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Synthesis of 2,2-Di-*C*-methyl-2-deoxy- and 4,4-Di-*C*-methyl-4-deoxypyranosides via Michael Addition of Conjugated Enopyranosiduloses

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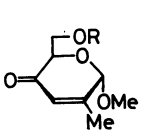
Three hexopyranosides having *gem*-di-*C*-methyl group at 2- or 4-positions were synthesized by Michael addition to 2-enopyranosid-4-ulose and 3-enopyranosid-2-ulose derivatives, respectively, followed by hydroboration. A heptopyranosid-6-ulose having *gem*-di-*C*-methyl group at C-4 was also synthesized from 4-enopyranosid-6-ulose derivative in a similar way.

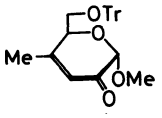
In recent years, carbohydrates have been used widely as chiral sources for synthesis of natural products.[1] *gem*-Dialkylation of carbohydrates has progressed on this utilization. For example, the following *gem*-dialkyl groups have been constructed: a) *C*-cyano-*C*-nitromethyl as well as *C*-methyl-*C*-nitromethyl group from the *C*-nitromethylene group by Michael addition,[2] b) *C*-(ethoxycarbonylmethyl)-*C*-methyl group by enolate alkylation of the ulose derivative,[3] c) *C*-formylmethyl-*C*-vinyl group from *C*-[2-(vinyloxy)ethylidene] group by Claisen rearrangement.[4] On the other hand, introduction of *gem*-dimethyl group into the carbohydrate skeleton has not yet been reported except a recently published paper[5] and our preliminary one,[6] although *gem*-dimethylation has been achieved for non-carbohydrate compounds by several methods.[7-11] In this paper we should like to report on the synthesis of *gem*-di-*C*-methylpyranosides by Michael addition of methylcuprates(I) to conjugated enopyranosiduloses. This method has been proved to be useful for construction of *gem*-dimethyl function at C-2 and C-4 positions of hexopyranosides, while the method by hydrogenolytic cleavage of spirocyclopropane ring for that at C-3 position.[6]

Results and Discussion

Four kinds of conjugated enopyranosiduloses **2**—**5** were used for this study. The first two branched-chain enopyranosiduloses **2** and **3** were derived from a common starting compound, i.e., methyl 6-*O*-trityl-α-D-*glycero*-2-enopyranosid-4-ulose (**6**).[12] Conjugate 1,4-addition of a lithium (cyano)dimethylcuprate(I), $Me_2Cu(CN)Li_2$, to **6** followed by treatment with chlorotrimethylsilane, gave the corresponding enol trimethylsilyl ether **7**. Dehydrosilylation of **7** with *p*-benzoquinone in the presence of palladium(II) acetate[13] afforded **2** in 55% yield from **6**. Alternatively, the enone **2** was prepared from methyl 4,6-*O*-benzylidene-2-deoxy-2-*C*-methyl-α-D-altropyranoside (**9**) via the 3-enopyranoside **8**, which was formed selectively by treatment of the 3-mesylate **10** of **9** with potassium *t*-butoxide. Palladium-catalyzed enone formation[14] was proved to be effective for the enolate **8** to give enone **1**, which was converted into **2** by a conventional tritylation. The total yield of **2** from **9** was 11.4%. The latter route proved to be rather convenient than the previous one[15] in the steps of elimination and enone formation.



1 R=H
2 R=Tr



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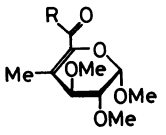
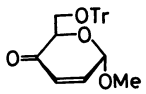


4 R=H
5 R=Me



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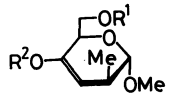
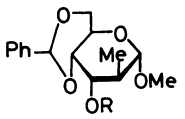


7 R^1=Tr, R^2=TMS
8 R^1, R^2=PhCH

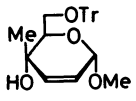


9 R=H
10 R=Ms

On the other hand, the enone **3** was already prepared[16] by pyridinium chlorochromate oxidation of 1,2-adduct **11** obtained by treatment of **6** with methyllithium. In the addition reaction the ratio of **11** and its 4-epimer was proved to be 4:3, while with methylcerium(III) reagent[17] instead of methyllithium **11** was obtained exclusively in a quantitative yield. Thus it is noteworthy that the methylcerium reagent tends to facilitate axial attack of carbanion, which was also observed in the reaction of methyl 3,4-dideoxy-6-*O*-trityl-α-D-*glycero*-3-enopyranosid-2-ulose.[18] Furthermore, oxidation of **11** with pyridinium fluoroformate[19] instead of chloroformate gave **3** in a higher yield (86%), indicating that this less acidic oxidant are convenient and effective for allylic alcohol.

The enone **4** was derived from methyl 6-*O*-benzyl-2,3-di-*O*-methyl-α-D-glucopyranoside (**12**)[20] according to a similar strategy to Hanessian et al.[21] Swern oxidation of **12** gave the corresponding 4-ulose, which was converted stereoselectively with methylmagnesium iodide into the 4-*C*-methyl derivative **13** of D-*galacto* configuration in 77% yield in two steps. Methylation of **13** followed by hydrogenolytic removal of 6-*O*-benzyl group and Swern oxidation gave a dialdose **14** in 79% yield. Then, **4** was obtained in 65% yield by treatment of **14** with calcium hydroxide. As shown in

Table 1 the reaction of **4** with various methylcuprates(I) gave in good yields the 1,2-adduct **15**, from which the enone **5** was derived quantitatively by Swern oxidation.



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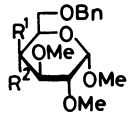
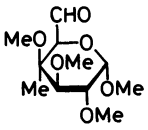


12 $R^1=H$, $R^2=OH$
13 $R^1=OH$, $R^2=Me$



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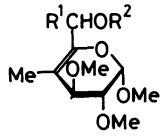


15 $R^1=Me$, $R^2=H$
16 $R^1=Me$, $R^2=Ac$
17 $R^1=R^2=H$

The reaction of these enones **2**, **3**, and **5** with lithium (cyano)dimethylcuprate(I), $Me_2Cu(CN)Li_2$, gave preferentially 1,4-adducts, *gem*-di-*C*-methyl-pyranosiduloses **18**, **19**, and **20**, respectively, in high yields as shown in Table 1. In the case of **3** very small amount of by-product, the *β*-anomer of **19**, was isolated. On the other hand, the reaction of the enal **4** afforded an epimeric mixture of 1,2-adduct **15** together with small amount of reduced product **17**. The distinct difference of regioselectivity in the addition reactions between **4** and **5** coincide with the fact that aldehydes react easily with lithium organocuprates, while ketones not.[22]

Table 1. Reaction of Methyl Branched Enones **2**—**5** with Lithium Methylcuprates (I)

Enone	Product	Yield/%	
		Me_2CuLi	$Me_2Cu(CN)Li_2$
2	**18**	72	77
	5-epimer of **18**	8.4	3.1
3	**19**	82	93
	β-anomer of **19**	6.9	4.1
4[a]	**15**	62	90
	17	12	trace
5	**20**	83	89

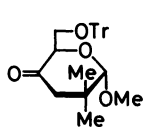
a) With $Me_5Cu_2Li_3$ the yield of **15** was 93%.

Thus, it was turned out that *gem*-dimethylation in hexopyranoside ring could be performed very easily using conjugate addition to the enopyranosiduloses. Furthermore, in the cases of **18** and **19** asymmetric carbons lost during the enone formation was also recovered by hydroboration of the silyl enolates[23] e.g., **18** → **21** → **24** or **19** → **23** → **26**. The enolates **21** and **23** were obtained by quenching the above mentioned Michael addition with chlorotrimethylsilane in good yields. Hydroborations of **21** and **23** were examined using various reagents and the products were analyzed after hydrolysis and acetylation. As summarized in Table 2, hydroboration with 3 equivalents of diborane gave the best results. In the case of **21**, only 2-deoxy-2,2-di-*C*-methyl-hexopyranoside derivative **24** was obtained as hydroboration product, where a small amount of 3-deoxy-D-*erythro*-hexopyranoside **25** and 3-enopyranoside **22** were also formed. In the case of **23**, 4-deoxy-4,4-di-*C*-methyl-D-*xylo*- **26** and D-*arabino*-hexopyranoside derivatives **28** were obtained in a ratio of 3 to 1, and 3-deoxy-D-*erythro*-hexopyranoside **27** was also formed. Hydroboration with borane formed in situ from sodium borohydride and Lewis acids such as titanium(III) chloride[24] and cobalt(II) chloride[25] gave also the desired products in moderate yields, although recovery of the uloses were increased. On the other hand, hydroboration with disiamylborane and 9-borabicyclo[3.3.1]nonane (9-BBN) gave small amount of the reduced by-products, **25** and **27**, while the uloses were recovered in high yield. Only in the case of **23** hydroboration with disiamylborane afforded **26**, albeit in 17% yield, stereoselectively. The structures of **24**, **26**, and **28** were confirmed on the basis of two acetyl signals and the coupling constants of methine protons

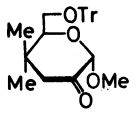
Table 2. Hydroboration[a] of **21** and **23**

Enolate	Reagent	Product[b] and Yield/%						Recovered ulose/%	
21	Borane (1.1 equiv)	**24**	Trace					**18**	70
21	Borane (3.0 equiv)	**24**	43	**25**	6.4	**22**	5.8		
21	Borane (9.0 equiv)	**24**	44	**25**	8.6	**22**	4.6		
21	$NaBH_4$, $TiCl_3$	**24**	12.5	**25**	12.5	**22**	10	**18**	30
21	$NaBH_4$, $CoCl_2$	**24**	26	**25**	Trace	**22**	2.0	**18**	51
21	Disiamylborane	**24**	Trace	**25**	14			**18**	76
21	9-BBN[c]	**24**	Trace	**25**	7.8			**18**	70
23	Borane (1.1 equiv)	**26**	26	**28**	5.3	**27**	9.0		
23	Borane (3.0 equiv)	**26**	29	**28**	9.7	**27**	13		
23	Borane (9.0 equiv)	**26**	22	**28**	6.3	**27**	13.5		
23	$NaBH_4$, $CoCl_2$	**26**	24	**28**	12	**27**	Trace		
23	$NaBH_4$, $TiCl_3$	**26**	27	**28**	9.1	**27**	16		
23	Disiamylborane	**26**	17			**27**	13	**19**	43
23	9-BBN[c]	**26**	Trace			**27**	7.9	**19**	57

a) Followed by treatment with alkaline hydrogen peroxide. b) Isolated after acetylation with acetic anhydride and pyridine. c) 9-Borabicyco[3.3.1]nonane.



18



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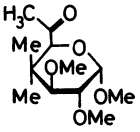

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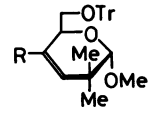
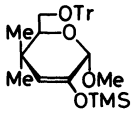


21 R = OTMS
22 R = H



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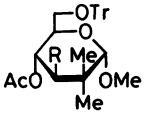
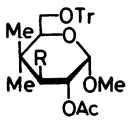
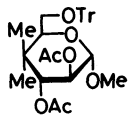


24 R = OAc
25 R = H



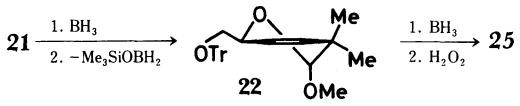
26 R = OAc
27 R = H



28

with acetoxyl groups, i.e., $J_{3,4}$=8.0 Hz, $J_{2,3}$=7.8 Hz, and $J_{2,3}$=4.0 Hz, respectively. While those of **25** and **27** by one acetyl signal and the coupling constants of methine protons with acetoxyl group, i.e., $J_{3ax,4}$=7.8 Hz and $J_{2,3ax}$=13.3 Hz, respectively.

The formation of the deoxygenated derivatives, **25** and **27**, may be rationalized by trans β-elimination[26] of trimethylsiloxyborane from the hydroboration products, giving the corresponding de(trimethylsilyloxy) derivative. Actually in the reaction of **21**, the de(trimethylsilyloxy) intermediate **22** was isolated. Further hydroboration of **22** followed by oxidation may give **25**, where the stereoselectivity was well-explained by a half-chair conformation as depicted in the following scheme.



Thus, Michael addition of lithium methylcuprate to 2-enopyranosid-4-ulose and 3-enopyranosid-2-ulose derivatives, followed by hydroboration-oxidation, opened the synthetic routes of hexopyranosides having *gem*-di-*C*-methyl group at 2- and 4-positions, respectively.

Experimental

General Methods. Melting points determined with a Yanagimoto micro melting point apparatus, were uncorrected. Optical rotations were measured in chloroform, by using a 0.5-dm tube with a Carl Zeiss LEP-Al polarimeter. Infrared spectra were recorded on a Hitachi EPI-G2 grating spectrometer. ^{1}H and ^{13}C NMR spectra were recorded at 100 MHz with a JEOL JMN PS-100 spectrometer and at 22.5 MHz with a JEOL FX-90Q spectrometer, respectively, in $CDCl_3$ with tetramethylsilane as internal standard. Column chromatography was performed on silica gel (Wakogel C-300: Wako Pure Chemical Industries, Ltd.) ^{1}H and ^{13}C NMR data of pyranosides having *gem*-di-*C*-methyl group are summarized in Table 3.

Methyl 2,3-Dideoxy-2-*C*-methyl-6-*O*-trityl-α-D-*glycero*-hex-2-enopyranosid-4-ulose (2). To a mixture of palladium(II) acetate (112 mg, 0.5 mmol) and *p*-benzoquinone (54 mg, 0.5 mmol) was added under argon a solution of **7** (460 mg, 0.95 mmol), whose preparation is described below, in acetonitrile (4 ml). The mixture was stirred at 50 °C for 6 h, and fractionated directly on a silica-gel column with benzene-acetone (15 : 1) to give **2** (241 mg, 62%). IR and NMR data of **2** coincided with the reported data.[15]

Methyl 3,4-Dideoxy-4-*C*-methyl-6-*O*-trityl-α-D-*glycero*-hex-3-enopyranosid-2-ulose (3). A solution of pyridinium fluorochromate (2.36 g, 11.9 mmol) and **11** (2.72 g, 6.6 mmol) in dichloromethane (84 ml) was stirred at room temperature for 6 h. The undissolved materials were filtered off, and the filtrate was washed with 2.5% aqueous sodium hydroxide and water, and dried with potassium carbonate. Evaporation of the filtrate gave a syrup, which was purified on a short column of silica gel with hexane-ethyl acetate (18 : 1) to afford **3** (2.33 g, 86%) as a colorless syrup. ^{1}H NMR data was identical with those reported.[16]

Methyl 4-Deoxy-2,3-di-*O*-methyl-4-*C*-methyl-β-L-*threo*-hexodialdo-4-enopyranoside-(1,5) (4). To a solution of **14** (500 mg, 2.0 mmol) in tetrahydrofuran (5 ml) and water (5 ml), was added 0.5 M (1 M=1 mol dm^{-3}) aqueous solution of barium hydroxide (4 ml). The mixture was kept at room temperature for 6 h, then saturated with ammonium chloride and extracted with chloroform. The extract was washed with aqueous sodium chloride, dried over magnesium sulfate, and evaporated to give a crude mixture of products, which was fractionated on a column of silica gel with hexane-acetone (5 : 1) to give **4** (284 mg, 65%), methyl 2,3-di-*O*-methyl-4-*C*-methylene-β-L-*threo*-hexodialdo-4-enopyranoside-(1,5) (17 mg, 3.9%), and starting material (29 mg, 5.8%).

4: Mp 148—150 °C, $[\alpha]_D^{20}$ +31.2° (*c* 0.7, $CHCl_3$). IR (KBr) 1680 (CO) and 1640 cm^{-1} (C=C), ^{1}H NMR δ=5.06 (1H, d, H-1), 3.92 (1H, dd, $J_{1,2}$=2.2 Hz, H-2), 3.60 (1H, d, $J_{2,3}$=7.8 Hz, H-3), 9.76 (1H, s, H-6), 2.12 (3H, s, C-Me), 3.44 (3H, s, OMe) and 3.52 (6H, s, OMe).

Found: C, 55.38; H, 7.48%. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46%.

The *exo*-methylene compound was a syrup, and had $[\alpha]_D^{20}$ +10.1° (*c* 0.88, $CHCl_3$). ^{1}H NMR δ=4.96 (1H, d, $J_{1,2}$=3.0 Hz, H-1), 3.6—3.7 (2H, m, H-2 and H-3), 3.98 (1H, bs, H-5), 9.54 (1H, bs, H-6), 3.52 (3H, s, OMe), and 3.56 (6H, s, OMe).

Found: C, 55.41: H, 7.60%. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46%.

Methyl 4,7-Dideoxy-4-*C*-methyl-2,3-di-*O*-methyl-β-L-*threo*-hept-4-enopyranosid-6-ulose (5). To a suspension of cerium(III) chloride (318 mg, 1.3 mmol) in tetrahydrofuran (5 ml), was added an ethereal solution of methyllithium (1.2 M solution, 1.1 ml, 1.3 mmol) at −78 °C, and then after 1 h a solution of **4** (260 mg, 1.1 mmol) in tetrahydrofuran (5 ml). The mixture was kept at −78 °C for 4 h and poured into a saturated ammonium chloride solution and extracted with dich-

Table 3. ^{1}H and ^{13}C NMR Data of Pyranosides Having *gem*-Di-*C*-methyl Group

Compound	1	2	3	4	5	6	C-Me	OMe	Others
18(^{1}H)	4.36s		2.08, 2.50d (J=15.4)		4.02dd ($J_{5,6}$=4.2)	3.30dd, 3.42t ($J_{5,6'}$=$J_{6,6'}$=8.8)	0.94s 1.18s	3.44s	7.1—7.5m (Tr)
18(^{13}C)	103.08d	37.39s	47.24t	205.51s	73.16	61.64t	25.23q 25.82q	54.57q	a)
19(^{1}H)	4.58s		1.96dd (J=1.0), 2.64d (J=14.2)		4.16dd ($J_{5,6}$=7.4)	3.20t, 3.18dd ($J_{5,6'}$=$J_{6,6'}$=3.8)	1.76bs 1.78s	3.60s	7.1—7.6m (Tr)
19(^{13}C)	100.24	202.58	51.04	39.88	75.53	63.07	20.43 26.82	54.94	b)
24(^{1}H)	5.16s		5.22d ($J_{3,4}$=$J_{4,5}$=8.0)	5.08t	3.86m	3.12dd, 3.20t	0.96s 1.12s	3.38s	1.86s, 2.00s (OAc) 7.2—7.6m (Tr)
24(^{13}C)	105.52	40.80	68.28	69.74	75.06	62.86	19.93 20.60	55.00	22.16, 20.74 (Me) 170.48, 169.55 (C=O)[c]
			1.62bt ($J_{3',4}$=$J_{3',3}$=7.8)						
25(^{1}H)	4.20s		1.44dd ($J_{3,4}$=4.4)	5.00ddd ($J_{4,5}$=6.6)	3.96ddd ($J_{5,6}$=4.0)	3.16dd, 3.24t ($J_{6,6'}$=$J_{5,6'}$=8.0)	0.92s 1.04s	3.32s	2.02s (OAc) 7.2—7.6m (Tr)
25(^{13}C)	99.66	35.34	43.99	70.28	71.69	62.28	19.86 21.13	57.20	21.33, 164.62 (OAc)[d]
26(^{1}H)	4.42d ($J_{1,2}$=4.0)	4.56dd ($J_{2,3}$=7.8)	4.72bd		3.2—3.6m (2H)	3.12dd ($J_{5,6}$=4.0, $J_{6,6'}$=6.8)	0.88s 0.90s	3.60s	2.08s, 2.12s (OAc) 7.2—7.6m (Tr)
26(^{13}C)	98.76	69.45	81.75	38.70	75.88	64.14	20.67 23.43	53.12	24.10, 24.75 (Me) 167.38, 168.94 (C=O)[e]
28(^{1}H)	4.60d ($J_{1,2}$=1.2)	4.22bdd ($J_{2,3}$=4.0)	4.26bd		3.2—3.5m (2H)	3.14dd ($J_{5,6}$=2.8, $J_{6,6'}$=5.4)	0.82s 0.86s	3.64s	2.02bs (6H) (OAc) 7.2—7.6m (Tr)
28(^{13}C)	100.12	73.16	78.77	39.02	77.51	65.98	19.72 22.80	55.69	27.38, 22.94 (Me) 166.23, 178. 46 (C=O)[f]

a) 85.85 (Ph_3C), 125.87, 126.65, 127.77, and 142.91 (Ph). b) 87.01 (Ph_3C), 127.00, 127.81, 128.68, and 144.06 (Ph). c) 86.63 (Ph_3C), 126.90, 127.72, 128.75, and 143.78 (Ph). d) 85.62 (Ph_3C), 126.43, 127.53, 128.23, and 143.66 (Ph). e) 81.94 (Ph_3C), 127.37, 127.49, 128.68, and 144.06(Ph). f) 85.45 (Ph_3C), 127.26, 127.92, 128.39, and 144.14 (Ph).

loromethane. The extract was washed with aqueous sodium chloride, dried with sodium sulfate, and evaporated to give crude 1,2-adduct as a syrup. The syrup was oxidized with dimethyl sulfoxide (0.3 ml) and oxalyl dichloride (0.2 ml) in dichloromethane (4.5 ml) in the same manner as described for compound **14**. Crude **5** was purified on a column of silica gel with hexane-ether (3:1), yield, 206 mg (82%); syrup, IR (NaCl) 1700 (C=O) and 1660 cm^{-1} (C=C). ^{1}H NMR δ=4.96 (1H, d, $J_{1,2}$=3.6 Hz, H-1), 3.44 (1H, dd, $J_{2,3}$=6.4 Hz, H-2), 3.72 (1H, d, H-3), 1.88 and 1.96 (each 3H, each s, CMe), 3.50 (3H, s, OMe) and 3.58 (6H, s, OMe).

Found: C, 57.66; H, 8.17%. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88%.

Preparation of Enol Trimethylsilyl Ethers 7, 21, and 23 from Enones 6, 2, and 3. To a reaction mixture of an enone with lithium (cyano)dimethylcuprate(I) as described latter, was added after 4 h at −78 °C triethylamine (1.7 ml per 1.0 mmol of enone), hexamethylphosphoric triamide (0.3 ml per 1.0 mmol of enone), and chlorotrimethylsilane (1.7 ml per 1.0 mmol of enone). Being kept at 0 °C for 1 h, the mixture was processed in the same manner as described for **13**. The enol ethers were used for further reaction without purification.

Methyl 2,3-Dideoxy-2-*C*-methyl-4-*O*-trimethylsilyl-6-*O*-trityl-α-D-*threo*-hex-3-enopyranoside (7). Treatment of **6**[12] as described above gave **7** quantitatively, which was characterized only by ^{1}H NMR δ=4.72 (1H, d, $J_{1,2}$=4.8 Hz, H-1), 2.54 (1H, dq, $J_{2,Me}$=6.8 Hz, H-2), 4.66 (1H, bs, H-3), 4.22 (1H, dd, $J_{5,6}$=4.4 Hz, $J_{6,6'}$=8.0 Hz, H-5), 3.40 (1H, t, $J_{5,6'}$=8.0 Hz, H-6), 3.52 (1H, dd, H-6'), 0.12 (9H, s, SiMe), 1.02 (3H, d, C-Me), 3.62 (3H, s, OMe) and 7.2—7.6 (15H, m, Tr).

Methyl 2,3-Dideoxy-2,2-di-*C*-methyl-4-*O*-trimethylsilyl-α-D-*glycero*-hex-3-enopyranoside (21). Treatment of **2** as described above gave **21** quantitatively, which was characterized only by ^{1}H NMR δ=4.62 (1H, s, H-1), 4.68 (1H, bs, H-3), 3.0—3.4 (2H, m, H-5 and H-6'), 3.84 (1H, dd, $J_{5,6}$=4.0 Hz, $J_{6,6'}$=6.6 Hz, H-6), 0.18 (9H, s, SiMe), 0.98 and 1.00 (each 3H, each s, C-Me), 3.56 (3H, s, OMe), and 7.2—7.6 (15H, m, Tr).

Methyl 3,4-Dideoxy-4,4-di-*C*-methyl-2-*O*-trimethylsilyl-6-*O*-trityl-α-D-*glycero*-hex-2-enopyranoside (23). Treatment of **3**[16] as described above gave **23** quantitatively, which was characterized only by ^{1}H NMR δ=4.70 (1H, s, H-1), 4.94 (1H, s, H-3), 3.92 (1H, dd, $J_{5,6}$=3.8 Hz, $J_{5,6'}$=6.2 Hz, H-5), 3.36 (1H, dd, $J_{6,6'}$=7.0 Hz, H-6), 3.28 (1H, dd, H-6'), 0.18 (9H, s, SiMe), 0.76 and 0.84 (each 3H, each s, C-Me), 3.66 (3H, s, OMe) and 7.2—7.6 (15H, m, Tr).

Methyl 6-*O*-Benzyl-2,3-di-*O*-methyl-4-*C*-methyl-α-D-galactopyranoside (13). Swern oxidation of **12**,[20] as described for **14**, gave the corresponding 4-ulose in 84% yield. To a solution of methylmagnesium iodide (2.17 mmol) in ether (5 ml) was added the ulose (227 mg, 0.72 mmol) at 0 °C. After 12 h at the same temperature, the solution was mixed with saturated aqueous ammonium chloride and extracted with dichloromethane. The extract was washed with aqueous sodium chloride, dried over magnesium sulfate, and evaporated. The crude mixture of products was fractionated on a column of silica gel with hexane-ethanol (18:1) to give **13** (187 mg, 81%) and its 4-epimer (23 mg, 10%).

13: Syrup, $[\alpha]_D^{20}$ +62.5° (*c* 0.86, $CHCl_3$); ^{1}H NMR δ=4.96 (1H, d, $J_{1,2}$=3.6 Hz, H-1), 3.24 (1H, dd, H-2), 3.6—3.8 (4H, m, H-3, H-5, H-6 and H-6'), 1.06 (3H, s, C-Me), 3.44, 3.52, and 3.60 (each 3H, each s, OMe), 4.64 (2H, bs, $CH_2C_6H_5$) and 7.44 (5H, bs, C_6H_5).

Found: C, 63.08; H, 7.56%. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46%.

4-Epimer of **13**: Syrup $[\alpha]_D^{20}$ +43.1° (*c* 0.81, $CHCl_3$);

^{1}H NMR δ=5.02 (1H, d, $J_{1,2}$=3.6 Hz, H-1), 3.26 (1H, dd, $J_{2,3}$=6.6 Hz, H-2), 3.6—3.8 (4H, m, H-3, H-5, H-6, and H-6′), 1.32 (3H, s, C-Me), 3.68 (6H, s, OMe), 4.62 (2H, bs, $CH_2C_6H_5$) and 7.44 (5H, bs, C_6H_5).

Found: C, 62.66; H, 7.28%. Calcd for $C_{17}H_{24}O_6$: C, 62.95%; H, 7.46%.

When this reaction was performed at −78 °C, only **13** was obtained in 90% yield. Furthermore, treatment of the ulose with methyllithium in ether at −78 °C for 5 h and at room temperature overnight, gave **13** and its 4-epimer 42 and 36% yields, respectively.

Methyl 2,3,4-Tri-*O*-methyl-4-*C*-methyl-α-D-*galacto*-hexodialdo-pyranoside-(1,5) (14). Treatment of **13** with sodium hydride in *N,N*-dimethylformamide for 4 h and then with methyl iodide at 0 °C, gave the 4-*O*-methyl derivative in 94% yield, which was hydrogenolyzed under 3 atm (1 atm=1.01×10^5 Pa) in the presence of 10% palladium on carbon in methanol and water (10 : 1) at room temperature overnight to give the *O*-debenzylated derivative in 93% yield.

To a solution of oxalyl dichloride (0.92 ml, 10.8 mmol) in dichloromethane (30 ml) was added a solution of dimethyl sulfoxide (0.94 ml, 12.9 mmol) in dichloromethane (10 ml) at −78 °C and then the *O*-debenzylated derivative (2.1 g, 8.5 mmol) at −78 °C. The reaction mixture was kept at −78 °C for 30 min, quenched with triethylamine, poured into water, and extracted with chloroform. The extract was washed with water, dried over magnesium sulfate, and evaporated to give **14** (1.87 g, 90%) as colorless syrup, $[\alpha]_D^{20}$ +41.6° (*c* 1.30, $CHCl_3$); ^{1}H NMR δ=5.02 (1H, d, $J_{1,2}$=3.0 Hz, H-1), 3.28 (1H, dd, $J_{2,3}$=8.0 Hz, H-2), 3.62 (1H, d, H-3), 3.88 (1H, bs, H-5), 9.62 (1H, bs, H-6), 1.40 (3H, s, C-Me) and 3.38, 3.42, 3.48, and 3.54 (each 3H, each s, OMe).

Found: C, 53.45; H, 8.27%. Calcd for $C_{11}H_{20}O_6$: C, 53.22; H, 8.12%.

Reaction of Enones 2—5 with Lithium Dimethylcuprate-(I). To a suspension of copper(I) iodide (0.68 g, 3.6 mmol) in ether (10 ml) was added methyllithium (6 ml of 1.2 M ethereal solution, 7.2 mmol) at 0 °C under an atmosphere of argon, and then a solution of an enone (1.2 mmol) in ether (5 ml). The reaction mixture was kept at 0 °C for 4 h and processed in the same manner as described for **13** to give a mixture of products, which was fractionated on a column of silica gel with the solvent system given below in individual cases.

Reaction of Enones 2—5 with Lithium (Cyano)dimethylcuprate(I). To a suspension of copper(I) cyanide (424 mg, 4.73 mmol) in ether (13 ml), was added methyllithium (12.9 ml of 1.2 M ethereal solution, 9.5 mmol) at −78 °C. When the solution became clear, a solution of an enone (1.58 mmol) in ether (6.5 ml) was added, and the same temperature was kept for 4 h. The reaction mixture was processed in the same manner as described above and the results are summarized in Table 1.

A Mixture 15 of Methyl 4,7-Dideoxy-2,3-di-*O*-methyl-4-*C*-methyl-α-D-*xylo*-hept-4-enopyranoside and Its 6-Epimer. The reactions of **4** as described above gave a mixture of unseparable two epimers **15** and methyl 4-deoxy-2,3-di-*O*-methyl-4-*C*-methyl-β-L-*threo*-hex-4-enopyranoside (**17**), which were separated on a silica gel column with hexane-ethyl acetate (3 : 1). The epimeric mixture **15** was only characterized by ^{1}H NMR.

15: Syrup, ^{1}H NMR (major): δ=4.80 (d, $J_{1,2}$=2.0 Hz, H-1), 3.46 (H-2), 3.62 (bd, $J_{2,3}$=6.6 Hz, H-3), 4.54 (bq, $J_{6,7}$=6.4 Hz, H-6), 1.36 (d, H-7), 1.58 (bs, C-Me) and 3.46 (s, OMe), (minor): δ=4.76 (d, $J_{1,2}$=2.0 Hz, H-1), 1.34 (d, H-7) and 3.38 (s, OMe).

Furthermore, conventional acetylation of **15** with acetic anhydride and pyridine gave **16** as colorless syrup, **16**: ^{1}H NMR (major) δ=4.96 (d, H-1), 3.56 (H-2), 3.74 (d, $J_{2,3}$=8.8 Hz, H-3), 5.76 (q, H-6), 1.74 (bs, C-Me), 1.42 (d, H-7), 2.08 (s, OAc) and 3.56 (bs, OMe), (minor) δ=4.94 (d, $J_{1,2}$=2.2 Hz, H-1), 3.78 (d, H-3), 5.76 (q, $J_{6,7}$=6.2 Hz, H-6), 1.40 (d, H-7) and 3.50 (s, OMe).

17: Syrup, $[\alpha]_D^{23}$ +28.5° (*c* 0.43, $CHCl_3$), IR (NaCl) 3500 (OH) and 1610 cm^{-1} (C=C); ^{1}H NMR δ=4.76 (1H, d, $J_{1,2}$=3.6 Hz, H-1), 3.22 (1H, dd, $J_{2,3}$=5.8 Hz, H-2), 3.68 (1H, d, H-3), 3.38 (2H, bs, H-6), 1.74 (3H, bs, C-Me) and 3.42, 3.44, and 3.50 (each 3H, each s, OMe).

Found: C, 54.88; H, 8.27%. Calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31%.

Methyl 2,3-Dideoxy-2,2-di-*C*-methyl-6-*O*-trityl-α-D-*glycero*-hexopyranosid-4-ulose (18). The reactions of **2** with lithium methylcuprates(I) as described above gave a mixture of **18** and its 5-epimer, methyl 2,3-dideoxy-2,2-di-*C*-methyl-6-*O*-trityl-β-L-*glycero*-hexopyranosid-4-ulose, which were separated on a column of silica gel with hexane-ethyl acetate (15 : 1).

18: Syrup, $[\alpha]_D^{23}$ +104.1° (*c* 2.2, $CHCl_3$); IR (NaCl) 1740 cm^{-1} (C=O). The ^{1}H and ^{13}C NMR data are given in Table 3.

Found: C, 78.25; H, 7.09%. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02%.

5-Epimer of **18**: Syrup, $[\alpha]_D^{23}$ +38.6° (*c* 1.41, $CHCl_3$); IR (NaCl) 1740 cm^{-1} (C=O), ^{1}H NMR δ=4.36 (1H, s, H-1), 2.12, and 2.48 (each 1H, each d, J=16.0 Hz, H-3 and H-3′), 4.12 (1H, dd, $J_{5,6}$=3.6 Hz, $J_{5,6'}$=5.4 Hz, H-5), 3.4—3.6 (2H, m, H-6), 1.02 and 1.00 (each 3H, each s, C_2-Me), 3.38 (3H, s, OMe) and 7.1—7.5 (m, Tr).

Found: C, 78.05; H, 7.02%. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02%.

Methyl 3,4-Dideoxy-4,4-di-*C*-methyl-6-*O*-trityl-α-D-*glycero*-hexopyranosid-2-ulose (19). The reaction of **3** with lithium methylcuprates(I) as described above gave crude **19**, which was purified on a column of silica gel with hexane-ethyl acetate (10 : 1), syrup, $[\alpha]_D^{23}$ +27.1° (*c* 1.5, $CHCl_3$), IR (NaCl) 1740 cm^{-1} (C=O). The ^{1}H and ^{13}C NMR data are given in Table 3.

Found: C, 77.93; H, 7.24%. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02%.

Methyl 4,7-Dideoxy-2,3-di-*O*-methyl-4,4-di-*C*-methyl-α-D-*xylo*-heptopyranosid-6-ulose (20). The reactions of **5** with lithium methylcuprates(I) as described above gave crude **20**, which was purified on a column of silica gel with hexane-ethyl acetate (4 : 1), syrup, $[\alpha]_D^{23}$ +55.2° (*c* 0.44, $CHCl_3$), ^{1}H NMR δ=4.68 (1H, d, $J_{1,2}$=3.2 Hz, H-1), 3.4—3.6 (2H, m, H-2), 1.36 and 1.56 (each 3H, each s, C_4-Me), 1.82 (3H, s, C_6-Me), 3.52 (6H, s, OMe) and 3.46 (3H, s, OMe).

Found: C, 58.29; H, 9.20%. Calcd for $C_{12}H_{22}O_5$: C, 58.51; H, 9.00%.

Hydroborations of 21 and 23. (i) With Borane in Tetrahydrofuran. To a solution of a enol trimethylsilyl ether (503 mg, 1.0 mmol) in tetrahydrofuran (6.5 ml), was added calculated amount of borane (the amount given in Table 2, 1 M solution in tetrahydrofuran) at 0 °C under an atmosphere of argon. Being kept at room temperature for 6 h, the reaction mixture was poured into water (10 ml). To a separated organic layer was added, at 0 °C with vigorous stirring, 10%

aqueous sodium hydroxide (5 ml) and hydrogen peroxide (30%, 5 ml) and the stirring was continued at 45 °C for 30 min. The reaction mixture was extracted with chloroform and the extract was washed with aqueous sodium chloride, dried over magnesium sulfate, and evaporated to give a mixture of products as a colorless syrup. The mixture was acetylated conventionally with acetic anhydride (2 ml) and pyridine (3 ml). In the case of **21**, fractionation of the products on a column of silica gel with hexane-ethyl acetate (15 : 1) afforded **22**, **24**, and **25** in the yields given in Table 2, while in the case of **23** with hexane-ethyl acetate (25 : 1) **26**, **27**, and **28**.

(ii) With Sodium Borohydride and Titanium(III) Chloride. To a mixture of sodium borohydride (100 mg, 2.6 mmol) and 18-crown-6 (132 mg, 0.5 mmol) in tetrahydrofuran (10 ml) was added titanium(III) chloride (85 mg, 0.55 mmol), and the mixture was stirred at 30 °C for 1 h under argon. After the color of the solution turned to be dark violet, a solution of enol silyl ether (503 mg, 1.0 mmol) in tetrahydrofuran (5.5 ml) was added, and the mixture was stirred at the same temperature for 8 h. To the mixture was added methanolic sodium methoxide (3 ml of 3 M solution) and then 30% aqueous H_2O_2 (5 ml). Being kept at 40 °C for 1 h, the reaction mixture was processed in the same manner as described above.

(iii) With Sodium Borohydride and Cobalt(II) Chloride. To a suspension of cobalt(II) chloride (325 mg, 2.5 mmol) in tetrahydrofuran (8 ml), was added with stirring at 0 °C under argon sodium borohydride (195 mg, 5 mmol). After 1 h a solution of enol silyl ether (0.66 mmol) in tetrahydrofuran (3 ml) was added after stirring at room temperature for 1.5 h, and the mixture was stirred at room temperature for 8 h. The successive oxidation was performed as described for hydroboration with titanium(III) chloride and sodium borohydride.

(iv) With Disiamylborane. To a 0.6 M solution of disiamylborane (2 ml) in tetrahydrofuran was added a solution of enol silyl ether (503 mg, 1.0 mmol) in tetrahydrofuran (6 ml) at room temperature, and the mixture was stirred at room temperature for 8 h. The oxidation was performed in the same manner as described above.

(v) With 9-Borabicyclo[3.3.1]nonane (9-BBN). To a 0.5 M solution of 9-borabicyclo[3.3.1]nonane (2.4 ml) in tetrahydrofuran was added a solution of enol silyl ether (503 mg, 1.0 mmol) in tetrahydrofuran (5.5 ml). The mixture was heated under reflux for 6 h. The oxidation was performed in the same manner as described above.

Methyl 3,4-Di-*O*-acetyl-2-deoxy-2,2-di-*C*-methyl-6-*O*-trityl-α-D-*arabino*-hexopyranoside (24). Hydroboration of **21** with 3 equivalents of diborane in the same manner as described above gave a mixture of **24**, methyl 4-*O*-acetyl-2,3-dideoxy-2,2-di-*C*-methyl-6-*O*-trityl-α-D-*erythro*-hexopyranoside (**25**), and methyl 2,3,4-trideoxy-2,2-di-*C*-methyl-6-*O*-trityl-α-D-*glycero*-hex-3-enopyranoside (**22**).

24: Syrup, $[\alpha]_D^{23}$ +150.6° (*c* 1.2, $CHCl_3$), IR (NaCl) 1720 cm^{-1} (C=O). The ^1H and ^{13}C NMR data are given in Table 3.

Found: C, 72.11; H, 6.85%. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81%.

25: Syrup, $[\alpha]_D^{23}$ +13.7° (*c* 0.97, $CHCl_3$), IR (NaCl) 1720 cm^{-1} (C=O). The ^1H and ^{13}C NMR data are given in Table 3.

Found: C, 75.68; H, 7.50%. Calcd for $C_{30}H_{34}O_5$: C, 75.92; H, 7.22%.

22: Syrup, $[\alpha]_D^{23}$ +12.0° (*c* 1.14, $CHCl_3$), IR (NaCl) 1680 cm^{-1} (C=C), ^1H NMR δ=4.44 (1H, s, H-1), 5.62 (1H, bd, $J_{3,4}$=9.2 Hz, H-3), 5.58 (1H, bdd, $J_{4,5}$=4.6 Hz, H-4), 3.82 (1H, bdd, $J_{5,6}$=4.0 Hz, $J_{5,6'}$=6.8 Hz, H-5), 3.12 (2H, m, H-6), 1.02 and 1.10 (each 3H, each s, C_2-Me), 3.52 (3H, s, OMe) and 7.2—7.6 (15H, m, Tr).

Found: C, 80.96; H, 7.43%. Calcd for $C_{28}H_{30}O_3$: C, 81.13; H, 7.29%.

Methyl 2,3-Di-*O*-acetyl-4-deoxy-4,4-di-*C*-methyl-6-*O*-trityl-α-D-*xylo*-hexopyranoside (26) and Methyl 2,3-Di-*O*-acetyl-4-deoxy-4,4-di-*C*-methyl-6-*O*-trityl-α-D-*arabino*-hexpyranoside (28). Hydroboration of **23** in the same manner as described above gave **26**, **28**, and methyl 2-*O*-acetyl-3,4-dideoxy-4,4-di-*C*-methyl-6-*O*-trityl-α-D-*erythro*-hexopyranoside (**27**).

26: Syrup, $[\alpha]_D^{23}$ +91.5° (*c* 0.89, $CHCl_3$), IR (NaCl) 1700 and 1710 cm^{-1} (C=O). The ^1H and ^{13}C NMR data are given in Table 3.

Found: C, 72.02; H, 6.92%. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81%.

28: Syrup, $[\alpha]_D^{23}$ +113.1° (*c* 1.3, $CHCl_3$), IR (NaCl) 1720 cm^{-1} (C=O). The ^1H and ^{13}C NMR data are given in Table 3.

Found: C, 71.96; H, 6.79%. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81%.

27: Mp 128—130 °C, $[\alpha]_D^{23}$ +51.2° (*c* 1.2, $CHCl_3$), IR (NaCl) 1710 cm^{-1} (C=O), ^1H NMR δ=4.87 (1H, dd, $J_{1,2}$=3.4 Hz, $J_{1,3}$=0.6 Hz, H-1), 4.89 (1H, ddd, $J_{2,3}$=5.3 Hz, $J_{2,3'}$=13.3 Hz, H-2), 1.42 and 1.76 (each 1H, each dd, $J_{3,3'}$=11.5 Hz, H-3 and H-3'), 3.74 (1H, dd, $J_{5,6}$=3.8 Hz, $J_{5,6'}$=9.8 Hz, H-5), 3.10 (1H, dd, $J_{6,6'}$=9.8 Hz, H-6), 3.22 (1H, t, H-6'), 0.78 and 0.82 (each 3H, each s, C-Me), 2.16 (3H, s, OAc), 3.58 (3H, s, OMe) and 7.2—7.6 (m, Tr). The data for H-1, H-2, H-3, and H-3', were obtained by simulation.

Found: C, 75.63; H, 6.95%. Calcd for $C_{30}H_{34}O_5$: C, 75.92; H, 7.22%.

^1H NMR data of deacetylated **27**: δ=4.86 (1H, d, $J_{1,2}$=3.8 Hz, H-1), 3.58 (1H, dt, $J_{2,3}$=3.8 Hz, $J_{2,3'}$=6.2 Hz, H-2), 1.44 and 1.64 (each 1H, each dd, $J_{3,3'}$=12.0 Hz, H-3 and H-3'), 3.59 (1H, dd, $J_{5,6}$=4.0 Hz, $J_{5,6'}$=7.6 Hz, H-5), 3.14 (1H, dd, $J_{6,6'}$=7.6 Hz, H-6), 3.28 (1H, t, H-6'), 0.72 and 0.80 (each 3H, each s, C-Me), 3.60 (3H, s, OMe) and 7.2—7.6 (m, Tr).

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