March 1993 Chem. Pharm. Bull. 41(3) 491—501 (1993)

Chemistry of Oxo-Sugars. (2). Regio- and Stereo-Selective Synthesis of Methyl D-Hexopyranosiduloses and Identification of Their Forms Existing in Solutions[1)]

Hong-Min Liu, Yoshiyuki Sato, and Yoshisuke Tsuda*

Faculty of Pharmaceutical Sciences, Kanazawa University, 13–1 Takara-machi, Kanazawa 920, Japan.

Received August 21, 1992

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 H_2O (D_2O) were investigated by means of ^{13}C-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; ^{13}C-NMR

Oxo derivatives of sugars, so-called oxo-sugars, are biologically important in carbohydrate metabolism[2)] 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 preferentialy 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 H_2O 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

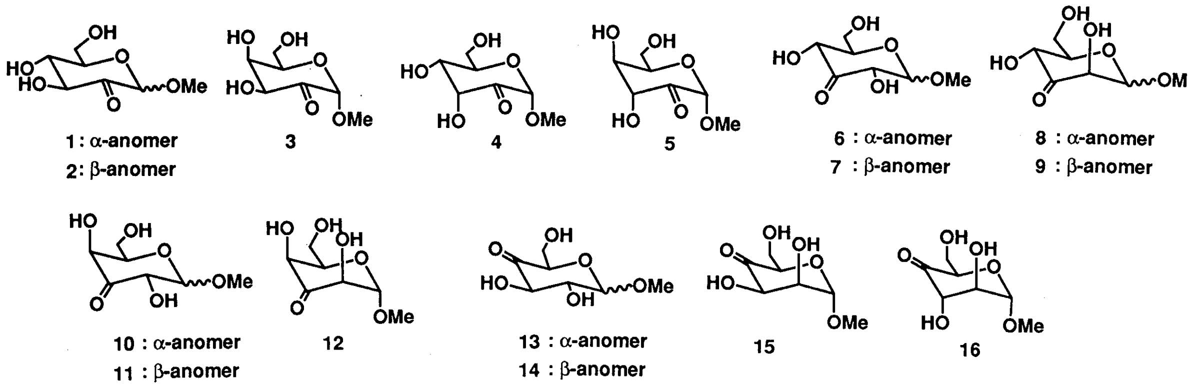


Chart 1

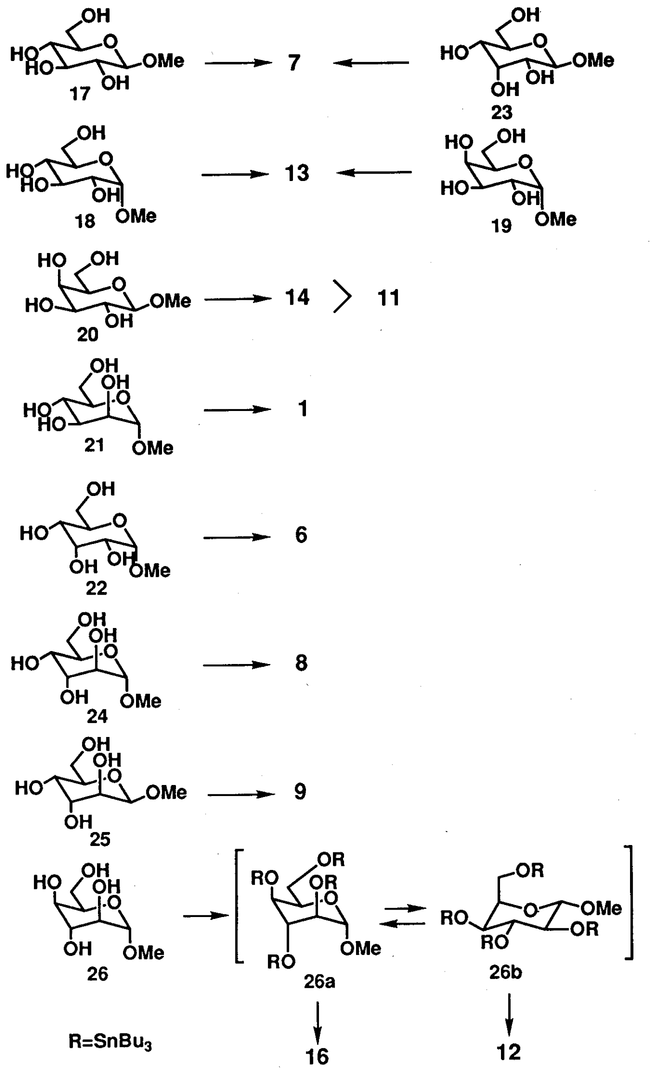


Chart 2. Oxidation of Non-Protected Methyl Glycosides by the (Bu$_3$Sn)$_2$O–Br$_2$ Method

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 (Bu$_3$Sn)$_2$O–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 (Bu$_3$Sn)$_2$O–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.

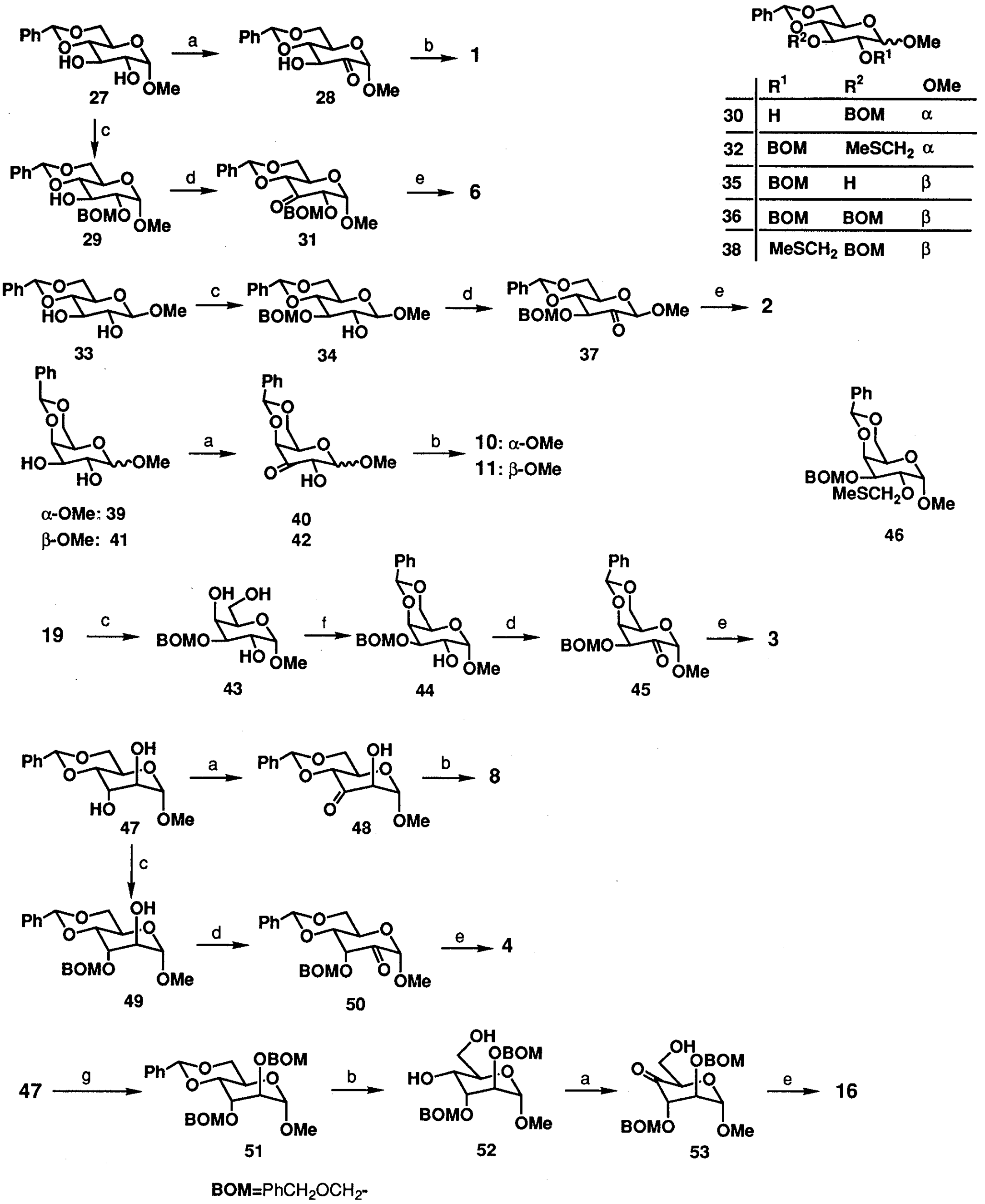
Regioselective Synthesis of Oxoglycosides through Oxidation of Partially Protected Glycosides Me α-D-*arabino*-2-OG (**1**) was prepared as follows. Previously, Tsuda *et al.*[6] reported that Me 4,6-*O*-benzylidene-α-D-Glc (**27**) was oxidized by the (Bu$_3$Sn)$_2$O–Br$_2$ method to the 2-oxo derivative **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 ^{13}C-nuclear magnetic resonance (NMR) spectrum of **1** (in D$_2$O) was identical with that of the specimen described in the above section. This was reduced by NaBH$_4$ 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 method[7] 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 ^{1}H–^{1}H and ^{1}H–^{13}C 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 (Bu$_3$Sn)$_2$O–Br$_2$ oxidation, it was oxidized with dimethyl sulfoxide (DMSO)–acetic anhydride (Ac$_2$O) 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**). NaBH$_4$ 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 byproducts in this alkylation. The position of the BOM group in **34** was proved on the basis of the ^{1}H–^{1}H and ^{1}H–^{13}C 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–Ac_2O 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 $NaBH_4$ 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 $(Bu_3Sn)_2O$–Br_2 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. $NaBH_4$ 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 $(Bu_3Sn)_2O$–Br_2 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 ^{13}C-NMR spectrum of this compound was superimposable on that of the minor



	R^1	R^2	OMe
30	H	BOM	α
32	BOM	$MeSCH_2$	α
35	BOM	H	β
36	BOM	BOM	β
38	$MeSCH_2$	BOM	β

a: i) $(Bu_3Sn)_2O$, ii) Br_2; b: 40—60% AcOH, 70—100°C; c: i) Bu_2SnO, ii) BOMCl; d: DMSO—Ac_2O; e: H_2/Pd; f: $PhCH(OMe)_2$/*p*-TsOH; g: i) *n*-BuLi, ii) BOMCl

Chart 3

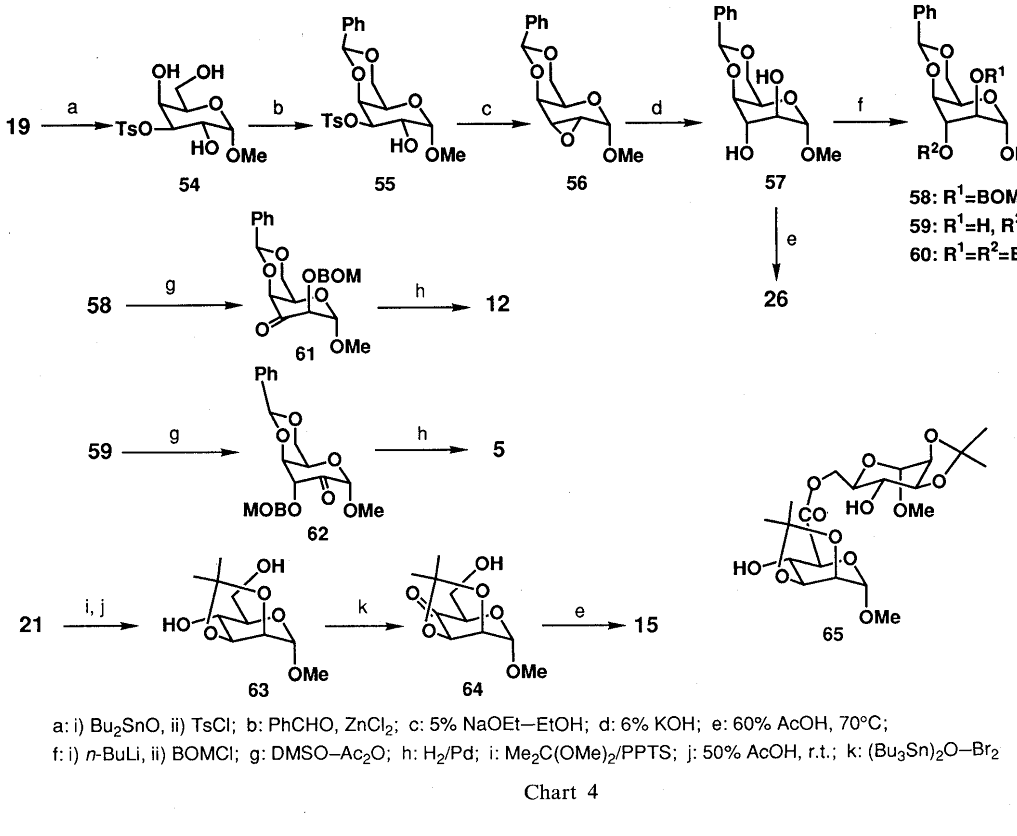
product obtained by the direct oxidation of Me β-D-Gal (**20**). NaBH$_4$ reduction of **11** gave Me β-D-Gal (**20**) as a single product.

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 method[7] 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 ^{1}H–^{1}H and ^{1}H–^{13}C COSY spectra. This was converted to the 4,6-*O*-benzylidene derivative **44** (92%), which was oxidized with DMSO–Ac$_2$O 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. NaBH$_4$ 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 (Bu$_3$Sn)$_2$O–Br$_2$ method to the 3-oxo derivative **48**. The position of the carbonyl group in **48** was confimed 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] NaBH$_4$ 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 method[7] 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 ^{1}H–^{1}H and ^{1}H–^{13}C COSY spectra. The signals at δ3.94 (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–Ac$_2$O 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. NaBH$_4$ reduction of **4** gave Me α-D-All (**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 mol eq 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 (Bu$_3$Sn)$_2$O–Br$_2$ 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-tosylation[9] followed by benzylidenation, epoxide formation, and stereoselective opening of the epoxide ring (Chart 4). Alkylation of **57** with 1.5 mol eq 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



a: i) Bu$_2$SnO, ii) TsCl; b: PhCHO, ZnCl$_2$; c: 5% NaOEt–EtOH; d: 6% KOH; e: 60% AcOH, 70°C; f: i) *n*-BuLi, ii) BOMCl; g: DMSO–Ac$_2$O; h: H$_2$/Pd; i: Me$_2$C(OMe)$_2$/PPTS; j: 50% AcOH, r.t.; k: (Bu$_3$Sn)$_2$O–Br$_2$

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 $(Bu_3Sn)_2O$ 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 pyridin-d_5; its carbonyl carbon signal appeared at δ 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 δ 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 δ 207.5 in pyridine-d_5 and at δ 208.0 in D_2O.

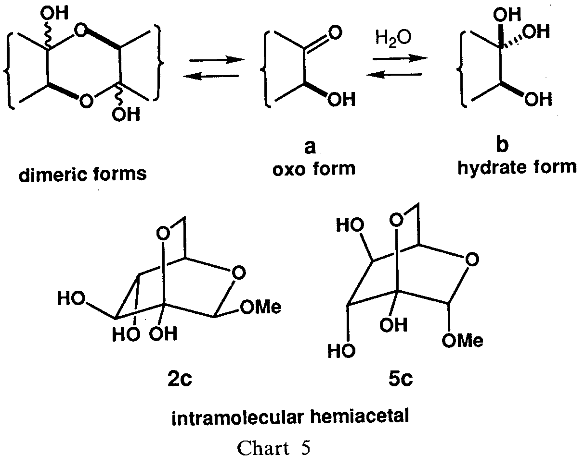


Chart 5

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 δ 208.2 and the masked carbonyl carbon at δ 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 δ 208.2 and that of the hydrate form at δ 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 δ 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).

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**.

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.

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 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 $CDCl_3$ 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 ^{13}C-NMR peaks ascribable to the hydrate form **50b** in $CDCl_3$ 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 D_2O, 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 D_2O 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 D_2O (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 D_2O. 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 D_2O (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 ≥ 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 ^{1}H and 100 MHz for ^{13}C) spectrometer in $CDCl_3$ 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 D_2O (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 × 1 m) packed with 1.5% OV-1 on Shimalite W (80—100 mesh) and a flame ionization detector (FID), using N_2 (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 μl) was directly injected into a GC column. Column chromatography was performed on silica gel (Wako-gel C-200). For TLC, Merck precoated plates GF_{254} were used and spots were developed by spraying 5% H_2SO_4 and heating the plates until coloration took place. Identities were confirmed by comparisons of TLC behavior and of ^{1}H- and ^{13}C-NMR spectra.

Reduction of an Oxoglycoside with $NaBH_4$ and GC Analysis of the Product An oxoglycoside (2—5 mg) in MeOH (1—2 ml) was treated with $NaBH_4$ (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), $(Bu_3Sn)_2O$ (2 mol eq), and molecular sieves 3A (large excess) in $CHCl_3$ (30—50 ml) was heated under reflux for 3 h, then cooled. To this mixture, bromine (*ca.* 2 mol eq) 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 $CHCl_3$ to remove tin compounds, then eluted with AcOEt or $CHCl_3$–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 ^{13}C-NMR spectrum of the oxidation product in D_2O showed only seven peaks corresponding to **1b** (hydrate form), no other peaks being observed in the spectrum.

Reduction of this compound with $NaBH_4$ 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. ^{1}H-NMR (pyridine-d_5): 3.29 (OMe).

$NaBH_4$ 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). ^{1}H-NMR (pyridine-d_5): 3.34 (OMe).

Reduction of **8** with $NaBH_4$ 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). ^{1}H-NMR (pyridine-d_5): 3.56 (OMe).

$NaBH_4$ 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 mol eq of $(Bu_3Sn)_2O$ (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}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}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), $(Bu_3Sn)_2O$ (1.27 g, 3 mol eq), 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 mol eq) 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}H-NMR (pyridine-d_5): 3.40 (OMe). MS: 193 ($M^+ + 1$, 0.6). The ^{13}C-NMR spectrum of this compound in D_2O was superimposable on that of the oxidation product of Me α-D-Man (**21**).

Benzyloxymethylation 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 mol eq) 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 mol eq) 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—107 °C. IR: 3340. ^{1}H-NMR: 3.40 (3H, s, OMe), 3.53 (1H, t, J = 10.0 Hz, H-4), 3.62 (1H, dd, J = 4.3, 10.0 Hz, H-2), 3.74 (1H, t, J = 10.0 Hz, H-6), 3.85 (1H, dt, J = 4.7, 10.0 Hz, H-5), 4.13 (1H, t, J = 10.0 Hz, H-3), 4.28 (1H, dd, J = 4.7, 10.0 Hz, H-6), 4.85 (1H, d, J = 4.3 Hz, H-1), and benzylidene and BOM groups. MS: 402 (M^+, 2). *Anal.* Calcd for $C_{22}H_{26}O_7$: 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—88 °C. IR: 3340. ^{1}H-NMR: 3.40 (3H, s, OMe), 3.54 (1H, t, J = 9.5 Hz, H-4), 3.67 (1H, dd, J = 4.0, 9.5 Hz, H-2), 3.71 (1H, t, J = 10.0 Hz, H-6), 3.81 (1H, dt, J = 4.9, 10.0 Hz, H-5), 3.99 (1H, t, J = 9.5 Hz, H-3), 4.26 (1H, dd, J = 4.9, 10.0 Hz, H-6), 4.76 (1H, d, J = 4.0 Hz, H-1), and benzylidene and BOM groups. MS: 402 (M^+, 0.5). *Anal.* Calcd for $C_{22}H_{26}O_7 \cdot 3/2H_2O$: C, 61.53; H, 6.81. Found: C, 61.56; H, 6.83.

DMSO–Ac_2O 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—168 °C. IR (KBr): 1745. ^{1}H-NMR: 3.42 (3H, s, OMe), 3.90 (1H, t, J = 10.0 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 Hz, H-1), and benzylidene and BOM groups. MS: 400 (M^+, 0.5). *Anal.* Calcd for $C_{22}H_{24}O_7 \cdot 1/2H_2O$: 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}H-NMR: 2.10 (3H, s, SMe), 3.41 (3H, s, OMe), 3.59 (1H, t, J = 10.0 Hz, H-4), 3.73 (1H, t, J = 10.0 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 Hz, H-3), 4.27 (1H, dd, J = 4.7, 10.0 Hz, H-6), 4.81 (1H, d, J = 4.3 Hz, H-1), 4.86, 4.90 (each 1H, d, J = 11.0 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—88 °C. IR (KBr): 1736. ^{1}H-NMR (pyridine-d_5): 3.29 (OMe). MS: 193 ($M^+ + 1$, 4). HRMS: Calcd for $C_7H_{13}O_6$ ($M^+ + 1$): 193.0711. Found: 193.0667. This product was identical with the oxidation product of Me α-D-All (**22**).

Benzyloxymethylation 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—135 °C. ^{1}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 Hz, H-4), 3.79 (1H, t, J = 10 Hz, H-6), 3.82 (1H, br t, J = 8.4 Hz, H-3), 4.35 (1H, d, J = 8.0 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 $C_{22}H_{26}O_7$: 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—117 °C. ^{1}H-NMR: 3.54—3.47 (2H, m, H-3,5) 3.54 (3H, s, OMe), 3.56 (1H, t, J = 9.0 Hz, H-4), 3.78 (1H, t, J = 10 Hz, H-6), 3.84 (1H, br t, J = 8.5 Hz, H-2), 4.36 (1H, dd, J = 4.9, 10 Hz, H-6), 4.39 (1H, d, J = 8 Hz, H-1), and benzylidene and BOM groups. MS: 402 (M^+, 0.2). *Anal.* Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.61; H, 6.64.

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

DMSO–Ac_2O 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—157 °C. IR (KBr): 1756 (weak). ^{1}H-NMR: 4.83, 4.84 (total 1H, each s, H-1), 3.63, 3.66 (total 3H, each s, OMe). *Anal.* Calcd for $C_{22}H_{24}O_7 \cdot 1/2H_2O$: C, 64.54; H, 6.15. Found: C, 64.68; H, 6.21.

The 2-*O*-Methylthiomethyl Derivative **38**: Colorless oil. ^{1}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 Hz, H-4), 3.65 (1H, dd, J = 8, 9 Hz, H-2), 3.77 (1H, t, J = 10 Hz, H-6), 3.96 (1H, t, J = 9 Hz, H-3), 4.35 (1H, dd, J = 5, 10 Hz, H-6), 4.40 (1H, d, J = 8 Hz, H-1), 4.60, 4.65 (each 1H, d, J = 11.6 Hz, OCH_2S), and benzylidene and BOM groups. MS: 401 ($M^+ - CH_2SCH_3$, 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}H-NMR (pyridine-d_5): 3.53 (OMe). MS: 193 ($M^+ + 1$, 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—148 °C. IR (KBr): 1741. ^{1}H-NMR (500 MHz): 3.02 (1H, d, J = 8.0 Hz, OH), 3.44 (3H, s, OMe), 3.87 (1H, d, J = 1.5 Hz, H-5), 4.18 (1H, dd, J = 1.5, 12.7 Hz, H-6), 4.42 (1H, d, J = 12.7 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 Hz, H-1), and a benzylidene group. MS: 280 (M^+, 0.04), 279 ($M^+ - 1$, 0.2), 107 (100). *Anal.* Calcd for $C_{14}H_{16}O_6$: 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}H-NMR (pyridine-d_5): 3.35 (OMe). MS: 192 (M^+, 0.9). HRMS: Calcd for $C_7H_{11}O_6$ ($M^+ - 1$): 191.0555; $C_6H_9O_5$ ($M^+ -$ 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. ^{1}H-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 $C_{14}H_{16}O_6 \cdot 1/2H_2O$: 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 $CHCl_3$–MeOH (4 : 1) to give **11** (64 mg, 93%) as a gum. IR (film): 1727 (weak). ^{1}H-NMR (pyridine-d_5): 3.60 (OMe). MS: 191 (M^+-1, 0.3), 161 (M^+-OMe, 3). HRMS: Calcd for $C_7H_{11}O_6$ (M^+-1): 191.0555; $C_6H_9O_5$ (M^+-OMe): 161.0449. Found: 191.0508; 161.0398. The ^{13}C-NMR spectrum of this compound in D_2O was superimposable on that of the minor constituent in the oxidation product of Me *β*-D-Gal (**20**).[6]

Reduction of **11** with $NaBH_4$ gave Me *β*-D-Gal (**20**) as a single product.

Benzyloxymethylation of Me *α*-D-Gal (19) by the Dibutyltin Oxide Method A mixture of Me *α*-D-Gal (**19**, 1.2 g) and Bu_2SnO (3.1 g, 2 mol eq) 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 mol eq) 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 $CHCl_3$. Subsequent elution with $CHCl_3$–AcOEt (1 : 3) gave the 3-*O*-BOM derivative **43** (1.4 g, 72%) as a gum. IR: 3425. ^{1}H-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, br d, 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 $NaHCO_3$ and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with brine, dried, and concentrated to dryness. Chromatography of the residue gave, from the $CHCl_3$–AcOEt (3 : 1) eluate, **44** (1.3 g, 92%), as colorless needles from ether, mp 92—93 °C. IR (KBr): 3455. ^{1}H-NMR: 3.43 (3H, s, OMe), 3.61 (1H, br s, 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 $C_{22}H_{26}O_7 \cdot 1/3H_2O$: C, 64.70; H, 6.58. Found: C, 64.62; H, 6.46.

DMSO–Ac_2O Oxidation of the 3-*O*-BOM Derivative (44) Compound **44** (0.27 g) was treated with DMSO (1.6 ml) and Ac_2O (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. ^{1}H-NMR: 3.47 (3H, s, OMe), 4.03 (1H, d, J=12.5 Hz, H-6), 4.05 (1H, br s, 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 $C_{22}H_{24}O_7$ (M^+): 400.1539. Found: 400.1522.

The 2-*O*-Methylthiomethyl Derivative **46**: Colorless oil. ^{1}H-NMR: 3.45 (3H, s, OMe), 3.64 (1H, br s, 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, SCH_2O), 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. ^{1}H-NMR (pyridine-d_5): 3.39 (OMe). MS: 161 (M^+-OMe, 0.7). HRMS: Calcd for $C_6H_9O_5$ (M^+-OMe): 161.0449. Found: 161.0439.

Reduction of **3** with $NaBH_4$ 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 H_2O, the mixture was lyophilized, and the residue was chromatographed to give, from the $CHCl_3$–MeOH (3 : 1) eluate, **8** as a gum (92 mg, 89%). This was identical with the oxidation product of Me *α*-D-Alt (**24**).

Benzyloxymethylation of Me 4,6-*O*-Benzylidene-*α*-D-Alt (47) (1) Compound **47** (0.45 g) was stannylated with Bu_2SnO and benzyloxymethylated (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. ^{1}H-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 $C_{22}H_{26}O_7 \cdot 1/3H_2O$: C, 64.70; H, 6.58. Found: C, 64.85; H, 6.57.

(2) A stirred solution of **47** (1.40 g) in CH_3CN (50 ml) was treated with 15% *n*-BuLi in hexane (2.2 ml, 1.0 mol eq) and then with BOMCl (0.7 ml, 1.0 mol eq) at 0 °C. The mixture was stirred at 40 °C for 4 h, poured into water and extracted with CH_2Cl_2. 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 CH_3CN (40 ml) was treated with 15% *n*-BuLi in hexane (0.6 ml, 2.5 mol eq) and BOMCl (0.2 ml, 2.5 mol eq) 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. ^{1}H-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 Ac_2O (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. ^{1}H-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 $C_{22}H_{24}O_7 \cdot H_2O$: 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). ^{1}H-NMR (pyridine-d_5): 3.46 (OMe). MS: 161 (M^+-OMe, 5). HRMS: Calcd for $C_6H_9O_5$ (M^+-OMe): 161.0449; $C_6H_8O_5$ (M^+-MeOH): 160.371. Found: 161.0420; 160.0359.

Reduction of **4** with $NaBH_4$ gave Me *α*-D-All (**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. ^{1}H-NMR: 3.38 (3H, s, OMe), 3.81 (1H, br d, J=9.3 Hz, H-6), 3.85 (2H, br s, H-4, 5), 3.90 (1H, d, J=9.3 Hz, H-6), 3.94 (1H, br s, 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), $(Bu_3Sn)_2O$ (3.2 g, 5 mol eq), and molecular sieves 3A (10 g) in CH_2Cl_2 (50 ml) was heated under reflux for 4 h. To the cooled mixture, a further crop of $(Bu_3Sn)_2O$ (3.2 g, 5 mol eq) 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 $CHCl_3$–benzene and then eluted with $CHCl_3$–AcOEt to give the 4-oxo derivative **53** (0.2 g, 68%) as a colorless gum. IR: 3580, 3475, 1747. ^{1}H-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. ^{1}H-NMR (pyridine-d_5): 3.40 (OMe). MS: 161 (M^+-OMe, 1). HRMS: Calcd for $C_6H_9O_5$ (M^+-OMe): 161.0449. Found: 161.0423.

Reduction of **16** with $NaBH_4$ 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 method[9] gave the 3-*O*-tosylate derivative **54**, mp 124—125 °C, as colorless needles from $CHCl_3$–AcOEt.[9] ^{1}H-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, br d, J=9.7 Hz, H-2), 4.08 (1H, br dt, J=6.0, 4.0 Hz, H-5), 4.26 (1H, br d, 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. ^{1}H-NMR (500 MHz): 3.42 (3H, s, OMe), 3.65 (1H, br s, H-5), 4.00 and 4.23 (each 1H, dd, J=1.4, 13.0 Hz, H-6), 4.16 (1H, br d, 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 4 N 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. ^{1}H-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, br t, 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 4 N 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. ^{1}H-NMR (500 MHz): 3.47 (3H, s, OMe), 3.67 (1H, br d, J=9.0 Hz, H-3), 3.90 (1H, s, H-5), 3.95 (1H, br s, 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 *C1* conformation. Crystal data: orthorhombic, a=10.173(2) Å, b=16.728(3) Å, c=7.915(3) Å, V=1347.0(6) Å^3, Z=4, D_C=1.39 g/cm^3. 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).

Benzyloxymethylation 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 mol eq) at 0 °C for 15 min, then BOMCl (0.75 ml, 1.5 mol eq) 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. ^{1}H-NMR: 3.43 (3H, s, OMe), 3.69 (1H, dd, J=2.5, 4.5 Hz, H-2), 3.80 (1H, br d, 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. ^{1}H-NMR: 3.45 (3H, s, OMe), 3.70 (1H, br s, H-2), 3.87 (1H, br s, H-5), 3.96 (1H, br s, H-3), 4.00 (1H, br s, 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. ^{1}H-NMR (500 MHz): 3.45 (3H, s, OMe), 3.81 (1H, br s, 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 × 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. ^{1}H-NMR (500 MHz): 3.48 (3H, s, OMe), 4.21 (1H, dd, J=2.5, 13.2 Hz, H-6), 4.27 (1H, br s, 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. ^{1}H-NMR (500 MHz, pyridine-d_5): 3.61 (OMe). MS: 191 (M^+, 0.2), 161 (2), 160 (40). HRMS: Calcd for $C_6H_9O_5$ ($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. ^{1}H-NMR (500 MHz): 3.50 (3H, s, OMe), 3.99 (1H, br d, 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). ^{1}H-NMR (500 MHz, pyridine-d_5): 3.43 (OMe). HRMS: Calcd for $C_6H_9O_5$ ($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] ^{1}H-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 Bistributyltin Oxide–Bromine Method (Modified Procedure) A mixture of **63** (0.4 g), $(Bu_3Sn)_2O$ (1.28 g, 3 mol eq) 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 mol eq) was added at 0 °C and, after 10 min, bromine (*ca.* 5 mol eq) 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. ^{1}H-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. ^{1}H-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. ^{1}H-NMR (pyridine-d_5): 3.47 (OMe). MS: 193 ($M^+ + 1$, 0.9), 161 ($M^+ -$OMe, 6). HRMS: Calcd for $C_7H_{13}O_6$ ($M^+ + 1$): 193.0712. Found: 193.0682.

$NaBH_4$ reduction of **15** gave Me α-D-Man (**21**) as major product.

Acknowledgement The authors thank Drs. F. Kiuchi and S. Hosoi of this Faculty for X-ray analysis and valuable discussions.

References and Notes

1) *a*) Part XXVII of Utilization of Sugars in Organic Synthesis; *b*) Part XXVI: Y. Tsuda and H.-M. Liu, *Chem. Pharm. Bull.*, **40**, 1975 (1992).
2) *a*) O. Gabriel, *Adv. Chem. Ser.*, **117**, 387 (1973); *b*) S. Matsuhashi and J. L. Strominger, *Methods Enzymol.*, **8**, 310 (1966); *c*) A. Melo, W. H. Elliott, and L. Glaser, *J. Biol. Chem.*, **243**, 1467 (1968); *d*) O. Gabriel and L. C. Lindquist, *ibid.*, **243**, 1479 (1968).
3) *a*) K. Shimada, T. Nambara, I. Uchida, and S. M. Kupchan, *Heterocycles*, **12**, 1445 (1979); *b*) K. Shimada, T. Kyuno, and T. Nambara, *ibid.*, **15**, 335 (1981); *c*) K. Shimada, T. Kyuno, T. Nambara, and I. Uchida, *Chem. Pharm. Bull.*, **30**, 4075 (1982); *d*) F. Abe and T. Yamauchi, *ibid.*, **33**, 3662 (1985); *e*) T. Yamauchi, F. Abe, and A. S. C. Wan, *ibid.*, **35**, 4813 (1987); *f*) H.-M. Liu, F. Kiuchi, and Y. Tsuda, *ibid.*, **40**, 1366 (1992); *g*) A. De Bruyn and J. Van Beeumen, *Carbohydr. Res.*, **228**, 445 (1992).
4) *a*) B. Lindberg and O. Theander, *Acta Chem. Scand.*, **8**, 1870 (1954); *b*) O. Theander, *ibid.*, **11**, 1557 (1957); *c*) A. Assarsson and O. Theander, *ibid.*, **12**, 1507 (1958); *d*) O. Theander, *ibid.*, **12**, 1887 (1958).
5) Abbreviations: Me = methyl, OG = hexopyranosidulose, Glc = glucopyranoside, Gal = galactopyranoside, Man = mannopyranoside, All = allopyranoside, Alt = altropyranoside, Ido = idopyranoside, Gul = gulopyranoside, and Tal = talopyranoside.
6) Y. Tsuda, M. Hanajima, N. Matsuhira, Y. Okuno, and K. Kanemitsu, *Chem. Pharm. Bull.*, **37**, 2344 (1989).
7) M. E. Haque, T. Kikuchi, K. Yoshimoto, and Y. Tsuda, *Chem. Pharm. Bull.*, **33**, 2243 (1985).
8) The same product **49** was more conveniently prepared by benzyloxymethylation of **47** with 1 mol eq of *n*-BuLi and BOMCl in CH_3CN (see Experimental).
9) Y. Tsuda, M. Nishimura, T. Kobayashi, Y. Sato, and K. Kanemitsu, *Chem. Pharm. Bull.*, **39**, 2883 (1991).
10) *Cf.*, T. Ogawa and M. Matsui, *J. Am. Chem. Soc.*, **98**, 1629 (1976).
11) A part of this work was presented at the 37th Annual Meeting of the Japanese Society of Pharmacognosy, Chiba, Nov. 1990, Abstract Papers 2A-4.
12) In aqueous solution, D-*ribo*-hexos-3-ulose exists as a mixture of at least ten isomeric forms with predominance of the 3-oxo forms and the hydrate form of the β-anomer [P. E. Morris, Jr., K. D. Hope, and D. E. Kiely, *J. Carbohydr. Chem.*, **8**, 515 (1989)].
13) Y. Tsuda, M. E. Haque, and K. Yoshimoto, *Chem. Pharm. Bull.*, **31**, 1612 (1983).
14) The reaction was accompanied with epimerization. The ratio of the products depends on the reaction conditions. Details will be presented in a future publication.
15) *a*) R. G. Ault, W. N. Haworth, and E. L. Hirst, *J. Chem. Soc.*, **1935**, 1012; *b*) *Idem*, *ibid.*, **1935**, 517.