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Synthesis of *p*-trifluoroacetamidophenyl (4,6-dideoxy-4-formamido-3-*C*-methyl-2-*O*-methyl-α-L-mannopyranosyl)-(1→3)-(2-*O*-methyl-α-D-rhamnopyranosyl)-(1→3)-(2-*O*-methyl-α-L-fucopyranosyl)-(1→3)-(α-L-rhamnopyranosyl)-(1→2)-6-deoxy-α-L-talopyranoside: a spacer-armed pentasaccharide glycopeptidolipid antigen of *Mycobacterium avium* serovar 14

István Bajza [a,*], Katalin E. Kövér [b], András Lipták [a,c,*]

[a] *Research Group for Carbohydrates of the Hungarian Academy of Sciences, Debrecen, P.O.B 55, H-4010 Hungary*

[b] *Institute of Organic Chemistry, L. Kossuth University, Debrecen, P.O.B. 20, H-4010 Hungary*

[c] *Institute of Biochemistry, L. Kossuth University, Debrecen, P.O.B 55, H-4010 Hungary*

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Abstract

Syntheses of *p*-trifluoroacetamidophenyl glycosides of the haptenic pentasaccharide and the non-reducing disaccharide unit of the title pentasaccharide are reported. The synthesis of the terminal *N*-formylkansosamine unit started from methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyran-4-uloside which, after C-3 methylation, was transformed into a glycosyl donor [3-*O*-benzyl-4-*N*-benzylformamido-4,6-dideoxy-3-*C*-methyl-2-*O*-methyl-α,β-L-mannopyranosyl trichloroacetimidate (**20**), and used for the synthesis of *p*-trifluoroacetamidophenyl (4-formamido-4,6-dideoxy-3-*C*-methyl-2-*O*-methyl-α-L-mannopyranosyl)-(1→3)-6-deoxy-2-*O*-methyl-α-D-mannopyranoside (**29**). Ethyl (3-*O*-benzyl-4-*N*-benzylformamido-4,6-dideoxy-3-*C*-methyl-2-*O*-methyl-α-L-mannopyranosyl)-(1→3)-4-*O*-benzyl-6-deoxy-2-*O*-methyl-l-thio-α-D-mannopyranoside (**31**), prepared by glycosylation of ethyl 4-*O*-benzyl-6-deoxy-2-*O*-methyl-1-thio-α-D-mannopyranoside with **20**, served as glycosyl donor in a 2+3 block synthesis of the title pentasaccharide.

Keywords: Branched-chain sugar; Spacer, *p*-trifluoroacetamidophenyl; Oligosaccharide synthesis; Block synthesis

* Corresponding authors.

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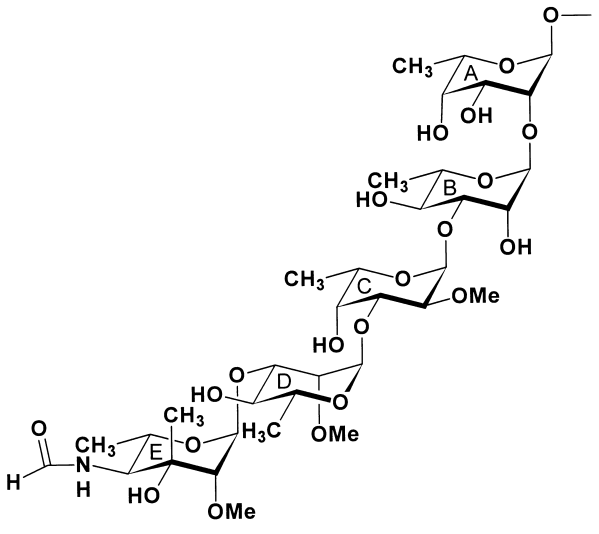
1. Introduction

The pioneering work of Brennan [1] and Aspinall et al. [2] laid the foundation of the molecular basis of the exact serodiagnosis of infections caused by mycobacteria. Many pulmonary infections, especially in patients suffering from acquired immunodeficiency syndrome (AIDS), are connected with mycobacteria of the *Mycobacterium avium–Mycobacterium scrofulaceum* complex. Different serovars of this complex possess highly antigenic glycopeptidolipids (GPLs) on their cell surface. Thus the outer oligosaccharide haptens, after conjugation with suitable proteins, might aid the serodiagnosis of mycobacterial infections. Among these haptens, the pentasaccharide of *M. avium* serovar 14 has the most complex structure [3,4] (Scheme 1). Here rhamnose occurs in both enantiomeric forms and the terminal *N*-formyl-α-L-kansosamine (4-*N*-formamido-4,6-dideoxy-3-*C*-methyl-2-*O*-methyl-α-L-mannopyranose) is a highly functionalised branched-chain aminosugar. Although kansosamine has not been isolated in free form, its derivatives were found in the surface antigen of *M. kansasii* [5] [4-(2-*O*-methyl)propionamido] and in the antibiotic sibiromycin [6] (4-*N*-methylated). For the preparation of *N*-formyl-α-L-kansosamine, four different methods have been published [4,7–9], and the synthesis of some oligosaccharide fragments of the pentasaccharide have also been reported. The B–A disaccharide (with benzyl [10], methyl [11], and *p*-nitrophenyl [12,13] aglycons), and the E–D [4] and D–C [4] disaccharides (with the allyl aglycon) were also reported.



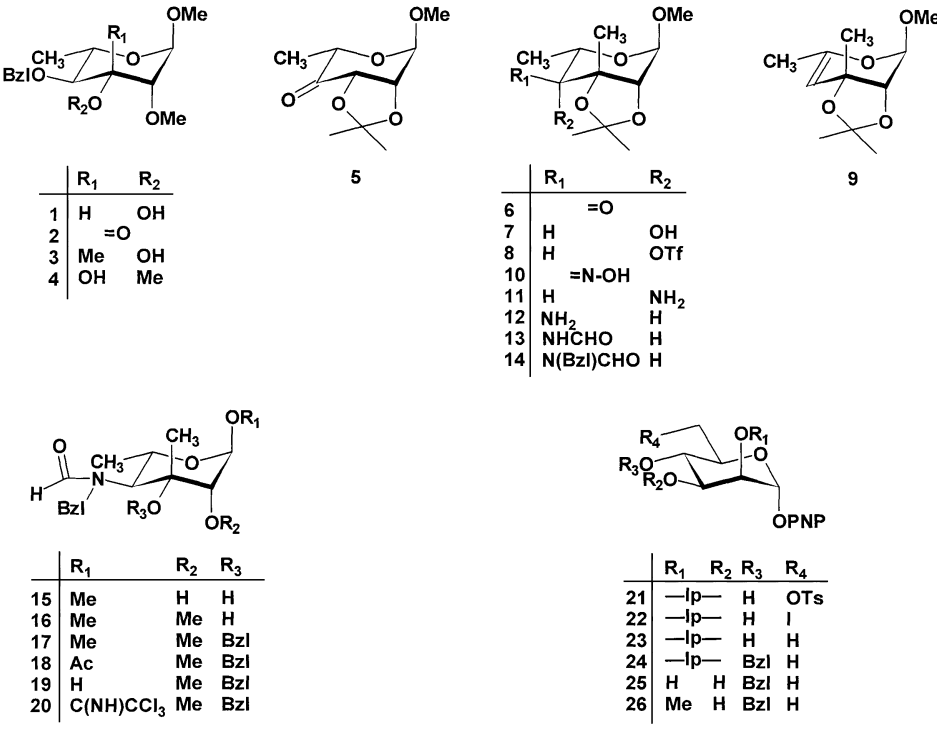
Scheme 1.

Two trisaccharide segments (C–B–A with the *o*-aminopropyl [14] and *p*-nitrophenyl aglycons [12], and E–D–C [4] with the allyl aglycon), and the tetrasaccharide D–C–B–A [12] with the *p*-nitrophenyl aglycon have also been prepared.

2. Results and discussion

For the synthesis of *N*-formyl-L-kansosamine on a preparative scale we applied two known synthetic strategies [15,16]. Firstly, the addition of methyl magnesium iodide to **2** (Scheme 2) obtained by oxidation of methyl 4-*O*-benzyl-2-*O*-methyl-α-L-rhamnopyranoside [17] (**1**) with pyridinium chlorochromate [18] gave diastereomers **3** and **4** in a molar ratio of 1:1.2. The stereochemical assignment of compounds **3** and **4** was based on homonuclear NOE measurements [19]. In compound **3**, the irradiation of the 3-*C*-methyl protons resulted in the signal enhancement of H-2 (14%) and H-5 (8%), while no effect was observed at the resonance frequency of H-4. These spectral data showed the proximity of the 3-*C*-Me group to H-5, confirming its *axial* position. In the case of compound **4**, signal intensity enhancements were observed at H-4 (9%) and at H-2 (11%) indicating the equatorial orientation of the 3-*C*-Me group. The low yields of **3** (19%) and **4** (13%) prompted us to proceed with our second synthetic strategy.

Methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyran-4-uloside (**5**) was *C*-methylated [20] with methyl iodide in the presence of strong inorganic or organic bases, to give methyl 6-deoxy-2,3-*O*-isopropylidene-3-*C*-methyl-α-L-*lyxo*-hexopyran-4-uloside (**6**). Reduction of compound **6** with $NaBH_4$ yielded exclusively 6-deoxy-talopyranoside derivative **7**, which was converted into 4-*O*-triflate **8**. Treatment of compound **8** with sodium azide afforded methyl 4,6-dideoxy-2,3-*O*-isopropylidene-3-*C*-methyl-α-L-*erythro*-hex-4-enopyranoside (**9**), instead of the desired 4-azido-L-rhamnopyranoside derivative. The reason of this elimination may have been the presence of the axial 3-*C*-Me group, which prevented the attack of the nucleophile, since successful azide displacements of the 4-*O*-trifluoromethanesulphonyl derivative in 6-deoxy-α-L-talopyranoside [21] and D-talopyranoside [22] were reported to yield 4-azido-L-rhamno- and 4-azido-D-mannopyranoside derivatives. Catalytic reduction (Pd-C) of oxime **10**, prepared from **6**, gave exclusively the 6-deoxy-*talo* isomer (**11**), but the



Scheme 2.

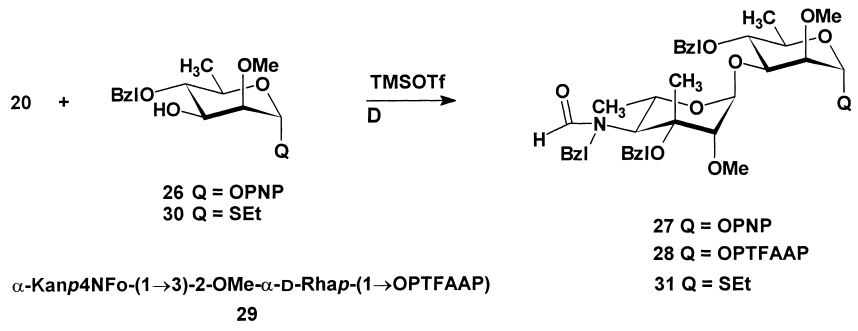
$LiA1H_4$ reduction of **10** resulted in a 1:1 mixture of 6-deoxy-L-*talo*- (**11**) and 6-deoxy-L-*manno*-isomers (**12**) [23]. Compound **12** was isolated in 41% yield. After *N*-formylation of **12** with acetic-formic anhydride (→**13**) and *N*-benzylation (→**14**), the 2,3-*O*-isopropylidene group was removed (→**15**) and the HO-2 function was selectively methylated to give compound **16**. The remaining free HO-3 group of **16** was benzylated to yield the fully protected *N*-formyl-α-L-kansosamine derivative (**17**). Acetolysis of compound **17** (→**18**), followed by deacetylation (→**19**) and imidation in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) [24] gave donor **20**.

For the preparation of *p*-nitrophenyl 4-*O*-benzyl-2-*O*-methyl-α-D-rhamnopyranoside (**26**), *p*-nitrophenyl 2,3-*O*-isopropylidene-α-D-mannopyranoside [25] was selectively tosylated at HO-6 (→**21**), and the tosyloxy group was transformed into a 6-deoxy-6-iodo function (**22**). Compound **22** was reduced by $LiA1H_4$ to give **23**, and the latter was benzylated and deisopropylidenated to give **25**. Treatment of **25** with methyl iodide under phase-transfer condition [26] gave **26**. The structure of all these compounds was verified by ^1H and ^{13}C NMR data, and the physical parameters of compounds **23–25** were compared with those of their L-enantiomers [27].

The glycosylation of compound **26** with trichloroacetimidate **20** (Scheme 3), catalysed by trimethylsilyl triflate, yielded the fully protected disaccharide **27** in 35% yield, whose structure was confirmed by ^1H and ^{13}C NMR spectroscopy (Table 1). The nitro group in **27** was catalytically reduced, and the amine formed was trifluoroacetylated to give **28**. Deprotection of **28** was achieved by catalytic hydrogenolysis yielding the spacer-armed disaccharide **29** (for NMR data, see Table 2).

Ethyl 4-*O*-benzyl-2-*O*-methyl-1-thio-α-D-rhamnopyranoside [12] (**30**) was glycosylated with donor **20**, yielding disaccharide **31** (75%) as the E–D synthon (Scheme 1; Table 1) for the block synthesis of the target pentasaccharide. The considerable difference in yields of the glycosylations of **26** and **30** with donor **20** may have been due to the different electronic effects of the aglycons since the substitution pattern of the two acceptors was the same.

Previously, we have reported [12] the synthesis of the *p*-nitrophenyl glycoside of the tetrasaccharide hapten isolated from *M. avium* serovar 20. This tetrasaccharide was the D–C–B–A part of our target pentasaccharide. An intermediate of the unprotected tetrasaccharide [12], *p*-nitrophenyl (3-*O*-acetyl-4-*O*-benzyl-2-*O*-methyl-α-D-rhamnopyranosyl)-(1→3)-(4-*O*-benzyl-2-*O*-methyl-α-L-fuco-



Scheme 3.

Table 1
NMR data for disaccharides **27** and **31** in $CDCl_3$ (δ in ppm)

Atom no.	**27**a		**27**b		**31**a		**31**b	
	δ ^{13}C	δ ^{1}H	δ ^{13}C	δ ^{1}H	δ ^{13}C	δ ^{1}H	δ ^{13}C	δ ^{1}H
1	95.88	5.64	96.22	5.60	80.61	5.38	80.61	5.34
2	76.39	3.84	77.2	3.81	77.96	3.75	78.70	3.71
3	73.98	4.20	74.16	4.27	74.38	3.97	74.78	4.04
4	79.54	3.54	80.09	3.55	80.02	3.48	80.33	3.47
5	69.51	3.76	69.30	3.71	68.38	4.10	68.20	4.0
6	18.33	1.30	18.13	1.23	18.12	1.33	18.03	1.26
1′	94.45	5.11	96.76	5.08	93.44	5.00	95.49	4.99
2′	81.03	3.46	82.53	3.77	80.90	3.45	82.25	3.66
3′	78.5		80.15		78.5		80.23	
4′	62.50	4.40	65.81	3.23	62.50	4.40	65.43	3.21
5′	65.27	4.13	63.77	5.04	65.14	4.04	63.89	5.00
6′	17.35	0.63	18.69	0.73	17.33	0.62	18.58	0.71
3′-CMe	17.50	1.45	18.30	1.53	17.33	1.40	18.30	1.54
2-OMe	59.20	3.58	59.68	3.55	58.83	3.48	59.37	3.52
2′-OMe	58.94	3.51	58.94	3.56	57.94	3.48	57.78	3.46
4-OCH_2Ph	74.38	4.69 + 4.75	74.73	4.57 + 4.98	74.43	4.71 + 4.73	74.94	4.54 + 4.98
3′-OCH_2Ph	63.36	4.45 + 4.48	63.72	4.45	63.26	4.43	63.52	4.40
NCH_2Ph	50.2	3.85 + 5.40	55.97	4.58 + 4.98	50.09	3.83 + 5.4	55.92	4.40
NC*H*O	161.61	7.49	163.32	8.36	161.71	7.49	163.27	8.33
S$CH_2$$CH_3$					25.48	2.63	25.36	2.61
S$CH_2$$CH_3$					14.98	1.29	15.02	1.26
Ph	126.0–140.0		126.0–140.0		126.0–140.0	7.1–7.4	126.0–140.0	7.1–7.4
PNP-C1	161.14		161.45					
PNP-C2,C6	116.33	7.15	116.38	7.13				
PNP-C3,C5	125.83	8.19	125.76	8.17				
PNP-C4	142.72		142.53					

pyranosyl)-(1→3)-(2,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-*endo*-3,4-*O*-benzylidene-6-deoxy-α-L-talopyranoside, was saponified to afford the tetrasaccharide acceptor for the preparation of our target pentasaccharide. Unfortunately neither imidate **20** nor the previously prepared phenyl 4-(*N*-benzylformamido)-4,6-dideoxy-3-*C*-methyl-2-*O*-methyl-1-thio-α-L-mannopyranoside reacted with this acceptor.

The trisaccharide acceptor *p*-nitrophenyl (4-*O*-benzyl-2-*O*-methyl-α-L-fucopyranosyl)-(1→3)-(2,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-*endo*-3,4-*O*-benzylidene-6-deoxy-α-L-talopyranoside [12] (**32**) reacted readily with the disaccharide donor **31** in the presence of NIS/TfOH as promotor [28], yielding the fully protected pentasaccharide **33** in a yield of 55% (Scheme 4). The complete ^{1}H and ^{13}C NMR assignment of compound **33** was not possible since signals of the CH_2 protons of the benzyl groups appeared in the informative region of the ^{1}H NMR spectrum. The *E* and *Z* isomerism of the N-CHO group also made the interpretation of the spectrum more difficult. The assignable chemical shift values for compound **33** are presented in Table 3.

Table 2
NMR data for disaccharide **29** in CD_3OD (δ in ppm)

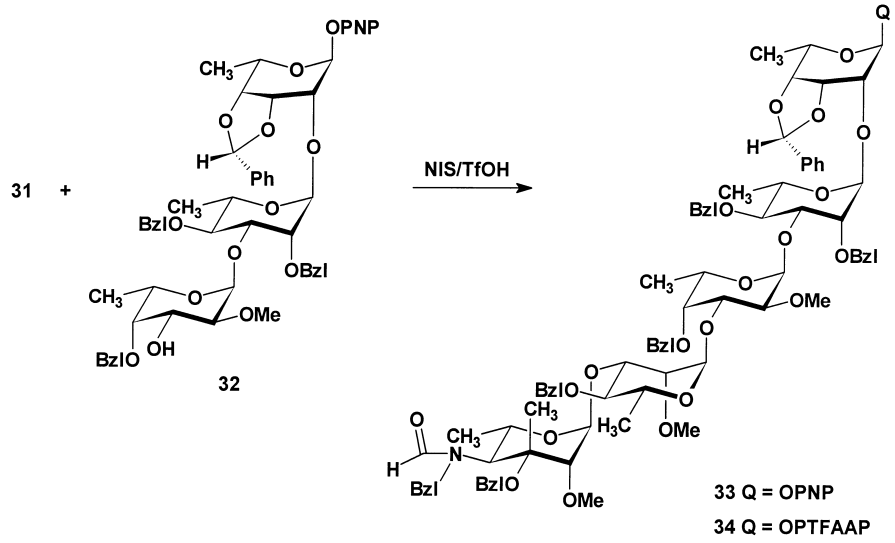
Atom no.	δ^1H		δ^{13}C	
	29a	**29**b	**29**a	**29**b
1	5.60		96.3	
2	3.88		76.8	
3	4.06		75.1	
4	3.49		71.0	
5	3.68		69.5	
6	1.24		17.2	
OMe	3.30–3.32		~58.9	
Ph	7.56–7.11		122.8–117	
1′	5.04	5.15	94.6	94.8
2′	3.12	3.17	84.3	
4′	3.26		60.3	
5′	4.00	4.05	67.5	
6′	1.17	1.20	17.7	
OMe	3.49–3.52		~58.9	
NC*H*O	8.16	8.55	136.9	131
CH_3(3′)	1.32	1.39	19	

The fully protected pentasaccharide **33** was converted into *p*-trifluoroacetamidophenyl glycoside **34**, and then deprotected as described for disaccharide **29**. Full assignment of the ^{1}H and ^{13}C spectra of the pentasaccharide **35** was achieved by ^{1}H-^{1}H COSY and TOCSY experiments as well as ^{1}H/^{13}C HSQC and HSQC–TOCSY experiments [29,30] (Table 4). The spectral parameters were in full accord with the target structure.

3. Experimental

General.—Melting points (uncorrected) were determined on a Kofler hot-stage apparatus. NMR spectra were recorded at 25 °C with a Bruker WP 200 SY (^{1}H, 200 MHz; ^{13}C, 50 MHz) or a Bruker Avance DRX 500 (^{1}H, 500.13 MHz; ^{13}C, 125.76 MHz) spectrometer for solutions in $CDCl_3$ (internal Me_4Si) or in CD_3OD. Proton chemical shifts (δ) are given in ppm relative to the signal for internal Me_4Si ($CDCl_3$). Carbon chemical shifts were referenced to the solvent signal. Column chromatography was performed on Kieselgel 60 (Merck, 230 mesh) and fractions were monitored by TLC on Kieselgel 60 F_{254} (Merck) by detection with UV light and then charring with H_2SO_4. Unless noted otherwise, optical rotations were measured for solutions in $CHCl_3$ at 20 °C with a Perkin Elmer 241 polarimeter, using a 10 cm (1 mL) cell. Concentration of solutions was performed at 40 °C.

*Methyl 4-*O*-benzyl-2-*O*-methyl-*α*-*L*-arabino-hexopyranosid-3-ulose* (**2**).—Methyl 4-*O*-benzyl-6-deoxy-2-*O*-methyl-*α*-*L*-mannopyranoside (**1**) (1.96 g, 6.94 mmol) was dissolved in CH_2Cl_2 (200 mL), pyridinium chlorochromate (6.5 g, 34.7 mmol) was added, and the mixture was stirred for 12 h at room temperature. The mixture was chromatographed (7:3 hexane–EtOAc) to yield **2** (1.62 g, 83%) as a



α-Kan*p*4NFo-(1→3)-2-OMe-α-D-Rha*p*-(1→3)-2-OMe-α-L-Fuc*p*-(1→3)-α-L-Rha*p*-(1→2)-6d-α-L-Tal*p*-(1→OPTFAAP)

35

Scheme 4.

Table 3
NMR data for pentasaccharide **33** in $CDCl_3$ (δ in ppm)

Residue	Atom no.	$\delta^{13}C$	$\delta^{1}H$
6d-α-L-Tal*p*	1	98.7	5.64
	2	71.44	4.26
	3	74.84	4.60
	6	17-19	1.2-1.4
	benzylidene	104.74	5.85
	$J_{C1,H1}$	175.1 Hz	
α-L-Rha*p*	1	94.40	5.11
	2	77.5	3.68
	3	76.82	4.27
	6	17-19	1.2-1.4
	$J_{C1,H1}$	168.2 Hz	
α-L-Fuc*p*	1	98.97	5.08
	2	79.85	3.85
	3	79.50	3.55
	4	78.33	3.83
	5	67.58	3.90
	6	18	0.95
	2-OMe	58.89	3.12
	$J_{C1,H1}$	167.3 Hz	
α-D-Rha*p*	1	98.45	5.26
	2	80.30	3.47
	3	74.09	4.09
	4	76.32	3.68
	5	68.78	3.90
	6	17-19	1.2-1.4
	2-OMe	58.89 or 58.38	3.45 or 3.41
	$J_{C1,H1}$	172.1 Hz	
α-Kan*p*-4NFo	1	93.50	5.07
	6	17-19	1.2-1.4
	2-OMe	58.89 or 58.38	3.45 or 3.41
	CHO	162.31	8.32
	N-Bzl	50.03	3.84
	$J_{C1,H1}$	166.3 Hz	

Table 4
NMR data for pentasaccharide **35** in CD_3OD (δ in ppm)

Residue	Atom no.	$\delta^{1}H$	$\delta^{13}C$
6d-α-L-Tal*p*	1	5.62	98.1
	2	4.03	77.8
	3	4.12	71
	4	3.63	70.6
	5	3.80	69.8
	6	1.25	17.2
α-L-Rha*p*	1	5.03	103.44
	2	4.10	75.1
	3,4	3.82,3.79	78.3
	5	3.63	72.1
	6	1.12	16.7
α-L-Fuc*p*	1	5.17	99.3
	2	3.73	77.5
	3,4,5	3.93,3.98,4.03	75,67.1,70
	6	1.21	17.4
	2-OMe	3.49,3.52,3.54	58.8-59
α-D-Rha*p*	1	5.39	98.7
	2	3.67	78.2
	3	4.05	76.3
	4	3.75	72.3
	5	4.02	68.3
	6	1.20	17.5
	2-OMe	3.49,3.52,3.54	58.8-59
α-Kan*p*-4NFo	1	5.08	94.9
	2	3.11 3.15	84.6
	4	3.24 3.28	53.5
	5	4.08	70.6
	6	1.22	15.8
	2-OMe	3.49,3.52,3.54	58.8-59
	NC*H*O	8.2 and 8.0	131 and 137
	CH_3(3)	1.37 and 1.31	19.1

colourless syrup; $[\alpha]_D$ −183.5° (*c* 0.45); IR: 1730 cm^{-1} (C=O); ^1H NMR: δ 7.20–7.30 (m, 5 H, Ph), 4.79 (d, 1 H, $J_{1,2}$ 2 Hz, H-1), 4.01 (d, 1 H, $J_{4,5}$ 9.2 Hz, H-4), 3.88 (dd, 1 H, $J_{5,Me(6)}$ 6 Hz, H-5), 3.55 (d, 1 H, H-2), 3.28 and 3.26 (2 s, each 3 H, 2 OCH_3), 1.32 (d, 3 H, CH_3). Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.11; H, 7.05.

*Methyl 4-*O*-benzyl-6-deoxy-3-*C*-methyl-2-*O*-methyl*-α-L-manno-(**3**) and altro-*pyranoside* (**4**).—A solution of compound **2** (196 mg, 0.7 mmol) in Et_2O (2 mL) was added dropwise to a solution of Grignard reagent prepared from CH_3I (875 mg, 14.1 mmol) and Mg (343 mg, 14.1 mmol) in Et_2O (5 mL), and the mixture was stirred for 1 h at room temperature. The reaction was quenched by addition of a chilled NH_3-solution (10 mL), then the mixture was diluted with Et_2O (20 mL), extracted with water (2×10 mL), dried, and concentrated. Chromatography of the residue (8:2 hexane–EtOAc) gave pure **3** (40 mg, 19%) and **4** (28 mg, 13%), isolated as colourless syrups. Compound **3**: $[\alpha]_D$ −67.1° (*c* 0.43); ^1H NMR: δ 7.40 (m, 5 H, Ph), 4.72 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 3.61 (dd, 1 H, $J_{4,5}$ 10, $J_{5,Me(6)}$ 6 Hz, H-5), 3.48 and 3.36 (2 s, each 3 H, 2 OCH_3), 3.20 (d, 1 H, H-4), 3.08 (d, 1 H, H-2), 1.38 (s, 3 H, CH_3), 1.25 (d, 3 H, CH_3); Compound **4**: $[\alpha]_D$ −56.1° (*c* 0.3); ^1H NMR: δ 7.4 (m, 5 H, Ph), 4.72 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.66 (s, 2 H, CH_2Ph), 3.92 (dd, 1 H, $J_{4,5}$ 9.5, $J_{5,6}$ 6 Hz, H-5), 3.46 and 3.41 (2 s, each 3 H, 2 OCH_3), 3.19 (d, 1 H, H-4), 3.09 (d, 1 H, H-2), 1.15 (s, 3 H CH_3), 1.14 (d, 3 H, CH_3). Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.90; H, 8.05.

*Methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-lyxo-hexopyran-4-uloside* (**5**).—To a solution of methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-mannopyranoside (1.0 g, 4.6 mmol) in dry CH_2Cl_2 (50 mL) was added pyridinium chlorochromate (5.0 g, 23 mmol), and the mixture was stirred for 3.5 h at room temperature. Conventional work-up (see **2**)

yielded pure **5** (0.92 g, 91%), isolated as a colourless syrup; $[\alpha]_D$ −35.8° (*c* 0.77); IR: 1740 cm^{-1} (C=O); ^1H NMR: δ 4.85 (s, 1 H, H-1), 4.44 (s, 2 H, H-2,3), 4.26 (d, 1 H, $J_{5,Me(6)}$ 7 Hz, H-5), 3.47 (s, 3 H, OCH_3), 1.49 and 1.37 (2 s, each 3 H, Ip CH_3), 1.41 (d, 3 H, CH_3). Anal. Calcd for $C_{10}H_{16}O_6$: C, 55.54; H, 7.46. Found: C, 55.03; H, 7.18.

Methyl 6-deoxy-2,3-O-*isopropylidene-3*-C-*methyl*-α-L-lyxo-*hexopyran-4-uloside* (**6**).—A solution of BuLi (15% in hexane; 2.1 mL, 4.8 mmol) was added dropwise at −40 °C under Ar to a solution of diisopropylamine (672 μL, 4.8 mmol) in dry THF (50 mL). The light-yellow mixture was stirred for 20 min at −40 °C, then cooled to −78 °C, and a solution of **5** (0.91 g, 4.2 mmol) in dry THF (5 mL) was added dropwise. After stirring for 1 h at −78 °C, hexamethylphosphoric triamide (1.1 mL) and CH_3I (2.2 mL, 34 mmol) was added, and the mixture was allowed to warm up to room temperature. Then, an aqueous solution of NH_4Cl (10%, 12 mL) was added, the mixture was diluted with CH_2Cl_2 (200 mL), the organic layer was washed with water, dried, and concentrated. The residue was chromatographed (8:2 hexane–EtOAc) to yield pure **6** (800 mg, 83%), isolated as a colourless syrup; $[\alpha]_D$ −65.8° (*c* 0.38); IR: 1740 cm^{-1} (C=O); ^1H NMR: δ 4.92 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1), 4.34 (d, 1 H, $J_{5,Me(6)}$ 6.8 Hz, H-5), 4.07 (d, 1 H, H-2), 350 (s, 3 H, OCH_3), 1.49 and 1.37 (2 s, each 3 H, Ip CH_3), 1.43 (s, 3 H, CH_3), 1.41 (d, 3 H, CH_3). Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 56.96; H, 7.70.

Methyl 6-deoxy-2,3-O-*isopropylidene-3*-C-*methyl*-α-L-*talopyranoside* (**7**).—To the chilled solution of **6** (500 mg, 2.18 mmol) in MeOH (10 mL) was added $NaBH_4$ (150 mg, 3.9 mmol), and the mixture was stirred for 1 h, then boiled under reflux for 20 min, and concentrated. CH_2Cl_2 (50 mL) was added, the organic layer was washed with water until neutral, dried, and concentrated to yield **7** (480 mg, 95%), isolated as a colourless syrup; $[\alpha]_D$ −58.0° (*c* 0.35); ^1H NMR: δ 4.93 (s, 1 H, H-1), 3.88 (dd, 1 H, $J_{4,5}$ 1, $J_{5,Me(6)}$ 6.5 Hz, H-5), 3.75 (s, 1 H, H-2), 3.40 (s, 3 H, OCH_3), 3.17 (dd, 1 H, $J_{4,OH}$ 5 Hz, H-4), 2.48 (d, 1 H, OH), 1.57 and 1.38 (2 s, each 3 H, Ip CH_3), 1.42 (s, 3 H, CH_3), 1.34 (d, 3 H, CH_3). Anal. Calcd for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68. Found: C, 56.16; H, 8.42.

Methyl 6-deoxy-2,3-O-*isopropylidene-3*-C-*methyl*-*4*-O-*trifluoromethanesulfonyl*-α-L-*talopyranoside* (**8**).—To the solution of **7** (220 mg, 0.95 mmol) in dry CH_2Cl_2 (8 mL) containing pyridine (400 μL) was added dropwise triflic anhydride (210 μL, 1.24 mmol) at −70 °C, and the mixture was stirred for 90 min. After work-up via extractions and purification on a short column of silica (9:1 hexane–EtOAc) pure **8** was obtained as a colourless syrup (304 mg, 88%); $[\alpha]_D$ −17.8° (*c* 0.95); ^1H NMR: δ 4.94 (s, 1 H, H-1), 4.35 (s, 1 H, H-4), 4.03 (d, 1 H, $J_{5,Me(6)}$ 6 Hz, H-5), 3.78 (s, 1 H, H-2), 3.40 (s, 3 H, OCH_3), 1.55 and1.40 (2 s, each 3 H, Ip CH_3), 1.50 (s, 3 H, CH_3), 1.38 (d, 3 H, CH_3). Anal. Calcd for $C_{12}H_{19}F_3O_7S$: C, 39.56; H, 5.26. Found: C, 39.16; H, 5.02.

Methyl 4,6-dideoxy-2,3-O-*isopropylidene-3*-C-*methyl*-α-L-erythro-*hex-4-enopyranoside* (**9**).—To the solution of **8** (300 mg, 0.82 mmol) in dry DMF (5 mL) was added NaN_3 (150 mg, 2.46 mmol) and dicyclohexyl-18-crown-6 (10 mg, 0.03 mmol), and the mixture was stirred for 6 h at room temperature. The mixture was then poured into 0.1 M HCl (10 mL), extracted with Et_2O (2×20 mL), and the combined organic layer was washed with water until neutral, dried, and concentrated. Chromatography (95:5 hexane–EtOAc) of the residue yielded **9** (150 mg, 87%), isolated as a colourless oil; $[\alpha]_D$ −18.3° (*c* 0.65); ^1H NMR: δ 5.02 (d, 1 H, $J_{1,2}$ 2 Hz, H-1), 4.60 (s, 1 H, H-4), 3.81 (d, 1 H, H-2), 3.45 (s, 3 H, OCH_3), 1.80, 1.48, 1.42, and 1.43 (4 s, each 3 H, 4 CH_3). Anal. Calcd for $C_{11}H_{19}O_4$: C, 61.37; H, 8.90. Found: C, 60.56; H, 8.92.

Methyl 6-deoxy-2,3-O-*isopropylidene-3*-C-*methyl*-α-L-lyxo-*hexopyran-4-uloside-oxime* (**10**).—To a solution of **6** (5.8 g, 25.2 mmol) in EtOH (150 mL) was added hydroxylamine hydrochloride (8.85 g, 127.4 mmol) and Na_2CO_3 (15 g, 141.5 mmol), and the mixture was stirred for 15 h at 80 °C. Inorganic salts were filtered off, the filtrate was concentrated, and CH_2Cl_2 (300 mL) was added. The organic layer was washed with water until neutral, dried, and concentrated to yield **10** (6.2 g, 99%) as a colourless oil which was sufficiently pure for the next transformation; $[\alpha]_D$ −78.0° (*c* 0.55); ^1H NMR: δ 4.72 (dd, 1 H, $J_{5,6}$ 5 Hz, H-5), 4.57 (s, 1 H, H-1), 3.92 (s, 1 H, H-2), 3.87 (s, 3 H, OCH_3), 3.38 (s, 3 H, OCH_3), 1.55 (s, 3 H, CH_3), 1.53 and 1.45 (2 s, each 3 H, Ip CH_3), 1.44 (d, 3 H, CH_3). Anal. Calcd for $C_{11}H_{19}NO_5$: C, 53.86; H, 7.81. Found: C, 54.16; H, 7.92.

Methyl 4-amino-4,6-dideoxy-2,3-O-*isopropylidene-3*-C-*methyl*-α-L-*mannopyranoside* (**12**).—A solution of **10** (6.0 g, 24.5 mmol) and $LiAlH_4$ (8.83 g, 233 mmol) in 1,4-dioxane (400 mL) was stirred for 4 h at 100 °C. The mixture was chilled, and the

excess of hydride was decomposed by addition of EtOAc (200 mL) and water. Then the organic layer was washed with water until neutral, dried, and concentrated. Chromatography (9:1 hexane–EtOAc) of the residue yielded **12** (2.27 g, 41%), isolated as a syrup. The corresponding L-*talo* isomer was isolated in 38% yield; $[\alpha]_D$ −40.1° (*C* 0.99); ^{1}H NMR: δ 4.87 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 3.79 (d, 1 H, H-2), 3.51 (dd, 1 H, $J_{4,5}$ 10, $J_{5,Me(6)}$ 6.5 Hz, H-5), 3.38 (s, 3 H, OCH_3), 2.84 (d, 1 H, H-4), 1.51 and 1.37 (2 s, each 3 H, Ip CH_3), 1.31 (s, 3 H, CH_3). Anal. Calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.05. Found: C 57.10; H, 9.00; N, 5.95.

Methyl 4,6-dideoxy-4-formamido-2,3-O-*isopropylidene-3*-C-*methyl*-α-L-*mannopyranoside* (**13**).—To a solution of **12** (880 mg, 3.8 mmol) in MeOH (20 mL) was added acetic–formic anhydride (3 mL, 35.6 mmol) and the mixture was stirred for 30 min, then concentrated. Chromatography (8:2 hexane–acetone) of the residue gave **13** (980 mg, 99%), isolated as a syrup; $[\alpha]_D$ −76.0° (*c* 0.72); ^{1}H NMR: δ 8.18 and 7.98 (2 d, 1 H, CHO), 7.22 and 6.70 (2 m, 1 H, NH), 4.64 and 4.54 (2 d, 1 H, $J_{1,2}$ 1 Hz, H-1), 3.05 and 3.04 (2 d, 1 H, $J_{4,5}$ 10 Hz, H-4), 3.75 and 3.65 (2 dd, 1 H, $J_{5,Me(6)}$ 6 Hz, H-5), 3.43 (d, 1 H, H-2), 3.30 and 3.28 (2 s, 3 H, OCH_3), 1.49 and 1.40 (2 s, each 3 H, Ip CH_3), 1.23 and 1.22 (2 s, 3 H, CH_3), 1.19 and 1.17 (2 d, 3 H, CH_3). Anal. Calcd for $C_{12}H_{21}NO_5$: C, 55.58; H, 8.16. Found: C, 55.04; H, 8.01.

Methyl 4-N-*benzylformamido-4,6-dideoxy-2,3*-O-*isopropylidene-3*-C-*methyl*-α-L-*mannopyranoside* (**14**).—A solution of **13** (980 mg, 1.77 mmol), benzyl bromide (1 mL, 3.9 mmol) and powdered KOH (2 g) in dry DMF (20 mL) was stirred for 1.5 h at room temperature. Then the mixture was diluted with EtOAc (200 mL), washed with water until neutral, dried, and concentrated. Chromatography (8:2 hexane–EtOAc) of the residue yielded **14** (1.0 g, 75%), isolated as a syrup; $[\alpha]_D$ −2.9° (*c* 0.6); ^{1}H NMR: δ 8.2 and 8.05 (2 d, 1 H, CHO), 7.3–7.2 (m, 5 H, Ph), 4.64 and 4.59 (2 s, 1 H, H-1), 4.08 (dd, $J_{4,5}$ 10, $J_{5,6}$ 6 Hz, H-5), 3.58 and 3.51 (2 s, 1 H, H-2), 332 (s, 3 H, OCH_3), 2.91 (d, 1 H, H-4), 1.41 and 1.40 (2 s, 3 H, CH_3), 0.85 (d, 3 H, CH_3). Anal. Calcd for $C_{19}H_{27}NO_5$: C, 65.31; H, 7.79. Found: C, 64.90; H, 7.80.

Methyl 4-N-*benzylformamido-4,6-dideoxy-3*-C-*methyl*-α-L-*mannopyranoside* (**15**).—Compound **14** (280 mg, 0.8 mmol) was dissolved in aq 70% HOAc (20 mL) and the solution was kept for 4 h at 80 °C, then concentrated. The residue was chromatographed (9:1 CH_2Cl_2–MeOH) to yield syrupy **15** (208 mg, 84%); $[\alpha]_D$ −11.41° (*c* 0.60); ^{1}H NMR: δ 8.35 and 8.05 (2 s, 1 H, CHO), 7.2–7.3 (m, 5 H, Ph), 5.40 (bs, 1 H, OH), 4.64 and 4.62 (2 s, 1 H, H-1), 4.0 (dd, 1 H, $J_{4,5}$ 10, $J_{5,Me(6)}$ 6 Hz, H-5), 3.57 and 3.52 (2 s, 1 H, H-2), 3.30 (s, 3 H, OCH_3), 2.90 (d, 1 H, H-4), 1.40 and 1.39 (2 s, 3 H, CH_3), 1.25 (s, 1 H, OH), 0.80 (d, 3 H, CH_3). Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49. Found: C, 62.16; H, 7.52.

Methyl 4-N-*benzylformamido-4,6-dideoxy-3*-C-*methyl-2*-O-*methyl*-α-L-*mannopyranoside* (**16**).—To a solution of **15** (200 mg, 0.65 mmol) in dry DMF (10 mL) was added NaH (29 mg, 0.98 mmol), and the mixture was stirred at room temperature for 40 min, then chilled, and CH_3I (52 μL, 0.85 mmol) was injected. After 15 min, MeOH (0.5 mL) was added, the mixture was concentrated, and the residue was chromatographed (7:3 hexane–acetone) to yield **16** (169 mg, 80%), isolated as a syrup; $[\alpha]_D$ −32.01° (*c* 0.87); ^{1}H NMR: δ 8.40 and 8.15 (2 s, 1 H, CHO), 7.20–7.40 (m, 5 H, Ph), 4.50 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 4.00 (dd, 1 H, $J_{4,5}$ 10, $J_{5,Me(6)}$ 6 Hz, H-5), 3.50 and 3.48 (2 s, 3 H, OCH_3), 3.37 and 3.34 (2 s, 3 H, OCH_3), 3.10 and 3.03 (2 d, 1 H, H-2), 2.58 (bs, 1 H, OH), 1.41 and 1.32 (2 s, 3 H, CH_3), 0.77 (d, 3 H, CH_3). Anal. Calcd for $C_{17}H_{27}NO_5$: C, 63.14; H, 7.79. Found: C, 63.06; H, 7.90.

Methyl 3-O-*benzyl-4*-N-*benzylformamido-4,6-dideoxy-3*-C-*methyl-2*-O-*methyl*-α-L-*mannopyranoside* (**17**).—To a solution of **16** (1.56 g, 4.8 mmol) in dry DMF (70 mL) was added NaH (300 mg, 9.6 mmol), and the mixture was stirred for 2 h at room temperature. Benzyl bromide (1.5 mL, 6.2 mmol) was added and the mixture was stirred for 3 h. After processing (see **16**) pure **17** (1.0 g, 50%) was isolated as a colourless glass; $[\alpha]_D$ −48.0° (*c* 0.35); ^{1}H NMR: δ 8.32 and 8.15 (2 s, 1 H, CHO), 7.20 and 7.43 (2 m, 10 H, 2 Ph), 4.91 and 4.05 (2 dd, 1 H, $J_{4,5}$ 11, $J_{5,Me(6)}$ 6 Hz, H-5), 4.72 and 4.70 (2 d, 1 H, $J_{1,2}$ 1 Hz, H-1), 4.50 and 4.42 (2 d, each 1 H, PhCH_2), 4.49 (s, 2 H, PhCH_2), 3.47 and 3.45 (2 s, 3 H, OCH_3), 3.41 (d, 1 H, H-2), 3.37 and 3.50 (2 s, 3 H, OCH_3), 3.21 (d, 1 H, H-4), 1.60 and 1.45 (2 s, 3 H, CH_3), 0.78 (d, 3 H, CH_3). Anal. Calcd for $C_{24}H_{31}NO_5$: C, 69.71; H, 7.56. Found: C, 70.06; H, 7.82.

1-O-*Acetyl-3*-O-*benzyl-4*-N-*benzylformamido-4,6-dideoxy-3*-C-*methyl-2*-O-*methyl*-α-L-*mannopyranose* (**18**).—To a solution of **17** (300 mg, 0.72 mmol) in Ac_2O (2 mL) was added H_2SO_4 in Ac_2O (4%, 2 mL), and the mixture was stirred for

30 min at room temperature. The solution was poured into ice-cold aq $NaHCO_3$, extracted with CH_2Cl_2 (20 mL), and the organic layer was separated, dried, and concentrated. Chromatography (97:3 CH_2Cl_2-EtOAc) of the residue yielded syrupy **18** (221 mg, 70%); $[\alpha]_D$ −28.0° (*c* 0.55); ^{1}H NMR: δ 8.32 and 8.13 (2 s, 1 H, CHO), 7.20–7.50 (m, 10 H, Ph), 6.12 and 6.20 (2 d, 1 H, $J_{1,2}$ 1 Hz, H-1), 5.08 and 4.20 (2 dd, 1 H, $J_{4,5}$ 10, $J_{5,Me(6)}$ 6 Hz, H-5), 4.50 (d, 1 H, H-2), 4.50-4.43 (m, 4 H, $PhCH_2$), 3.52 and 3.51 (2 s, 3 H, OCH_3), 3.32 (d, 1 H, H-4), 2.10 and 2.12 (2 s, 3 H, Ac), 1.52 and 1.60 (2 s, 3 H, CH_3), 0.75 (d, 3 H, CH_3). Anal. Calcd for $C_{25}H_{31}NO_6$: C 68.01; H, 7.08. Found: C, 67.76; H, 7.02.

3-O-*Benzyl-4*-N-*benzylformamido-4,6-dideoxy-3*-C-*methyl-2*-O-*methyl*-α-L-*mannopyranosyl trichloroacetimidate* (**20**).—To a solution of **18** (100 mg, 0.23 mmol) in dry DMF (5 mL) was added hydrazine acetate (30 mg, 0.3 mmol), and the solution was kept for 30 min at 50 °C. Then, EtOAc (20 mL) was added, and the organic layer was washed with water, dried, and concentrated to give **19** (80 mg, 87%) which was used without purification ($[\alpha]_D$ +33.2° (*c* 0.29)). A solution of the foregoing material (80 mg, 0.2 mmol), trichloroacetonitrile (190 μL, 1.9 mmol) and DBU (50 mL, 0.34 mmol) in dry CH_2Cl_2 (5 mL) was stirred for 10 min at room temperature, then concentrated. The residue was chromatographed (7:3 hexane–acetone +1% Et_3N) to yield **20** (100 mg, 91%; 6:4, E:Z) as a syrup; $[\alpha]_D$ −21.3° (*c* 0.42); ^{1}H NMR: δ 8.68 and 8.56 (2 s, 1 H, NH), 8.34 and 8.13 (2 s, 1 H, CHO), 7.20–7.50 (m, 10 H, Ph), 6.35 and 6.29 (2 d, 1 H, $J_{1,2}$ 2 Hz, H-1), 5.17 and 4.29 (2 dd, 1 H, $J_{4,5}$ 10, $J_{5,Me(6)}$ 6 Hz, H-5), 4.50 (bs, 4 H, $PhCH_2$), 3.72 and 3.65 (2 bs, 1 H, H-2), 3.56 and 3.54 (2 s, 3 H, OCH_3), 3.30 (d, 1 H, H-4), 1.60 (s, 3 H, CH_3), 0.79 (d, 3 H, CH_3). Anal. Calcd for $C_{25}H_{29}C_{13}N_2O_5$: C, 55.21; H, 5.38. Found: C, 55.16; H, 5.12.

p-*Nitrophenyl 2,3*-O-*isopropylidene-6*-O-p-*toluenesulfonyl*-α-D-*mannopyranoside* (**21**).—*p*-Toluenesulfonyl chloride (290 mg, 1.5 mmol) was added to a solution of *p*-nitrophenyl 2,3-*O*-isopropylidene-α-D-mannopyranoside (100 mg, 0.3 mmol) in dry pyridine (8 mL), and the solution was kept for 1.5 h at 60 °C. After concentration, chromatography (7:3 hexane–acetone) of the residue yielded **21** (96 mg, 70%), isolated as a syrup; $[\alpha]_D$ +52.6° (*c* 0.63); ^{1}H NMR: δ 8.15 and 7.10 (2 m, each 2 H, *p*-subst. Ph), 7.70 and 7.32 (2 m, each 2 H, *p*-Ts), 5.78 (s, 1 H, H-1), 4.38 (d, 1 H, $J_{2,3}$ 5 Hz, H-2), 4.3 (m, 3 H, H-3,4,5), 3.50 (m, 2 H, H-6a,6b), 2.90 (s, 1 H, OH), 2.45 (s, 3 H, *p*-Ts CH_3), 1.55 and 1.42 (2 s, each 3 H, Ip CH_3); ^{13}C NMR: δ 115.66 (acetalic C), 94.71 (C-1), 67.63 (C-6), 25.1 and 26.82 (2 Ip CH_3), 20.32 (*p*-Ts CH_3). Anal. Calcd for $C_{22}H_{25}NO_{10}S$: C, 57.01; H, 5.44. Found: C, 56.96; H, 5.12.

p-*Nitrophenyl 6-deoxy-6-iodo-2,3*-O-*isopropylidene*-α-D-*mannopyranoside* (**22**).—A solution of **21** (580 mg, 1.2 mmol) and NaI (4 g, 24 mmol) in dry DMF (10 mL) was kept for 5 h at 100 °C, then cooled, diluted with CH_2Cl_2 (200 mL), extracted with water, and concentrated. Chromatography (7:3 hexane–EtOAc) of the residue afforded **22** (380 mg, 73%), isolated as a syrup; $[\alpha]_D$ +85.3° (*c* 0.36); ^{1}H NMR: δ 8.22 and 7.20 (2 m, each 2 H, *p*-subst. Ph), 5.90 (d, 1 H, $J_{1,2}$ 1 Hz, H- 1), 4.42 (dd, 1 H, $J_{2,3}$ 6 Hz, H-2), 4.32 (dd, 1 H, $J_{3,4}$ 7 Hz, H-3), 3.50 (ni, 2 H, H-5,6a), 3.31 (dd, 1 H, $J_{5,6a}$ 7, $J_{6a,6b}$ 11 Hz, H-6b), 3.12 (ddd, 1 H, $J_{4,5}$ 7, $J_{4,OH}$ 2 Hz, H-4), 2.05 (s, 1 H, OH), 1.60 and 1.42 (2 s, each 3 H, Ip CH_3); ^{13}C NMR: δ 116.82 (acetalic C), 96.17 (C-1), 26.2 and 27.95 (2 Ip CH_3), 5.11 (C-6). Anal. Calcd for $C_{15}H_{18}INO_7$: C, 39.93; H, 4.02. Found: C, 40.16; H, 3.92.

p-*Nitrophenyl 6-deoxy-2,3*-O-*isopropylidene*-α-D-*mannopyranoside* (**23**).—To a solution of **22** (380 mg, 0.84 mmol) in dry THF (15 mL) was added $LiAlH_4$ (96 mg, 2.5 mmol), and the mixture was stirred for 20 h at room temperature. The excess of hydride was decomposed by addition of EtOAc (100 mL) and water, and the organic layer was washed with water until neutral, dried, concentrated. Chromatography (7:3 CH_2Cl_2–acetone) of the residue yielded **23** (144 mg, 53%), isolated as a syrup; $[\alpha]_D$ + 115.4° (*c* 0.24); ^{1}H NMR: δ 8.20 and 7.28 (2 m, each 2 H, *p*-subst. Ph), 5.82 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 4.45 (dd, 1 H, $J_{2,3}$ 6, $J_{3,4}$ 6.5 Hz, H-3), 4.39 (dd, 1 H, H-2), 3.75 (dd, 1 H, $J_{4,5}$ 9.5, $J_{5,Me(6)}$ 6 Hz, H-5), 3.40 (dd, 1 H, H-4), 1.55 and 1.40 (2 s, each 3 H, Ip CH_3), 1.21 (d, 1 H, CH_3). Anal. Calcd for $C_{15}H_{19}NO_7$: C, 55.38; H, 5.89. Found: C, 55.16; H, 5.92.

p-*Nitrophenyl 4*-O-*benzyl-6-deoxy-2,3*-O-*isopropylidene*-α-D-*mannopyranoside* (**24**).—To a chilled solution of **23** (140 mg, 0.43 mmol) and benzyl bromide (67 μL, 0.56 mmol) in DMF (10 mL) was added KOH (2.5 g), and the mixture was stirred for 40 min at 0 °C. EtOAc (100 mL) was added, and the organic layer was washed with water until neutral, dried, and concentrated. Chromatography

(95:5 hexane–EtOAc) of the residue yielded **24** (133 mg, 75%), isolated as a syrup; $[\alpha]_D$ +121° (*c* 0.17); ^{1}H NMR: δ 8.19 and 7.13 (2 m, each 2 H, *p*-subst. Ph), 7.32 (m, 5 H, Ph), 5.79 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 4.92 and 4.66 (2 d, each 1 H, $PhCH_2$), 4.45 (t, 1 H, $J_{2,3}$ 6, $J_{3,4}$ 6 Hz, H-3), 4.38 (dd, 1 H, H-2), 3.72 (dd, 1 H, $J_{4,5}$ 9.5, $J_{5,Me(6)}$ 6 Hz, H-5), 3.31 (dd, 1 H, H-4), 1.56 and 1.42 (2 s, each 3 H, Ip CH_3), 1.22 (d, 1 H, CH_3). Anal. Calcd for $C_{22}H_{25}NO_7$: C, 63.60; H, 6.07. Found: C, 63.46; H, 6.22.

p-*Nitrophenyl 4*-O-*benzyl-6-deoxy*-α-D-*mannopyranoside* (**25**).—To a solution of **24** (500 mg, 1.2 mmol) in CH_2Cl_2 (10 mL) were added CF_3CO_2H (1 mL) and water (0.5 mL), and the mixture was stirred vigorously for 10 min at room temperature. After concentration, flash chromatography (7:3 hexane–EtOAc) of the residue gave **25** (405 mg, 90%), isolated as a syrup; $[\alpha]_D$ +105.2° (*c* 0.58); ^{1}H NMR: δ 8.20 and 7.28 (2 m, each 2 H, *p*-subst. Ph), 7.32 (m, 5 H, Ph), 5.90 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 4.91 and 4.60 (2 d, each 1 H, CH_2Ph), 5.2 and 3.2 (2 s, each 1 H, OH). Anal. Calcd for $C_{19}H_{21}NO_7$: C, 60.79; H, 5.64. Found: C, 61.0; H, 5.88.

p-*Nitrophenyl 4*-O-*benzyl-6-deoxy-2*-O-*methyl*-α-D-*mannopyranoside* (**26**).—A mixture of **25** (200 mg, 0.53 mmol), Bu_4NBr (300 mg), and CH_3I (3 mL, 9.3 mmol) in CH_2Cl_2 (10 mL) and aq 20% NaOH (6 mL) was stirred vigorously overnight. The organic layer was separated, washed with water, concentrated, and the residue was chromatographed (7:3 hexane–EtOAc) to yield **26** (186 mg, 90%) as a syrup; $[\alpha]_D$ +118.0° (*c* 0.15); ^{1}H NMR: δ 8.20 and 7.30 (2 m, each 2 H, *p*-subst. Ph), 7.32 (m, 5 H, Ph), 5.85 (d, 1 H, $J_{1,2}$ 2 Hz, H-1), 5.21 (d, 1 H, $J_{OH,3}$ 7 Hz, OH), 4.88 and 4.58 (2 d, each 1 H, $PhCH_2$), 3.95 (m, 1 H, $J_{2,3}$ 3.5, $J_{3,4}$ 9 Hz, H-3), 3.58 (dd, 1 H, H-2), 3.47 (dd, 1 H, $J_{5,6}$ 6, $J_{4,5}$ 9.5 Hz, H-5), 3.46 (s, 3 H, OCH_3), 3.30 (t, 1 H, H-4), 1.1 (d, 3 H, CH_3). Anal. Calcd for $C_{20}H_{23}NO_7$: C, 61.69; H, 5.95. Found: C, 61.50; H, 5.92.

p-*Nitrophenyl* (*3*-O-*benzyl-4*-N-*benzylformamido-4,6-dideoxy-3*-C-*methyl-2*-O-*methyl*-α-L-*mannopyranosyl*)-(*1*→*3*)-*4*-O-*benzyl-6-deoxy-2*-O-*methyl*-α-D-*mannopyranoside* (**27**).—A mixture of **26** (29 mg, 0.074 mmol) and **20** (50 mg, 0.09 mmol) in dry CH_2Cl_2 (5 mL), containing 4 Å molecular sieves (100 mg) was stirred for 30 min at 0 °C under Ar, then cooled to −30 °C. A solution of TMSOTf (17 μL, 0.3 equiv.), in dry CH_2Cl_2 (1 mL) was injected and after 15 min the reaction was quenched with pyridine (0.5 mL). Then the mixture was diluted with CH_2Cl_2 (20 mL), filtered, and concentrated. Chromatography (7:3 hexane–EtOAc) of the residue yielded **27** (20 mg, 35%), isolated as a syrup; $[\alpha]_D$ +52.9° (*c* 1.03). ^{1}H and ^{13}C NMR data (500 and 125 MHz, respectively) are presented in Table 1. "a" and "b" denote the two isomers present due to the formamido group. Anal. Calcd for $C_{43}H_{50}N_2O_{11}$: C, 66.99; H, 6.54; N, 3.64. Found: C, 66.85, H, 6.48, N, 3.65.

p-*Trifluoroacetamidophenyl* (*4-formamido-4,6-dideoxy-3*-C-*methyl-2*-O-*methyl*-α-L-*mannopyranosyl*)-(*1*→*3*)-*6-deoxy-2*-O-*methyl*-α-D-*mannopyranoside* (**29**).—Compound **27** (15 mg, 0.03 mmol) in EtOAc (10 mL) was treated with H_2 in the presence of Adam's catalyst (PtO_2, 10 mg) for 2 h at room temperature. Pyridine (200 μL) and trifluoroacetic anhydride (150 μL) were added, and the mixture was stirred for an additional 1 h. After filtration, the filtrate was concentrated and the residue was chromatographed (7:3 hexane–EtOAc) to yield **28** (11 mg). A mixture of **28** (11 mg) and $Pd(OH)_2$ (40 mg) in MeOH (5 mL) was stirred vigorously under H_2 overnight. After filtration and concentration, the residue was purified on a short column of silica gel (98:2 CH_2Cl_2–MeOH) to yield **29** (4 mg, 24%) as a glass; $[\alpha]_D$ −4.52° (*c* 0.24; MeOH). ^{1}H and ^{13}C NMR data (recorded in CD_3OD at 500 and 125 MHz, respectively) are presented in Table 2.

Ethyl (*3*-O-*benzyl-4*-N-*benzylformamido-4,6-dideoxy-3*-C-*methyl-2*-O-*methyl*-α-L-*mannopyranosyl*)-(*1*→*3*)-*4*-O-*benzyl-6-deoxy-2*-O-*methyl-1-thio*-α-D-*mannopyranoside* (**31**).—A mixture of ethyl 4-*O*-benzyl-6-deoxy-2-*O*-methyl-1-thio-α-D-mannopyranoside (**30**) (23 mg, 0.074 mmol), **20** (50 mg, 0.09 mmol) and 4 Å molecular sieves (100 mg) in dry CH_2Cl_2 (3 mL) was stirred for 30 min at 0 °C under Ar. The mixture was cooled to −30 °C, and TMSOTf (17 μL, 0.3 equiv.) in CH_2Cl_2 (1 mL) was injected. After 15 min, pyridine (500 mL) was added, and the mixture was diluted with CH_2Cl_2, filtered, and the filtrate was concentrated. Chromatography (7:3 hexane–EtOAc) of the residue gave **31** (38 mg, 75%), isolated as a syrup; $[\alpha]_D$ +56.8° (*c* 0.37). ^{1}H and ^{13}C NMR data (500 and 125 MHz, respectively) are presented in Table 1. "a" and "b" denote the two isomers present due to the formamido group. Anal. Calcd for $C_{39}H_{51}NO_8S$: C, 67.50; H, 7.41. Found: C, 67.42; H, 7.23.

p-*Nitrophenyl* (*3*-O-*benzyl-4*-N-*benzylformamido-4,6-dideoxy-3*-C-*methyl-2*-O-*methyl*-α-L-*mannopyranosyl*)-(*1*→*3*)-(*4*-O-*benzyl-6-deoxy-2*-O-*methyl*-α-

D-*mannopyranosyl)-(1→3)-(4*-O-*benzyl-2*-O-*methyl*-α-L-*fucopyranosyl)-(1→3)-(2,4-di*-O-*benzyl-6-deoxy*-α-L-*mannopyranosyl)-(1→2)-3,4*-O-endo-*benzylidene*-α-L-*talopyranoside* (**33**).—A mixture of **31** (30 mg, 0.046 mmol), **32** [12] (48 mg, 0.074 mmol) and 4 Å molecular sieves (100 mg) in dry CH_2Cl_2 (5 mL) was stirred for 30 min at 0 °C, then cooled to −40 °C. A solution of NIS (14 mg, 0.055 mmol) and TfOH (0.6 mL, 0.005 mmol) in CH_2Cl_2 (1 mL) was added dropwise and the mixture was allowed to warm up to 0 °C. After 40 min the mixture was diluted with CH_2Cl_2 (20 mL), extracted with aq $Na_2S_2O_3$ (10 mL) and aq $NaHCO_3$ (10 mL), and the organic layer was dried and concentrated. The residue was chromatographed (8:2 hexane–EtOAc) to yield **33** (40 mg, 55%), isolated as a syrup; $[\alpha]_D$ −23.2° (*c* 0.19); ^1H and ^{13}C NMR data (500 and 125 MHz, respectively) are given in Table 3. Anal. Calcd for $C_{90}H_{104}N_2O_{23}$: C, 68.34; H, 6.63. Found: C, 68.12; H, 6.58.

p-*Trifluoroacetamidophenyl (4-formamido-4,6-dideoxy-3*-C-*methyl-2*-O-*methyl*-α-L-*mannopyranosyl)-(1→3)-(6-deoxy-2*-O-*methyl*-α-D-*mannopyranosyl)-(1→3)-(2*-O-*methyl*-α-L-*fucopyranosyl)-(1→3)-(6-deoxy*-α-L-*mannopyranosyl)-(1→2)*-α-L-*talopyranoside* (**35**).—A solution of **33** (35 mg, 0.02 mmol) in EtOAc (10 mL) was stirred vigorously under H_2 in the presence of Adam's catalyst (PtO_2, 10 mg) for 2 h at room temperature. Pyridine (200 μL) and trifluoroacetic anhydride (150 μL) were added, and the mixture was stirred for an additional 1 h. After filtration and concentration of the filtrate, resulting **34** (16 mg) was dissolved in MeOH (10 mL), and $Pd(OH)_2$ (50 mg) was added. The mixture was stirred vigorously under H_2 overnight, then filtrated followed by concentration of the filtrate. The residue was purified on a column of silica (98:2 CH_2Cl_2–MeOH) to yield pure **35** (5 mg, 25%), isolated as a syrup; $[\alpha]_D$ −17.9° (*c* 0.21; MeOH). ^1H and ^{13}C NMR data (500 and 125 MHz, respectively) are given in Table 4.

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