

Chemistry of Oxo-Sugars. (2). Regio- and Stereo-Selective Synthesis of Methyl D-Hexopyranosiduloses and Identification of Their Forms Existing in Solutions¹⁾

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Sixteen oxo derivatives of methyl D-hexopyranosides with various regio- and stereo-chemistries were selectively synthesized by direct oxidation of non-protected methyl glycosides by the bistributyltin oxide-bromine method or by oxidation of partially protected glycosides followed by deprotection. The forms of these oxoglycosides existing in pyridine-*d*₅ and in H₂O (D₂O) were investigated by means of ¹³C-NMR spectroscopy, and it was found that interconversion between oxo and hydrate forms of oxoglycosides readily takes place.

Keywords oxoglycoside; oxo-hydrate interconversion; regioselective oxidation; bistributyltin oxide-bromine oxidation; hexopyranosidulose; ¹³C-NMR

Oxo derivatives of sugars, so-called oxo-sugars, are biologically important in carbohydrate metabolism²⁾ and are sometimes found in nature as glycosides.³⁾ However, very little is known about their chemistry, because of difficulty of their selective synthesis, high susceptibility to solvation, and instability particularly towards bases. The pioneering work by Theander *et al.*⁴⁾ resulted in the synthesis of some oxo derivatives of methyl α - and β -D-glucoside, though the yields were extremely poor, and the products were not well characterized except for the 3-oxo derivative of Me β -D-Glc.⁵⁾ They also reported^{4d)} that the 2- and 3-oxoglucosides decomposed in 0.16% lime-water with a half-life of *ca.* 1 min.

Recently, Tsuda *et al.*⁶⁾ reported details of a new method for regioselective mono-oxidation of glycosides by bistributyltin oxide and bromine. Thus, many oxoglycosides are now easily available by direct oxidation of common glycosides. By this method, a particular secondary hydroxyl group is selectively oxidized, even if an unprotected primary hydroxyl group is present. The following two rules appear to be hold: (1) the axial hydroxyl in a *cis*-1,2-glycol system is preferentially oxidized (*cis*-glycol control) and (2) glycosides with an axial anomeric linkage are oxidized at O-4, while those with an equatorial anomeric linkage are oxidized at O-3 (anomeric control).

In this paper, we firstly apply this method to the

oxidation of non-protected glycosides which bear so far unexamined stereochemical arrangements of hydroxyl groups, in order to check the validity of the above two rules. Next, the assigned structures of resulting oxoglycosides were unequivocally proved by alternative syntheses starting from partially protected glycosides.

We prepared, in high yields, sixteen methyl D-hexopyranosiduloses (OG, hereafter)⁵⁾ with a carbonyl group at position 2, 3, or 4 (shown in Chart 1), most of which were new compounds. The forms of these compounds existing in pyridine-*d*₅ and H₂O solutions were also examined.

Results and Discussion

Direct Oxidation of Methyl Glycosides by the Bistributyltin Oxide-Bromine Method Me α - and β -D-Glc (18 and 17) are oxidized to the 4-oxo and 3-oxo derivatives [Me α -D-xylo-4-OG (13) and Me β -D-ribo-3-OG (7)], respectively.⁶⁾ Me α -D-Gal (19), in which the above rules reinforce each other, gives a single product 13, whereas Me β -D-Gal (20), where the above two rules are operating competitively, gives a mixture of the 4-oxo and the 3-oxo derivatives [Me β -D-xylo-4-OG (14) and Me β -D-xylo-3-OG (11)] with predominance of the former (4:1), indicating the preference of rule 1.⁶⁾ The structure of the minor product 11 was now definitively determined by an alternative synthesis (see below).

Oxidation of Me α -D-Man (21), in which the two rules

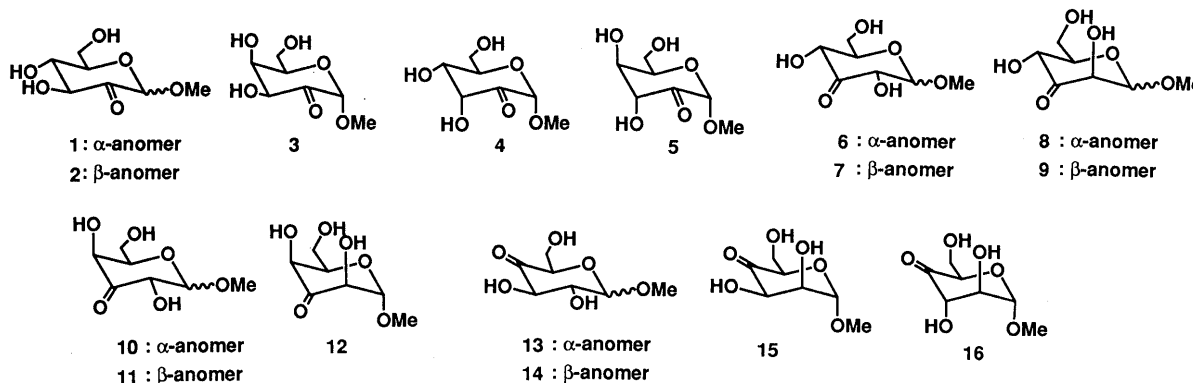


Chart 1

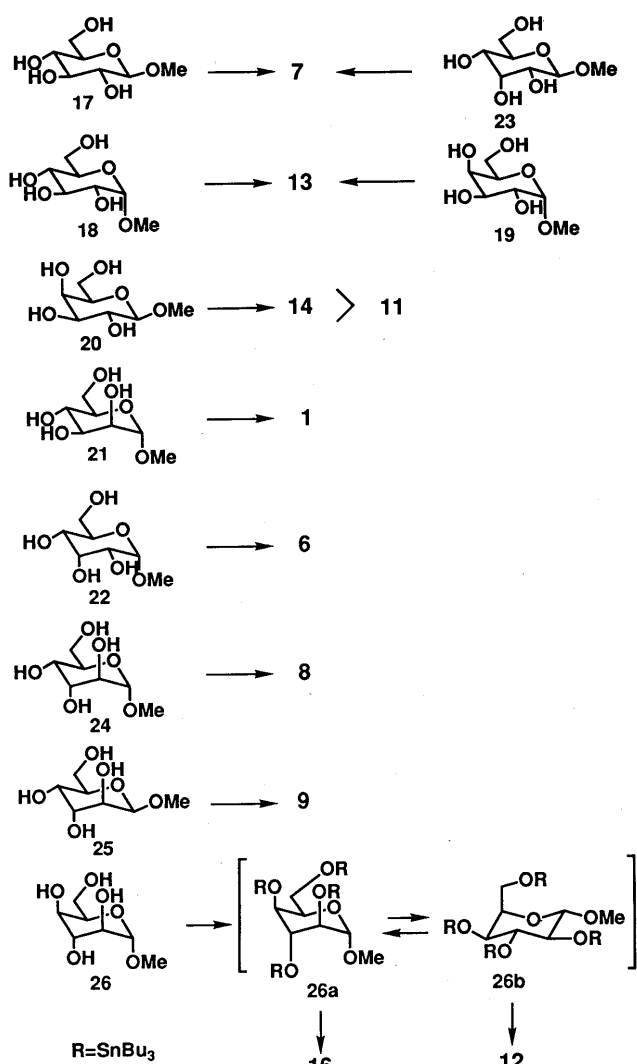


Chart 2. Oxidation of Non-Protected Methyl Glycosides by the $(\text{Bu}_3\text{Sn})_2\text{O}-\text{Br}_2$ Method

are again operating competitively, was reported to give the 2-oxo derivative [Me α -D-arabino-2-OG (1)] as a major product together with a minor product which was assumed to be the 4-oxo derivative 15.⁶⁾ Re-examination of this oxidation has now revealed that the real oxidation product is only 1 and the minor product is the derivative formed from 1 by contact with a base during the isolation procedure (details have been presented in a separate paper).^{1b)} The structure of the latter compound is now revised to 8 (Me α -D-arabino-3-OG) on the basis of confirmatory syntheses of both 15 and 8 (see below).

Oxidation of Me α - and β -D-All (22 and 23) gave the 3-oxo derivatives, Me α -D-ribo-3-OG (6) and Me β -D-ribo-3-OG (7), respectively, each as a sole product. Me α - and β -D-Alt (24 and 25) again gave the 3-oxo derivatives (Me α - and β -D-arabino-3-OG, 8 and 9), respectively, each as a single product. These five examples indicate that rule 1 is operating in preference to rule 2.

In Me α -D-Ido (26), all secondary hydroxy groups are in *trans* and axial orientations. Oxidation of 26 by the $(\text{Bu}_3\text{Sn})_2\text{O}-\text{Br}_2$ method gave two products, Me α -D-lyxo-3-OG (12) and Me α -D-arabino-4-OG (16), in a ratio of *ca.* 5:3. This result can be explained by assuming that 26 is in an equilibrium between 26a and 26b. Following rule 2, the

former (26a) should be oxidized to the 4-oxo derivative (16) and the latter (26b) to the 3-oxo derivative (12).

The above results indicate that non-protected glycosides (except for Me α -D-Ido) are regioselectively oxidized by the $(\text{Bu}_3\text{Sn})_2\text{O}-\text{Br}_2$ method in accordance with the rules already proposed; rule 1 is superior to rule 2 when the two rules are operating competitively.

The structures of all of the above-obtained oxoglycosides were proved by alternative syntheses through oxidation of partially protected glycosides, as described below.

Regioselective Synthesis of Oxoglycosides through Oxidation of Partially Protected Glycosides Me α -D-arabino-2-OG (1) was prepared as follows. Previously, Tsuda *et al.*⁶⁾ reported that Me 4,6-*O*-benzylidene- α -D-Glc (27) was oxidized by the $(\text{Bu}_3\text{Sn})_2\text{O}-\text{Br}_2$ method to the 2-oxo derivative 28 in high yield. Several re-examinations of the reported procedure revealed that the yield of the desired oxidation product 28 was variable (30–93%), with considerable recovery of the starting material 27 when the reaction was incomplete. Modification of the reported procedure (changing the solvent from chloroform to toluene and increasing the amount of the reagents—see Experimental) made it possible to isolate 28 consistently in more than 90% yield. Deprotection of 28 with 40% AcOH on heating at 100°C for 10 min furnished Me α -D-arabino-2-OG (1) as a gum in 84% yield. The ¹³C-nuclear magnetic resonance (NMR) spectrum of 1 (in D₂O) was identical with that of the specimen described in the above section. This was reduced by NaBH₄ to give Me α -D-Glc (18) and Me α -D-Man (21) in a ratio of 7:1, as expected.

Alkylation of 27 with benzyloxymethyl (BOM) chloride in acetonitrile by the dibutyltin oxide method⁷⁾ gave the 2-*O*-BOM derivative 29 regioselectively (70%), as expected, together with a small amount (20%) of the 3-*O*-BOM derivative 30. The position of the BOM group in 29 was elucidated on the basis of ¹H–¹H and ¹H–¹³C chemical shift correlation (COSY) spectra. The signals of two protons at δ 3.62 (dd, *J*=4.3, 10 Hz) and 4.13 (t, *J*=10 Hz) were assigned to H-2 and H-3, respectively, since H-2 was coupled with H-1 (δ 4.85, d, *J*=4.3 Hz). These proton signals corresponded to the carbon signals at δ 81.4 and 69.8, respectively, indicating that 29 is the 2-*O*-alkyl derivative. Although 29 was inert to $(\text{Bu}_3\text{Sn})_2\text{O}-\text{Br}_2$ oxidation, it was oxidized with dimethyl sulfoxide (DMSO)–acetic anhydride (Ac₂O) to yield the ketone 31 (51%) accompanied with a methylthiomethyl derivative 32 (48%). Deprotection of 31 by hydrogenolysis over activated Pd black in EtOH–AcOEt gave Me α -D-ribo-3-OG (6) in 99% yield; this product was identical with the specimen obtained by the oxidation of Me α -D-All (22). NaBH₄ reduction of 6 gave a mixture of Me α -D-All (22) and Me α -D-Glc (17) in a ratio of 14:1.

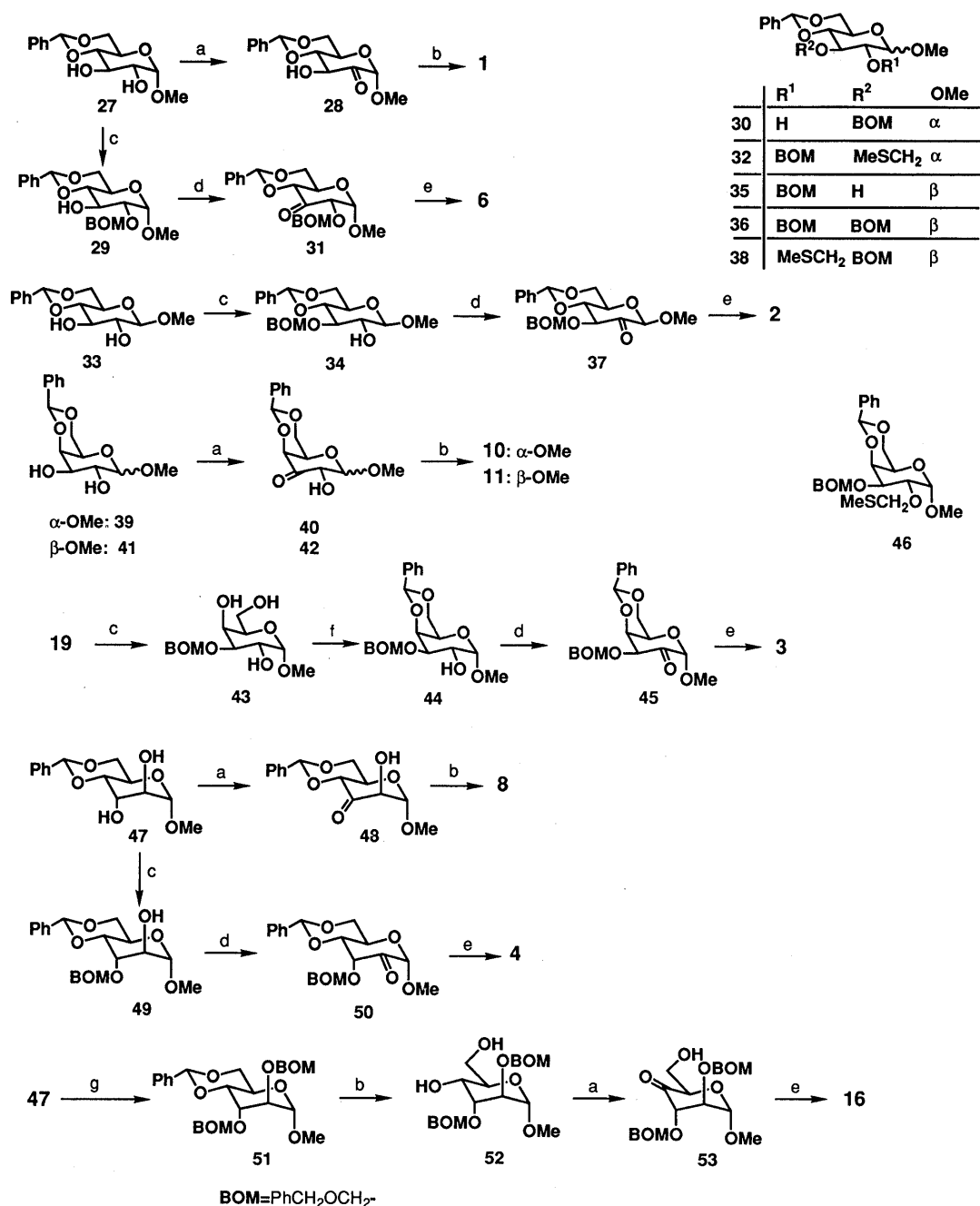
Me β -D-arabino-2-OG (2) was prepared as follows. Me 4,6-*O*-benzylidene- β -D-Glc (33) was benzyloxymethylated as above to give the 3-*O*-BOM derivative 34 regioselectively (54%). The 2-*O*-BOM derivative 35 (21%) and 2,3-di-*O*-BOM derivative 36 (16%) were found as by-products in this alkylation. The position of the BOM group in 34 was proved on the basis of the ¹H–¹H and ¹H–¹³C COSY spectra. Two protons at δ 3.53 (br dt, *J*=1.8, 8 Hz) and 3.82 (br t, *J*=8.4 Hz) were assigned as H-2 and H-3, respectively, since the former was coupled

with H-1 at δ 4.35 (d, $J=8$ Hz) and OH ($J=1.8$ Hz). These proton signals corresponded to the carbon signals at δ 74.2 and 80.1, respectively, indicating that **34** is the 3-*O*-alkyl derivative. Therefore **35** is the 2-*O*-alkyl derivative. Oxidation of **34** with DMSO-Ac₂O gave the 2-oxo derivative **37** (43%) (for the structure of this compound in solutions, see the next section), but with significant formation of the undesired methylthiomethyl derivative **38** (55%). Deprotection of **37** as above gave Me β -D-*arabino*-2-OG (**2**) as a gum in 64% yield. This was reduced by NaBH₄ to a mixture of Me β -D-Man and Me β -D-Glc (**17**) in a ratio of 20:1.

Oxidation of Me 4,6-*O*-benzylidene- α -D-Gal (**39**) by the

(Bu₃Sn)₂O-Br₂ method in toluene gave a single product **40** (59%) with recovery of the starting material (35%). The doublet signal of the anomeric proton (δ 5.19, d, $J=4.5$ Hz) of **40** proved that this is the 3-oxo derivative. Deprotection of this with 50% AcOH gave Me α -D-*xylo*-3-OG (**10**) in 85% yield. NaBH₄ reduction of **10** gave Me α -D-Gal (**19**) and Me α -D-Gul in a ratio of *ca.* 1:1.

Similarly, oxidation of Me 4,6-*O*-benzylidene- β -D-Gal (**41**) with the (Bu₃Sn)₂O-Br₂ method gave the 3-oxo derivative **42** (H-1: δ 4.29, d, $J=8.0$ Hz) in 89% yield. Deprotection of **42** with 60% AcOH gave Me β -D-*xylo*-3-OG (**11**) in 93% yield. The ¹³C-NMR spectrum of this compound was superimposable on that of the minor



a: i) (Bu₃Sn)₂O, ii) Br₂; b: 40—60% AcOH, 70—100°C; c: i) Bu₂SnO, ii) BOMCl; d: DMSO-Ac₂O;
e: H₂/Pd; f: PhCH(OMe)₂/p-TsOH; g: i) *n*-BuLi, ii) BOMCl

Chart 3

product obtained by the direct oxidation of Me β -D-Gal (20). NaBH₄ reduction of 11 gave Me β -D-Gal (20) as a single product.

Me α -D-lyxo-2-OG (3) was synthesized as follows. Alkylation of Me α -D-Gal (19) with BOM chloride in dioxane by the dibutyltin oxide method⁷⁾ gave the 3-O-BOM derivative 43 regioselectively (72%), as expected. The position of the BOM group in 43 was elucidated on the basis of the ¹H-¹H and ¹H-¹³C COSY spectra. This was converted to the 4,6-O-benzylidene derivative 44 (92%), which was oxidized with DMSO-Ac₂O to give the 2-oxo derivative 45 (71%) accompanied with the methylthiomethyl derivative 46 (20%). Deprotection of 45 by hydrogenolysis over activated Pd in EtOH-acetone gave Me α -D-lyxo-2-OG (3) as a gum in 84% yield. NaBH₄ reduction of 3 gave Me α -D-Gal (19) and Me α -D-Tal in a ratio of 1:3.

In order to confirm the structure of the oxidation products of altrosides, Me α -D-arabino-3-OG (8) was synthesized as follows. Me 4,6-O-benzylidene- α -D-Alt (47) was oxidized by the (Bu₃Sn)₂O-Br₂ method to the 3-oxo derivative 48. The position of the carbonyl group in 48 was confirmed by the doublet anomeric proton signal (δ 4.92, J =1.5 Hz). Deprotection of 48 with 50% AcOH yielded 8, which was identical with the direct oxidation product of Me α -D-Alt (24) and also with the minor product previously reported in the oxidation of Me α -D-Man (21).⁶⁾ NaBH₄ reduction of 8 gave Me α -D-Alt (24) and Me α -D-Man (21) in a ratio of 8:1 as expected. Reduction of the corresponding β -anomer (9) gave Me β -D-Man and Me β -D-Alt (25) in ratio of 3:1, thus supporting the correctness of the structure.

The other possible isomer, Me α -D-ribo-2-OG (4) was prepared as follows. Alkylation of 47 with BOM chloride

in dioxane by the dibutyltin oxide method⁷⁾ gave the 3-O-BOM derivative 49 regioselectively (84%).⁸⁾ The position of the BOM group at O-3 in 49 was proved by the ¹H-¹H and ¹H-¹³C COSY spectra. The signals at δ 3.94 (d, J =2 Hz) and 4.13 (dd, J =3.2, 2 Hz), assignable to H-2 and H-3, are correlated to the carbon signals at δ 70.0 and 73.3, being shifted by -0.2 and +4.1 ppm compared to those of 47, respectively. Oxidation of 49 with DMSO-Ac₂O gave the 2-oxo derivative 50 in 96% yield. Deprotection of 50 by hydrogenolysis in EtOH-acetone gave Me α -D-ribo-2-OG (4) in 91% yield. NaBH₄ reduction of 4 gave Me α -D-Alt (22) and Me α -D-Alt (24) in a ratio of 5:4.

The structures of the oxidation products of Me α -D-Ido (26) were proved as follows. Dialkylation of 47 with 2 moleq of *n*-BuLi and BOM chloride followed by hydrolysis with 60% AcOH gave, in 67% yield, Me 2,3-di-O-BOM- α -D-Alt (52), which on oxidation by the (Bu₃Sn)₂O-Br₂ method (using a modification of the original procedure—see Experimental) gave the 4-oxo derivative (53) in 67% yield. The presence of the carbonyl absorptions (δ_c 207.2 and IR: 1747 cm⁻¹) and the absence of an aldehydic proton indicated it to be the 4-oxo derivative 53. Deprotection of 53 by hydrogenolysis gave Me α -D-arabino-4-OG (16) in 83% yield. The other two possible oxidation products, 5 and 12, were prepared from Me 4,6-O-benzylidene- α -D-Ido (57), which, in turn, was prepared from Me α -D-Gal (19) through regioselective mono-tosylation⁹⁾ followed by benzylidenation, epoxide formation, and stereoselective opening of the epoxide ring (Chart 4). Alkylation of 57 with 1.5 moleq of *n*-BuLi and BOM chloride gave a mixture of the 2-O-BOM (58), 3-O-BOM (59), and 2,3-di-O-BOM (60) derivatives in 11%, 27%, and 49% yields. They were separated by recycling preparative

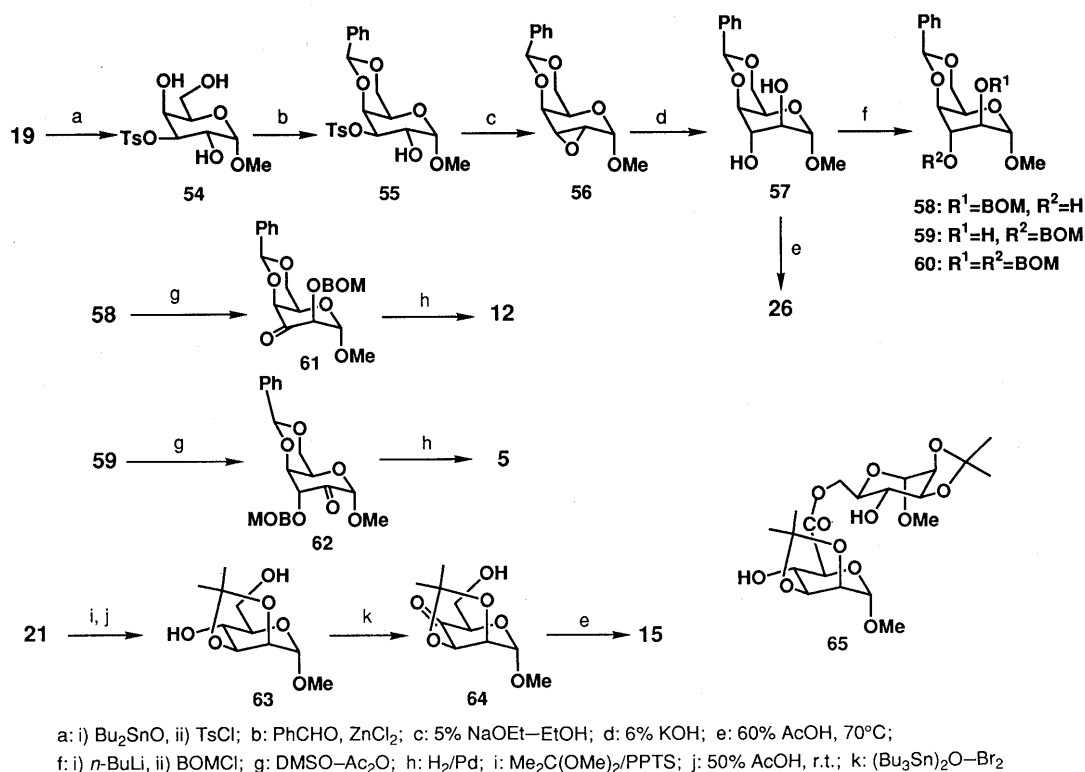


Chart 4

high-performance liquid chromatography (HPLC) and the structure of each product was elucidated by examination of the ^1H - ^{13}C COSY spectra. Oxidation of **58** with DMSO- Ac_2O followed by deprotection of the resulting 3-oxo derivative (**61**) by hydrogenolysis in EtOH-acetone gave Me α -D-lyxo-3-OG (**12**) in 63% yield. Similarly, oxidation of **59** with DMSO- Ac_2O followed by hydrogenolysis gave Me α -D-xylo-2-OG (**5**) in 68% yield. Of the above three products, the ^{13}C -NMR spectra (in both D_2O and pyridine- d_5) of **12** and **16** were superimposable on those of the two oxidation products of Me α -D-Ido (**26**), and that of **5** was obviously different from either component in the oxidation of **26**.

Me α -D-lyxo-4-OG (**15**), previously assigned as a minor oxidation product⁶⁾ of Me α -D-Man (**21**), was regioselectively synthesized as follows. Oxidation of Me 2,3-O-isopropylidene- α -D-Man (**63**) with $(\text{Bu}_3\text{Sn})_2\text{O}$ and bromine in CH_2Cl_2 using modification of the original procedure (see Experimental) gave a mixture of the 4-oxo derivative **64** (76%) and a dimeric ester **65** (20%).¹⁰⁾ Deprotection of **64** with 60% AcOH on heating at 70°C for 40 min gave Me α -D-lyxo-4-OG (**15**) as a gum in 86% yield, and its ^{13}C -NMR spectrum was obviously different from that of **8**. Reduction of **15** with NaBH_4 gave Me α -D-Man (**21**) as a major product.

All of the above-synthesized oxoglycosides were purified by chromatography on a silica gel column with ethyl acetate or chloroform-methanol and the dried samples could be stored in a refrigerator at -30°C for at least 6 months.

Forms of Oxoglycosides in Solutions¹¹⁾ ^{13}C -NMR spectra of the above oxoglycoside derivatives in pyridine- d_5 and in H_2O (D_2O) are listed in Tables Ia and Ib. Their ^1H - and ^{13}C -NMR spectra show that they exist in different forms depending on the solvents.¹²⁾

Me β -D-ribo-3-OG (**7**) showed peaks ascribable only to the oxo form **7a** in pyridine- d_5 ; its carbonyl carbon signal appeared at $\delta 207.3$. However, in D_2O it showed two sets of peaks, ascribable to the oxo form **7a** and the hydrate form **7b** in a ratio of 5:3. The signal of the masked carbonyl carbon in **7b** appeared at $\delta 94.6$. After evaporation of D_2O , the spectrum of **7** in pyridine- d_5 was identical with that in pyridine- d_5 , indicating that **7a** and **7b** are interconvertible depending on the solvents.

Me α -D-ribo-3-OG (**6**) was only in the oxo form **6a** in both pyridine- d_5 and D_2O , since the spectra in the two

solvents were essentially identical, showing the carbonyl absorption at $\delta 207.5$ in pyridine- d_5 and at $\delta 208.0$ in D_2O .

Me α -D-arabino-3-OG (**8**) showed the oxo form **8a** and the hydrate form **8b** in a ratio of ca. 6:1 in pyridine- d_5 , exhibiting signals of the carbonyl carbon at $\delta 208.2$ and the masked carbonyl carbon at $\delta 97.0$, but it gave a complex spectrum (a mixture of an oxo form, a hydrate form, and dimeric forms) in D_2O , showing the carbonyl carbon at $\delta 208.2$ and that of the hydrate form at $\delta 96.3$.

Me β -D-arabino-3-OG (**9**) showed only the oxo form **9a** in pyridine- d_5 , showing a carbonyl carbon signal at $\delta 208.7$, while it gave only a hydrate form **9b** in D_2O ,

TABLE Ia. ^{13}C -NMR Data for Oxoglycosides in Pyridine- d_5

Compd.	C1	C2	C3	C4	C5	C6	OMe
1a	102.7	201.7	78.9	74.9	75.7	62.0	55.0
2a	101.1	200.2	78.4	75.7	80.7	62.2	56.2
3a	101.8	203.7	76.0	75.9	73.7	61.8	55.0
4a	103.3	205.7	77.3	74.3	69.9	62.4	54.8
4b	103.0	93.3	76.0	71.2	67.2	63.4	55.5
5a	104.4	202.4	71.0	68.7	65.8	62.2	55.4
5c	104.6	100.9	80.7	75.7	71.0	65.2	55.7
6a	103.9	76.4	207.5	77.3	73.5	62.2	55.0
7a	106.2	78.0	207.3	73.2	77.7	61.7	56.5
8a	104.1	76.3	208.2	71.6	77.6	62.3	54.3
8b	103.0	73.3	97.0	70.2	76.2	62.0	55.7
9a	103.7	79.3	208.7	72.1	76.1	62.5	56.3
10a	104.1	74.7	207.1	75.7	74.4	60.8	55.1
11a	106.9	76.6	207.4	77.0	74.7	60.5	56.7
11b	104.1	74.1	98.3	69.2	75.3	61.8	56.3
12a	105.4	77.6	207.8	77.5	73.8	61.4	56.2
12b	101.1	71.4	90.6	69.8	67.0	62.8	54.8
13a	100.4	74.0	76.8	205.2	74.5	59.9	55.3
14a	105.1	77.7	79.0	205.4	78.8	60.7	56.7
15a	101.9	75.2	76.1	207.6	76.1	60.6	55.2
16a	106.3	77.6	79.5	211.4	78.5	62.4	55.0

a: Oxo form. b: Hydrate form. 5c: Intramolecular hemiacetal form (see Chart 5).

TABLE Ib. ^{13}C -NMR Data for Oxoglycosides in D_2O

Compd.	C1	C2	C3	C4	C5	C6	OMe
1b	102.1	94.0	74.9	69.6	73.0	61.8	55.8
2b	103.2	93.5	76.8	69.6	77.2	61.8	58.4
2c	103.2	101.8	73.8	67.5	71.1	67.0	57.6
3b	102.7	93.4	71.9	70.3	69.5	62.0	55.8
4b	102.2	92.5	74.0	68.3	66.2	61.9	56.3
5b	102.5	91.0	72.9	70.0	68.3	61.8	56.3
6a	101.6	75.5	208.0	75.3	72.6	61.4	56.0
7a	106.5	78.2	207.4	73.5	78.0	62.0	57.7
7b	102.7	74.2	94.6	70.8	75.4	61.4	57.4
8a	103.4	76.4	208.7	72.0	77.6	61.4	55.7
8b	102.0	72.8	96.3	71.2	75.7	61.8	55.9
9b	101.3	75.9	94.8	68.6	73.6	62.2	57.6
10a	102.7	73.9	206.8	75.1	73.0	60.9	56.1
10b	100.0	70.5	94.0	72.9	69.2	62.1	56.4
11b	103.7	72.5	95.2	72.4	75.3	61.9	57.9
12a	104.0	76.7	207.5	76.7	72.9	60.5	57.7
12b	102.4	72.2	91.6	72.0	71.0	62.2	56.1
13a	100.1	73.6	76.3	205.5	74.5	59.6	56.6
13b	99.9	71.0	74.1	94.6	73.3	59.9	55.9
14b	104.1	73.0	78.0	94.2	76.8	59.9	57.9
15a	101.2	74.0	75.2	207.6	74.8	59.7	56.3
15b	101.7	69.9	74.3	94.2	70.9	59.9	55.7
16a	105.1	75.6	77.7	211.8	77.6	61.6	56.2
16b	101.8	71.7	74.5	93.7	73.5	59.7	56.6

a: Oxo form. b: Hydrate form. 2c: Intramolecular hemiacetal form (see Chart 5).

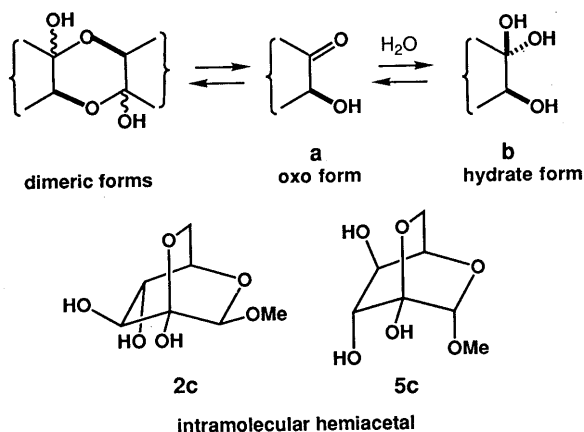


Chart 5

TABLE II. Ratio of Existence Forms of Oxoglycosides in Pyridine- d_5 and D_2O ^{a)}

Compd.	Pyridine- d_5			D_2O		
	a	b	Others	a	b	Others
1	95 ^{b)}	0	5	0	100	0
2	45	30	25 ^{c)}	0	90	10 ^{d)}
3	100	0	0	0	100	0
4	37	38	25 ^{e)}	0	85	15 ^{e)}
5	60	0	40 ^{f)}	0	100	0
6	100	0	0	100	0	0
7	100	0	0	65	35	0
8	85	15	0	42	43	15 ^{c)}
9	100	0	0	0	100	0
10	100	0	0	35	65	0
11	35	65	0	0	100	0
12	80	20	0	40	60	0
13	82	12	6 ^{e)}	75	25	0
14	100	0	0	0	75	25 ^{e)}
15	100	0	0	65	35	0
16	100	0	0	85	15	0

a: Oxo form. b: Hydrate form. a) The ratio was calculated from the ^{13}C -NMR. b) 1 showed a very complex spectrum, immediately after dissolution in pyr- d_5 . The ratio is based on the spectrum at 1 h after dissolution. c) May be a mixture of dimeric forms. d) An intramolecular hemiacetal 2c. e) May be a dimeric form. f) Mainly an intramolecular hemiacetal 5c.

exhibiting a masked carbonyl adsorption at δ 94.8.

Me α -D-xylo-3-OG (10) showed only the oxo form in pyridine- d_5 (C=O: δ 207.1), but gave two forms corresponding to the hydrate and oxo forms in D_2O in a ratio of ca. 2:1. On the other hand, the corresponding β -anomer (11) showed both oxo and hydrate forms in pyridine- d_5 in a ratio of ca. 1:2, showing the carbonyl and masked carbonyl peaks at δ 207.4 and 98.3, respectively. It gave only the hydrate form 11b in D_2O , exhibiting a masked carbonyl carbon signal at δ 95.2.

Me α -D-lyxo-3-OG (12) gave a mixture of the oxo and hydrate forms in both pyridine- d_5 and D_2O , but the ratio was different (4:1 in pyridine- d_5 and 2:3 in D_2O). The carbonyl and masked carbonyl carbons appeared at δ 207.8 and 90.6 in pyridine- d_5 and δ 207.5 and 91.6 in D_2O , respectively.

In contrast to the 3-oxo derivatives, the 2-oxo derivatives completely changed form depending on the solvents. Me β -D-arabino-2-OG (2) in pyridine- d_5 gave major peaks ascribable to the oxo form 2a (though it was unstable), which completely disappeared in D_2O . The spectrum in D_2O was ascribable to the hydrate form 2b and the third form 2c in a ratio of 9:1. The signals of the masked carbonyl carbons in these compounds appeared at δ 93.5 and 101.8, respectively. The structure of the third compound was tentatively assigned as an intramolecular hemiacetal 2c, because the C-6 signal of this compound appeared at too low a field (δ 67.0) to allow its assignment as a CH_2OH group of a normal pyranoside structure. Evaporation of the solvent regenerated the oxo form 2a in pyridine- d_5 , though it was accompanied with significant decomposition of the compound.

Me α -D-arabino-2-OG (1) gave a very complex spectrum due to a mixture of the oxo form, the hydrate form, and dimeric forms in pyridine- d_5 , when the spectrum was measured immediately after its dissolution in the solvent. However, after about 1 h, the spectrum converged into a

TABLE III. ^{13}C -NMR Data for Glycoside Derivatives in $CDCl_3$ ^{a)}

Compd.	C1	C2	C3	C4	C5	C6	OMe
28	100.8	198.8	74.7	83.9	62.8	68.6	55.4
29	99.5	80.5	69.8	81.4	61.9	69.0	55.3
30	100.1	72.4	77.3	80.6	62.6	69.1	55.5
31	102.0	78.4	195.4	82.2	65.4	69.4	55.6
32	99.7	78.3	74.6	81.9	62.2	69.0	55.2
34	104.4	74.2	80.1	80.0	65.5	68.7	57.5
35	103.6	80.6	72.9	82.0	66.0	68.7	57.4
37a ^{b)}	102.9	196.1	81.7	78.8	66.5	68.5	57.8
37b ^{b)}	101.6	92.9	81.2	78.7	66.5	68.4	57.1
37b ^{b,c)}	105.6	101.5	82.3	79.9	66.9	68.9	56.6
38	104.9	76.3	78.8	80.0	66.2	68.8	57.2
40	103.2	81.0	200.7	73.9	64.8	68.8	56.0
42	105.5	76.5	201.3	80.0	68.5	66.3	57.2
43	99.8	68.1	77.6	69.6	69.4	62.9	55.4
44	100.3	67.5	76.7	75.4	62.6	69.3	55.5
45	101.2	196.6	90.0	75.3	63.5	68.7	55.3
46	99.8	73.0	75.9	75.2	62.3	69.4	55.6
47	101.8	70.2	69.2	76.3	58.4	69.2	55.7
48	104.2	76.4	199.2	80.3	66.3	69.4	55.1
49	101.9	70.0	73.3	75.9	58.6	69.3	55.7
50b ^{b)}	103.5	92.4	78.3	77.3	58.5	69.2	56.1
51	100.6	71.2	74.9	76.2	58.4	69.4	55.7
52	100.1	77.6	74.5	68.4	65.2	63.2	55.4
53	103.7	79.7	79.7	207.2	76.6	62.2	55.4
54	99.8	66.5	81.5	69.5	69.5	62.2	55.2
55	100.3	66.4	78.7	74.8	62.5	69.0	55.8
56	96.8	49.0	49.6	68.7	59.8	69.2	55.9
57	102.6	67.8	67.8	75.6	58.9	69.8	55.7
58	101.5	74.5	69.1	75.8	59.8	69.5	55.5
59	102.6	66.4	74.1	74.4	59.5	70.1	55.9
60	102.3	74.1	75.9	76.8	61.1	69.3	55.4
61	103.0	78.5	199.2	77.5	64.5	68.7	55.7
62	100.4	199.7	78.1	79.3	63.2	68.7	56.2
63	98.3	78.4	75.4	69.1	69.5	62.1	55.0
64	98.1	75.1	77.9	203.3	74.4	61.9	55.9

a) Data for protecting groups are omitted. b) a: Oxo form. b: Hydrate form. c) Data in pyridine- d_5 .

simple pattern ascribable to the oxo form 1a (which gradually changed into a different compound—this change will be discussed in a separate communication).^{1b)} In D_2O , 1 gave a spectrum of only the hydrate form 1b. Evaporation of D_2O and dissolution of the residue in pyridine- d_5 regenerated the oxo form 1a.

Me α -D-lyxo-2-OG (3) showed only the oxo form in pyridine- d_5 (C=O: δ 203.7), but showed only the hydrate form in D_2O , giving the masked carbonyl peak at δ 93.4.

Me α -D-ribo-2-OG (4) showed the presence of an oxo form and a hydrate form in a ratio of 1:1 in pyridine- d_5 (C=O: δ 205.7; masked C=O: δ 93.3) accompanied with other peaks ascribable probably to a dimeric form, but in D_2O it gave peaks ascribable to the hydrate form (masked C=O: δ 92.5) and a dimeric form.

Me α -D-xylo-2-OG (5) gave the oxo form 5a and another form (assignable as an intramolecular hemiacetal 5c) in a ratio of 3:2 in pyridine- d_5 (C=O: δ 202.4), but gave only the hydrate form 5b in D_2O (masked C=O: δ 91.0).

Such an oxo-hydrate form interconversion was also observed for the 4,6-O-benzylidene derivative 37, in which all hydroxyl groups had been masked, thus excluding the possibility of intermolecular hemiacetal formation. In $CDCl_3$ solution, compound 37 showed two sets of peaks, one being ascribable to the oxo form 37a and the other

to the hydrate form **37b** (Table III). However, it gave only one set of peaks ascribable to a hydrate **37b** in pyridine-*d*₅ solution (this may be due to water contaminating in the solvent). Although compound **37** showed only one spot on thin-layer chromatography (TLC), it was less mobile than the original compound **34**, suggesting that it behaved as the hydrate form on the plate. In the IR spectrum, a solid sample of **37** exhibited a weak carbonyl absorption at 1756 cm⁻¹, and the sample was analyzed as a semi-hydrate. On the contrary, the isomer **31** gave peaks ascribable to only the oxo form **31a** in both CDCl₃ and pyridine-*d*₅ solutions. The IR spectrum of **31** exhibited a strong carbonyl absorption at 1745 cm⁻¹. On the other hand, another isomer **50** did not show the carbonyl absorption in the IR spectrum, and gave ¹³C-NMR peaks ascribable to the hydrate form **50b** in CDCl₃ solution (see Table III).

The above results indicate that 2-oxoglycosides, either α or β , have high affinity for a hydroxylic solvent, forming a hemiacetal (hydrate) form, while most of the 3-oxoglycosides, either α or β , are rather stable and exist in oxo forms in large proportions even in hydroxylic solvents.

Me α -D-xylo-4-OG (**13**) showed mainly two sets of peaks in a ratio of *ca.* 6:1, major peaks being ascribable to the oxo form **13a** (C=O: δ 205.2) and minor peaks to the hydrate form **13b**. In D₂O, it again showed two sets of peaks, which were almost the same as those in pyridine-*d*₅. The carbonyl and the masked carbonyl carbons in D₂O were at δ 205.5 and 94.6, respectively.

On the other hand, Me β -D-xylo-4-OG (**14**) showed the peaks ascribable only to the oxo form **14a** in pyridine-*d*₅ (C=O: δ 205.4), and mainly to the hydrate form **14b** in D₂O (masked C=O: δ 94.2).

Me α -D-lyxo-4-OG (**15**) showed only an oxo form in pyridine-*d*₅ (C=O: δ 207.6), but showed two forms, the oxo form **15a** and the hydrate form **15b**, with a preference for the former, in D₂O. The carbonyl and masked carbonyl carbons appeared at δ 207.6 and 94.2, respectively. Similarly, Me α -D-arabino-4-OG (**16**) gave only the oxo form in pyridine-*d*₅ (C=O: δ 211.4), and gave two forms, the oxo form and the hydrate form, in D₂O (masked C=O: δ 93.7).

The above results are summarized in Table II, from which we reached the following conclusions. (1) All oxoglycosides, more or less, change their forms depending on the solvents. Preference for hydration is observed with all 2-oxoglycosides. The relative hydration capability of oxoglycosides is in the order of 2-oxo > 4-oxo $\geq$ 3-oxo glycosides: 2-oxoglycosides are the most reactive and 3-oxoglycosides are the most stable to hydration. (2) In the 3-oxo and 4-oxo glycosides, β -anomers are more reactive to hydration than the corresponding α -anomers.

In addition to the above observations, all oxoglycosides were found to be, more or less, unstable, gradually decomposing on standing in pyridine-*d*₅. 2-Oxoglycosides were more unstable than 3-oxo and 4-oxo derivatives in pyridine-*d*₅; they gradually changed into 3-oxo derivatives mainly through an intramolecular hydride shift, then underwent further decomposition. This new rearrangement of 2-oxoglycosides and decomposition of oxoglycosides in pyridine will be discussed in detail in a future publication.^{1b)}

Experimental

Unless otherwise stated, the following procedures were adopted. Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken in chloroform solutions and the data are given in cm⁻¹. NMR spectra were measured on a JEOL GX-400 (400 MHz for ¹H and 100 MHz for ¹³C) spectrometer in CDCl₃ solutions (for protected compounds) with tetramethylsilane as an internal standard and the chemical shifts are given in δ values. Data for protecting groups are omitted. Oxoglycosides were measured as 0.1–0.3 M solutions in pyridine-*d*₅ or in D₂O (internal standard: dioxane). Mass spectra (MS) and high resolution MS (HRMS) were taken with a Hitachi M-80 machine at 70 eV and M⁺ and/or major peaks are indicated as *m/z* (%). Gas chromatographic (GC) analyses were carried out with a Shimadzu GC4CM-PF gas chromatograph with a glass column (4 mm $\times$ 1 m) packed with 1.5% OV-1 on Shimalite W (80–100 mesh) and a flame ionization detector (FID), using N₂ (45–60 ml/min) as a carrier gas. Trimethylsilyl (TMS) derivatives were prepared as follows. A sample (1–2 mg) in dry pyridine (2 drops) was shaken vigorously with hexamethyldisilazane (2 drops) and trimethylsilyl chloride (1 drop). After 10 min at room temperature, the mixture was centrifuged and the supernatant (0.5–1 μ l) was directly injected into a GC column. Column chromatography was performed on silica gel (Wako-gel C-200). For TLC, Merck precoated plates GF₂₅₄ were used and spots were developed by spraying 5% H₂SO₄ and heating the plates until coloration took place. Identities were confirmed by comparisons of TLC behavior and of ¹H- and ¹³C-NMR spectra.

Reduction of an Oxoglycoside with NaBH₄ and GC Analysis of the Product An oxoglycoside (2–5 mg) in MeOH (1–2 ml) was treated with NaBH₄ (2–5 mg) at room temperature for 1 h. The mixture was neutralized with 1 N HCl and concentrated to dryness. The residue was dissolved in MeOH and concentrated. This procedure was repeated several times to remove borate complexes completely. The residue was converted to a TMS derivative and analyzed by GC. The relative retention times of the reference glycosides are as follows: Me β -D-Glc 1.00, Me α -D-Glc 0.88, Me β -D-Gal 0.79, Me α -D-Ido 0.69, Me α -D-Gal 0.67, Me α -D-Tal 0.63, Me β -D-Man 0.61, Me α -D-Man 0.56, Me β -D-All 0.50, Me α -D-All 0.50, Me α -D-Gul 0.44, Me β -D-Alt 0.44, and Me α -D-Alt 0.42.

Oxidation of a Glycoside by the Bistributyltin Oxide-Bromine Method (General Procedure)⁶⁾ A mixture of a glycoside (0.1–0.5 g), (Bu₃Sn)₂O (2 moleq), and molecular sieves 3A (large excess) in CHCl₃ (30–50 ml) was heated under reflux for 3 h, then cooled. To this mixture, bromine (*ca.* 2 moleq) was added at 0°C with stirring until the solution was faintly colored, then the mixture was rapidly poured onto a column of silica gel. The column was washed thoroughly with CHCl₃ to remove tin compounds, then eluted with AcOEt or CHCl₃-MeOH to yield an oxoglycoside.

Oxidation of Me α -D-Man (21) Me α -D-Man (**21**, 0.5 g) was oxidized as described above to give the oxidation product (0.26 g, 53%) with recovery of **21** (0.21 g, 42%). The ¹³C-NMR spectrum of the oxidation product in D₂O showed only seven peaks corresponding to **1b** (hydrate form), no other peaks being observed in the spectrum.

Reduction of this compound with NaBH₄ gave Me α -D-Glc (**18**) and Me α -D-Man (**21**) in a ratio of 7:1.

Oxidation of Me α -D-All (22) Me α -D-All (**22**, 50 mg) was oxidized as described above to yield **6** (45 mg, 91%) as a solid. IR (KBr): 1736. ¹H-NMR (pyridine-*d*₅): 3.29 (OMe).

NaBH₄ reduction of **6** gave Me α -D-Glc (**18**) and Me α -D-All (**22**) in a ratio of 1:14.

Oxidation of Me β -D-All (23) Me β -D-All (**23**, 70 mg) was oxidized as described above to yield **7** (58 mg, 84%) as colorless prisms, mp 130°C. This product was identified with the specimen obtained by oxidation of Me β -D-Glc (**17**).⁶⁾

Oxidation of Me α -D-Alt (24) Me α -D-Alt (**24**, 0.23 g) was oxidized as described above to yield **8** (0.19 g, 84%) as a gum. IR (film): 3415, 1739. MS: 160 (M⁺ - MeOH, 5), 103 (100). ¹H-NMR (pyridine-*d*₅): 3.34 (OMe).

Reduction of **8** with NaBH₄ gave Me α -D-Man (**21**) and Me α -D-Alt (**24**) in a ratio of 8:1.

Oxidation of Me β -D-Alt (25) Me β -D-Alt (**25**, 0.15 g) was oxidized as described above to give **9** (0.12 g, 82%) as a gum. IR (film): 3400, 1726 (weak). MS: 175 (M⁺ - OH, 0.5), 103 (100). ¹H-NMR (pyridine-*d*₅): 3.56 (OMe).

NaBH₄ reduction of **9** gave Me β -D-Man and Me β -D-Alt (**25**) in a ratio of 3:1.

Oxidation of Me α -D-Ido (26) Me α -D-Ido (26, 0.2 g) was oxidized with 4 moleq of $(\text{Bu}_3\text{Sn})_2\text{O}$ (2.46 g) and bromine and worked up as described in the general procedure to yield a mixture of **12** and **16** (167 mg, 84%) as a gum. $^1\text{H-NMR}$ (pyridine- d_5): OMe 3.61 for **12** and 3.40 for **16**. The structures of these products were proved by alternative syntheses of **12** and **16** (see below) and comparisons of their $^{13}\text{C-NMR}$ spectra with that of the above mixture.

Oxidation of Me 4,6-*O*-Benzylidene- α -D-Glc (27) (Modified Procedure) A mixture of Me 4,6-*O*-benzylidene- α -D-Glc (27, 200 mg), $(\text{Bu}_3\text{Sn})_2\text{O}$ (1.27 g, 3 moleq), and molecular sieves 3A (2 g) in dry toluene (30 ml) was heated under reflux for 5 h and then cooled. To the mixture, Br_2 (ca. 3 moleq) was added with stirring at 0°C , and stirring was continued for 10 min. The mixture was directly poured onto a silica gel column. The column was washed with benzene to remove tin compounds, then eluted with benzene-AcOEt (2:1) to yield **28** (189 mg, 95%), which was identical with the previously reported specimen.⁶⁾

Methyl α -D-arabino-Hexopyranosid-2-ulose (1) Compound **28** (100 mg) in AcOH (4 ml) and water (6 ml) was heated at 100°C for 10 min. After addition of water, the mixture was lyophilized and the residue was purified by chromatography (CHCl_3 :MeOH=3:1) to give **1** (57 mg, 84%) as a solid mass. IR (KBr): 1746 (weak). $^1\text{H-NMR}$ (pyridine- d_5): 3.40 (OMe). MS: 193 ($\text{M}^+ + 1$, 0.6). The $^{13}\text{C-NMR}$ spectrum of this compound in D_2O was superimposable on that of the oxidation product of Me α -D-Man (**21**).

Benzylloxymethylation of Me 4,6-*O*-Benzylidene- α -D-Glc (27) by the Dibutyltin Oxide Method A mixture of **27** (1 g) and Bu_2SnO (1.36 g, 2 moleq) in MeOH (40 ml) was heated under reflux for 3 h, then the solvent was evaporated off *in vacuo*. The glassy solid residue was dissolved in CH_3CN (40 ml) and the solution was stirred with BOM chloride (BOMCl) (1.39 g, 2.5 moleq) for 10 h at room temperature. The solvent was evaporated off below 30°C , and the residue was separated by flash chromatography (solvent; hexane: CHCl_3 :AcOEt=2:1:1) to yield the 2-*O*-BOM derivative **29** (1.0 g, 70%) and the 3-*O*-BOM derivative **30** (0.28 g, 20%).

The 2-*O*-BOM Derivative **29**: Colorless needles from hexane-acetone, mp $105\text{--}107^\circ\text{C}$. IR: 3340. $^1\text{H-NMR}$: 3.40 (3H, s, OMe), 3.53 (1H, t, $J=10.0\text{ Hz}$, H-4), 3.62 (1H, dd, $J=4.3$, 10.0 Hz, H-2), 3.74 (1H, t, $J=10.0\text{ Hz}$, H-6), 3.85 (1H, dt, $J=4.7$, 10.0 Hz, H-5), 4.13 (1H, t, $J=10.0\text{ Hz}$, H-3), 4.28 (1H, dd, $J=4.7$, 10.0 Hz, H-6), 4.85 (1H, d, $J=4.3\text{ Hz}$, H-1), and benzylidene and BOM groups. MS: 402 (M^+ , 2). Anal. Calcd for $\text{C}_{22}\text{H}_{26}\text{O}_7$: C, 65.66; H, 6.51. Found: C, 65.42; H, 6.69.

The 3-*O*-BOM Derivative **30**: Colorless needles from acetone, mp $86\text{--}88^\circ\text{C}$. IR: 3340. $^1\text{H-NMR}$: 3.40 (3H, s, OMe), 3.54 (1H, t, $J=9.5\text{ Hz}$, H-4), 3.67 (1H, dd, $J=4.0$, 9.5 Hz, H-2), 3.71 (1H, t, $J=10.0\text{ Hz}$, H-6), 3.81 (1H, dt, $J=4.9$, 10.0 Hz, H-5), 3.99 (1H, t, $J=9.5\text{ Hz}$, H-3), 4.26 (1H, dd, $J=4.9$, 10.0 Hz, H-6), 4.76 (1H, d, $J=4.0\text{ Hz}$, H-1), and benzylidene and BOM groups. MS: 402 (M^+ , 0.5). Anal. Calcd for $\text{C}_{22}\text{H}_{26}\text{O}_7 \cdot 3/2\text{H}_2\text{O}$: C, 61.53; H, 6.81. Found: C, 61.56; H, 6.83.

DMSO-Ac₂O Oxidation of the 2-*O*-BOM Derivative 29 A mixture of **29** (450 mg), DMSO (6 ml), and Ac_2O (5 ml) was stirred at room temperature for 10 h. The mixture was poured into aqueous NaHCO_3 and extracted with ether. Concentration of the extract gave a solid, which was washed with ether and recrystallized from ether-acetone to give **31**. Chromatography of the ether washings eluting with CHCl_3 -AcOEt (2:1) gave a further crop of **31** (total yield, 230 mg, 51%) and the 3-*O*-methylthiomethyl derivative **32** (249 mg, 48%).

The 3-Oxo Derivative **31**: Colorless needles from ether-acetone, mp $166\text{--}168^\circ\text{C}$. IR (KBr): 1745. $^1\text{H-NMR}$: 3.42 (3H, s, OMe), 3.90 (1H, t, $J=10.0\text{ Hz}$, H-6), 4.07 (1H, dt, $J=4.6$, 10.0 Hz, H-5), 4.23 (1H, dd, $J=1.2$, 10.0 Hz, H-4), 4.39 (1H, dd, $J=4.6$, 10.0 Hz, H-6), 4.46 (1H, dd, $J=1.2$, 4.3 Hz, H-2), 4.97 (1H, d, $J=4.3\text{ Hz}$, H-1), and benzylidene and BOM groups. MS: 400 (M^+ , 0.5). Anal. Calcd for $\text{C}_{22}\text{H}_{24}\text{O}_7 \cdot 1/2\text{H}_2\text{O}$: C, 64.54; H, 6.15. Found: C, 64.82; H, 6.11.

The 3-*O*-Methylthiomethyl Derivative **32**: Colorless oil: IR: 1360, no OH absorption. $^1\text{H-NMR}$: 2.10 (3H, s, SMe), 3.41 (3H, s, OMe), 3.59 (1H, t, $J=10.0\text{ Hz}$, H-4), 3.73 (1H, t, $J=10.0\text{ Hz}$, H-6), 3.74 (1H, dd, $J=4.7$, 10.0 Hz, H-2), 3.85 (1H, dt, $J=4.7$, 10.0 Hz, H-5), 4.22 (1H, t, $J=10.0\text{ Hz}$, H-3), 4.27 (1H, dd, $J=4.7$, 10.0 Hz, H-6), 4.81 (1H, d, $J=4.3\text{ Hz}$, H-1), 4.86, 4.90 (each 1H, d, $J=11.0\text{ Hz}$, OCH_2S), and benzylidene and BOM groups. MS: 462 (M^+ , 0.2).

Methyl α -D-ribo-Hexopyranosid-3-ulose (6) Compound **31** (200 mg) in AcOEt-EtOH (35 ml) was hydrogenated over activated Pd black [commercial Pd black (150 mg) was treated with concentrated HCl for a few min and washed with water several times, then with EtOH] under a

hydrogen pressure of 4 kg/cm^2 for 9 h. Removal of the catalyst and the solvent followed by chromatography of the residue eluting with CHCl_3 -MeOH (5:1) gave **6** (95 mg, 99%), as colorless plates from CHCl_3 -MeOH, mp $86\text{--}88^\circ\text{C}$. IR (KBr): 1736. $^1\text{H-NMR}$ (pyridine- d_5): 3.29 (OMe). MS: 193 ($\text{M}^+ + 1$, 4). HRMS: Calcd for $\text{C}_7\text{H}_{13}\text{O}_6$ ($\text{M}^+ + 1$): 193.0711. Found: 193.0667. This product was identical with the oxidation product of Me α -D-AlI (**22**).

Benzylloxymethylation of Me 4,6-*O*-Benzylidene- β -D-Glc (33) by the Dibutyltin Oxide Method Compound **33** (2.0 g) was treated with Bu_2SnO and BOMCl (4 eq) as described for **27**. Chromatography of the product eluting with hexane-AcOEt (1:1) gave the 3-*O*-BOM derivative **34** (1.55 g, 54%), the 2-*O*-BOM derivative **35** (0.6 g, 21%), and the di-*O*-BOM derivative **36** (0.59 g, 16%).

The 3-*O*-BOM Derivative **34**: Colorless needles from ether-hexane, mp $134\text{--}135^\circ\text{C}$. $^1\text{H-NMR}$: 3.46 (1H, dt, $J=5$, 10 Hz, H-5), 3.53 (1H, br dt, $J=1.8$, 8.3 Hz, H-2), 3.59 (3H, s, OMe), 3.64 (1H, t, $J=9\text{ Hz}$, H-4), 3.79 (1H, t, $J=10\text{ Hz}$, H-6), 3.82 (1H, br t, $J=8.4\text{ Hz}$, H-3), 4.35 (1H, d, $J=8.0\text{ Hz}$, H-1), 4.36 (1H, dd, $J=5$, 10 Hz, H-6), and benzylidene and BOM groups. MS: 402 (M^+ , 0.4%). Anal. Calcd for $\text{C}_{22}\text{H}_{26}\text{O}_7$: C, 65.66; H, 6.51. Found: C, 65.69; H, 6.56.

The 2-*O*-BOM Derivative **35**: Colorless needles from ether-hexane, mp $115\text{--}117^\circ\text{C}$. $^1\text{H-NMR}$: 3.54—3.47 (2H, m, H-3,5), 3.54 (3H, s, OMe), 3.56 (1H, t, $J=9.0\text{ Hz}$, H-4), 3.78 (1H, t, $J=10\text{ Hz}$, H-6), 3.84 (1H, br t, $J=8.5\text{ Hz}$, H-2), 4.36 (1H, dd, $J=4.9$, 10 Hz, H-6), 4.39 (1H, d, $J=8\text{ Hz}$, H-1), and benzylidene and BOM groups. MS: 402 (M^+ , 0.2). Anal. Calcd for $\text{C}_{22}\text{H}_{26}\text{O}_7$: C, 65.66; H, 6.51. Found: C, 65.61; H, 6.64.

The 2,3-Di-*O*-BOM Derivative **36**: Colorless oil. $^1\text{H-NMR}$ (100 MHz): 3.50 (3H, s, OMe), 4.38 (1H, d, $J=7.6\text{ Hz}$, H-1), 3.5—5.0 (6H, m, H-2,3,4,5,6), and benzylidene and 2 $\times$ BOM groups. MS: 552 (M^+ , 0.2).

DMSO-Ac₂O Oxidation of the 3-*O*-BOM Derivative (34) A mixture of **34** (1.0 g), DMSO (18 ml), and Ac_2O (12 ml) was stirred overnight at room temperature, then poured into water and extracted with ether. Chromatography of the product gave the 2-*O*-methylthiomethyl derivative **38** (628 mg, 55%) from the CHCl_3 -AcOEt (9:1) eluate and the 2-oxo derivative **37** (433 mg, 43%) from the CHCl_3 -AcOEt (4:1) eluate.

The 2-Oxo Derivative **37**: Colorless needles from AcOEt, mp $154\text{--}157^\circ\text{C}$. IR (KBr): 1756 (weak). $^1\text{H-NMR}$: 4.83, 4.84 (total 1H, each s, H-1), 3.63, 3.66 (total 3H, each s, OMe). Anal. Calcd for $\text{C}_{22}\text{H}_{24}\text{O}_7 \cdot 1/2\text{H}_2\text{O}$: C, 64.54; H, 6.15. Found: C, 64.68; H, 6.21.

The 2-*O*-Methylthiomethyl Derivative **38**: Colorless oil. $^1\text{H-NMR}$: 2.20 (3H, s, SMe), 3.43 (1H, dt, $J=5$, 10 Hz, H-5), 3.55 (3H, s, OMe), 3.61 (1H, t, $J=9.5\text{ Hz}$, H-4), 3.65 (1H, dd, $J=8$, 9 Hz, H-2), 3.77 (1H, t, $J=10\text{ Hz}$, H-6), 3.96 (1H, t, $J=9\text{ Hz}$, H-3), 4.35 (1H, dd, $J=5$, 10 Hz, H-6), 4.40 (1H, d, $J=8\text{ Hz}$, H-1), 4.60, 4.65 (each 1H, d, $J=11.6\text{ Hz}$, OCH_2S), and benzylidene and BOM groups. MS: 401 ($\text{M}^+ - \text{CH}_2\text{SCH}_3$, 0.9).

Methyl β -D-arabino-Hexopyranosid-2-ulose (2) Compound **37** (300 mg) in EtOH-AcOEt (1:1, 30 ml) was shaken with activated Pd black (150 mg) under hydrogen pressure of 4 kg/cm^2 for 9 h at room temperature. Removal of the catalyst and the solvent left a gum, which was purified by chromatography to give **2** (102 mg, 64%), from the CHCl_3 -MeOH (3:1) eluate, as a colorless gum. IR (film): 3400, 1726 (weak). $^1\text{H-NMR}$ (pyridine- d_5): 3.53 (OMe). MS: 193 ($\text{M}^+ + 1$, 0.05).

Reduction of **2** with NaBH_4 gave Me β -D-Man and Me β -D-Glc (**17**) in a ratio of 20:1.

Methyl 4,6-*O*-Benzylidene- α -D-xylo-hexopyranosid-3-ulose (40) Me 4,6-*O*-benzylidene- α -D-Gal (**39**, 0.3 g) was oxidized and worked up as described in the general procedure. The column was washed thoroughly with benzene to remove tin compounds, then eluted with benzene- CHCl_3 to yield the 3-oxo derivative **40** (0.175 g, 59%) as colorless needles from AcOEt, mp $146\text{--}148^\circ\text{C}$. IR (KBr): 1741. $^1\text{H-NMR}$ (500 MHz): 3.02 (1H, d, $J=8.0\text{ Hz}$, OH), 3.44 (3H, s, OMe), 3.87 (1H, d, $J=1.5\text{ Hz}$, H-5), 4.18 (1H, dd, $J=1.5$, 12.7 Hz, H-6), 4.42 (1H, d, $J=12.7\text{ Hz}$, H-6), 4.56 (1H, s, H-4), 4.96 (1H, dd, $J=4.5$, 8.0 Hz, H-2), 5.19 (1H, d, $J=4.5\text{ Hz}$, H-1), and a benzylidene group. MS: 280 (M^+ , 0.04), 279 ($\text{M}^+ - 1$, 0.2), 107 (100). Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{O}_6$: C, 59.99; H, 5.75. Found: C, 59.11; H, 5.68.

Methyl α -D-xylo-Hexopyranosid-3-ulose (10) Compound **40** (100 mg) was hydrolyzed with 50% AcOH (5 ml) at 100°C for 15 min and worked up as described for **1** to give **10** (58 mg, 85%) as a gum. IR (film): 1728. $^1\text{H-NMR}$ (pyridine- d_5): 3.35 (OMe). MS: 192 (M^+ , 0.9). HRMS: Calcd for $\text{C}_7\text{H}_{11}\text{O}_6$ ($\text{M}^+ - 1$): 191.0555; $\text{C}_6\text{H}_9\text{O}_5$ ($\text{M}^+ - \text{OMe}$): 161.0449. Found: 191.0621; 161.0440.

NaBH_4 reduction of **10** gave Me α -D-Gal (**19**) and Me α -D-Gul in a ratio of ca. 1:1.

Methyl 4,6-*O*-Benzylidene- β -D-xylo-hexopyranosid-3-ulose (42) Me 4,6-*O*-Benzylidene- β -D-Gal **41** (175 mg) was oxidized and worked up as described for **40** to give the 3-oxo derivative **42** (155 mg, 89%) as colorless needles from AcOEt, mp 199–201 °C. IR: 3440, 1741. ¹H-NMR (500 MHz): 3.29 (1H, d, *J* = 4.0 Hz, OH), 3.66 (3H, s, OMe), 4.19 (1H, dd, *J* = 1.9, 12.7 Hz, H-6), 4.29 (1H, d, *J* = 8.0 Hz, H-1), 4.49 (1H, dd, *J* = 1.5, 12.7 Hz, H-6), 4.56 (1H, d, *J* = 1.0 Hz, H-4), 4.70 (1H, dd, *J* = 4.0, 8.0 Hz, H-2), 5.35 (1H, dd, *J* = 1.5, 1.9 Hz, H-5), and a benzylidene group. MS: 279 (*M*⁺ – 1, 1), 248 (*M*⁺ – OMe, 3), 107 (100). *Anal.* Calcd for C₁₄H₁₆O₆ · 1/2H₂O: C, 58.13; H, 5.92. Found: C, 58.41; H, 5.70.

Methyl β -D-xylo-Hexopyranosid-3-ulose (11) Compound **42** (100 mg) was heated in 60% AcOH (5 ml) at 100 °C for 10 min. The mixture was lyophilized and the residue was purified by chromatography eluting with CHCl₃–MeOH (4:1) to give **11** (64 mg, 93%) as a gum. IR (film): 1727 (weak). ¹H-NMR (pyridine-*d*₅): 3.60 (OMe). MS: 191 (*M*⁺ – 1, 0.3), 161 (*M*⁺ – OMe, 3). HRMS: Calcd for C₇H₁₁O₆ (*M*⁺ – 1): 191.0555; C₆H₉O₅ (*M*⁺ – OMe): 161.0449. Found: 191.0508; 161.0398. The ¹³C-NMR spectrum of this compound in D₂O was superimposable on that of the minor constituent in the oxidation product of Me β -D-Gal (**20**).⁶¹

Reduction of **11** with NaBH₄ gave Me β -D-Gal (**20**) as a single product.

Benzylloxymethylation of Me α -D-Gal (19) by the Dibutyltin Oxide Method A mixture of Me α -D-Gal (**19**, 1.2 g) and Bu₂SnO (3.1 g, 2 moleq) in MeOH (70 ml) was heated under reflux for 3 h. Evaporation of the solvent gave the crude stannylene derivative. This was dissolved in dioxane (80 ml) and treated with BOMCl (0.5 g, 2 moleq) under stirring at room temperature, then at 80 °C for 2 h. The mixture was concentrated to dryness and the residue was chromatographed. Tin compound(s) was removed by eluting the column with CHCl₃. Subsequent elution with CHCl₃–AcOEt (1:3) gave the 3-*O*-BOM derivative **43** (1.4 g, 72%) as a gum. IR: 3425. ¹H-NMR: 3.76–3.84 (3H, m, H-3,5,6), 3.92 (1H, dd, *J* = 5.4, 11.3 Hz, H-6), 3.99 (1H, dd, *J* = 3.9, 9.7 Hz, H-2), 4.08 (1H, brd, *J* = 3.9 Hz, H-4), 4.86 (1H, d, *J* = 3.9 Hz, H-1) and a BOM group. MS: 315 (*M*⁺ + 1, 0.2), 59 (100).

Benzylidenation of Me 3-*O*-BOM- α -D-Gal (43) A mixture of **43** (1.1 g), 1,1-dimethoxytoluene (2 ml), and *p*-TsOH (8 mg) in dimethyl formamide (DMF) (6 ml) was heated at 60 °C for 2 h with continuous removal of the formed MeOH under reduced pressure. The mixture was poured into aqueous NaHCO₃ and extracted with CHCl₃. The CHCl₃ layer was washed with brine, dried, and concentrated to dryness. Chromatography of the residue gave, from the CHCl₃–AcOEt (3:1) eluate, **44** (1.3 g, 92%), as colorless needles from ether, mp 92–93 °C. IR (KBr): 3455. ¹H-NMR: 3.43 (3H, s, OMe), 3.61 (1H, brs, H-5), 3.93 (1H, dd, *J* = 3.0, 10.0 Hz, H-2), 3.98 (1H, dd, *J* = 1.5, 12.5 Hz, H-6), 4.15 (1H, dd, *J* = 3.0, 10.0 Hz, H-3), 4.20 (1H, dd, *J* = 1.5, 12.5 Hz, H-6), 4.31 (1H, d, *J* = 3.0 Hz, H-4), 4.92 (1H, d, *J* = 3.5 Hz, H-1), and benzylidene and BOM groups. MS: 403 (*M*⁺ + 1, 1), 402 (*M*⁺, 0.8), 91 (100). *Anal.* Calcd for C₂₂H₂₆O₇ · 1/3H₂O: C, 64.70; H, 6.58. Found: C, 64.62; H, 6.46.

DMSO–Ac₂O Oxidation of the 3-*O*-BOM Derivative (44) Compound **44** (0.27 g) was treated with DMSO (1.6 ml) and Ac₂O (1.4 ml) at 35 °C for 8 h to give, after chromatography, the 2-oxo derivative **45** (0.19 g, 71%) and the 2-*O*-methylthiomethyl derivative **46** (63 mg, 20%).

The 2-Oxo Derivative **45**: Colorless gum. IR: 1751. ¹H-NMR: 3.47 (3H, s, OMe), 4.03 (1H, d, *J* = 12.5 Hz, H-6), 4.05 (1H, brs, H-5), 4.26 (1H, dd, *J* = 2.0, 12.5 Hz, H-6), 4.49 (1H, d, *J* = 3.9 Hz, H-3), 4.82 (1H, s, H-1), 4.86 (1H, d, *J* = 3.9 Hz, H-4), and benzylidene and BOM groups. HRMS: Calcd for C₂₂H₂₄O₇ (*M*⁺): 400.1539. Found: 400.1522.

The 2-*O*-Methylthiomethyl Derivative **46**: Colorless oil. ¹H-NMR: 3.45 (3H, s, OMe), 3.64 (1H, brs, H-5), 3.99 (1H, dd, *J* = 1.5, 12.2 Hz, H-6), 4.13 (1H, dd, *J* = 3.5, 10.5 Hz, H-3), 4.22 (1H, dd, *J* = 3.9, 10.5 Hz, H-2), 4.23 (1H, d, *J* = 12.2 Hz, H-6), 4.31 (1H, d, *J* = 3.5 Hz, H-4), 4.94, 4.92 (each 1H, d, *J* = 8.0 Hz, SCH₂O), 5.01 (1H, d, *J* = 3.4 Hz, H-1), and benzylidene and BOM groups. MS: 462 (*M*⁺, 0.06).

Methyl α -D-lyxo-Hexopyranosid-2-ulose (3) Compound **45** (130 mg) in EtOH–acetone (3:1, 40 ml) was hydrogenated over activated Pd black (120 mg) for 3 h and worked up as described above to give **3** (52 mg, 84%) as a colorless gum. IR (KBr): 1747. ¹H-NMR (pyridine-*d*₅): 3.39 (OMe). MS: 161 (*M*⁺ – OMe, 0.7). HRMS: Calcd for C₆H₉O₅ (*M*⁺ – OMe): 161.0449. Found: 161.0439.

Reduction of **3** with NaBH₄ gave Me α -D-Gal (**19**) and Me α -D-Tal in a ratio of 1:3.

Methyl α -D-arabino-Hexopyranosid-3-ulose (8) Me 4,6-*O*-benzylidene- α -D-Alt (**47**, 0.2 g) was oxidized as described in the general procedure to give the 3-oxo derivative **48** (0.15 g, 76%).

This was heated with 50% AcOH at 100 °C for 10 min. After addition of H₂O, the mixture was lyophilized, and the residue was chromatographed to give, from the CHCl₃–MeOH (3:1) eluate, **8** as a gum (92 mg, 89%). This was identical with the oxidation product of Me α -D-Alt (**24**).

Benzylloxymethylation of Me 4,6-*O*-Benzylidene- α -D-Alt (47) (1) Compound **47** (0.45 g) was stannylated with Bu₂SnO and benzylloxymethylated (50 °C, 3 d) in a similar manner to that described for **27**. Chromatography of the product gave, from the benzene–AcOEt (1:2) eluate, the 3-*O*-BOM derivative **49** (0.54 g, 84%) as colorless needles from ether, mp 100–102 °C. IR (KBr): 3460. ¹H-NMR (500 MHz): 3.41 (3H, s, OMe), 3.75 (1H, t, *J* = 9.0 Hz, H-6), 3.94 (1H, d, *J* = 2.0 Hz, H-2), 3.99 (1H, dd, *J* = 3.2, 9.6 Hz, H-4), 4.13 (1H, dd, *J* = 2.0, 3.2 Hz, H-3), 4.22–4.34 (2H, m, H-5,6), 4.58 (1H, s, H-1), and benzylidene and BOM groups. MS: 401 (*M*⁺ – 1, 0.09), 56 (100). *Anal.* Calcd for C₂₂H₂₆O₇ · 1/3H₂O: C, 64.70; H, 6.58. Found: C, 64.85; H, 6.57.

(2) A stirred solution of **47** (1.40 g) in CH₃CN (50 ml) was treated with 15% *n*-BuLi in hexane (2.2 ml, 1.0 moleq) and then with BOMCl (0.7 ml, 1.0 moleq) at 0 °C. The mixture was stirred at 40 °C for 4 h, poured into water and extracted with CH₂Cl₂. Chromatography of the product gave the 3-*O*-BOM derivative **49** (1.26 g, 64%) with recovery of the starting material (16%).

(3) A stirred solution of **47** (0.15 g) in CH₃CN (40 ml) was treated with 15% *n*-BuLi in hexane (0.6 ml, 2.5 moleq) and BOMCl (0.2 ml, 2.5 moleq) at 0 °C for 2 h, then at room temperature for 10 h. Chromatography of the product gave the di-*O*-BOM derivative **51** (0.23 g, 84%) as a colorless gum. ¹H-NMR (500 MHz): 3.78 (1H, t, *J* = 11.0 Hz, H-6), 3.96–4.00 (2H, m, H-3,4), 4.25–4.34 (3H, m, H-2,5,6), 4.61 (1H, s, H-1), and benzylidene and 2 × BOM groups. MS: 522 (*M*⁺, 0.2).

Methyl α -D-ribo-Hexopyranosid-2-ulose (4) Compound **49** (230 mg) was oxidized with DMSO (1.6 ml) and Ac₂O (1.4 ml) at 50 °C for 3 h and worked up as usual to give **50** (220 mg, 96%) as colorless needles from AcOEt, mp 128–130 °C. IR (KBr): 3475, 3330, no CO absorption. ¹H-NMR (500 MHz): 3.46 (3H, s, OMe), 3.77 (1H, t, *J* = 10.0 Hz, H-6), 4.00 (1H, dd, *J* = 3.0, 10.0 Hz, H-4), 4.04 (1H, d, *J* = 3.0 Hz, H-3), 4.21 (1H, dt, *J* = 5.4, 10.0 Hz, H-5), 4.36 (1H, dd, *J* = 5.4, 10.0 Hz, H-6), 4.40 (1H, s, H-1). *Anal.* Calcd for C₂₂H₂₄O₇ · H₂O: C, 63.15; H, 6.26. Found: C, 62.89; H, 6.45.

Compound **50** (160 mg) in EtOH–acetone (4:1, 50 ml) was hydrogenated over activated Pd black (120 mg) for 3 h and worked up as usual to give **4** (70 mg, 91%) as a colorless gum. IR (film): 1746 (weak). ¹H-NMR (pyridine-*d*₅): 3.46 (OMe). MS: 161 (*M*⁺ – OMe, 5). HRMS: Calcd for C₆H₉O₅ (*M*⁺ – OMe): 161.0449; C₆H₈O₅ (*M*⁺ – MeOH): 160.371. Found: 161.0420; 160.0359.

Reduction of **4** with NaBH₄ gave Me α -D-Alt (**22**) and Me α -D-Alt (**23**) in a ratio of 5:4.

Methyl α -D-arabino-Hexopyranosid-4-ulose (16) Compound **51** (0.18 g) was hydrolyzed with 60% AcOH on heating at 50 °C for 5 h to give **52** as a colorless oil (0.12 g, 80%). IR (KBr): 3455. ¹H-NMR: 3.38 (3H, s, OMe), 3.81 (1H, brd, *J* = 9.3 Hz, H-6), 3.85 (2H, brs, H-4, 5), 3.90 (1H, d, *J* = 9.3 Hz, H-6), 3.94 (1H, brs, H-2), 4.03 (1H, d, *J* = 3.4 Hz, H-3), 4.61 (1H, s, H-1), and 2 × BOM groups. MS: 313 (*M*⁺ – BOM, 7).

A mixture of compound **52** (0.3 g), (Bu₃Sn)₂O (3.2 g, 5 moleq), and molecular sieves 3A (10 g) in CH₂Cl₂ (50 ml) was heated under reflux for 4 h. To the cooled mixture, a further crop of (Bu₃Sn)₂O (3.2 g, 5 moleq) was added and the mixture was treated with bromine at 0 °C with stirring. After 10 min of stirring, the mixture was poured onto a silica gel column, and the column was washed with CHCl₃–benzene and then eluted with CHCl₃–AcOEt to give the 4-oxo derivative **53** (0.2 g, 68%) as a colorless gum. IR: 3580, 3475, 1747. ¹H-NMR (500 MHz): 3.38 (3H, s, OMe), 3.87, 3.90 (each 1H, dd, *J* = 3.5, 11.4 Hz, H-6), 3.94 (1H, dd, *J* = 2.7, 9.0 Hz, H-2), 4.14 (1H, t, *J* = 3.5 Hz, H-5), 4.71 (1H, d, *J* = 9.0 Hz, H-3), 4.96 (1H, d, *J* = 2.7 Hz, H-1), and 2 × BOM groups. MS: 432 (*M*⁺, 0.1).

Compound **53** (150 mg) in EtOH–acetone (1:1, 40 ml) was hydrogenated over activated Pd black (140 mg) for 3 h to give **16** (52 mg, 84%) as a colorless gum. IR (film): 3400, 3360, 1738. ¹H-NMR (pyridine-*d*₅): 3.40 (OMe). MS: 161 (*M*⁺ – OMe, 1). HRMS: Calcd for C₆H₉O₅ (*M*⁺ – OMe): 161.0449. Found: 161.0423.

Reduction of **16** with NaBH₄ gave Me α -D-Alt (**24**) and Me α -D-Ido (**26**) in a ratio of 5:1.

Methyl α -D-Idopyranoside (26) This was synthesized as follows.

Me-3-*O*-Tosyl- α -D-Gal (**54**): Tosylation of Me α -D-Gal (**18**) by the dibutyltin oxide method⁹⁾ gave the 3-*O*-tosylate derivative **54**, mp 124–125 °C, as colorless needles from CHCl₃–AcOEt.⁹⁾ ¹H-NMR: 3.38

(3H, s, OMe), 3.80 (1H, dd, $J=4.0$, 13.0 Hz, H-6), 3.85 (1H, dd, $J=6.0$, 13.0 Hz, H-6), 3.98 (1H, brd, $J=9.7$ Hz, H-2), 4.08 (1H, brdt, $J=6.0$, 4.0 Hz, H-5), 4.26 (1H, brd, $J=4.0$ Hz, H-4), 4.60 (1H, dd, $J=4.0$, 9.7 Hz, H-3), 4.81 (1H, d, $J=3.9$ Hz, H-1), and a tosyl group. *Anal.* Calcd for $C_{14}H_{20}O_8S$: C, 48.28; H, 5.75. Found: C, 48.03; H, 6.04. This compound was dimorphic to the specimen reported by Tsuda *et al.*¹³ (colorless prisms from MeOH, mp 153–154°C).

Me 4,6-*O*-Benzylidene-3-*O*-tosyl- α -D-Gal (**55**): A mixture of **54** (0.76 g), $ZnCl_2$ (0.7 g) and benzaldehyde (4 ml) was stirred at room temperature for 12 h. The resulting solution was poured into aqueous $NaHCO_3$ and extracted with AcOEt. Concentration of the dried extract and chromatography of the residue gave **55** (0.91 g, 96%) as colorless prisms from $CHCl_3$ -AcOEt, mp 173–174°C. IR (KBr): 3560, 1598, 1485. 1H -NMR (500 MHz): 3.42 (3H, s, OMe), 3.65 (1H, brs, H-5), 4.00 and 4.23 (each 1H, dd, $J=1.4$, 13.0 Hz, H-6), 4.16 (1H, brd, $J=10.0$ Hz, H-2), 4.23 (1H, dd, $J=1.4$, 13.0 Hz, H-6), 4.35 (1H, d, $J=4.0$ Hz, H-4), 4.81 (1H, dd, $J=4.0$, 10.0 Hz, H-3), 4.89 (1H, d, $J=3.4$ Hz, H-1) and benzylidene and tosyl groups. MS: 436 (M^+ , 21). *Anal.* Calcd for $C_{21}H_{24}O_8S$: C, 57.79; H, 5.54. Found: C, 57.74; H, 5.52.

Me 2,3-Anhydro-4,6-*O*-benzylidene- α -D-Gul (**56**): Compound **55** (0.8 g) in 5% EtONa-EtOH (35 ml) was heated at 50°C for 30 min. The cooled solution was neutralized with 4N HCl at 0°C and concentrated to dryness. Chromatography of the residue gave **56** (0.44 g, 91%) as colorless needles from $CHCl_3$ -AcOEt, mp 175–176°C. IR (KBr): 1448, 1340, 1146. 1H -NMR (500 MHz): 3.10 (1H, d, $J=4.0$ Hz, H-2), 3.46 (3H, s, OMe), 3.53 (1H, dd, $J=4.0$, 5.5 Hz, H-3), 3.60 (1H, brt, $J=3$ Hz, H-5), 4.14 (1H, dd, $J=3.0$, 13.0 Hz, H-6), 4.24 (1H, d, $J=13.0$ Hz, H-6), 4.32 (1H, dd, $J=3.0$, 5.5 Hz, H-4), 5.06 (1H, s, H-1), and a benzylidene group. MS: 264 (M^+ , 3). *Anal.* Calcd for $C_{14}H_{16}O_5$: C, 63.62; H, 6.10. Found: C, 63.67; H, 6.09.

Me 4,6-*O*-Benzylidene- α -D-Ido (**57**): A solution of **56** (0.54 g) in dioxane (15 ml) and 6% KOH (30 ml) was heated under reflux for 12 h, then neutralized with 4N HCl at 0°C. The solvent was evaporated off and the residue was chromatographed with $CHCl_3$ -AcOEt (1:1) to give **57** (0.52 g, 89%) as colorless prisms from $CHCl_3$ -AcOEt, mp 145–147°C. IR (KBr): 3490. 1H -NMR (500 MHz): 3.47 (3H, s, OMe), 3.67 (1H, brd, $J=9.0$ Hz, H-3), 3.90 (1H, s, H-5), 3.95 (1H, brs, H-2), 4.09–4.12 (2H, m, H-4,6), 4.36 (1H, dd, $J=1.5$, 13.0 Hz, H-6), 4.91 (1H, s, H-1), and a benzylidene group. MS: 282 (M^+ , 2). *Anal.* Calcd for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43. Found: C, 59.59; H, 6.42. An X-ray crystallographic analysis of **57** revealed that the compound has a *Ci* conformation. Crystal data: orthorhombic, $a=10.173(2)$ Å, $b=16.728(3)$ Å, $c=7.915(3)$ Å, $V=1347.0(6)$ Å³, $Z=4$, $D_c=1.39$ g/cm³. Space group, $P2_12_12_1$. $R=0.039$. The other data are available on request to the authors.

Me α -D-Ido (**26**): Compound **57** (0.5 g) was hydrolyzed with 60% AcOH (25 ml) at 70°C for 5 h and worked up as usual to give **26** (0.3 g, 88%) as a colorless gum. ^{13}C -NMR (CD_3OD , 500 MHz): 55.7 (OMe), 62.6 (C-6), 70.0 (C-4), 71.1 (C-2,5), 71.8 (C-3), 103.4 (C-1).

Benzylloxymethylation of Me 4,6-*O*-Benzylidene- α -D-Ido (57**)** A stirred solution of **57** (1.0 g) in tetrahydrofuran (THF, 50 ml) was treated with 15% *n*-BuLi in hexane (2.3 ml, 1.5 moleq) at 0°C for 15 min, then BOMCl (0.75 ml, 1.5 moleq) was added dropwise and the mixture was stirred at 0°C for 2 h, then at room temperature for 5 h. The mixture was poured into water and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. Chromatography of the residue gave the 2-*O*-BOM derivative **58** (0.16 g, 11%), the 3-*O*-BOM derivative **59** (0.38 g, 27%), and the 2,3-di-*O*-BOM derivative **60** (0.9 g, 49%).

The 2-*O*-BOM Derivative **58**: Colorless needles from AcOEt, mp 103–105°C. IR (KBr): 3495. 1H -NMR: 3.43 (3H, s, OMe), 3.69 (1H, dd, $J=2.5$, 4.5 Hz, H-2), 3.80 (1H, brd, $J=2.5$ Hz, H-5), 4.02 (1H, dd, $J=3.0$, 4.5 Hz, H-3), 4.12 (1H, t, $J=3.0$ Hz, H-4), 4.13 (1H, dd, $J=2.7$, 12.8 Hz, H-6), 4.33 (1H, dd, $J=1.0$, 12.8 Hz, H-6), 4.90 (1H, d, $J=2.5$ Hz, H-1), and benzylidene and BOM groups. MS: 402 (M^+ , 0.4). *Anal.* Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.53; H, 6.54.

The 3-*O*-BOM Derivative **59**: Colorless needles from AcOEt, mp 131–133°C. 1H -NMR: 3.45 (3H, s, OMe), 3.70 (1H, brs, H-2), 3.87 (1H, brs, H-5), 3.96 (1H, brs, H-3), 4.00 (1H, brs, H-4), 4.01 (1H, dd, $J=1.5$, 13.0 Hz, H-6), 4.29 (1H, dd, $J=1.5$, 13.0 Hz, H-6), 4.85 (1H, s, H-1), and benzylidene and BOM groups. MS: 402 (M^+ , 0.1). *Anal.* Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.74; H, 6.54.

The 2,3-Di-*O*-BOM Derivative **60**: Colorless needles from AcOEt, mp 104–106°C. 1H -NMR (500 MHz): 3.45 (3H, s, OMe), 3.81 (1H, brs, H-5), 3.87 (1H, dd, $J=3.7$, 7.0 Hz, H-2), 4.10–4.13 (3H, m, H-3,4,6),

4.34 (1H, d, $J=13.0$ Hz, H-6), 4.86 (1H, d, $J=3.7$ Hz, H-1), and benzylidene and 2 $\times$ BOM groups. MS: 522 (M^+ , 0.2). *Anal.* Calcd for $C_{30}H_{34}O_8$: C, 68.95; H, 6.56. Found: C, 68.75; H, 6.78.

Methyl α -D-lyxo-Hexopyranosid-3-ulose (12**)** The 2-*O*-BOM derivative **58** (0.15 g) was oxidized with DMSO (1.6 ml) and Ac_2O (1.4 ml) at 50°C for 1.5 h to give the 3-oxo derivative **61** (0.12 g, 80%) as colorless needles from benzene-ether, mp 149–151°C. IR (KBr): 1749. 1H -NMR (500 MHz): 3.48 (3H, s, OMe), 4.21 (1H, dd, $J=2.5$, 13.2 Hz, H-6), 4.27 (1H, brs, H-5), 4.39 (1H, d, $J=13.2$ Hz, H-6), 4.40 (1H, d, $J=4.4$ Hz, H-2), 4.42 (1H, d, $J=2.5$ Hz, H-4), 4.93 (1H, d, $J=4.4$ Hz, H-1), and benzylidene and BOM groups. *Anal.* Calcd for $C_{22}H_{24}O_7$: C, 65.99; H, 6.04. Found: C, 65.53; H, 5.96.

Hydrogenation of **61** (75 mg) in acetone-EtOH (1:1, 30 ml) over activated Pd black (70 mg) for 3 h gave **12** (28 mg, 78%) as a colorless oil. IR (film): 3290, 1727. 1H -NMR (500 MHz, pyridine- d_5): 3.61 (OMe). MS: 191 (M^+ , 0.2), 161 (2), 160 (40). HRMS: Calcd for $C_6H_8O_5$ (M^+ -OMe): 161.0449; $C_6H_8O_5$ (M^+ -MeOH): 160.0371. Found: 161.0440; 160.0395.

Reduction of **12** with $NaBH_4$ gave Me α -D-Tal, Me α -D-Ido (**26**) and Me α -D-Man (**21**) in a variable ratio.¹⁴

Methyl α -D-xylo-Hexopyranosid-3-ulose (5**)** The 3-*O*-BOM derivative **59** (0.38 g) was oxidized with DMSO (3.2 ml) and Ac_2O (2.8 ml) at 50°C for 3 h to give the 2-oxo derivative **62** (310 mg, 82%) as colorless needles from benzene-ether, mp 150–152°C. IR (KBr): 1752. 1H -NMR (500 MHz): 3.50 (3H, s, OMe), 3.99 (1H, brd, $J=2.0$ Hz, H-5), 4.17 (1H, dd, $J=2.0$, 12.7 Hz, H-6), 4.29 (1H, dd, $J=2.2$, 3.5 Hz, H-4), 4.35 (1H, dd, $J=1.0$, 12.7 Hz, H-6), 4.56 (1H, d, $J=3.5$ Hz, H-3), 4.90 (1H, s, H-1), and benzylidene and BOM groups. *Anal.* Calcd for $C_{22}H_{24}O_7 \cdot 1/3H_2O$: C, 65.02; H, 6.11. Found: C, 65.25; H, 6.02.

Compound **62** (0.10 g) was hydrogenated in EtOH-acetone (1:1, 30 ml) over activated Pd black for 4 h to give **5** (40 mg, 83%) as a colorless gum. IR (film): 3490, 1696 (weak). 1H -NMR (500 MHz, pyridine- d_5): 3.43 (OMe). HRMS: Calcd for $C_6H_8O_5$ (M^+ -OMe): 161.0449; $C_6H_8O_5$ (M^+ -MeOH): 160.0371. Found: 161.0455; 160.0397.

Reduction of **5** with $NaBH_4$ gave Me α -D-Ido (**26**) and Me α -D-Gul in a ratio of ca. 1:1.

Methyl 2,3-*O*-Isopropylidene- α -D-Mannopyranoside (63**)** A mixture of Me α -D-Man (**21**, 1 g), 2,2-dimethoxypropane (3 ml), and pyridinium *p*-toluenesulfonate (PPTS, 15 mg) in DMF (50 ml) was stirred at room temperature for 5 h. The solution was poured into aqueous $NaHCO_3$ and extracted with ether several times. Concentration of the dried extract yielded a colorless solid. Recrystallization of this from ether gave the diisopropylidene derivative as colorless prisms (1.03 g, 73%), mp 75–76°C (lit. 76–77°C).¹⁵ This (1 g) was heated with 50% AcOH (35 ml) for 2 h. The solution was poured into aqueous $NaHCO_3$ and extracted with AcOEt. Concentration of the dried extract gave **63** (0.71 g, 83%) as prisms from ether, mp 105–106°C (lit. 105°C).¹⁵ 1H -NMR: 3.34 (3H, s, OMe), 3.51 (1H, dd, $J=3.7$, 10.0 Hz, H-5), 3.67 (1H, dd, $J=6.0$, 10.0 Hz, H-4), 3.80 (2H, d, $J=3.7$ Hz, H-6), 4.09 (1H, s, H-2), 4.11 (1H, d, $J=6.0$ Hz, H-3), 4.88 (1H, s, H-1), and an isopropylidene group. MS: 234 (M^+ , 0.1), 100 (100).

Oxidation of Me 2,3-*O*-Isopropylidene- α -D-Man (63**) by the Bistrityltin Oxide-Bromine Method (Modified Procedure)** A mixture of **63** (0.4 g), $(Bu_3Sn)_2O$ (1.28 g, 3 moleq) and molecular sieves 3A (2.0 g) in CH_2Cl_2 (35 ml) was heated under reflux for 3 h, then cooled. To this stirred mixture, $(Bu_3Sn)_2O$ (0.85 g, 2 moleq) was added at 0°C and, after 10 min, bromine (ca. 5 moleq) was added at 0°C with stirring until the solution became faintly colored. The mixture was poured onto a column of silica gel, and the column was washed thoroughly with $CHCl_3$, then eluted with $CHCl_3$ -AcOEt (2:1) to yield the 4-oxo derivative **64** (0.3 g, 76%) and the dimeric ester **65** (79 mg, 20%).

The 4-Oxo Derivative **64**: Colorless gum. IR: 1737. 1H -NMR: 3.48 (3H, s, OMe), 3.93 (1H, d, $J=5.0$ Hz, H-6), 4.14 (1H, t, $J=5.0$ Hz, H-6), 4.22 (1H, t, $J=5.0$ Hz, H-5), 4.40 (1H, d, $J=6.0$ Hz, H-2), 4.44 (1H, d, $J=6.0$ Hz, H-3), 4.93 (1H, s, H-1), and an isopropylidene group. MS: 233 (M^+ +1, 5), 217 (M^+ -Me, 15), 201 (M^+ -OMe), 85 (100).

The Dimeric Ester **65**: Colorless gum. IR: 1725, 1370, 1095. 1H -NMR (500 MHz): 1.34 (6H, s), 1.52 (6H, s), 3.40 (3H, s), 3.46 (3H, s), 3.65 (1H, m), 3.80 (1H, m), 4.00 (1H, dd, $J=6.5$, 7.8 Hz), 4.14 (3H, m), 4.23 (2H, dd, $J=7.8$, 14.0 Hz), 4.33 (1H, dd, $J=3.0$, 12.0 Hz), 4.65 (1H, dd, $J=5.0$, 12.0 Hz), 4.97 (1H, s), 4.91 (1H, s). ^{13}C -NMR (125 MHz): 25.6, 26.0, 27.2, 27.9, 55.2, 55.7, 64.5, 67.9, 69.2, 69.5, 70.3, 74.6, 75.5, 76.3, 77.8, 98.6, 98.8, 109.7, 110.0, 170.0. MS: 449 (M^+ -Me, 7), 249 (M^+ -215, 2), 100 (100).

$NaBH_4$ reduction of **65** in MeOH regenerated **63**.

Methyl α -D-lyxo-Hexopyranosid-4-ulose (15) Compound **64** (0.24 g) was hydrolyzed with 60% AcOH (10 ml) at 70 °C for 40 min. Chromatography of the product gave **15** as a gum (0.17 g, 86%). IR: 3434, 1737. ¹H-NMR (pyridine-*d*₅): 3.47 (OMe). MS: 193 (*M*⁺ + 1, 0.9), 161 (*M*⁺ - OMe, 6). HRMS: Calcd for C₇H₁₃O₆ (*M*⁺ + 1): 193.0712. Found: 193.0682.

NaBH₄ reduction of **15** gave Me α -D-Man (**21**) as major product.

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