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SYNTHESIS OF METHYL 2,3-*O*-D-GLYCOPYRANOSYLIDENE-α-D-MANNOPYRANOSIDES HAVING VARIOUS SUBSTITUENTS

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ABSTRACT

The title compounds were obtained by condensation of D-glucono-, D-galactono-, or L-*glycero*-D-*gluco*-heptono-1,5-lactones with methyl 2,3-di-*O*-(trimethylsilyl)-α-D-mannopyranosides having various substituents on C-4 and C-6, in the presence of trimethylsilyl trifluoromethanesulfonate as the catalyst. Except for a 6-acetoxyl group on a lactone component and a (*tert*-butyldiphenylsiloxy) group, the usual *C*-substituents, such as benzyloxy, allyloxy, azido, acyloxy, (methylthio)methoxy, and methoxy, did not prevent occurrence of this condensation.

INTRODUCTION

In the preceding paper[1], a new method for the synthesis of D-glucopyranosylidene acetals by the use of the trimethylsilyl trifluoromethanesulfonate as the catalyst was described, and it was shown that the reaction was accompanied by a side reaction when the D-glucono-1,5-lactone derivative had an acetyl group on O-6.

The new method has now been extended to preparation of the title compounds, and the effect, on the reaction, of various substituents on the lactone and diol component has been examined.

RESULTS AND DISCUSSION

Preparation of lactone components. — As the lactone components, 6-(benzyloxycarbonyl)amino- (**16**) and 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-D-glucono-1,5-lactone (**17**), 4-azido-2,3-di-*O*-benzyl-4-deoxy-D-glucono-1,5-lactone (**18**) and its 6-acetate (**19**), 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-D-galactono-1,5-lactone (**20**)

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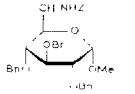
and its 4-azido-6-*O*-benzyl analog (**21**), and 7-*O*-acetyl-2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-L-*glycero*-D-*gluco*-heptono-1,5-lactone (**22**) were used, in addition to per-*O*-benzyl- (**14**) and 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-D-gluconono-1,5-lactone (**15**), already described[1].

Acetolysis of methyl 2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-α-D-glucopyranoside (**1**), which was obtained from the corresponding 6-azido-6-deoxy derivative[2], in 56% yield, by successive reduction and benzyloxycarbonylation, gave an anomeric mixture of the corresponding 1,*N*-diacetyl derivative (**2**) in 93% yield, and this was deacetylated with sodium methoxide to **3** in 65% yield. Oxidation of **3** with pyridinium chlorochromate[3], or bromine, gave **16** in 68 and 56% yield, respectively. Compound **17** was prepared in 94% yield by chlorochromate oxidation of the corresponding aldose[2], which was newly prepared from the 1-acetate (**4**). Partial deacetylation of 1,6-di-*O*-acetyl-4-azido-2,3-di-*O*-benzyl-4-deoxy-α,β-D-glucopyranose[4] with benzylamine gave the corresponding 6-acetate (**5**) in 94% yield. Oxidation of **5** with chlorochromate, and of deacetylated **5** with bromine, gave **19** and **18**, respectively, in 86 and 66% yield.

Mesylation of methyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranoside[5] gave the corresponding 6-mesylate (**6**) in quantitative yield. The usual treatment of **6** and of methyl 2,3,6-tri-*O*-benzyl-4-*O*-mesyl-α-D-glucopyranoside[6] with sodium azide in *N*,*N*-dimethylformamide gave the corresponding 6-azido (**7**) and 4-azido derivatives (**8**) in 71 and 77% yields, respectively. Acetolysis of **7** and **8** gave the corresponding 1-acetates (**9** and **11**) in 89 and 76% yields, respectively. Deacetylation of **9** and **11** with sodium methoxide gave the corresponding galactose derivatives (**10** and **12**), each in quantitative yield. Oxidation of **10** and **12** with pyridinium chloro-



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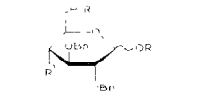
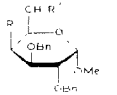
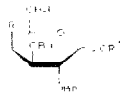


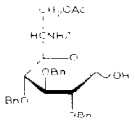
2 R¹ = OBn, R² = NHAc, R³ = Ac
3 R = OBn, R² = NHZ, R³ = H
4 R = OBn, R² = N₃, R³ = Ac
5 R = N₃, R² = OH, R³ = H



6 R¹ = OBn, R² = OMs
7 R = OBn, R² = N₃
8 R = N₃, R² = OBn



9 R = OBn, R² = N₃, R³ = Ac
10 R = OBn, R² = N₃, R³ = H
11 R = N₃, R² = OBn, R³ = Ac
12 R = N₃, R² = OBn, R³ = H



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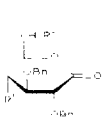
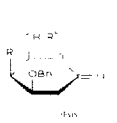


14 R¹ = R² = OBn
15 R = OAc, R² = OAc
16 R¹ = OBn, R² = NHZ
17 R = OBn, R² = N₃
18 R¹ = N₃, R² = OH
19 R = N₃, R² = Ac



20 R¹ = OBn, R² = N₃
21 R = N₃, R² = OBn

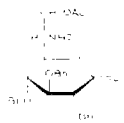


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TABLE I

^{1}H-N M R PARAMETERS OF D-GLUCONO-(**16–19**) AND D-GALACTONO-1,5-LACTONES (**20** AND **21**)

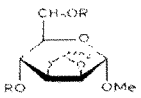
Compound	*Chemical shifts (δ)[a] and coupling constants (Hz)*							
	H-2 ($J_{2,3}$)	*H-3* ($J_{3,4}$)	*H-4* ($J_{4,5}$)	*H-5* ($J_{5,6}$)	*H-6* ($J_{5,6'}$)	*H-6'* ($J_{6,6'}$)	OCH_2Ph[b] {NCO_2CH_2Ph}	*OAc* {*OH*}
16	4.03d	3.78dd	3.49dd	4.4m	3.3–3.6m		4.85 and 4.49ABq, 4.59 and 4.47ABq,	—
	(5.5)	(6.0)	(9.0)				4.47 and 4.28ABq, {5.03s}	
17	4.10d	3.90dd	3.77dd	4.5oct	3.63dd	3.43dd	4.90 and 4.70ABq, 4.67 and 4.49ABq,	—
	(5.0)	(6.0)	(9.2)	(2.7)	(4.0)	(11.6)	4.62 and 4.49ABq	
18[c]	4.03d			3.4–4.0m			5.11 and 4.63ABq, 4.85 and 4.54ABq	{3.2bs}
	(7.0)							
19[c]	3.92d	3.60dd	3.40dd	3.78oct	4.27	4.08dd	5.04 and 4.58ABq, 4.69 and 4.49ABq	1.70s
	(6.7)	(8.0)	(10.0)	(3.0)	(4.5)	(12.2)		
20	4.47d	3.88dd	4.02t	4.20oct	3.62dd	3.39dd	5.22 and 4.82ABq, 5.04 and 4.67ABq,	—
	(9.5)	(2.0)	(2.0)	(6.6)	(7.0)	(10.0)	4.87 and 4.72ABq	
21	4.38d	4.00dd	4.25dd	4.2–4.3m	3.6–3.8m		5.21 and 4.78ABq, 4.78s, 4.60s	—
	(9.0)	(3.2)	(3.0)					

[a]Phenyl-proton signals commonly appeared at δ 7.1–7.5. [b]ABq showed coupling constants of 10–12 Hz. [c]Measured in benzene-d_6, and the others in chloroform-*d*.

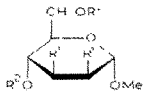
methane gave **20** and **21** in 86 and 68% yields, respectively. Partial deacetylation of 1,7-di-*O*-acetyl-2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-α,β-L-*glycero*-D-*gluco*-heptopyranose[7] with benzylamine gave **13** in 80% yield, and this was then oxidized to **22** in 85% yield.

Recently, the conformations of free (in dimethyl sulfoxide-d_6)[8] and peracetylated (in organic solvents)[9] D-glucono-1,5-lactone were assigned as $^4H_3$ ($J_{2,3}$ 8.5, $J_{3,4}$ 7.5, and $J_{4,5}$ 8.1 Hz) and a distorted half-chair ($J_{2,3}$ 8.6–8.7, $J_{3,4}$ 9.1–9.2, and $J_{4,5}$ 8.8–9.2 Hz), respectively. However, the ^{1}H-n.m.r. parameters of **16** and **17**, shown in Table I, indicate a sofa conformation in which C-4 is exoplanar. Also, the conformation of the D-galactono-1,5-lactones **20** and **21** is deduced to be a flattened $^4C_1$.

Preparation of 1,2-diol components. — As the diol components, the 4,6-di-*O*-benzyl[1] (**29**), 4,6-di-*O*-acetyl[10] (**30**), 4,6-di-*O*-benzoyl (**31**), 4,6-di-*O*-allyl (**32**), 4,6-di-*O*-(methylthio)methyl (**33**), and 4,6-di-*O*-(*tert*-butyldiphenylsilyl) (**34**) derivatives of methyl 2,3-di-*O*-(trimethylsilyl)-α-D-mannopyranoside were used. Reaction of methyl 2,3-*O*-isoporpylidene-α-D-mannopyranoside with allyl bromide–sodium hydride, with dimethyl sulfoxide–acetic acid–acetic anhydride, and with *tert*-butylchlorodiphenylsilane–imidazole[11] gave the corresponding 4,6-di-*O*-allyl (**23**), 4,6-di-*O*-(methylthio)methyl (**24**), and 4,6-di-*O*-(*tert*-butyldiphenylsilyl) derivatives (**25**) in 95, 52, and 95% yield, respectively. Partial hydrolysis of **23–25** with 90% acetic acid gave the corresponding *O*-deisopropylidenated products (**26–28**) in quantitative yield. Treatment of methyl 4,6-di-*O*-benzoyl-α-D-mannopyranoside[12] and of **26–28** in dichloromethane with hexamethyldisilazane in the presence of trifluoroacetic acid as the catalyst gave the corresponding 2,3-di-*O*-(trimethylsilyl) derivatives (**31–34**) in quantitative yield.



23 R = $CH_2CH{=}CH_2$
24 R = CH_2SMe
25 R = $Si(CMe_3)Ph_2$

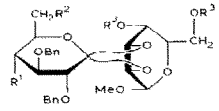


26 R^1 = OH, R^2 = $CH_2CH{=}CH_2$
27 R^1 = OH, R^2 = CH_2SMe
28 R^1 = OH, R^2 = $Si(CMe_3)Ph_2$
29 R^1 = $OSiMe_3$, R^2 = Bn
30 R^1 = $OSiMe_3$, R^2 = Ac
31 R^1 = $OSiMe_3$, R^2 = Bz
32 R^1 = $OSiMe_3$, R^2 = $CH_2CH{=}CH_2$
33 R^1 = $OSiMe_3$, R^2 = CH_2SMe
34 R^1 = $OSiMe_3$, R^2 = $Si(CMe_3)Ph_2$

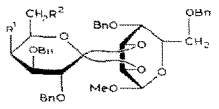
Methyl 2,3-O-D-glycopyranosylidene-α-D-mannopyranosides. — As already described[1], a lactone component in dichloromethane was condensed with 1.3–1.5 equivalents of a diol component for 2–3 days at room temperature in the presence of $Me_3SiO_3SCF_3$ (5–10 mol%), and the products were separated as far as possible by various types of chromatography.

The reaction of **29** with the lactone components **14–22** gave the orthoesters **35–40** and **46–48**, respectively, as summarized in Table II. The ratio of the two isomers in the products was estimated from the intensities of the signals of the orthoester carbon atom in the ^{13}C-n.m.r. spectra when the compounds were inseparable. In the case of **48**, the two isomers could be separated as *O*-deacetylated compounds (**49a,b**) by treatment with methanolic ammonia. In the case of **19**, having a 6-*O*-acetyl group, the yield of the product (**40**) was again lower, as observed with **15**, and the *O*-deacetylated product (**39**) was produced as a by-product; the acetyl group may have been removed as trimethylsilyl acetate[13]. Interestingly, compound **18**, having a free hydroxyl group at C-6 gave a rather better yield than **19**. The 7-*O*-acetyl group in **22** showed no important effect on this condensation.

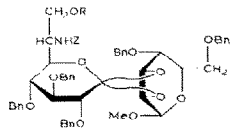
From the yields given in Table II, the order of substituents on D-glucono-1,5-lactone favorable to formation of orthoesters is $N_3 \geq OBn \cong NHZ > OH \gg OAc$ for substituents at C-6, and $N_3 > OBn$ for those at C-4, and the D-galactono-1,5-lactone derivative **20** gave a better yield than the corresponding D-glucono-1,5-lactone derivative (**17**). The result for **22** indicates that the new method will be applicable for the synthesis of such natural products as[14] destomycin B.



35 R^1 = R^2 = OBn, R^3 = Bn
36 R^1 = OBn, R^2 = OAc, R^3 = Bn
37 R^1 = OBn, R^2 = NHZ, R^3 = Bn
38 R^1 = OBn, R^2 = N_3, R^3 = Bn
39 R^1 = N_3, R^2 = OH, R^3 = Bn
40 R^1 = N_3, R^2 = OAc, R^3 = Bn
41 R^1 = R^2 = OBn, R^3 = Ac
42 R^1 = R^2 = OBn, R^3 = Bz
43 R^1 = R^2 = OBn, R^3 = $CH_2CH{=}CH_2$
44 R^1 = R^2 = OBn, R^3 = CH_2SMe
45 R^1 = R^2 = OBn, R^3 = H



46 R^1 = OBn, R^2 = N_3
47 R^1 = N_3, R^2 = OBn



48 R = Ac
49 R = H

The results of similar reactions of **14** with various methyl 1,2-di-*O*-(trimethylsilyl)-α-D-mannopyranosides (**30–34**) are summarized in Table III. Two isomeric products (**41** and **42**) from **30** and **31** could not be separated, but, they were successfully separated after conversion into the same compound (**45**) by deacylation with methanolic ammonia. The condensation product (**43**) from **32** could be separated by flash column-chromatography. It is characteristic that the reaction of **14** with **33** gave only one isomer. The reaction of **14** with **34** gave a complex mixture of products, indicating that the *O*-*tert*-butyldiphenylsilyl group is not a suitable protecting-group, probably due to gradual removal by the catalyst used. As expected from the mechanism already described[1], acyl groups on a 1,2-diol component

TABLE II

METHYL 2,3-*O*-D-GLYCOPYRANOSYLIDENE-α-D-MANNOPYRANOSIDES

Aldono-1,5-lactone	*Methyl α-D-mannoside*	*Products*	*Yield (%)*	*^{13}C-n.m.r. data (p.p.m.) in $CDCl_3$*			*Ratio[a] (to 1.0)*	$[\alpha]_D$	
				C-1'	*C-1*	*C=O*		*(degrees)*	c[b]
14[c]	**29**	**35a**	44.8	119.0	97.4	—	1.0	+10	0.2
		35b	26.6	120.4	97.5	—	0.6	+28	1.06
15[c]	**29**	**36**[d]	30.0	118.9	97.3	170.5	1.0	+36	0.87
				120.4	97.9		1.0		
16	**29**	**37**[d]	70.2	118.9	97.3	156.3	1.0	+23	1.92
				120.4	97.5		1.3		
17	**29**	**38**[d]	82.2	118.8	97.4	—	1.0	+43	2.05
				120.2	97.6	—	1.0		
18	**29**	**39a**	28.6	119.0	97.3	—	1.0	+84	0.94
		39b	26.0	120.4	97.6	—	0.9	+100	1.08
19	**29**	**40**[d]	28.3	118.8	97.3	170.6	1.0	+72	7.9
				120.2		170.4	0.9		
		39[d]	14.0	119.0	97.3	—	1.0	—	—
				120.4	97.6		1.0		
20	**29**	**46a**	55.4	119.4	97.4	—	1.0	+19	0.84
		46b	32.8	120.9	97.6	—	0.6	+29	0.90
21	**29**	**47a**	31.3	119.2	97.2	—	1.0	+28	4.8
		47b	38.3	120.5	99.6	—	1.2	+32	4.2
22	**29**	**48**[d]	52.0	118.8	97.3	170.8	1.0	+25	1.98
				120.6	97.6	155.7	1.0		
—	—	**49a**[e]	—	118.8	97.3	156.2	—	+36	0.51
		49b[e]		120.5	97.8	156.1		+46	0.72

[a]Ratios were calculated from actual yields, or from the intensities of the C-1' signal in the spectra of the mixtures. [b]Measured in $CHCl_3$. [c]Data cited from ref. 1. [d]A mixture of two isomers. [e]Compound **49** was obtained from **48** by deacetylation.

TABLE III

METHYL 2,3-*O*-D-GLYCOPYRANOSYLIDENE-α-D-MANNOPYRANOSIDES

Glucono-1,5-lactone	*Methyl α-D-mannoside*	*Products*	*Yield (%)*	*^{13}C-n.m.r. data (p.p.m.) in $CDCl_3$*			*Ratio[a] (to 1.0)*	$[\alpha]_D$	
				C-1'	*C-1*	*C=O*		*(degrees)*	*c[b]*
14	**30**	**41**[c]	59.2	119.3	97.6	169.5	1.0	+29.8	1.59
				120.8	97.7	170.5	2.5		
14	**31**	**42**[c]	60.0	119.4	97.6	165.1	1.0	+31.4	1.26
				120.8		166.0	2.2		
14	**32**	**43a**	46.2	118.9	97.5	—	1.0	+30.5	1.10
		43b	37.0	120.3	97.3	—	0.8	+39.5	1.89
14	**33**	**44**	61.3	119.1	97.9	—	1.0	+42.9	0.65
				—	—	—	0		
—	—	**45a**[d]	—	119.0	97.3	—	—	+6.5	1.81
—	—	**45b**[d]	—	120.2	97.7	—	—	+42.0	1.78

[a]Ratios were calculated from actual yields of two isomers, or from the intensities of the C-1' signal in the spectra of the mixtures. [b]Measured in $CHCl_3$. [c]A mixture of two isomers. [d]Compound **45** was obtained from **41** or **42** by deacetylation.

caused no side reaction. It is obvious that the usual protecting-groups for the diol component can be used in this condensation, except for *O*-silyl groups.

In both Tables II and III, two isomers were distinguished by means of the chemical shift of the orthoester carbon atoms (C-1'). One isomer possesses lower (δ 120.2–120.9), and the other higher (δ 118.8–119.4), chemical shifts. Interestingly, the former isomers always have higher values of specific optical rotation than the latter. It was reported[15] that the chemical shift of the (*R*)-orthoester carbon atom of destomycin A, in which destomic acid lactone is linked to the *cis*-diol grouping at C-2 and C-3 of a D-talopyranoside residue, is 121.2 p.p.m.[16]. Therefore, the absolute configurations of the two isomers herein described may be tentatively assigned as (*R*) and (*S*), respectively.

These absolute configurations would be controlled by two factors in the reaction pathway already given[1]: *i.e.*, (*i*) which one of the trimethylsilyl groups on O-2 and O-3 in **29–34** forms a glycosidic bond first; and (*ii*) from which side of the plane of the 1,5-lactone ring the ring-closure (to afford a spiro, cyclic ring) occurs. It is characteristic that diol components having electron-withdrawing substituents at C-4 and C-6 gave the (*R*) isomer preponderantly, whereas those having electron-releasing substituents mainly gave the (*S*) isomer. This fact indicates a possibility for the stereoselective formation of the (*R*) or the (*S*) isomer.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Solutions were evaporated under diminished pressure at a bath temperature not exceeding 50°. Optical rotations were measured in a 0.5-dm tube with a Carl Zeiss LEP-Al polarimeter for solutions in chloroform, unless stated otherwise. I.r. spectra were recorded with a Hitachi model EPI-G2 spectrometer. ^{1}H-N.m.r. spectra were recorded with a JEOL SP-100 spectrometer for solutions in chloroform-*d* containing tetramethylsilane as the internal reference. ^{13}C-N.m.r. data were recorded at 30° with a JEOL JNM-FX-100 spectrometer, operated in the pulse, Fourier-transform, proton-noise-decoupled mode, at 25.15 MHz, for solutions in chloroform-*d* containing tetramethylsilane. Mass spectra were recorded with a Hitachi model M-80 spectrometer (ion voltage, 70 eV).

Methyl 2,3,4-tri-O-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-α-D-glucopyranoside (**1**). — A solution of methyl 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-α-D-glucopyranoside[2] (5.0 g, 10.2 mmol) in methanol (100 mL) was hydrogenolyzed in the presence of platinum oxide (0.1 g), the catalyst filtered off, and the filtrate evaporated. To a solution of the dried, residual syrup in benzene (30 mL) and triethylamine (2.5 mL) was added benzyl chloroformate (1.75 mL), dropwise at 0° with stirring, and the mixture was kept overnight at room temperature. The mixture was poured into a cold, saturated solution of sodium hydrogencarbonate, and extracted with chloroform. The extract was washed with water, dried, and evaporated, to give **1**, which was purified on a column of silica gel (12:6:5 benzene–

hexane–acetone); yield, 3.42 g (55.9%); m.p. 88.5–89.7°, $[\alpha]_D$ +10.9° (*c* 1.08); ν_{max}^{KBr} 1700 and 1555 cm^{-1} (urethan); ^{1}H-n.m.r. (C_6D_6): δ 7.0–7.4 (m, 20 H, 4 Ph), 5.10 (s, 2 H, CO_2CH_2Ph), 4.36–5.04 (m, 6 H, 3 CH_2Ph), 4.50 (d, $J_{1,2}$ 3.3 Hz, H-1), 4.16 (dd, $J_{2,3}$ 9.2, $J_{3,4}$ 9.0 Hz, H-3), 3.39 (dd, H-2), 3.32 (dd, $J_{4,5}$ 9.2 Hz, H-4), 3.3–3.8 (m, 3 H, H-5,6), and 3.03 (s, 3 H, OMe).

Anal. Calc. for $C_{36}H_{39}NO_7$: C, 72.34; H, 6.58; N, 2.34. Found: C, 72.23; H, 6.57; N, 2.05.

1-O-Acetyl-6-(benzyloxycarbonyl)acetamido-2,3,4-tri-O-benzyl-6-deoxy-α,β-D-glucopyranose (**2**). — To a solution of **1** (3.21 g, 5.36 mmol) in chloroform (4.3 mL) and acetic anhydride (6.7 mL) was added, dropwise, conc. sulfuric acid (0.3 mL) at 0° with stirring. The mixture was kept for 3 h at room temperature, poured into ice–water, made neutral with sodium hydrogencarbonate, and then extracted with chloroform. The extract was washed with water, dried, and evaporated, to give syrupy **2**, which was purified on a column of silica gel (3:7 ether–hexane); yield 3.33 g (93.0%; $\alpha:\beta$ = 5:1); $[\alpha]_D$ +47.6° (*c* 1.74); ν_{max}^{NaCl} 1745 (ester) and 1700 cm^{-1} (urethan); ^{1}H-n.m.r. (C_6D_6): α anomer, δ 7.0–7.4 (m, 20 H, 4 Ph), 6.35 (d, $J_{1,2}$ 3.3 Hz, H-1), 4.28–5.12 (m, 8 H, 4 CH_2Ph), 3.99 (t, $J_{2,3} = J_{3,4}$ 9.2 Hz, H-3), 3.44 (dd, H-2), 3.25 (t, $J_{4,5}$ 9.2 Hz, H-4), 3.4–4.0 (m, 3 H, H-5,6), 2.35 (s, 3 H, NAc), and 1.60 (s, 3 H, Ac); β anomer, δ 7.0–7.4 (m, 20 H, 4 Ph), 5.60 (d, $J_{1,2}$ 8.0 Hz, H-1), 3.2–5.1 (m, 14 H, H-2,3,4,5,6 and 4 CH_2Ph), 2.42 (s, 3 H, NAc), and 1.55 (s, 3 H, Ac).

Anal. Calc. for $C_{39}H_{41}NO_9$: C, 70.15; H, 6.19; N, 2.10. Found: C, 70.34; H, 6.23; N, 2.11.

2,3,4-Tri-O-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-α,β-D-glucopyranose (**3**). — To a solution of **2** (3.10 g, 4.64 mmol) in methanol (70 mL) was added 0.1M methanolic sodium methoxide (4 mL). The mixture was kept for 1.5 h at room temperature, passed through a column of Dowex 50-W X-8 (H^+) resin (10 mL), and the effluent evaporated to give syrupy **3**, which was purified on a column of silica gel (30:15:4 benzene–hexane–acetone); yield 1.77 g (65.2%, $\alpha:\beta$ = 30:1); $[\alpha]_D$ +12.3° (*c* 1.09); ν_{max}^{NaCl} 1710 and 1520 cm^{-1} (urethan); ^{1}H-n.m.r. (C_6D_6) of α anomer: δ 7.0–7.4 (m, 20 H, 4 Ph), 5.08 (s, 2 H, CO_2CH_2Ph), 4.4–5.1 (m, 6 H, 3 CH_2Ph), 4.75 (d, $J_{1,2}$ 4.0 Hz, H-1), 4.15 (t, $J_{2,3} = J_{3,4}$ 9.5 Hz, H-3), and 3.3–4.2 (m, 5 H, H-2,4,5,6).

Anal. Calc. for $C_{35}H_{37}NO_7$: C, 72.02; H, 6.39; N, 2.40. Found: C, 71.73; H, 6.39; N, 2.40.

1-O-Acetyl-6-azido-2,3,4-tri-O-benzyl-6-deoxy-α,β-D-glucopyranose (**4**). — Acetolysis of methyl 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-α-D-glucopyranoside (24.8 g, 50.7 mmol) with acetic anhydride (50 mL) and conc. sulfuric acid (0.5 mL), as described for **2**, gave syrupy **4** ($\alpha:\beta$ = 10:1) in 94.6% yield; $[\alpha]_D$ +77.7° (*c* 10.9); ν_{max}^{NaCl} 2110 (azide) and 1750 cm^{-1} (ester); ^{1}H-n.m.r.: α anomer, δ 7.3–7.5 (m, 15 H, 3 Ph), 4.65–5.16 (m, 6 H, 3 CH_2Ph), 6.47 (d, $J_{1,2}$ 4.0 Hz, H-1), 3.8–4.0 (m, H-5), 3.96 (t, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 3.66 (dd, H-2), 3.3–3.7 (m, 3 H, H-4,5,6), and 2.12 (s, 3 H, Ac); β anomer, δ 7.3–7.5 (m, 15 H, 3 Ph), 4.39–5.02 (m,

6 H, 3 CH_2Ph), 5.61 (d, $J_{1,2}$ 8.0 Hz, H-1), 4.00 (dd, $J_{2,3}$ 9.6 Hz, H-2), 3.4–3.8 (m, 3 H, H-3,4,5), 3.59 (dd, $J_{5,6}$ 6.8, $J_{6,6'}$ 15.0 Hz, H-6), 3.15 (dd, $J_{5,6'}$ 8.6 Hz, H-6'), and 2.04 (s, 3 H, Ac).

Anal. Calc. for $C_{29}H_{31}N_3O_6$: C, 67.29; H, 6.04; N, 8.12. Found: C, 67.05; H, 6.07; N, 8.01.

6-O-Acetyl-4-azido-2,3-di-O-benzyl-4-deoxy-α,β-D-glucopyranose (**5**). — A solution of 1,6-di-*O*-acetyl-4-azido-2,3-di-*O*-benzyl-4-deoxy-α,β-D-glucopyranose[2] (237 mg, 0.50 mmol) in benzylamine (0.5 mL) was stirred for 30 min at room temperature, poured into M hydrochloric acid, and extracted with chloroform. The usual processing of the extract, and separation of the products by preparative t.l.c. (2:1 hexane–ethyl acetate), gave **5** ($\alpha:\beta$ = 4:1) in 94.1% yield: $[\alpha]_D$ +10.2° (*c* 1.06); ν_{max}^{NaCl} 2110 (azide) and 1750 cm^{-1} (ester).

Anal. Calc. for $C_{22}H_{25}N_3O_6$: C, 61.81; H, 5.90; N, 9.83. Found: C, 62.06; H, 5.79; N, 9.78.

Preparation of substituted D-*glucono-1,5-lactones* (**16–19**). — Oxidation of C-1 of D-glucopyranoses was conducted by three methods. The ^{1}H-n.m.r. parameters are summarized in Table I.

(*i*) *Pyridinium chlorochromate oxidation.* To a stirred solution of **3** (0.85 g, 1.45 mmol) in dry dichloromethane was added pyridinium chlorochromate (0.63 g). The mixture was stirred for 23 h at room temperature, poured into ether (100 mL), and the insoluble material filtered off. The filtrate was evaporated, to give syrupy 2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-D-glucono-1,5-lactone (**16**; 579 mg, 68.4%), which was purified on a column of silica gel (20:10:1 benzene–hexane–acetone); $[\alpha]_D$ +55.7° (*c* 1.61); ν_{max}^{NaCl} 1760 (lactone), 1715, and 1620 cm^{-1} (urethan).

Anal. Calc. for $C_{35}H_{35}NO_7$: C, 72.27; H, 6.07; N, 2.41. Found: C, 72.53; H, 6.17; N, 2.11.

Similar oxidation of 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-α,β-D-glucopyranose[2] (4.0 g, 8.4 mmol) gave 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-D-glucono-1,5-lactone (**17**) in 94.1% yield (3.75 g); $[\alpha]_D$ +102.9° (*c* 11.2); ν_{max}^{NaCl} 2110 (azide) and 1750 cm^{-1} (lactone).

Anal. Calc. for $C_{27}H_{27}N_3O_5$: C, 68.48; H, 5.75; N, 8.87. Found: C, 68.55; H, 5.72; N, 8.74.

6-*O*-Acetyl-4-azido-2,3-di-*O*-benzyl-4-deoxy-D-glucono-1,5-lactone (**19**) was obtained by similar oxidation of **5** (203 mg, 0.48 mmol) in 79.7% yield (161 mg); $[\alpha]_D$ +88° (*c* 2.16); ν_{max}^{NaCl} 2110 (azide) and 1750 cm^{-1} (ester and lactone).

Anal. Calc. for $C_{22}H_{23}N_3O_6$: C, 62.16; H, 5.45; N, 9.88. Found: C, 61.98; H, 5.55; N, 9.79.

(*ii*) *Bromine oxidation.* To a suspension of **3** (0.74 g, 1.27 mmol) and barium carbonate (1.24 g) in water (7.5 mL) and 1,4-dioxane (15 mL) was added bromine (1 mL), with stirring. The mixture was stirred for 8 h at room temperature, the excess of bromine was removed with sodium sulfite, the insoluble material was filtered off, and the filtrate was extracted with chloroform. The extract was washed

with water, dried, and evaporated to give syrupy **16** (412 mg, 55.9%).

4-Azido-2,3-di-*O*-benzyl-4-deoxy-D-glucono-1,5-lactone (**18**) was obtained, by similar oxidation of 4-azido-2,3-di-*O*-benzyl-4-deoxy-α,β-D-glucopyranose[17] (1.62 g, 4.20 mmol), in 65.8% yield (1.06 g); $[\alpha]_D$ +92° (*c* 0.81); ν_{max}^{NaCl} 3400 (OH), 2100 (azide), and 1755 cm^{-1} (lactone).

Anal. Calc. for $C_{20}H_{21}N_3O_5$: C, 62.65; H, 5.52; N, 10.96. Found: C, 62.92; H, 5.48; N, 10.69.

(*iii*) *Dimethyl sulfoxide oxidation.* A solution of 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-α,β-D-glucopyranose[2] (268 mg, 0.56 mmol) in dimethyl sulfoxide (3.5 mL) and acetic anhydride (2.3 mL) was stirred for 17 h at room temperature, and poured into a solution of saturated sodium hydrogencarbonate. The mixture was extracted with chloroform, and the extract was washed with water, dried, and evaporated, to give **17** and the corresponding (methylthio)methyl glycoside in 54.7 (146 mg) and 16.9% (51 mg) yield (α:β = 2:1), respectively.

(Methylthio)methyl 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-α,β-D-glucopyranoside had $[\alpha]_D$ +29.3° (*c* 1.91); ν_{max}^{NaCl} 2110 cm^{-1} (azide).

Anal. Calc. for $C_{29}H_{33}N_3O_5S$: C, 65.03; H, 6.21; N, 7.85; S, 5.99. Found: C, 65.37; H, 6.09; N, 7.30; S, 5.86.

*Methyl 2,3,4-tri-*O*-benzyl-6-O-(methylsulfonyl)-α-*D*-galactopyranoside* (**6**). — To a solution of methyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranoside[6] (4.0 g, 8.62 mmol) in dry pyridine (15 mL) was added, dropwise, methanesulfonyl chloride (1 mL) with stirring at 0°. The mixture was stirred for 5 h at room temperature, and then the usual processing gave crude **6** (4.7 g), which was purified on a column of silica gel (9:1 hexane–ethyl acetate); $[\alpha]_D$ +18.6° (*c* 1.02); ^{1}H-n.m.r. (C_6D_6): δ 7.0–7.4 (m, 15 H, 3 Ph), 4.22–4.95 (m, 6 H, 3 CH_2Ph), 4.64 (d, $J_{1,2}$ 3.7 Hz, H-1), 4.28 (dd, $J_{5,6}$ 7.6, $J_{6,6'}$ 10.2 Hz, H-6), 4.09 (dd, $J_{2,3}$ 10.0 Hz, H-2), 4.01 (dd, $J_{5,6'}$ 4.6 Hz, H-6′), 3.88 (dd, $J_{3,4}$ 2.8 Hz, H-3), 3.78 (ddd, $J_{4,5}$ 1.2 Hz, H-5), 3.55 (dd, H-4), 3.31 (s, 3 H, OMs), and 3.16 (s, 3 H, OMe).

Anal. Calc. for $C_{29}H_{34}O_8S$: C, 64.18; H, 6.32; S, 5.91. Found: C, 64.12; H, 6.25; S, 6.02.

*Methyl 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-α-*D*-galactopyranoside* (**7**). — A suspension of **6** (4.7 g) and sodium azide (790 mg, 12.2 mmol) in *N*,*N*-dimethylformamide (35 mL) was heated for 20 h at 130°, poured into water, cooled, and extracted with ethyl ether. The extract was washed with water, dried, and evaporated. Separation of the products on a column of silica gel (9:1 hexane–ethyl acetate) gave **7** (2.98 g, 70.7%) and methyl 3,6-anhydro-2,4-di-*O*-benzyl-α-D-galactopyranoside (0.42 g, 13.7%).

Compound 7: $[\alpha]_D$ +10.7° (*c* 2.11); ν_{max}^{NaCl} 2100 cm^{-1} (azide); ^{1}H-n.m.r. (C_6D_6): δ 7.1–7.4 (m, 15 H, 3 Ph), 4.36–5.09 (m, 6 H, 3 CH_2Ph), 4.73 (d, $J_{1,2}$ 3.8 Hz, H-1), 4.18 (dd, $J_{2,3}$ 10.0 Hz, H-2), 3.92 (dd, $J_{3,4}$ 3.4 Hz, H-3), 3.3–3.7 (m, 3 H, H-4,5,6), 3.24 (s, 3 H, OMe), and 2.74 (dd, $J_{5,6'}$ 2.8, $J_{6,6'}$ 12.0 Hz, H-6′).

Anal. Calc. for $C_{28}H_{31}N_3O_5$: C, 68.70; H, 6.38; N, 8.58. Found: C, 68.32; H, 6.36; N, 8.54.

Methyl 3,6-anhydro-2,4-di-*O*-benzyl-α-D-galactopyranoside: $[\alpha]_D$ +19.2° (*c* 1.1); ^{1}H-n.m.r. (C_6D_6): δ 7.1–7.4 (m, 10 H, 2 Ph), 4.13–5.01 (m, 4 H, 2 CH_2Ph), 4.77 (d, $J_{1,2}$ 2.5 Hz, H-1), 4.55 (d, $J_{3,4}$ 0, $J_{4,5}$ 2.0 Hz, H-4), 4.50 (d, $J_{2,3}$ 5.4 Hz, H-3), 4.24 (dd, $J_{5,6}$ 2.7, $J_{5,6'}$ 0 Hz, H-5), 4.01 (dd, $J_{6,6'}$ 10.0 Hz, H-6), 3.86 (d, H-6'), 3.72 (dd, H-2), and 3.36 (s, 3 H, OMe); *m/z* 356 (M^+).

Anal. Calc. for $C_{21}H_{24}O_5$: C, 70.76; H, 6.79. Found: C, 70.82; H, 6.69.

Methyl 4-azido-2,3,6-tri-O-benzyl-4-deoxy-α-D-galactopyranoside (**8**). — Reaction of methyl 2,3,6-tri-*O*-benzyl-4-*O*-(methylsulfonyl)-α-D-glucopyranoside (4.1 g, 7.5 mmol) with sodium azide (730 mg), as described for **7**, gave **8** in 76.2% yield (2.82 g); $[\alpha]_D$ +1.7° (*c* 0.71); ν_{max}^{NaCl} 2110 cm^{-1} (azide); ^{1}H-n.m.r. (C_6D_6): δ 7.1–7.5 (m, 15 H, 3 Ph), 4.35–4.72 (m, 4 H, 2 CH_2Ph), 4.65 (d, $J_{1,2}$ 3.0 Hz, H-1), 4.39 (s, 2 H, CH_2Ph), 4.07 (dd, $J_{2,3}$ 10.0 Hz, H-2), 3.6–4.1 (m, 5 H, H-3,4,5,6), and 3.12 (s, 3 H, OMe).

Anal. Calc. for $C_{28}H_{31}N_3O_5$: C, 68.70; H, 6.38; N, 8.58. Found: C, 68.82; H, 6.34; N, 8.57.

1-O-Acetyl-6-azido-2,3,4-tri-O-benzyl-6-deoxy-α,β-D-galactopyranose (**9**). — Acetolysis of **7** (6.8 g, 13.9 mmol) with acetic anhydride (13 mL) and conc. sulfuric acid (0.3 mL), as described for **2**, gave syrupy **9** in 88.5% yield (6.36 g) (α:β = 2.8:1.0); $[\alpha]_D$ +51.0° (*c* 2.02); ν_{max}^{NaCl} 2110 (azide), and 1750 cm^{-1} (ester); ^{1}H-n.m.r.; α anomer: δ 7.2–7.4 (m, 15 H, 3 Ph), 6.36 (d, $J_{1,2}$ 4.0 Hz, H-1), 4.53–5.07 (m, 4 H, 2 CH_2Ph), 4.69 (s, 2 H, CH_2Ph), 4.15 (dd, $J_{2,3}$ 10.2 Hz, H-2), 3.8–4.0 (m, 3 H, H-3,4,5), 3.45 (dd, $J_{5,6}$ 6.8, $J_{6,6'}$ 12.3 Hz, H-6), 3.12 (dd, $J_{5,6'}$ 6.0 Hz, H-6'), and 2.12 (s, 3 H, Ac); β anomer: δ 7.3–7.5 (m, 15 H, 3 Ph), 5.62 (d, $J_{1,2}$ 8.0 Hz, H-1), 4.60–5.11 (m, 4 H, 2 CH_2Ph), 4.80 (s, 2 H, CH_2Ph), 3.99 (dd, $J_{2,3}$ 9.6 Hz, H-2), 3.86 (dd, 1 H, $J_{3,4}$ 2.7 Hz, H-4), 3.64 (dd, H-3), 3.5–3.7 (m, 1 H, H-5), 3.51 (dd, $J_{5,6}$ 6.0, $J_{6,6'}$ 14.3 Hz, H-6), 3.14 (dd, $J_{5,6'}$ 8.3 Hz, H-6'), and 2.03 (s, 3 H, Ac).

Anal. Calc. for $C_{30}H_{31}N_3O_6$: C, 67.29; H, 6.04; N, 8.12. Found: C, 67.41; H, 6.09; N, 8.01.

6-Azido-2,3,4-tri-O-benzyl-6-deoxy-α,β-D-galactopyranose (**10**). — Treatment of **9** (2.1 g, 4.06 mmol) with methanolic sodium methoxide (0.1M, 3 mL), as described for **3**, gave **10** in 98.0% yield (1.89 g); $[\alpha]_D$ +50.5° (*c* 1.09).

Anal. Calc. for $C_{27}H_{29}N_3O_5$: C, 68.19; H, 6.15; N, 8.84. Found: C, 68.22; H, 5.90; N, 8.75.

1-O-Acetyl-4-azido-2,3,6-tri-O-benzyl-4-deoxy-α,β-D-galactopyranose (**11**). — Acetolysis of **8** (6.10 g, 12.46 mmol) with acetic anhydride (20 mL) and conc. sulfuric acid (0.2 mL), as described for **2**, gave **11** and 1,6-di-*O*-acetyl-4-azido-2,3-di-*O*-benzyl-4-deoxy-α,β-D-galactopyranose[7] in yields of 4.9 g (76.0%, α:β = 10:1) and 1.1 g (18.8%, α:β = 20:1), respectively.

Compound **11**: $[\alpha]_D$ +35.6° (*c* 1.17); ν_{max}^{NaCl} 2110 (azide) and 1755 cm^{-1} (ester).

Anal. Calc. for $C_{29}H_{31}N_3O_6$: C, 67.29; H, 6.04; N, 8.12. Found: C, 67.46; H, 6.09; N, 8.02.

4-Azido-2,3,6-tri-O-benzyl-4-deoxy-α,β-D-galactopyranose (**12**). — Deacety-

lation of **11** (0.63 g, 1.22 mmol) with methanolic sodium methoxide (0.2M, 0.3 mL), as described for **3**, gave **12** in quantitative yield; $[\alpha]_D$ +20.2° (*c* 2.0); ν_{max}^{NaCl} 2110 cm^{-1} (azide).

Anal. Calc. for $C_{27}H_{29}N_3O_5$: C, 68.19; H, 6.15; N, 8.84. Found: C, 67.93; H, 6.24; N, 8.59.

*6-Azido-2,3,4-tri-*O*-benzyl-6-deoxy-*D*-galactono-1,5-lactone* (**20**). — Oxidation of **10** (4.0 g, 8.4 mmol) with pyridinium chlorochromate (4.33 g), as described for **16**, gave **20** in 86.1% yield (3.43 g); $[\alpha]_D$ +110° (*c* 0.69); ν_{max}^{NaCl} 2100 (azide) and 1760 cm^{-1} (lactone).

Anal. Calc. for $C_{27}H_{27}N_3O_5$: C, 68.48; H, 5.75; N, 8.87. Found: C, 68.29; H, 5.68; N, 8.92.

*4-Azido-2,3,6-tri-*O*-benzyl-4-deoxy-*D*-galactono-1,5-lactone* (**21**). — Oxidation of **12** (516 mg, 1.09 mmol) with pyridinium chlorochromate (700 mg) gave **21** in 76.7% yield (394 mg); $[\alpha]_D$ +61.4° (*c* 3.6); ν_{max}^{NaCl} 2110 (azide) and 1760 cm^{-1} (lactone).

Anal. Calc. for $C_{27}H_{27}N_3O_5$: C, 68.48; H, 5.75; N, 8.87. Found: C, 68.76; H, 5.81; N, 8.61.

*7-*O*-Acetyl-2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-*L*-glycero-*D*-gluco-heptono-1,5-lactone* (**22**). — Oxidation of **13** (0.90 g, 1.37 mmol) 2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-*L*-*glycero*-*D*-*gluco*-heptopyranose[8] (1.21 g, 2.0 mmol) with benzylamine (2.0 mL), as described for **5**, gave **13** in 79.9% yield (908 mg); $[\alpha]_D$ +20.6° (*c* 1.65); ν_{max}^{NaCl} 1730 and 1520 cm^{-1} (urethan).

Anal. Calc. for $C_{38}H_{41}NO_9$: C, 69.60; H, 6.30; N, 2.14. Found: C, 69.51; H, 6.22; N, 2.21.

*7-*O*-Acetyl-2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-*L*-glycero-*D*-gluco-heptono-1,5-lactone* (**22**). — Oxidation of **13** (0.90 g, 1.37 mmol) with pyridinium chlorochromate (0.85 g), as described for **16**, gave **22** in 84.8% yield (761 mg); $[\alpha]_D$ +54.7° (*c* 0.77); ν_{max}^{NaCl} 1750 (lactone and ester), 1720 and 1520 cm^{-1} (urethan).

Anal. Calc. for $C_{38}H_{39}NO_9$: C, 69.82; H, 6.01; N, 2.14. Found: C, 69.89; H, 6.05; N, 2.02.

*Methyl 4,6-di-*O*-allyl-2,3-*O*-isopropylidene-α-*D*-mannopyranoside* (**23**). — To a suspension of methyl 2,3-*O*-isopropylidene-α-D-mannopyranoside (1.53 g, 6.5 mmol) and sodium hydride (50%; 1.0 g, 21 mmol) in anhydrous *N*,*N*-dimethylformamide (20 mL) was added allyl bromide (2.40 g) dropwise. The mixture was stirred for 4 h at room temperature, poured into ice–water, and extracted with chloroform. The usual processing of the extract, and purification of the product by flash column-chromatography on silica gel (7:1 hexane–ethyl acetate) gave pure **23** as a syrup in 99.8% yield (2.05 g); $[\alpha]_D$ +108° (*c* 1.6); ^{1}H-n.m.r.: δ 5.7–6.1 (m, 2 H, 2 -CH=), 4.95–5.3 (m, 4 H, 2 $=CH_2$), 4.92 (s, H-1), 3.4–4.4 (m, 10 H, H-2,3,4,5,6 and 2 OCH_2), 3.38 (s, 3 H, OMe), and 1.52 and 1.35 (each s, 6 H, 2 CMe).

Anal. Calc. for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34. Found: C, 60.94; H, 8.50.

*Methyl 2,3-O-isopropylidene-4,6-di-O-[(methylthio)methyl]-α-*D*-mannopyranoside* (**24**). — To a solution of methyl 2,3-*O*-isopropylidene-α-D-mannopyranoside (1.99 g, 8.5 mmol) in anhydrous dimethyl sulfoxide (25 mL) was added a mixture of acetic anhydride (17 mL) and acetic acid (3 mL), with stirring. The solution was kept for 46 h at room temperature, poured into saturated sodium hydrogencarbonate, stirred overnight, and extracted with chloroform. The usual processing of the extract, and purification of the product by flash column-chromatography on silica gel (20:1 hexane–ethyl acetate), gave **24** as a syrup (1.57 g) in 52.1% yield; $[\alpha]_D$ +116° (*c* 5.2); ^{1}H-n.m.r.: δ 4.8–5.1 (ABq, 2 H, OCH_2S), 4.90 (s, H-1), 4.78 (s, 2 H, OCH_2S), 3.6–4.4 (m, 6 H, H-2,3,4,5,6), 3.43 (s, 3 H, OMe), 2.20 and 2.18 (each s, 6 H, 2 SMe), and 1.55 and 1.34 (each s, 6 H, 2 CMe).

Anal. Calc. for $C_{14}H_{26}O_6S_2$: C, 47.44; H, 7.39; S, 18.09. Found: C, 47.23; H, 7.16; S, 17.85.

*Methyl 4,6-di-O-(tert-butyldiphenylsilyl)-2,3-O-isopropylidene-α-*D*-mannopyranoside* (**25**). — To a solution of methyl 2,3-*O*-isopropylidene-α-D-mannopyranoside (1.43 g, 6.1 mmol) and imidazole (1.25 g, 18.4 mmol) in anhydrous *N,N*-dimethylformamide (10 mL) was added *tert*-butylchlorodiphenylsilane (4.2 g), and the mixture was stirred for 12 h at room temperature. The usual processing of the mixture, and purification of the product by flash column-chromatography on silica gel (20:1 hexane–ethyl acetate), gave pure **25** as a syrup (4.07 g) in 90.7% yield; $[\alpha]_D$ −18.7° (*c* 2.1); ^{1}H-n.m.r.: δ 7.1–7.6 (m, 20 H, 4 Ph), 4.86 (s, H-1), 4.26 (t, $J_{2,3} = J_{3,4}$ 6.4 Hz, H-3), 4.10 (d, H-2), 3.7–4.0 and 3.3–3.5 (m, 4 H, H-4,5,6), 3.49 (s, 3 H, Ome), and 1.25, 1.05, and 0.98 (each s, 18 H, 6 CMe).

Anal. Calc. for $C_{42}H_{54}O_6Si_2$: C, 70.94; H, 7.66. Found: C, 70.96; H, 7.50.

*O-Deisopropylidenation of methyl 2,3-O-isopropylidene-α-*D*-mannopyranoside derivatives* (**23–25**). — Reaction was generally performed as follows. A solution of the 2,3-*O*-isopropylidene derivative (3 mmol) in 3:1 acetic acid–water (40 mL) was stirred at 40°. After the reaction was complete, the acetic acid and water were removed by azeotropic evaporation with toluene, and the residual syrup was purified on a column of silica gel with (*A*) 1:1 or (*B*) 3:1 hexane–ethyl acetate.

Methyl 4,6-di-*O*-allyl-α-D-mannopyranoside (**26**): 98.1% yield (solvent *A*); $[\alpha]_D$ +69.2° (*c* 2.3).

Anal. Calc. for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.93; H, 8.09.

Methyl 4,6-di-*O*-[(methylthio)methyl]-α-D-mannopyranoside (**27**): 76.0% yield (solvent *A*); $[\alpha]_D$ +36.7° (*c* 1.9).

Anal. Calc. for $C_{11}H_{22}O_6S_2$: C, 42.02; H, 7.05; S, 20.39. Found: C, 41.65; H, 7.14; S, 20.54.

Methyl 4,6-di-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranoside (**28**): 87.2% yield (solvent *B*); $[\alpha]_D$ +17.7° (*c* 2.6).

Anal. Calc. for $C_{39}H_{50}O_6Si_2$: C, 69.81; H, 7.51. Found: C, 69.56; H, 7.69.

Preparation of 2,3-di-O-(trimethylsilyl) derivatives (**30–34**). — The 2,3-di-(trimethylsilyl) ethers were generally prepared as follows. To a solution of the methyl α-D-mannopyranoside derivative (3.0 mmol) and hexamethyldisilazane

(7.8–8.0 mmol) in dichloromethane (10 mL) was added trifluoroacetic acid (2 drops) at 0°, with stirring, and the mixture was stirred overnight at room temperature. After the reaction was complete, the mixture was evaporated. The residual syrup was separated by flash column-chromatography on silica gel with 10–20:1 hexane–ethyl acetate.

Methyl 4,6-di-*O*-acetyl-2,3-di-*O*-(trimethylsilyl)-α-D-mannopyranoside[9] (**30**): 91.8% yield; $[\alpha]_D$ +31.5° (*c* 3.6); ^{1}H-n.m.r.: δ 5.18 (t, $J_{3,4} = J_{4,5}$ 9.8 Hz, H-4), 4.57 (d, $J_{1,2}$ 2.0 Hz, H-1), 4.22 (dd, $J_{5,6}$ 5.3, $J_{6,6'}$ 12.0 Hz, H-6), 4.08 (dd, $J_{5,6'}$ 3.4 Hz, H-6'), 3.7–4.1 (m, 3 H, H-2,3,5), 3.37 (s, 3 H, OMe), 2.04 and 2.06 (each s, 6 H, 2 Ac), and 0.12 (s, 18 H, 6 SiMe).

Anal. Calc. for $C_{17}H_{34}O_8Si_2$: C, 48.31; H, 8.11. Found: C, 48.36; H, 8.07.

Methyl 4,6-di-*O*-benzoyl-2,3-di-*O*-(trimethylsilyl)-α-D-mannopyranoside (**31**): 98.6% yield; $[\alpha]_D$ +31.1° (*c* 3.0); ^{1}H-n.m.r.: δ 8.0–8.2 and 7.4–7.6 (m, 10 H, 2 Ph), 5.72 (t, $J_{3,4} = J_{4,5}$ 10.0 Hz, H-4), 4.67 (d, $J_{1,2}$ 2.2 Hz, H-1), 4.56 (dd, $J_{5,6}$ 3.6, $J_{6,6'}$ 11.8 Hz, H-6), 4.39 (dd, $J_{5,6'}$ 5.0 Hz, H-6'), 3.92 (t, $J_{2,3}$ 2.2 Hz, H-2), 4.0–4.3 (m, 2 H, H-3,5), 3.45 (s, 3 H, OMe), and 0.16 (s, 18 H, 6 SiMe).

Anal. Calc. for $C_{27}H_{38}O_8Si_2$: C, 59.31; H, 7.01. Found: C, 59.35; H, 6.93.

Methyl 4,6-di-*O*-allyl-2,3-di-*O*-(trimethylsilyl)-α-D-mannopyranoside (**32**): 98.1% yield; $[\alpha]_D$ +55.4° (*c* 1.7); ^{1}H-n.m.r.: δ 5.7–6.2 (m, 2 H, 2 CH=), 5.1–5.5 (m, 4 H, 2 $=CH_2$), 4.57 (d, $J_{1,2}$ 2.0 Hz, H-1), 3.6–4.4 (m, 10 H, H-2,3,4,5,6 and 2 CH_2O), 3.45 (s, 3 H, OMe), and 0.18 (s, 18 H, 6 SiMe).

Anal. Calc. for $C_{19}H_{38}O_6Si_2$: C, 54.50; H, 9.15. Found: C, 54.70; H, 9.14.

Methyl 4,6-di-*O*-[(methylthio)methyl]-2,3-di-*O*-(trimethylsilyl)-α-D-mannopyranoside (**33**): 72.5% yield; $[\alpha]_D$ +82.5° (*c* 1.7); ^{1}H-n.m.r.: δ 4.79 and 4.84 (m, 4 H, 2 OCH_2S), 4.57 (d, $J_{1,2}$ 2.0 Hz, H-1), 3.6–4.1 (m, 6 H, H-2,3,4,5,6), 3.39 (s, 3 H, OMe), 2.18 and 2.25 (each s, 6 H, 2 SMe), and 0.12 and 0.15 (each s, 18 H, 6 SiMe).

Anal. Calc. for $C_{17}H_{38}O_6S_2Si_2$: C, 44.50; H, 8.35; S, 13.98. Found: C, 44.68; H, 8.17; S, 13.66.

Methyl 4,6-di-*O*-(*tert*-butyldiphenylsilyl)-2,3-di-*O*-(trimethylsilyl)-α-D-mannopyranoside (**34**): 96.9% yield; $[\alpha]_D$ +32.0° (*c* 1.8); ^{1}H-n.m.r.: δ 7.5–8.0 (m, 20 H, 4 Ph), 4.71 (d, $J_{1,2}$ 2.0 Hz, H-1), 3.8–4.3 (m, 6 H, H-2,3,4,5,6), 3.66 (s, 3 H, OMe), 1.16 and 1.21 (each s, 18 H, 6 CMe), and 0.17 and 0.37 (each s, 18 H, 6 SiMe).

Anal. Calc. for $C_{45}H_{66}O_6Si_4$: C, 66.29; H, 8.16. Found: C, 66.66; H, 7.90.

Synthesis of methyl 2,3-O-D-glycopyranosylidene-α-D-mannopyranoside derivatives (**37–44** *and* **46–48**). — These compounds were generally synthesized as follows. To a solution of an aldono-1,5-lactone (1.0 mmol) and a methyl 2,3-di-*O*-(trimethylsilyl)-α-D-mannopyranoside (1.3–1.5 mmol) in anhydrous dichloromethane (2–3 mL) was added trimethylsilyl trifluoromethanesulfonate (0.05–0.1 mmol) in dichloromethane at 0°, and the mixture was kept for 2–4 days at room temperature. After the reaction was complete, the mixture was diluted with chloroform. The usual processing of the reaction mixture, and purification of

the product on a column of silica gel (flash column, or Lobar column) with hexane–ether or hexane–ethyl acetate gave pure products. The yields and physical constants of the pure isomers are summarized in Tables II and III.

Methyl 4,6-di-*O*-benzyl-2,3-*O*-[2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)-amino-6-deoxy-D-glucopyranosylidene]-α-D-mannopyranoside (**37**): reaction of **16** with **29** for 2 days gave a mixture (**37**) of two isomers as a syrup that could not be separated.

Anal. Calc. for $C_{56}H_{59}NO_{12}$: C, 71.70; H, 6.34; N, 1.49. Found: C, 71.69; H, 6.49; N, 1.25.

Methyl 2,3-*O*-(6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-D-glucopyranosylidene)-4,6-di-*O*-benzyl-α-D-mannopyranoside (**38**): reaction of **17** with **29** for 3 days gave a mixture (**38**) of two isomers as a syrup that could not be separated.

Anal. Calc. for $C_{48}H_{51}N_3O_{10}$: C, 69.47; H, 6.19; N, 5.06. Found: C, 69.18; H, 6.30; N, 5.04.

Methyl 2,3-*O*-(4-azido-2,3-di-*O*-benzyl-4-deoxy-D-glucopyranosylidene)-4,6-di-*O*-benzyl-α-D-mannopyranoside (**39**): reaction of **18** with **29** for 33 h, and separation of the product with 17:3 hexane–ethyl acetate, gave **39a** and **39b**.

Anal. Calc. for $C_{41}H_{45}N_3O_{10}$: C, 66.43; H, 6.13; N, 5.68. Found for **39a**: C, 66.57; H, 6.24; N, 5.57; and for **39b**: C, 66.27; H, 6.17; N, 5.53.

Methyl 2,3-*O*-(6-*O*-acetyl-4-azido-2,3-di-*O*-benzyl-4-deoxy-D-glucopyranosylidene)-4,6-di-*O*-benzyl-α-D-mannopyranoside (**40**): reaction of **19** with **29** for 2 days, and separation of the product by preparative t.l.c. (1:1 hexane–ether), gave **39** and **40**.

Anal. Calc. for $C_{43}H_{47}N_3O_{11}$: C, 66.06; H, 6.06; N, 5.37. Found: C, 66.45; H, 6.15; N, 5.47.

Methyl 2,3-*O*-(6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-D-galactopyranosylidene)-4,6-di-*O*-benzyl-α-D-mannopyranoside (**46**): reaction of **20** with **29** for 2 days, and separation of the product with 100:3 hexane–ethyl acetate, gave **46a** and **46b**.

Anal. Calc. for $C_{48}H_{51}N_3O_{10}$: C, 69.47; H, 6.19; N, 5.06. Found for **46a**: C, 69.41; H, 6.18; N, 4.73; and for **46b**: C, 69.38; H, 6.20; N, 4.99.

Methyl 2,3-*O*-(4-azido-2,3,6-tri-*O*-benzyl-4-deoxy-D-galactopyranosylidene)-4,6-di-*O*-benzyl-α-D-mannopyranoside (**47**): reaction of **21** with **29** for 3 days, and separation of the product with 7:3 hexane–ether, gave **47a** and **47b**.

Anal. Calc. for $C_{48}H_{51}N_3O_{10}$: C, 69.47; H, 6.19; N, 5.06. Found for **47a**: C, 69.42; H, 5.90; N, 5.09; and for **47b**: C, 69.33; H, 6.18; N, 5.12.

Methyl 2,3-*O*-[7-*O*-acetyl-2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)amino-6-deoxy-L-*glycero*-D-*gluco*-heptopyranosylidene]-4,6-di-*O*-benzyl-α-D-mannopyranoside (**48**): reaction of **22** with **29** for 43 h gave a mixture (**48**) of two isomers as a syrup that could not be separated.

Anal. Calc. for $C_{59}H_{63}NO_{14}$: C, 70.15; H, 6.29; N, 1.39. Found: C, 69.81; H, 6.24; N, 1.39.

Methyl 4,6-di-*O*-acetyl-2,3-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl-

idene)-α-D-mannopyranoside (**41**): reaction of **14** with **30** for 4 days gave a mixture (**41**) of two isomers as a syrup that could not be separated.

Anal. Calc. for $C_{45}H_{50}O_{13}$: C, 67.65; H, 6.31. Found: C, 67.36; H, 6.24.

Methyl 4,6-di-*O*-benzoyl-2,3-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosylidene)-α-D-mannopyranoside (**42**): reaction of **14** with **31** for 4 days gave a mixture (**42**) of two isomers as a syrup that could not be separated.

Anal. Calc. for $C_{55}H_{54}O_{13}$: C, 71.57; H, 5.90. Found: C, 71.46; H, 5.93.

Methyl 4,6-di-*O*-allyl-2,3-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosylidene)-α-D-mannopyranoside (**43**): reaction of **14** with **32** for 3 days, and separation of the product mixture with 15:1 hexane–ethyl acetate, gave **43a** and **43b**.

Anal. Calc. for $C_{47}H_{54}O_{11}$: C, 71.01; H, 6.85. Found: C, 70.75; H, 6.91.

Methyl 2,3-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosylidene)-4,6-di-*O*-[(methylthio)methyl]-α-D-mannopyranoside (**44**): reaction of **14** with **33** for 4 days, and purification of the product with 9:1 hexane–ethyl acetate (flash column), gave one isomer (**44**).

Anal. Calc. for $C_{45}H_{54}O_{11}S_2$: C, 64.72; H, 6.52; S, 7.68. Found: C, 64.77; H, 6.31; S, 7.57.

Deacylation of **40, 42,** *and* **48**. — The reaction was generally performed as follows. A solution of **40, 42,** or **48** (0.6 mmol) in anhydrous methanolic ammonia (1:1 methanol–saturated methanolic ammonia) was kept at room temperature. After the reaction was complete, the mixture was evaporated, to give a syrupy product (**39, 45,** or **49**) which was purified on a column of silica gel with hexane–ether or hexane–ethyl acetate. The physical data for the pure isomers are summarized in Tables II and III.

The reaction of **40** for 4 h gave **39** (93.4%), which was separated as already described for **39**.

Methyl 2,3-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosylidene)-α-D-mannopyranoside (**45**): the reaction of **42**, and separation of the product by preparative t.l.c. with 1:2 hexane–ethyl acetate, gave **45a** (30.3%) and **45b** (65.2%).

Anal. Calc. for $C_{41}H_{46}O_{11}$: C, 68.89; H, 6.49. Found for **45a**: C, 69.01; H, 6.60; and for **45b**: C, 68.77; H, 6.66.

Methyl 4,6-di-*O*-benzyl-2,3-*O*-[2,3,4-tri-*O*-benzyl-6-(benzyloxycarbonyl)-amino-6-deoxy-L-*glycero*-D-*gluco*-heptopyranosylidene]-α-D-mannopyranoside (**49**): the reaction of **48** for 6 h, and separation of the product with 83:17 hexane–ethyl acetate, gave **49a** (46.3%) and **49b** (45.1%).

Anal. Calc. for $C_{57}H_{61}NO_{13}$: C, 70.71; H, 6.35; N, 1.45. Found for **49a**: C, 70.72; H, 6.46; N, 1.34; and for **49b**: C, 70.52; H, 6.30; N, 1.30.

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