

Branched-chain Sugars. XXIX. Synthesis of Moenuronic Acid (4-C-Methyl-D-glucuronic Acid)¹⁾

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Moenuronic acid (4-C-methyl-D-glucuronic acid), a branched-chain sugar component of moenomycin A, was synthesized by the introduction of an axial C-methyl group into methyl 2,3-di-O-benzyl-6-O-trityl- α -D-xyllohexopyranosid-4-ulose by the reaction with methyllithium, followed by deprotection and platinum-catalyzed oxidation of the C-6 position. Stereoselectivities in a few reactions for the introduction of C-methyl group were examined.

Moenomycin A²⁾ is a phosphoglycolipid antibiotic, which inhibits strongly the formation of linear polysaccharide-chain of murein from disaccharide intermediates³⁾ in the cell-wall biosynthesis. A new branched-chain uronic acid called moenuronic acid (**1**; 4-C-methyl-D-glucuronic acid) was found as a component.⁴⁾ By the ethanolysis of moenomycin A, the moiety was isolated as the corresponding ethyl β -D-glucofuranosidurono-6,3-lactone(**2**), and the structure was determined by the IR, NMR, CD, and mass spectroscopic data of **2** and its diacetate (**3**).⁵⁾ This paper describes the first synthesis of **3**.

Results and Discussion

The introduction of an axial C-methyl group to the C-4 position of a D-xyllohexopyranosid-4-ulose and the following oxidation of C-6 position of the product are necessary for the synthesis of **1**.

For the former problem, a few pathways from benzyl⁶⁾ and methyl 2,3-di-O-benzyl-6-O-trityl- α -D-xyllohexopyranosid-4-uloses (**4** and **5**) and 4-C-methylene derivative (**6**) of **5** were examined. Compound **5** was synthesized by the oxidation of methyl 2,3-di-O-benzyl-6-O-trityl- α -D-glucopyranoside⁷⁾ with dimethyl sulfoxide-trifluoroacetic anhydride in quantitative yield. Compound **6** was obtained in 63% yield by the usual Wittig reaction of **5**.

It is known that the reaction of α -D-xyllohexopyranosid-4-uloses⁸⁾ or a α -L-threo-pentopyranosid-4-ulose⁹⁾

with methyllithium at a low temperature gives axial C-methyl derivatives, whereas that with methylmagnesium iodide affords equatorial C-methyl derivatives predominantly. Therefore, these reactions of **4** and **5** were examined at first. As shown in Table 1, reaction of **4** with methyllithium at -78°C in ether gave exclusively the axial attack product (**7**), while that with methylmagnesium iodide in ether at -78°C gave only the equatorial attack product (**8**). The Grignard reaction in ether-tetrahydrofuran (1:1) under reflux gave **7** and **8** in the ratio of 1 to 1. A similar tendency was also observed in the reaction of **5**, and the corresponding C-methyl derivatives (**9** and **10**) were obtained. Configuration of **7**–**10** was determined from the chemical shifts of axially (**7**: δ 15.79 ppm, **9**: δ 14.92 ppm) and equatorially (**8**: δ 22.03 ppm, **10**: δ 22.02 ppm) oriented C-methyl carbons in ^{13}C -NMR spectra.^{8–10)}

On the other hand, diazomethane reaction¹¹⁾ of **4** and **5** gave one epimer of the corresponding spiro epoxides (**11** and **12**) in 20 and 15% yields, respectively, together with larger amount of ring-expanded products (**13** and **14**). The structures of **13** and **14** were thoroughly proved by the ^1H -NMR spectra (see Experimental). While, epoxidation¹²⁾ of **6** with *m*-chloroperbenzoic acid gave a 1:1 mixture of the corresponding spiro epoxides (**12** and **15**) in 80% yield. Reduction of **11**, **12**, and **15** with lithium aluminium hydride gave **7**, **9**, and **10** in fairly good yields, respectively. From these facts, configurations of **11**, **12**,

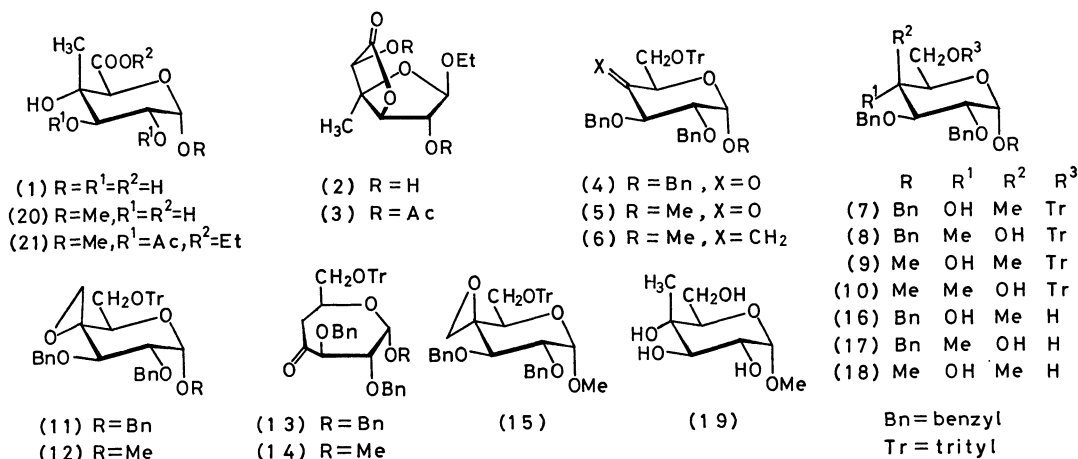


TABLE 1. COMPARISON OF STEREOSELECTIVITIES IN THE REACTIONS FOR THE INTRODUCTION OF A 4-C-METHYL GROUP INTO 4-6

Substrate	Reagent	Conditions		Ratio of products axial : equatorial attack	Yield/%
		Solvent	Temp/°C		
4	CH ₃ Li	Ether	-78	(7) 1 : 0	58
	CH ₃ MgI	Ether	-78	0 : 1 (8)	84
	CH ₃ MgI	Ether-THF	Boiling	(7) 1 : 1 (8)	72
5	CH ₃ Li	Ether	-78	(9) 1 : 0	95
	CH ₃ MgI	Ether	-78	0 : 1 (10)	84
	CH ₃ MgI	Ether	RT	(9) 1 : 2.2 (10)	93
4	CH ₂ N ₂	Ethanol	RT	(11) 1 : 0	20
5	CH ₂ N ₂	Ethanol	RT	(12) 1 : 0	15
6	<i>m</i> -ClC ₆ H ₄ CO ₃ H	CH ₂ Cl ₂	RT	(12) 1 : 1 (15)	81

TABLE 2. PHYSICAL CONSTANTS OF 4-C-METHYL-D-GLUCURONIC ACID DERIVATIVES

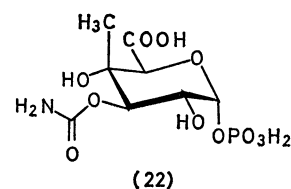
Derivatives	$\frac{[\alpha]_D^a}{^\circ}$	Chemical shifts (δ) and coupling constants (Hz) ^b										$\nu_{C=O}$ cm ⁻¹
		H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3	H-5	4-CH ₃	OAc	OCH ₂ (J_{gem})	CH ₃ (J_{CH_2, CH_3})	OMe		
2	−47.6	5.14 s	4.41 s	4.60 s	4.16 s	1.67 s	—	3.74 dq, 3.56 dq (9.0)	1.18 t (7.0)	—	1790	
3	+55.4	5.12 s	5.42 s	4.62 s	5.17 s	1.63 s	2.24 s 2.13 s	3.86 dq, 3.45 dq (9.0)	1.18 t (7.0)	—	1810 1750	
3 (reported)	—	5.14 s	5.42 s	4.60 s	5.19 s	1.63 s	2.25 s 2.13 s	3.70 m	1.19 t	—	1810 1750	
20	+87.0	4.77 d (4.0)	3.43 dd (10.5)	3.74 d	4.19 s	1.18 s	—	—	—	3.43 s	1730	
21	+112	5.03 d (3.4)	4.77 dd (10.4)	5.41 d	4.37 s	1.30 s	2.12 s 2.07 s	4.30 q	1.35 t (6.8)	3.44 s	1730	
22 (reported)	—	5.63 dd (3.5)	3.81 m (10.4)	5.00 d	4.48 s	1.25 s	—	—	—	—	—	

a) The rotational values of **2** and **20** were measured in ethanol and methanol, respectively. b) ¹H-NMR spectrum of **20** was taken in methanol-*d*. The spectrum of **2** showed signal of hydroxyl protons at δ 2.90 bs.

and **15** were established. Peroxy acid oxidation of methylene derivative such as **6** usually proceeds unselectively,¹²⁾ and the selectivities in the reaction of 4-uloses with methyllithium or diazomethane will be discussed in detail in the following papers.

For the oxidation of C-6 position, **7-9** were partially hydrolyzed with 70% acetic acid to give the corresponding de-*O*-tritylated products (**16-18**), respectively. However, attempted oxidation of **16** and **17** with chromium trioxide,¹³⁾ potassium permanganate,¹⁴⁾ and oxygen-platinum¹⁵⁾ gave commonly complex results, accompanying with the oxidation of the benzyl groups.^{6,16)} Therefore, *O*-benzyl groups of **18** were previously removed by hydrogenolysis to give methyl 4-*C*-methyl- α -D-glucopyranoside (**19**) in quantitative yield. Oxidation of **19** in slightly alkaline aqueous solution with oxygen in the presence of platinum-carbon gave the corresponding glucuronic acid (**20**) in 86% yield. Treatment of **20** with 0.1 M ethanolic hydrogen chloride for 16 h under reflux, and then base-catalyzed acetylation of the products gave **3** and methyl 2,3-di-*O*-acetyl-4-*C*-methyl- α -D-glucopyranosiduronic acid ethyl ester (**21**) in 28 and 55% yields, respectively. The formation of **21** implies the incomplete ethanolysis of the glycoside linkage of **20**. A similar ethanolysis of **21** for 3 d gave **2** in quantitative

yield. Physical constants of 4-*C*-methyl-D-glucuronic acid derivatives were summarized in Table 2, together with those of 3-*O*-carbamoyl-1-phosphate derivative (**22**) of **1**, obtained by hydrolysis of moenomycin A with trifluoroacetic acid and 2-propanol.⁴⁾



Although the rotational value and the magnetical non-equivalency of methylene protons in 1-ethoxyl group were not shown in the literature,⁵⁾ physical properties of **3** prove that **3** synthesized here is identical with that obtained from Moenomycin A. The non-equivalency of methylene protons will be attributed to the restricted rotation of 1-*O*-CH₂ bond, due to the steric hindrance between 1-ethoxyl and 5-acetoxyl groups oriented into the inside area of *cis*-fused five-membered ring. Data of **2** also support this deduction, though $\Delta\nu$ value of methylene protons is rather smaller. While, the coupling constants ($J_{1,2}$ and $J_{2,3}$) of **20-22** indicate their ⁴C₁ (D) conforma-

tions.

Thus, it was conclusively shown that synthesis of methyl glycoside (**20**) of **1** can be accomplished by the pathway of **5**→**9**→**18**→**19**→**20** in 73% overall yield.

Experimental

General Methods. Melting points were determined with a Mel-Temp hot-plate and are uncorrected. The solutions were evaporated under diminished pressure at a bath temperature not exceeding 50 °C. Specific rotations were measured with Carl Zeiss LEP-A1 or JASCO DIP-4 polarimeter, using chloroform as a solvent unless otherwise stated. IR spectra were recorded with Hitachi Model EPL-G2 spectrometer. ¹H-NMR spectra were taken with JEOL PS-100 spectrometer in chloroform-*d* unless otherwise stated, using tetramethylsilane as the internal standard. ¹³C-NMR data were recorded with JEOL FX-100 spectrometer at 25.16 MHz for the solutions in chloroform-*d*, using 8K data points, with proton-noise decoupling. Chemical shifts and coupling constants were recorded in δ (ppm) and Hz units, and IR frequencies in cm⁻¹. Column chromatography was performed on silica gel (Wakogel C-200) and preparative TLC on silica gel (Merck type 60).

Methyl 2,3-Di-O-benzyl-6-O-triphenylmethyl-α-D-xylo-hexopyranoside-4-ulose (5).

A solution of methyl 2,3-di-O-benzyl-6-O-trityl-α-D-glucopyranoside⁷⁾ (3 g, 4.86 mmol) in acetic anhydride (25 ml) and dimethyl sulfoxide (50 ml) was kept overnight at room temperature, poured into ice-water, and then extracted with ether. The usual processing of the extract and purification of the product on a column of silica gel with 15:1 hexane-ethyl acetate gave **5** as a syrup in 72% (2.15 g) yield. $[\alpha]_D^{25} + 47.1^\circ$ (*c* 1.2); IR: 1735 (C=O); NMR: 7.55–7.15 (m, 25 H, 5×Ph), 4.82 (d, 1 H, *J*_{1,2}=3.2, H-1), 4.52–4.98 (m, 4 H, 2×CH₂Ph), 4.36 (d, 1 H, *J*_{2,3}=10.0, H-3), 4.20 (dd, 1 H, H-5), 3.78 (dd, 1 H, H-2), 3.56 (dd, 1 H, *J*_{6,6'}=11.0, H-6), 3.53 (s, 3 H, OMe), 3.35 (dd, 1 H, *J*_{5,6'}=7.0, *J*_{5,6}=10.0, H-6'). Found: C, 78.53; H, 6.31%. Calcd for C₄₀H₃₈O₆: C, 78.15; H, 6.23%.

Methyl 2,3-Di-O-benzyl-4-deoxy-4-C-methylene-6-O-triphenylmethyl-α-D-xylo-hexopyranoside (6).

To an ice-cooled suspension of methyltriphenylphosphonium bromide (0.6 g, 1.68 mmol) in tetrahydrofuran (THF, 2 ml) was added butyllithium (10%, 8.7 ml, 1.36 mmol) in hexane with stirring, and to the resulting orange-coloured solution, a solution of **5** (1.02 g, 1.6 mmol) in THF (9 ml) was further added. After stirring the mixture for 30 min, the excess reagent was quenched with acetone, diluted with ether (20 ml), and then filtered. The filtrate was evaporated, and the residual syrup was purified on a column of silica gel with benzene to give **6** as a syrup in 63% (640 mg) yield. $[\alpha]_D^{25} + 40.3^\circ$ (*c* 0.9); IR: 1660 (C=C); NMR: 7.70–7.10 (m, 25 H, 5×Ph), 5.20–5.40 (bs, 2 H, methylene), 4.60–5.00 (m, 5 H, 2×CH₂Ph and H-1), 4.5–4.2 (m, 2 H, H-3 and 5), 3.53 (s, 3 H, OMe), 3.30–3.50 (m, 3 H, H-6, 6', and 2). Found: C, 80.52; H, 6.71%. Calcd for C₄₁H₄₀O₅: C, 80.36; H, 6.58%.

Reaction of 4-Uloses with Methyllithium. To a solution of **4** (120 mg, 0.174 mmol) in ether (2 ml) cooled with Dry Ice and acetone was added an excess amount of methyllithium (1.2 M, 1 ml) in ether with stirring, and then the mixture was kept at room temperature for 2 h, poured into saturated ammonium chloride solution. The usual processing of the ether layer and purification of the product on a column of silica gel with 3:1 hexane-ethyl acetate gave pure benzyl 2,3-di-O-benzyl-4-C-methyl-6-O-triphenylmethyl-

α-D-glucopyranoside (**7**) as a syrup in 58% (71 mg) yield. $[\alpha]_D^{25} + 26.8^\circ$ (*c* 1.1); ¹³C NMR: CMe, 15.79 ppm; ¹H NMR: 7.54–7.12 (m, 30 H, 6×Ph), 5.01–4.40 (m, 6 H, 3×CH₂Ph), 4.80 (d, 1 H, *J*_{1,2}=4.0, H-1), 4.00 (t, *J*_{5,6'}=5.8, H-5), 3.84 (d, 1 H, *J*_{2,3}=10.6, H-3), 3.36 (dd, 1 H, *J*_{5,6}=5.8, H-6), 3.36 (dd, 1 H, H-2), 3.25 (dd, 1 H, *J*_{6,6'}=11.6, H-6'), 2.32 (s, 1 H, OH), 0.98 (s, 3 H, CMe). Found: C, 79.42; H, 6.65%. Calcd for C₄₇H₄₆O₆: C, 79.86; H, 6.56%.

A similar reaction of **5** with methyllithium gave methyl 2,3-di-O-benzyl-4-C-methyl-6-O-triphenylmethyl-α-D-glucopyranoside (**9**) in 95% yield. $[\alpha]_D^{25} + 7.8^\circ$ (*c* 1.5); ¹³C NMR: CMe, 14.92 ppm; ¹H NMR: 7.60–7.14 (m, 25 H, 5×Ph), 5.03–4.52 (m, 4 H, 2×CH₂Ph), 4.59 (d, 1 H, *J*_{1,2}=3.8, H-1), 3.88 (dd, 1 H, *J*_{2,3}=10.0, H-2), 3.87 (t, 1 H, *J*_{5,6}=6.0, H-5), 3.51 (d, 1 H, H-3), 3.48 (s, 3 H, OMe), 3.39 (d, 2 H, H-6 and 6'), 2.37 (s, 1 H, OH), 1.00 (s, 3 H, CMe). Found: C, 78.29; H, 6.78%. Calcd for C₄₁H₄₂O₆: C, 78.07; H, 6.71%.

Reaction of 4-Uloses with Methylmagnesium Iodide. To a solution of methylmagnesium iodide, prepared from magnesium turnings (124 mg, 5.17 mmol) and methyl iodide (1 ml, 7 mmol), in ether (5 ml) chilled with Dry Ice and acetone was added dropwise a solution of **4** (187 mg, 2.72 mmol) in ether (2 ml) with stirring, and after 2 h, the reaction mixture was poured into saturated aqueous ammonium chloride solution. The usual processing of the ether layer and purification of the product on a column of silica gel with 3:1 hexane-ethyl acetate gave benzyl 2,3-di-O-benzyl-4-C-methyl-6-O-triphenylmethyl-α-D-galactopyranoside (**8**) as a syrup in 84% (160 mg) yield. $[\alpha]_D^{25} + 54.9^\circ$ (*c* 0.8); NMR: 7.64–7.14 (m, 30 H, 6×Ph), 5.10–4.25 (m, 6 H, 3×CH₂Ph), 4.98 (d, 1 H, *J*_{1,2}=3.5, H-1), 3.90 (dd, 1 H, *J*_{2,3}=9.5, H-2), 3.79 (t, 1 H, *J*_{5,6}=5.0, H-5), 3.59 (d, 1 H, H-3), 3.42 (d, 2 H, H-6 and 6'), 2.60 (s, 1 H, OH), 1.00 (s, 3 H, CMe). Found: C, 79.74; H, 6.62%. Calcd for C₄₇H₄₆O₆: C, 79.86; H, 6.56%.

The reaction of **4** (16.6 g, 24 mmol) with methylmagnesium iodide in ether-THF (1:1) at refluxing temperature and separation of the products on a flash column of silica gel with 6:1 hexane-ethyl acetate gave **7** and **8** in 35.2% (5.98 g) and 36.3% (6.15 g) yields, respectively.

A similar reaction of **5** (1.02 g, 1.6 mmol) with methylmagnesium iodide in ether at –78 °C and purification of the products on a flash column of silica gel with 6:1 hexane-ethyl acetate gave methyl 2,3-di-O-benzyl-4-C-methyl-6-O-triphenylmethyl-α-D-galactopyranoside (**10**) as a syrup in 84% (850 mg) yield. $[\alpha]_D^{25} + 18.2^\circ$ (*c* 1.0); NMR: 7.68–7.16 (m, 25 H, 5×Ph), 5.06–4.56 (m, 5 H, H-1 and 2×CH₂Ph), 3.90 (dd, 1 H, *J*_{1,2}=3.0, H-2), 3.70 (t, 1 H, *J*_{5,6}=4.0, H-5), 3.54 (d, 1 H, *J*_{2,3}=9.5, H-3), 3.52 (s, 3 H, OMe), 3.41 (d, 2 H, H-6 and 6'), 0.98 (s, 3 H, CMe). Found: C, 77.82; H, 6.83%. Calcd for C₄₁H₄₂O₆: C, 78.07; H, 6.71%.

When the reaction of **5** with methylmagnesium iodide in ether is carried out at room temperature, separation of the products on a flash column of silica gel with 6:1 hexane-ethyl acetate gave **9** and **10** in 29 and 64% yields, respectively.

Reaction of 4-Uloses and Diazomethane. To a solution of **4** (138 mg, 2.0 mmol) in ethanol (50 ml) was added dropwise a solution of diazomethane (4.0 mmol) in ether (20 ml) at 0 °C. After keeping the mixture at room temperature for 12 h, the solution was evaporated to give a syrup. Separation of the syrup on a preparative TLC gave a ring-expanded product, benzyl 2,3-di-O-benzyl-5-deoxy-7-O-triphenylmethyl-α-D-xylo-heptaseptanoside-4-ulose (**13**) and corresponding spiro epoxide, benzyl 4,4'-anhydro-2,3-di-O-benzyl-4-C-hydroxymethyl-6-O-triphenylmethyl-α-D-glucopyranoside (**14**).

pyranoside (**11**) in 60 and 20% yields, respectively.

11: syrup, $[\alpha]_D^{25} + 56.4^\circ$ (c 2.8); NMR: 7.6–7.1 (m, 30H, 6 $\times$ Ph), 5.0–4.40 (3 $\times$ ABq, 6H, J =11.0 and 12.0, 3 $\times$ CH₂Ph), 4.97 (d, 1H, $J_{1,2}$ =3.6, H-1), 4.64 (t, 1H, $J_{5,6}$ =4.0, H-5), 4.20 (d, 1H, $J_{2,3}$ =10.0, H-3), 3.55 (dd, 1H, H-2), 3.04 (d, 2H, H-6 and 6'), 3.06 and 2.43 (ABq, 2H, J =5.0, epoxy CH₂). Found: C, 80.38; H, 6.33%. Calcd for C₄₇H₄₄O₆: C, 80.09; H, 6.29%.

Compound **13** could not be completely purified, but the NMR and IR spectra could be analyzed. IR: 1720 (C=O); NMR: 7.50–7.10 (m, 30H, 6 $\times$ Ph), 5.03 (d, 1H, $J_{1,2}$ =1.8, H-1), 4.95–4.43 (m, 7H, 3 $\times$ CH₂Ph and H-6), 4.18 (d, 1H, $J_{2,3}$ =8.0, H-3), 3.74 (dd, 1H, H-2), 3.35–3.00 (m, 2H, H-7 and 7') 2.78 and 2.50 (dABq, 2H, $J_{A,B}$ =14.0, $J_{5,6}$ =11.0, $J_{5',6}$ =4.0, H-5 and 5').

A similar reaction of **5** and diazomethane and the separation of the products on preparative TLC gave a ring-expanded product, methyl 2,3-di-*O*-benzyl-5-deoxy-7-*O*-triphenylmethyl- α -D-xylo-heptaseptanosid-4-ulose (**14**), and the corresponding spiro epoxide, methyl 4,4'-anhydro-2,3-di-*O*-benzyl-4-*C*-hydroxymethyl-6-*O*-triphenylmethyl- α -D-glucopyranoside (**12**) 60 and 15% yields, respectively.

12: syrup; $[\alpha]_D^{25} + 17.8^\circ$ (c 0.8); NMR: 7.56–7.14 (m, 25H, 5 $\times$ Ph), 4.91–4.59 (m, 4H, 2 $\times$ CH₂Ph), 4.69 (d, 1H, $J_{1,2}$ =3.2, H-1), 4.36 (t, 1H, $J_{5,6}$ =4.2, H-5), 4.18 (d, 1H, $J_{2,3}$ =10.0, H-3), 3.64 (s, 3H, OMe), 3.58 (dd, 1H, H-2), 3.07 (d, 2H, H-6 and 6'), 3.02 and 2.42 (ABq, 2H, J =5.0, epoxy CH₂). Found: C, 78.01; H, 6.58%. Calcd for C₄₁H₄₀O₆: C, 78.32; H, 6.41%.

14: syrup, $[\alpha]_D^{25} + 19.5^\circ$ (c 0.9); IR: 1720 (C=O); NMR: 7.50–7.15 (m, 25H, 5 $\times$ Ph), 4.81 (d, 1H, $J_{1,2}$ =2.0, H-1), 4.82–4.03 (2 $\times$ ABq, 4H, 2 $\times$ CH₂Ph), 4.05–4.35 (m, 2H, $J_{2,3}$ =9.0, H-3 and 6), 3.71 (dd, 1H, H-2), 3.42 (s, 3H, OMe), 3.40–2.98 (m, 2H, H-7 and 7'), 2.79 and 2.55 (dABq, 2H, $J_{A,B}$ =14.0, $J_{5,6}$ =10.0, $J_{5',6}$ =2.0, H-5 and 5'). Found: C, 78.30; H, 6.38%. Calcd for C₄₁H₄₀O₆: C, 78.32; H, 6.41%.

Reduction of Spiro Epoxides with Lithium Aluminium Hydride. To a solution of **11** (200 mg, 0.28 mmol) in THF (20 ml) was added lithium aluminium hydride (LAH, 50 mg, 1.3 mmol) and then the mixture was refluxed for 2 h. The excess hydride was decomposed with water, and then filtered. The water layer was extracted with chloroform. The combined extract was washed with water, dried, and evaporated to give a syrupy **7** in quantitative yield, which was identical with that obtained by the reaction of **4** and methylolithium at -78°C .

A similar reduction of **12** (200 mg) in THF (20 ml) as above gave **9** in quantitative yield, which was identical with that obtained by the reaction of **5** and methylolithium at -78°C .

Reduction of **15** (200 mg) in THF (20 ml) as above gave **10** in quantitative yield, which was identical with that obtained by the reaction of **5** and methylmagnesium iodide at -78°C .

m-Chloroperoxybenzoic Acid Oxidation of 6. A solution of crude **6** (500 mg, 0.82 mmol) and *m*-chloroperoxybenzoic acid (630 mg, 3.65 mmol) in dichloroethane (50 ml) was stirred overnight at room temperature, and then washed successively with aqueous sodium hydroxide (0.1 M), water, saturated sodium chloride, and water, and then dried and evaporated. The residual syrup was separated on a column of silica gel with 5:1 hexane-ethyl acetate to give methyl 4,4'-anhydro-2,3-di-*O*-benzyl-4-*C*-hydroxymethyl-6-*O*-triphenylmethyl- α -D-glucopyranoside (**12**) and α -D-galactopyranoside (**15**) as syrups each in 21.3% (110 mg) yield. Physical constants of **12** were identical with the authentic sample

that was derived from the reaction of **5** and diazomethane. **15**: $[\alpha]_D^{25} + 4.4^\circ$ (c 0.8); NMR: 7.60–7.10 (m, 25H, 5 $\times$ Ph), 4.66 (d, 1H, $J_{1,2}$ =3.4, H-1), 4.53–4.98 (m, 4H, 2 $\times$ CH₂Ph), 4.14 (d, 1H, H-3), 4.12 (t, 1H, H-5), 3.73 (dd, 1H, $J_{2,3}$ =10.0, H-2), 3.41 (s, 3H, OMe), 3.26 (dd, 1H, $J_{5,6}$ =5.2, H-6'), 2.99 (dd, 1H, $J_{5,6}$ =6.2, $J_{6,6'}$ =10.0, H-6), 2.89 and 2.74 (ABq, 2H, J =5.0, epoxy CH₂). Found: C, 78.51; H, 6.62%. Calcd for C₄₁H₄₀O₆: C, 78.32; H, 6.41%.

De-O-tritylation of 4-C-Methyl Derivatives (7–9). A solution of **7** (1.47 g, 2.05 mmol) in acetic acid (70%, 30 ml) was heated at 100°C for 5 h, filtered at room temperature, and then evaporated. The resulting syrup was purified on a column of silica gel with 3:1 hexane-ethyl acetate gave pure benzyl 2,3-di-*O*-benzyl-4-*C*-methyl- α -D-glucopyranoside (**16**) as a syrup in 98% (1.1 g) yield. $[\alpha]_D^{25} + 88.7^\circ$ (c 1.1); NMR: 7.6–6.8 (m, 15H, 3 $\times$ Ph), 5.02–4.36 (m, 6H, 3 $\times$ CH₂Ph), 4.81 (dd, 1H, $J_{5,6}$ =3.5, H-6), 4.78 (d, 1H, $J_{1,2}$ =4.0, H-1), 4.74 (t, 1H, $J_{5,6}$ =3.5, H-5), 4.59 (dd, 1H, $J_{6,6'}$ =7.0, H-6'), 3.71 (d, 1H, H-3), 3.38 (dd, 1H, $J_{2,3}$ =10.0, H-2), 2.92 (bs, 1H, OH), 1.14 (s, 3H, CMe). Found: C, 72.11; H, 7.07%. Calcd for C₂₈H₃₂O₆: C, 72.39; H, 6.94%.

In a similar manner, de-*O*-tritylation of **8** (1.29 g, 1.8 mmol) and purification of the product on a column of silica gel with 3:1 hexane-ethyl acetate gave benzyl 2,3-di-*O*-benzyl-4-*C*-methyl- α -D-galactopyranoside (**17**) as a syrup in 96% (0.96 g) yield. $[\alpha]_D^{25} + 101^\circ$ (c 1.1), NMR: 7.6–7.1 (m, 15H, 3 $\times$ Ph), 5.1–4.4 (m, 6H, 3 $\times$ CH₂Ph), 4.88 (d, 1H, $J_{1,2}$ =4.0, H-1), 3.94–3.54 (m, 4H, H-3,5 and 6), 3.42 (dd, 1H, $J_{2,3}$ =10.0, H-2), 2.26 (s, 1H, OH), 1.18 (s, 3H, CMe). Found: C, 72.23; H, 7.15%. Calcd for C₂₈H₃₂O₆: C, 72.39; H, 6.94%.

In a similar manner, de-*O*-tritylation of **9** (6.3 g, 10 mmol) and purification of the products gave methyl 2,3-di-*O*-benzyl-4-*C*-methyl- α -D-glucopyranoside (**18**) in 90% (3.5 g) yield, together with a small amount of its 6-acetate as syrups.

18: $[\alpha]_D^{25} + 31.4^\circ$ (c 0.9); NMR: 7.6–7.1 and 5.10–4.52 (m, 14H, 2 $\times$ CH₂Ph), 4.61 (d, 1H, $J_{1,2}$ =4.0, H-1), 4.0–3.5 (m, 5H, H-2,3,4 and 6), 3.40 (s, 3H, OMe), 3.36 (bs, 1H, OH), 1.18 (s, 3H, CMe). Found: C, 67.77; H, 7.10%. Calcd for C₂₂H₂₈O₆: C, 68.02; H, 7.27%.

6-Acetate showed the following ¹H-NMR data: 7.6–7.1 and 5.16–4.52 (m, 14H, 2 $\times$ CH₂Ph), 4.59 (d, 1H, $J_{1,2}$ =4.0, H-1), 4.38 (dd, 1H, $J_{5,6}$ =2.0, $J_{6,6'}$ =12.0, H-6), 4.11 (dd, 1H, $J_{5,6}$ =6.0, H-6'), 3.75 (d, 1H, $J_{2,3}$ =9.5, H-3), 3.49 (dd, 1H, H-2), 3.40 (s, 3H, OMe), 2.16 (bs, 1H, OH), 2.05 (s, 3H, Ac), 1.17 (s, 3H, CMe).

Methyl 4-C-Methyl- α -D-glucopyranoside (19). The usual hydrogenation of **18** (3.9 g, 10 mmol) in ethanol in the presence of palladium-charcoal (10%) gave **19** as a syrup in quantitative (2.08 g) yield. $[\alpha]_D^{25} + 100^\circ$ (c 0.8, MeOH); NMR (CD₃OD): 4.67 (d, 1H, $J_{1,2}$ =4.0, H-1), 3.96–3.10 (m, 5H, H-2,3,5, and 6), 3.43 (s, 3H, OMe), 1.07 (s, 3H, CMe). Found: C, 46.50; H, 7.68%. Calcd for C₈H₁₆O₆: C, 46.15; H, 7.75%.

Methyl 4-C-Methyl- α -D-glucuronic Acid (20). Gaseous oxygen was bubbled into a solution of **19** (1.0 g, 4.8 mmol) in water at 90°C for 40 h in the presence of platinum-carbon (10%, 0.3 g), and pH of the reaction mixture was maintained about 8.0 with sodium hydrogencarbonate. After **19** has disappeared on TLC, the mixture was filtered, and treated with Amberlite (IR-120) and the filtrate was evaporated to give **20** as a syrup in 86% (917 mg) yield. Physical data of **20** were shown in Table 2. Found: C, 42.97; H, 6.01%. Calcd for C₈H₁₄O₇: C, 43.24; H, 6.35%.

Ethyl 2,5-Di-*O*-acetyl-4-*C*-methyl- β -D-glucofuranosidurono-6,3-

lactone (**3**) and Methyl 2,3-Di-O-acetyl-4-C-methyl- α -D-glucopyranosiduronic Acid Ethyl Ester (**21**). A solution of **20** (500 mg, 2.25 mmol) in ethanolic hydrogen chloride (0.1 M) was refluxed for 16 h, and then evaporated to give a syrup. Acetic anhydride (2 ml) was added to a solution of the syrup in pyridine (2 ml). After keeping overnight at room temperature, the mixture was evaporated together with ethanol to give a syrup. Separation of the syrup on a preparative TLC (benzene-acetone 8:1) gave **21** {mp 99–101 °C (from ether-hexane); Found: C, 50.27; H, 6.61%. Calcd for $C_{14}H_{22}O_9$: C, 50.29; H, 6.63%} and **3** (syrup; Found: C, 51.84; H, 6.26%. Calcd for $C_{13}H_{18}O_8$: C, 51.65; H, 6.00%) in 55% (414 mg) and 28% (190 mg) yields, respectively. Physical constants of **3** and **21** were shown in Table 2.

Ethyl 4-C-Methyl- β -D-glucofuranosidurono-6,3-lactone (2).

A similar ethanolysis of **21** (334 mg, 1.0 mmol) as above for 3 d gave syrupy **2** (Found: C, 49.47; H, 6.50%. Calcd for $C_9H_{14}O_6$: C, 49.54; H, 6.47%) in quantitative (218 mg) yield. Physical data of **2** were shown in Table 2.

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