, 10.7%. Calcd for $C_{28}H_{30}O_{10}S_2$: C, 56.93; H, 5.12; S, 10.7%.

Benzyl 6-Deoxy-2,3-O-methylene-α-D-glucopyranoside (**21**). A mixed solution of **19** (8 g, 18.4 mmol) and sodium borohydride (1.7 g, 45.7 mmol) in DMSO (100 ml) was heated at 80 °C for 3 h, and then poured into ice–water. The resulting solution was extracted with ether, and the extract was evaporated. The residual syrup was purified on a silica gel column (hexane–ethyl acetate 8:1) to give **21** (6.1 g, 81%) as a syrup. $[\alpha]_D$ +154° (*c* 0.85, $CHCl_3$), NMR: 7.50—7.20 (Ph; m), 5.24 (H-1; d, $J_{1,2}=3.0$), 5.13 (OCH_2O; s), 4.63 and 4.80 (CH_2Ph; ABq, $J=10.5$), 3.87 (H-3; t, $J_{2,3}=J_{3,4}=9.5$), 3.56 (H-5; dq, $J_{4,5}=9.5$, $J_{5,6}=6.5$), 3.45 (H-4; t), 3.35 (H-2; dd), 1.30 (H-6; d). Found: C, 62.64; H, 6.95%. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81%.

Methyl 6-Deoxy-2,3-O-methylene-α-D-glucopyranoside (**22**). Compound **16** was converted into **22** in a similar manner to that of **13** into **21**. Partial hydroxysis of **16** (24 gr, 8.16 mmol) in aqueous acetic acid (80%, 500 ml) at 35 °C for 1 d gave methyl 2,3-*O*-methylene-α-D-glucopyranoside (12 g, 68.5%) as a syrup. Monotosylation of the syrup (9.4 gr, 45.6 mmol) in pyridine (200 ml) with *p*-toluenesulfonyl chloride (9.9 g, 52 mmol) and purification of the products on a silica gel column (benzene–acetone 50:1) gave the 6-*O*-tosylate (12.6 g, 77%) as a syrup. NMR: 7.80 and 7.34 (Ph; each d, $J=8.0$), 5.13 (OCH_2O; s), 5.05 (H-1; d, $J_{1,2}=3.2$), 4.36 (H-6; dd, $J_{5,6}=4.0$, $J_{6,6'}=11.0$), 4.30 (H-6′; dd, $J_{5,6'}=2.4$), 3.9—3.4 (H-3, H-4, and H-5; m), 3.44 (OMe; s), 3.28 (H-2; dd, $J_{2,3}=9.5$), 2.44 (CMe; s). Found: C, 50.00; H, 5.60; S, 8.88%. Calcd for $C_{15}H_{20}O_8S$: C, 49.99; H, 5.59; S, 8.90%.

Reduction of 6-*O*-tosylate (9.18 g, 25.5 mmol) in THF (400 ml) with lithium aluminium hydride (LAH) (1.94 g, 50 mmol) and the purification of the product on a silica gel column gave pure **24** (2.0 g, 41.3%) as a syrup. $[\alpha]_D$ +202.3° (*c* 1.0, $CHCl_3$). Found: C, 50.21; H, 7.71%. Calcd for $C_8H_{14}O_5$: C, 50.52; H, 7.42%.

Methyl 6-Deoxy-2,3-O-methylene-α-D-allopyranoside (**23**). Compound **17** was converted into **23** as above. Partial hydrolysis of **17** and successive monotosylation of the product gave methyl 2,3-*O*-methylene-6-*O*-tosylsulfonyl-α-D-allopyranoside as a syrup in 62% yield. $[\alpha]_D$ +65.3° (*c* 1.0, $CHCl_3$). NMR: 7.79 and 7.36 (Ph; each d, $J=8.0$), 5.02 and 4.80 (OCH_2O; ABq, $J=2.0$), 4.58 (H-1; d, $J_{1,2}=5.0$), 4.4—4.1 (H-6 and H-6′; $J_{5,6}=2.4$, $J_{5,6'}=5.0$, $J_{6,6'}=10.8$), 4.06 (H-2; t, $J_{2,3}=5.0$), 3.95—3.65 (H-3 and H-5;

m, $J_{3,4}$=3.0, $J_{4,5}$=10.0), 3.50 (H-4; m), 3.34 (OMe; s), 3.24 (OH; s), 2.47 (CMe; s). Found: C, 49.76; H, 5.65; S, 8.75%. Calcd for $C_{15}H_{20}O_8S$: C, 49.99; H, 5.59; S, 8.90%.

Reduction of the above 6-*O*-tosylate with LAH gave **23** as a syrup in 83% yield. $[\alpha]_D$ +88.4° (*c* 2.75, $CHCl_3$); NMR: 5.27 and 5.03 (OCH_2O; ABq, J=2.0), 4.69 (H-1; d, $J_{1,2}$=5.0), 4.35—4.10 (H-3 and H-4; m), 3.64 (H-5; dq, $J_{5,6}$=6.3, $J_{4,5}$=10.0), 3.25 (H-4; dd, $J_{3,4}$=3.5), 3.40 (OMe; s), 2.56 (OH; s), 1.29 (H-6; d). Found: C, 50.41; H, 7.56%. Calcd for $C_8H_{14}O_5$: C, 50.52; H, 7.42%.

The coupling constants mentioned above indicate that **23** and the precursor exist in a flattened *C*1 conformation.

*Benzyl 2,3-Di-*O*-benzyl-6-deoxy-α-*D*-glucopyranoside (**24**).* To an ice-cooled solution of benzyl 2,3-di-*O*-benzyl-α-D-glucopyranoside[10] (28 g, 62 mmol) in pyridine (400 ml) was added *p*-toluenesulfonyl chloride (15.7 g, 82 mmol) portionwise for 4 h with stirring. After keeping overnight at room temperature, the reaction mixture was poured into ice–water and extracted with chloroform. The chloroform solution was evaporated, and the residual syrup was dried and dissolved in THF, and LAH (2.8 g, 74 mmol) was added to THF solution with stirring. After stirring for 3 h at room temperature, a mixture of ethyl acetate and water was added to the reaction mixture and the precipitates deposited were filtered off. The filtrate was extracted with chloroform, and evaporation of the extract gave a syrup (13.2 g) which was purified on a silica gel column (hexane–ethyl acetate 10:1) to give **24** as a syrup (10.2 g, 38%). $[\alpha]_D$ +51.5° (*c* 0.84, $CHCl_3$), NMR: 7.44—7.22 (Ph; m), 4.79 (H-1; d, $J_{1,2}$=3.0), 4.42—5.09 (CH_2Ph; m), 3.81 (H-4; t, $J_{3,4}$=$J_{4,5}$=9.5), 3.75 (H-5; dq, $J_{5,6}$=5.5), 3.50 (H-2; dd, $J_{2,3}$=9.5), 3.17 (H-3; t), 1.23 (H-6; d). Found: C, 71.60; H, 6.98%. Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71%.

Preparation of 4-*Uloses.* *Method A*: Oxidation with chromium oxide-pyridine is illustrated by the preparation of methyl 6-deoxy-2,3-*O*-methylene-α-D-*ribo*-hexopyranosid-4-ulose (**6**). To a mixture of pyridine (1.79 g, 22.6 mmol) and dichloromethane (40 ml) was added chromium trioxide (1.81 g, 18.1 mmol) in two portions, and the mixture was stirred for 20 min. To the mixture was added a solution of **22** (860 mg, 45 mmol) in dichloromethane (10 ml) and it was stirred for 20 min until **22** had disappeared on TLC. The mixture was poured into saturated sodium hydrogencarbonate, and the organic layer was processed conventionally to give a syrup which was purified on a silica gel column (benzene–acetone 5:1) to give **6** (382 mg, 45%). This fact implies the epimerrization at *C*-3 during the oxidation. IR: 1745 (C=O). Found: C, 50.82; H, 6.21%. Calcd for $C_8H_{12}O_5$: C, 51.06; H, 6.43%.

Method B: The DMSO–acetic anhydride oxidation is typically shown by the preparation of benzyl 2,3-di-*O*-benzyl-β-L-*threo*-pentopyranosid-4-ulose (**1**). A solution of **11** (0.5 g, 1.19 mmol) in DMSO (8 ml) and acetic anhydride (4 ml) was kept overnight at room temperature, poured into ice–water, and extracted with ether. The usual work up of the extract gave **1** as a syrup in 60% (0.3 g) yield. $[\alpha]_D$ +98.3° (*c* 1.25, $CHCl_3$), IR: 1740 (C=O). Found: C, 74.08; H, 6.51%. Calcd for $C_{26}H_{26}O_5$: C, 74.62; H, 6.26%.

Method C: The DMSO–trifluoroacetic anhydride oxidation is illustrated by the preparation of benzyl 2,3-di-*O*-benzyl-6-*O*-trityl-α-D-*xylo*-hexopyranosid-4-ulose (**5**). To a chilled solution of DMSO (143 mg, 2.01 mmol) and dichloromethane (2 ml) at −78 °C was added trifluoroacetic anhydride (318 mg, 1.51 mmol) in dichloromethane (2 ml) with stirring, and after 10 min, subsequently a solution of benzyl 2,3-di-*O*-benzyl-6-*O*-trityl-α-D-glucopyranosid (**25**)[12] (349 mg, 0.58 mmol) in dichloromethane (4 ml) dropwise. After stirring for 1 h, the reaction mixture was carefully neutralized at −78 °C with triethylamine, and then poured into ice-water. The resulting solution was extracted with chloroform, and the usual work up of the extract and purification of the product on a silica gel column gave pure **5** in 98% (341 mg) yield, which was crystallized from ethanol. Mp 131—136 °C; $[\alpha]_D$ +41.5° (*c* 1.42, $CHCl_3$). Found: C, 79.50; H, 6.01%. Calcd for $C_{46}H_{42}O_6$: C, 79.98; H, 6.13%.

In a similar manner, benzyl 2,3-*O*-methylene-β-L-*threo*-pentopyranosid-4-ulose (**2**), benzyl 2,3-*O*-benzyl-6-deoxy-α-D-*xylo*-hexopyranosid-4-ulose (**3**), benzyl 2,3-*O*-methylene-6-deoxy-α-D-*xylo*-hexopyranosid-4-ulose (**4**) were also obtained as syrups from **12**, **24**, and **21**, respectively. These compounds showed the correct analytical values, and the structures were confirmed by the NMR and IR spectra. However, the rotational values were not measured, because a small amount of impurities could not be removed, and they were directly used to the next reaction.

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