Carbohydrate Research, 241 (1993) 153–164
Elsevier Science Publishers B.V., Amsterdam

Iodonium ion-assisted synthesis of a haptenic tetrasaccharide fragment corresponding to the inner cell-wall glycopeptidolipid of *Mycobacterium avium* serotype 4

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(Received July 24th, 1992; accepted September 3rd, 1992)

ABSTRACT

Condensation of ethyl 2,4-di-*O*-benzoyl-1-thio-α-L-rhamnopyranoside with ethyl 3-*O*-benzyl-4-*O*-chloroacetyl-2-*O*-methyl-1-thio-β-L-fucopyranoside in the presence of iodonium di-*sym*-collidine perchlorate afforded exclusively ethyl 2,4-di-*O*-benzoyl-3-*O*-(3-*O*-benzyl-4-*O*-chloroacetyl-2-*O*-methyl-α-L-fucopyranosyl)-1-thio-α-L-rhamnopyranoside. This disaccharide derivative was extended at C-1 with 3-benzyloxycarbonylaminopropyl 6-deoxy-3,4-*O*-isopropylidene-α-L-talopyranoside, using *N*-iodosuccinimide and triflic acid as the catalyst, to furnish 3-benzyloxycarbonylaminopropyl 6-deoxy-2-*O*-[2,4-di-*O*-benzoyl-3-*O*-(3-*O*-benzyl-4-*O*-chloroacetyl-2-*O*-methyl-α-L-fucopyranosyl)-α-L-rhamnopyranosyl]-3,4-*O*-isopropylidene-α-L-talopyranoside (**20**). Selective removal of the chloroacetyl group from **20**, followed by condensation with ethyl 2,3-di-*O*-benzoyl-4-*O*-methyl-1-thio-α-L-rhamnopyranoside in the presence of the same thiophilic promoter, yielded a fully protected tetrasaccharide derivative. Deprotection of the latter gave the target compound 3-aminopropyl 6-deoxy-2-*O*-{3-*O*-[2-*O*-methyl-(4-*O*-methyl-α-L-rhamnopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-talopyranoside (**1**).

INTRODUCTION

It is well documented[1] that opportunistic members of the *M. avium* complex can be the causative agents of pulmonary and other organ infections. Renewal of interest in "atypical" mycobacteria stems from the observation that patients with an acquired immunodeficiency syndrome (AIDS) are vulnerable to disseminated infections by several serovariants of the *M. avium* complex[2]. For example, it has been established[3] that *M. avium* serotype 4 presents the majority of *M. avium* isolates from patients with AIDS from the eastern part of the USA. The structure of the serotype 4 haptenic oligosaccharide was established[3,4] as 4-*O*-Me-α-L-Rha*p*-(1 → 4)-2-*O*-Me-α-L-Fuc*p*-(1 → 3)-α-L-Rha*p*-(1 → 2)-6-deoxy-L-Tal*p*, the reducing

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end of which is α-linked to the hydroxyl group of an internal D-*allo*-threonine moiety of an invariant 3,4-di-*O*-methylrhamnopyranosylpeptidolipid.

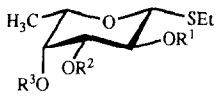
As part of a programme[5] on the design and preparation of immunodiagnostic reagents and synthetic vaccines, we now report the synthesis of the tetrasaccharide glycoside **1**, which contains a spacer to serve as a precursor of neoglycoproteins.

4-*O*-Me-α-L-Rha*p*-(1 → 4)-2-*O*-Me-α-L-Fuc*p*-(1 → 3)-α-L-Rha*p*-(1 → 2)-6-deoxy-L-Tal*p*-O$(CH_2)_3NH_2$

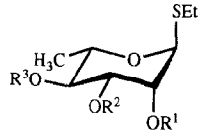
1

RESULTS AND DISCUSSION

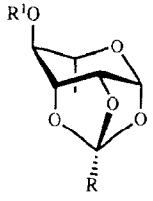
Preliminary studies[5] indicated that stereoselective formation of the 1,2-*cis* linkage between the fucose and rhamnose units in **1** was feasible using appropriately protected alkyl 1-thioglycosides. Thus, the presence of the 4-*O*-chloroacetyl group in ethyl 3-*O*-benzyl-4-*O*-chloroacetyl-2-*O*-methyl-1-thio-β-L-fucopyranoside (**5**) plays a pivotal role in the stereoselective introduction of the α linkage in the key disaccharide derivative **9**. Further, replacement of the 4-*O*-benzyl and 2-*O*-acetyl groups of the ethyl 1-thiorhamnopyranoside derivative **6** by benzoyl groups will exert the following beneficial effects. In the iodonium di-*sym*-collidine perchlorate (IDCP)-assisted glycosylation of ethyl 2,4-di-*O*-benzoyl-1-thio-α-L-rhamnopyranoside (**7**) with **5**, BzO-4 decreases the rate of cyclisation of **7** to give



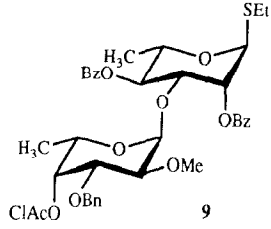
2 R^1 = Me, R^2R^3 = Me_2C
3 R^1 = Me, R^2 = R^3 = H
4 R^1 = Me, R^2 = Bn, R^3 = H
5 R^1 = Me, R^2 = Bn, R^3 = ClAc



6 R^1 = Ac, R^2 = H, R^3 = Bn
7 R^1 = R^3 = Bz, R^2 = H
17 R^1R^2 = CMe_2, R^3 = Me
18 R^1 = R^2 = H, R^3 = Me
19 R^1 = R^2 = Bz, R^3 = Me



8a R = CH_3, R^1 = Bn
8b R = Ph, R^1 = Bz



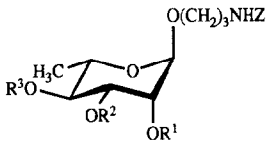
9

4-*O*-benzoyl-β-L-rhamnopyranose 1,2,3-orthobenzoate (**8b**) [the conversion of **6** into **8a** proceeds rapidly]. On the other hand, the coupling efficacy of **9** with the talose derivative **16** to give the trisaccharide derivative **20** rises[6] by the protection of HO-2 in **9** with a benzoyl group.

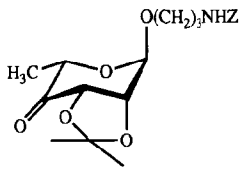
Synthesis of the requisite fucosyl acceptor **5** comprised methylation of known ethyl 3,4-*O*-isopropylidene-1-thio-β-L-fucopyranoside[7] (→ **2**), followed by deacetonation (→ **3**, 89% over the two steps), regioselective benzylation of the intermediate stannilydene complex of **3** with benzyl bromide in the presence of cesium fluoride[8] (→ **4**, 85%), and finally acylation with chloroacetic anhydride using sodium hydrogen carbonate[9] as the base.

Condensation of ethyl 2,4-di-*O*-benzoyl-1-thio-α-L-rhamnopyranoside[10] with **5** in the presence of IDCP afforded exclusively the α-linked key disaccharide derivative **9** (61%). The ^{1}H NMR data for **9** are given in Table I.

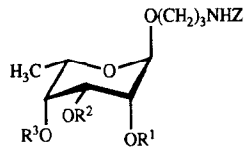
Further extension of **9** at C-1 and C-4′ involved the respective synthons 3-benzyloxycarbonylaminopropyl 6-deoxy-3,4-*O*-isopropylidene-α-L-talopyranoside (**16**) and ethyl 2,3-di-*O*-benzoyl-4-*O*-methyl-1-thio-α-L-rhamnopyranoside (**19**). Coupling of ethyl 2,3,4-tri-*O*-benzoyl-1-thio-α-L-rhamnopyranoside with 3-benzyloxycarbonylamino-1-propanol[11], using *N*-iodosuccinimide and catalytic triflic acid (NIS–TfOH)[12] as a promoter, afforded the glycoside **10**. Zemplén debenzoylation of **10** (→ **11**, 95%), followed by acetonation (→ **12**, 73%), and oxidation with tetrapropylammonium per-ruthenate in the presence of 4-methylmorpholine



10 $R^1 = R^2 = R^3 = Bz$
11 $R^1 = R^2 = R^3 = H$
12 $R^1,R^2 = CMe_2$, $R^3 = H$



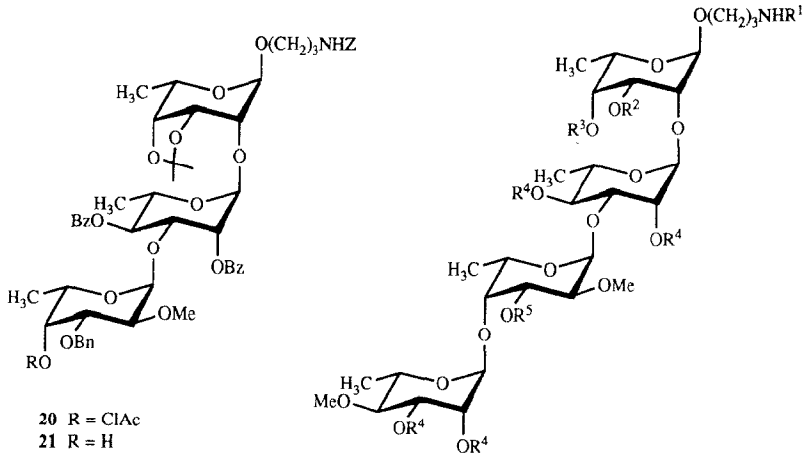
13



14 $R^1,R^2 = CMe_2$, $R^3 = H$
15 $R^1 = R^2 = R^3 = H$
16 $R^1 = H$, $R^2,R^3 = CMe_2$

N-oxide[13] gave 3-benzyloxycarbonylaminopropyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose (**13**, 85%). Stereoselective reduction of the ketone function in **13**, using sodium borohydride in ethanol (→ **14**, 90%), then deacetonation (→ **15**), and kinetically controlled acetonation with 2,2-dimethoxypropane catalysed by camphorsulfonic acid[14] afforded **16** (79% from **14**). Methylation of ethyl 2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside[15] with methyl iodide in the presence of sodium hydride and acid hydrolysis of the resulting crude **17** gave **18** that was benzoylated to give **19** (67% over the three steps).

Coupling of the disaccharide derivative **9** with **16** in dry 1,2-dichloroethane–ether at 20°C, using NIS–TfOH as a promoter, gave the trisaccharide derivative **20** (70%). The ^{1}H NMR data for **20** are given in Table I. Attempts to remove the chloroacetyl group from **20** with hydrazine dithiocarbonate[16] gave an intractable



20 R = ClAc
21 R = H

22 R^1 = Z, R^2,R^3 = CMe_2, R^4 = Bz, R^5 = Bn
23 R^1 = Z, R^2 = R^3 = H, R^4 = Bz, R^5 = Bn
24 R^1 = Z, R^2 = R^3 = R^4 = H, R^5 = Bn

mixture of products. However, treatment of **20** with hydrazine acetate[17] proceeded smoothly to afford **21** (79%).

NIS–TfOH-mediated glycosylation of **21** with **19** in dry 1,2-dichloroethane–ether at 0°C furnished the fully protected tetrasaccharide **22** (84%), the ^1H and ^{13}C NMR data for which are given in Tables I and II, respectively. Hydrolysis of **22** with acetic acid–water (→ **23**), followed by debenzoylation (→ **24**), and debenzylation gave the target 3-aminopropyl glycoside **1** (66% from **22**). The ^1H NMR data (Table I) of **1**, obtained by 2D COSY[18] and HOHAHA[19] measurements, are in full accord with the proposed structure.

The results of immunological inhibition experiments with **1** will be reported elsewhere.

EXPERIMENTAL

General methods—Pyridine and acetonitrile were dried by boiling under reflux over CaH_2 (5 g/L) and then distilled. Dichloromethane, 1,2-dichloroethane, and toluene were distilled from P_2O_5. *N*,*N*-Dimethylformamide was stirred with CaH_2 at room temperature and distilled under reduced pressure. Ether was distilled from $LiAlH_4$. Pyridine and acetonitrile were stored over 4A molecular sieves (Aldrich). Toluene and ether were stored over Na wire, and CH_2Cl_2 and 1,2-dichloroethane over alumina. Schleicher and Schüll DC Fertigfolien F 1500 LS 254 (Merck) were used for TLC. Compounds were detected by charring with 20% H_2SO_4 in MeOH. Optical rotations were recorded at 20°C with a Perkin–Elmer 241 polarimeter. Column chromatography was performed on Silica Gel 60 (70–230 mesh, Merck) and GPC was performed on Sephadex LH 20 (Pharmacia). ^1H NMR

TABLE I

The 300- and 400-MHz ^{1}H NMR data for glycosides **9**, **20**, **22**, and **1**

Residue	Proton (J)	δ (ppm) (J in Hz)			
		9 ($CDCl_3$) [a]	**20** ($CDCl_3$) [a]	**22** ($CDCl_3$) [a]	**1** (D_2O) [b]
Aminopropyl	H-1		3.58, 3.87	3.60, 3.89	3.60
	H-2 ($J_{2,3}$)		1.81 (6.3)	1.83	2.00
	H-3		3.30	3.30	3.15
6-Deoxy-α-L-Tal	H-1 ($J_{1,2}$)		4.86 (6.3)	4.88 (6.3)	4.95 (1.7)
	H-2 ($J_{2,3}$)		3.82 (2.6)	3.81 (2.6)	3.94
	H-3 ($J_{3,4}$)		4.62 (7.6)	4.63 (7.6)	4.06
	H-4 ($J_{4,5}$)		4.08	4.08 (1.8)	3.72
	H-5 ($J_{5,6}$)		4.08 (6.5)	4.25 (6.1)	4.05
	H-6		0.92	0.97	1.31
α-Rha	H-1 ($J_{1,2}$)	5.43 (1.7)	5.15 (1.8)	5.17 (1.7)	5.00 (1.7)
	H-2 ($J_{2,3}$)	5.56 (3.5)	5.57 (3.5)	5.55 (3.5)	4.15 (3.3)
	H-3 ($J_{3,4}$)	4.25 (9.8)	4.36 (9.9)	4.38 (9.9)	3.83
	H-4 ($J_{4,5}$)	5.55 (9.8)	5.51 (9.9)	5.54 (9.9)	3.76 (9.7)
	H-5 ($J_{5,6}$)	4.47 (6.4)	4.31 (6.3)	4.31 (6.3)	3.83 (6.6)
	H-6	1.33	1.29	1.29	1.24
α-Fuc	H-1 ($J_{1,2}$)	5.01 (3.7) [c]	5.05 (3.6)	5.09 (3.6)	5.43 (3.9)
	H-2 ($J_{2,3}$)	3.26 (10.1)	3.26 (10.1)	3.45 (10.3)	3.52 (10.6)
	H-3 ($J_{3,4}$)	3.68 (3.3)	3.67 (3.4)	3.61 (3.0)	4.05 (3.2)
	H-4 ($J_{4,5}$)	5.18 (1.5)	5.18 (1.4)	3.87	3.87
	H-5 ($J_{5,6}$)	4.05 (6.6)	3.75 (6.4)	3.74 (6.4)	4.21 (6.2)
	H-6	0.92	1.20	1.20	1.17
α-Rha	H-1 ($J_{1,2}$)			4.83 (1.7)	4.80 (1.8)
	H-2 ($J_{2,3}$)			5.54 (3.4)	4.10 (3.4)
	H-3 ($J_{3,4}$)			5.55 (9.6)	3.89 (9.6)
	H-4 ($J_{4,5}$)			3.37 (6.9)	3.34 (9.6)
	H-5 ($J_{5,6}$)			3.91 (6.6)	4.20 (6.6)
	H-6			1.08	1.24

[a] Chemical shifts are relative to that for internal Me_4Si. [b] Chemical shifts are relative to that for internal 4,4-dimethyl-4-silapentane-1-sulfonate. [c] $J_{C\text{-}1,H\text{-}1}$ 168.5 Hz.

spectra (300 and 400 MHz) were recorded at 25°C with a Bruker WM 300 or 400 MSL spectrometer. The 600-MHz 1D homonuclear Hartmann–Hahn spectrum (1D HOHAHA) of **1** was recorded with a MLEV-17 mixing sequence of 100 ms[19] on an AMX-600 (Bruker, Karlsruhe) spectrometer. ^{13}C NMR spectra (50 and 100 MHz) were recorded with a Jeol JNM-FX 200 or Bruker 400 MSL spectrometer. The ^{1}H and ^{13}C chemical shifts (δ) are given in ppm relative to that of Me_4Si ($CDCl_3$), or sodium 4,4-dimethyl-4-silapentane-1-sulfonate (D_2O). The liquid chromatography–mass spectrum (LC–MS) of **1** was recorded in the positive ion mode on a TSQ 70 triple quadrupole spectrometer equipped with an HP 59980A Particle Beam LC/MS interface, using ammonia for chemical ionisation.

TABLE II

The 400-MHz ^{13}C NMR data for **22** and **1**

Residue	Carbon atom (J)	δ (ppm) (J in Hz)	
		22 ($CDCl_3$) [a]	**1** (D_2O) [b]
Aminopropyl	C-1	65.3	65.7
	C-2	29.7	27.2
	C-3	38.3	38.0
6-Deoxy-α-L-Tal	C-1 ($J_{C-1,H-1}$)	99.0	99.7 (168.5)
	C-2	74.3	77.8
	C-3	71.6	
	C-4	76.5	
	C-5	67.6	
	C-6	17.5	16.3
α-Rha	C-1 ($J_{C-1,H-1}$)	95.8	103.1 (172.9)
	C-2	72.4	68.8
	C-3	75.4	
	C-4	72.8	70.5
	C-5	67.0	
	C-6	17.4	17.4
α-Fuc	C-1 ($J_{C-1,H-1}$)	99.5	98.5 (169.9)
	C-2	77.6	78.0
	C-3	78.9	68.4
	C-4	67.1	81.5
	C-5	65.9	
	C-6	15.4	16.3
α-Rha	C-1 ($J_{C-1,H-1}$)	98.7	102.7 (168.5)
	C-2	71.2	71.0
	C-3	71.5	70.8
	C-4	80.9	83.1
	C-5	67.1	67.7
	C-6	16.3	17.4

[a] Chemical shifts are relative to that for internal Me_4Si. [b] Chemical shifts are relative to that for internal 4,4-dimethyl-4-silapentane-1-sulfonate.

Ethyl 2-O-methyl-1-thio-β-L-fucopyranoside (**3**).—To a stirred solution of ethyl 3,4-*O*-isopropylidene-1-thio-β-L-fucopyranoside[7] (2.7 g, 10.9 mmol) in DMF (50 mL) were added NaH (0.4 g, 80%, 1.3 equiv) and MeI (0.8 mL, 1.2 equiv). The mixture was stirred for 2 h at 20°C, MeOH (10 mL) was added, and the mixture was concentrated. A solution of the residue in CH_2Cl_2 (50 mL) was washed twice with water, dried ($MgSO_4$), and concentrated. A solution of the resulting crude **2** in 9:1 HOAc–water (50 mL) was stirred for 2 h at 50°C, then concentrated, and toluene (2 × 50 mL) was evaporated from the residue. Column chromatography (97:3 CH_2Cl_2–MeOH) then yielded **3** (2.2 g, 89% based on ethyl 3,4-*O*-isopropylidene-1-thio-β-L-fucopyranoside); $[\alpha]_D$ +32° (*c* 1, $CHCl_3$). NMR data ($CDCl_3$): ^1H, δ 1.27 (t, 3 H, *J* 7.5 Hz, SCH_2CH_3), 1.32 (d, 3 H, $J_{5,6}$ 6.9 Hz, H-6,6,6), 2.74

(ABq, 2 H, SCH_2CH_3), 3.12 (d, 1 H, $J_{3,4}$ 5.9 Hz, H-4), 3.19 (t, 1 H, $J_{1,2} = J_{2,3} = 9.5$ Hz, H-2), 3.60 (dd, 1 H, H-3), 3.64 (s, 3 H, OMe), 3.77 (q, 1 H, H-5), and 4.32 (d, 1 H, H-1); ^{13}C, δ 14.7 (SCH_2CH_3), 16.3 (C-6), 24.7 (SCH_2CH_3), 60.9 (OCH_3), 71.7 (C-5), 74.3, 75.0, 80.4 (C-2,3,4), and 84.3 (C-1). Anal. Calcd for $C_9H_{18}O_4S$: C, 48.64; H, 8.16. Found: C, 48.49; H, 8.43.

Ethyl 3-O-benzyl-2-O-methyl-1-thio-β-L-fucopyranoside (**4**).—To a solution of **3** (2.2 g, 9.7 mmol) in dry MeOH was added dibutyltin oxide (3.1 g, 12.6 mmol). The mixture was boiled under reflux for 4 h, then concentrated under reduced pressure, and toluene (2 × 50 mL) was evaporated from the residue. A solution of the residue in DMF (50 mL) was stirred with CsF (1.9 g, 12.6 mmol) and benzyl bromide (2.5 g, 14.6 mmol) for 16 h at 20°C, then diluted with CH_2Cl_2 (50 mL), and the organic layer was washed with M KF (50 mL) and water (50 mL), dried ($MgSO_4$), and concentrated. Column chromatography [1:0 → 0:1 light petroleum (bp 40–60°C)–CH_2Cl_2] of the residue gave **4** (2.6 g, 85%); $[\alpha]_D$ +43° (*c* 1, $CHCl_3$). NMR data ($CDCl_3$): ^1H, δ 1.27 (t, 3 H, *J* 7.5 Hz, SCH_2CH_3), 1.32 (d, 3 H, $J_{5,6}$ 6.7 Hz, H-6,6,6), 2.76 (ABq, 2 H, SCH_2CH_3), 3.32 (t, 1 H, $J_{1,2}$ 9.5 Hz, H-2), 3.44 (ABq, 2 H, CH_2Ph), 3.52 (c, 2 H, H-3,4), 3.62 (s, 3 H, OMe), 3.78 (q, 1 H, H-5), 4.28 (d, 1 H, H-1), and 7.27–7.40 (c, 5 H, Ph); ^{13}C, δ 14.2 (SCH_2CH_3), 16.0 (C-6), 23.7 (SCH_2CH_3), 60.2 (OCH_3), 68.5 (C-5), 71.1 (CH_2Ph), 73.3, 78.7, 81.8 (C-2,3,4), 83.7 (C-1), 126.9–127.3 ($CH_{aromatic}$), and 137.4 ($C_{aromatic}$). Anal. Calcd for $C_{16}H_{24}O_4S$: C, 61.51; H, 7.74. Found: C, 61.73; H, 7.62.

Ethyl 3-O-benzyl-4-O-chloroacetyl-2-O-methyl-1-thio-β-L-fucopyranoside (**5**).—A suspension of **4** (1.5 g, 5.0 mmol), chloroacetic anhydride (1.7 g, 10.0 mmol), and $NaHCO_3$ (0.9 g, 10 mmol) in DMF (50 mL) was stirred for 17 h at 20°C, then diluted with CH_2Cl_2 (50 mL), washed with 0.9 M $NaHCO_3$ (50 mL) and water (50 mL), dried ($MgSO_4$), and concentrated. Column chromatography (CH_2Cl_2) of the residue gave **6** (1.8 g, 92%); $[\alpha]_D$ +34° (*c* 1, $CHCl_3$). NMR data ($CDCl_3$): ^1H, δ 1.22 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6,6,6), 1.32 (t, 3 H, *J* 7.5 Hz, SCH_2CH_3), 2.72 (ABq, 2 H, SCH_2CH_3), 3.25 (t, 1 H, $J_{1,2} = J_{2,3} = 9.5$ Hz, H-2), 3.48 (dd, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 3.60 (s, 3 H, OMe), 3.66 (q, 1 H, H-5), 4.18 (s, 2 H, CH_2Cl), 4.34 (d, 1 H, H-1), 4.63 (ABq, 2 H, CH_2Ph), 5.38 (d, 1 H, H-4), and 7.27–7.40 (c, 5 H, Ph); ^{13}C, δ 14.7 (SCH_2CH_3), 16.4 (C-6), 24.5 (SCH_2CH_3), 40.6 (CH_2Cl), 61.1 (OCH_3), 71.9 (CH_2Ph), 71.7, 72.3, 79.0, 80.4 (C-2,3,4,5), 84.5 (C-1), 126.9–127.3 ($CH_{aromatic}$), and 137.4 ($C_{aromatic}$). Anal. Calcd for $C_{18}H_{25}ClO_5S$: C, 55.59; H, 6.48. Found: C, 55.71; H, 6.39.

Ethyl 2,4-di-O-benzoyl-3-O-(3-O-benzyl-4-O-chloroacetyl-2-O-methyl-α-L-fucopyranosyl)-1-thio-α-L-rhamnopyranoside (**9**).—Iodonium di-*sym*-collidine perchlorate[20] (1.2 g, 2.6 mmol) was added to a stirred mixture of **5** (510 mg, 1.3 mmol), ethyl 2,4-di-*O*-benzoyl-1-thio-α-L-rhamnopyranoside[10] (420 mg, 1.0 mmol), and 4A powdered molecular sieves (1 g) in 1:5 1,2-dichloroethane–ether (12 mL). After 15 min at 20°C, TLC (97:3 CH_2Cl_2–acetone) showed the reaction to be complete. The mixture was filtered, diluted with CH_2Cl_2 (10 mL), washed with M sodium thiosulfate (10 mL), dried ($MgSO_4$), and concentrated. Column chromatography

[1:0 → 0:1 light petroleum (bp 40–60°C)–CH_2Cl_2] of the residue gave **9** (450 mg, 61%); $[\alpha]_D$ −52° (*c* 1, $CHCl_3$). ^{13}C NMR data ($CDCl_3$): δ 14.2 (SCH_2CH_3), 15.0 (C-6^F), 16.8 (C-6^R), 25.1 (SCH_2CH_3), 40.0 ($ClCH_2$), 58.8 (OCH_3), 65.4, 67.3, 73.0, 74.0, 75.7, 76.8 and 77.0 (C-2^R/5^R and C-2^F/5^F), 82.1 (C-1^R), 99.6 (C-1^F), and 126.7–132.8 ($CH_{aromatic}$ and $C_{aromatic}$). For the ^1H NMR data, see Table 1. Anal. Calcd for $C_{38}H_{43}ClO_{11}S$: C, 61.41; H, 5.83. Found: C, 61.73; H, 5.69.

3-Benzyloxycarbonylaminopropyl 2,3,4-tri-O-benzoyl-α-L-rhamnopyranoside (**10**).—To a solution of ethyl 2,3,4-tri-*O*-benzoyl-1-thio-α-L-rhamnopyranoside (1.1 g, 2.0 mmol) and 3-benzyloxycarbonylamino-1-propanol[11] (400 mg, 1.9 mmol) in 1:1 1,2-dichloroethane–ether (20 mL) were added 4A powdered molecular sieves (2 g), and the mixture was kept for 15 min at 0°C. A solution of *N*-iodosuccinimide (450 mg, 2.0 mmol) and trifluoromethanesulfonic acid (17 μL, 0.2 mmol) in 1:1 1,2-dichloroethane–ether (20 mL) was added and stirring was continued for 15 min. The mixture was filtered and diluted with CH_2Cl_2 (20 mL), and the organic layer was washed with M sodium thiosulfate (20 mL) and 0.9 M $NaHCO_3$ (20 mL), dried ($MgSO_4$), and concentrated. Column chromatography (95:5 CH_2Cl_2–acetone) of the residue gave **7** (1.1 g, 81%); $[\alpha]_D$ +39° (*c* 1, $CHCl_3$). ^{13}C NMR data ($CDCl_3$): δ 17.6 (C-6), 29.2 (C-2 spacer), 37.9 (C-3 spacer), 64.9 (C-1 spacer), 66.3 (CH_2Ph), 68.5 (C-5), 70.6, 71.2 and 72.6 (C-2,3,4), 97.1 (C-1), 127.7–133.1 ($CH_{aromatic}$ and $C_{aromatic}$), 156.4 (NHCO), 165.3 and 166.1 (Ph*C*OO). Anal. Calcd for $C_{37}H_{35}NO_{10}$: C, 67.99; H, 5.36. Found: C, 67.76; H, 5.48.

3-Benzyloxycarbonylaminopropyl 2,3-O-isopropylidene-α-L-rhamnopyranoside (**12**).—Potassium *tert*-butoxide (50 mg) was added to a solution of **10** (1.1 g, 1.6 mmol) in MeOH (20 mL), and the mixture was stirred for 2 h at 20°C, then neutralised with Dowex (H^+) resin, filtered, and concentrated. To a solution of the residue **11** (550 mg, 1.6 mmol) in acetone were added 2,2-dimethoxypropane and camphorsulfonic acid (20 mg). The mixture was stirred for 2 h at 20°C, then diluted with CH_2Cl_2 (10 mL), washed with 0.9 M $NaHCO_3$ (10 mL) and water (10 mL), dried ($MgSO_4$), and concentrated. Column chromatography (95:5 CH_2Cl_2–MeOH) of the residue gave **12** (460 mg, 73% based on **10**); $[\alpha]_D$ −13° (*c* 1, $CHCl_3$). NMR data ($CDCl_3$): ^1H, δ 1.28 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6,6,6), 1.35, 1.52 (2 s, 6 H, CMe_2), 1.81 (m, 2 H, H-2 spacer), 3.30 (t, 2 H, $J_{2,3}$ 6.3 Hz, H-3 spacer), 3.35 (m, 1 H, H-4), 3.48 (dt, 1 H, $J_{1a,2}$ 5.7, $J_{1a,1a}$ 11.3 Hz, H-1a spacer), 3.62 (dq, 1 H, $J_{4,5}$ 4.9 Hz, H-5), 3.76 (dt, 1 H, $J_{1b,2}$ 5.7 Hz, H-1b spacer), 4.07 (dd, 1 H, $J_{3,4}$ 6.4, $J_{2,3}$ 5.8 Hz, H-3), 4.10 (d, 1 H, H-2), 5.01 (s, 2 H, CH_2Ph), 5.30 (s, 1 H, H-1), and 7.28–7.35 (m, 5 H, Ph); ^{13}C, δ 17.2 (C-6), 25.9, 27.8 [$C(CH_3)_2$], 29.3 (C-2 spacer), 38.3 (C-3 spacer), 64.9 (C-1 spacer), 65.6 (C-5), 66.3 (CH_2Ph), 74.1, 75.6 and 78.3 (C-2,3,4), 96.8 (C-1), 109.1 [$C(CH_3)_2$], and 126.6–133.1 ($CH_{aromatic}$ and $C_{aromatic}$), 155.8 (NHCO). Anal. Calcd for $C_{19}H_{26}NO_7$: C, 60.00; H, 6.84. Found: C, 60.08; H, 6.77.

3-Benzyloxycarbonylaminopropyl 6-deoxy-2,3-O-isopropylidene-α-L-lyxo-hexopyranosid-4-ulose (**13**).—To a mixture of **12** (750 mg, 2.0 mmol), 4A powdered molecular sieves (2 g), and 4-methylmorpholine *N*-oxide (360 mg, 2.8 mmol) in 1,2-dichloroethane (15 mL) was added tetrapropylammonium per-ruthenate (0.5

mol%, 3 mg). The resulting green mixture was stirred for 10 min at 20°C when TLC (97:3 CH_2Cl_2–MeOH) showed the oxidation to be complete. The mixture was filtered through Celite, diluted with CH_2Cl_2 (10 mL), and washed with brine (2 × 10 mL), dried ($MgSO_4$), and concentrated. Column chromatography (98:2 CH_2Cl_2–MeOH) of the residue afforded **13** (630 mg, 85%); $[\alpha]_D$ −67° (*c* 1, $CHCl_3$). NMR data ($CDCl_3$): ^1H, δ 1.35 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6,6), 1.39, 1.47 (2 s, 6 H, CMe_2), 1.80 (m, 1 H, H-2, spacer), 3.28 (t, 2 H, $J_{2,3}$ 6.2 Hz, H-3 spacer), 3.56 (m, 1 H, H-1a spacer), 3.78 (m, 1 H, H-1b spacer), 4.22 (q, 1 H, H-5), 4.41 (2 d, 2 H, H-2,3), 5.01 (s, 2 H, CH_2Ph), 5.27 (s, 1 H, H-1), and 7.28–7.35 (m, 5 H, Ph); ^{13}C, δ 15.8 (C-6), 25.3 and 26.6 [$C(CH_3)_2$], 29.0 (C-2 spacer), 38.2 (C-3 spacer), 65.9 (C-1 spacer), 66.5 (CH_2Ph), 69.9 (C-5), 75.8 and 78.6 (C-2,3), 96.9 (C-1), 111.3 [$C(CH_3)_2$], 127.9–133.3 ($CH_{aromatic}$ and $C_{aromatic}$), 156.3 (NHCO), and 204.5 (C-4). Anal. Calcd for $C_{19}H_{25}NO_7$: C, 60.16; H, 6.60. Found: C, 60.25; H, 6.47.

*3-Benzyloxycarbonylaminopropyl 6-deoxy-2,3-*O*-isopropylidene-α-*L*-talopyranoside* (**14**).—Sodium borohydride (120 mg, 3.2 mmol) was added to a stirred and cooled (0°C) solution of **13** (630 mg, 1.6 mmol) in EtOH (20 mL). Stirring was continued for 10 min at 20°C, acetone (3 mL) was added, and the mixture was then diluted with CH_2Cl_2 (20 mL), dried ($MgSO_4$), and concentrated. Column chromatography (98:2 CH_2Cl_2–MeOH) of the residue gave **14** (570 mg, 90%); $[\alpha]_D$ −34° (*c* 1, $CHCl_3$). NMR data ($CDCl_3$): ^1H, δ 1.30 (d, 3 H, $J_{5,6}$ 6.6 Hz, H-6,6,6), 1.37 and 1.57 (2 s, 6 H, CMe_2), 1.80 (m, 2 H, H-2 spacer), 3.31 (t, 2 H, $J_{2,3}$ 5.7 Hz, H-3 spacer), 3.50 (t, 1 H, $J_{3,4}$ 4.8, $J_{4,5}$ 5.3 Hz, H-4), 3.55 (m, 1 H, H-1a spacer), 3.82 (m, 2 H, H-1b spacer and H-5), 4.02 (dd, 1 H, H-2, $J_{1,2}$ 1.4, $J_{2,3}$ 6.4 Hz, H-2), 4.20 (dd, 1 H, H-3), 5.00 (s, 2 H, CH_2Ph), 5.09 (s, 1 H, H-1), and 7.25–7.36 (m, 5 H, Ph); ^{13}C, δ 16.3 (C-6), 24.9, 25.5 [$C(CH_3)_2$], 29.1 (C-2 spacer), 38.1 (C-3 spacer), 64.3 (C-5), 65.1 (C-1 spacer), 66.1 (CH_2Ph), 66.4, 72.7, and 73.0 (C-2,3,4), 97.1 (C-1), 108.9 [$C(CH_3)_2$], 127.6–133.4 ($CH_{aromatic}$ and $C_{aromatic}$), and 156.1 (NHCO). Anal. Calcd for $C_{19}H_{26}NO_7$: C, 60.00; H, 6.84. Found: C, 60.12; H, 6.59.

*3-Benzyloxycarbonylaminopropyl 6-deoxy-3,4-*O*-isopropylidene-α-*L*-talopyranoside* (**16**).—A solution of **14** (570 mg, 1.5 mmol) in 9:1 acetic acid–water (20 mL) was heated to 50°C for 3 h, then concentrated, and toluene was evaporated repeatedly from the residue. To a solution of the resulting triol **15** (580 mg, 1.5 mmol) in acetone (20 mL) were added 2,2-dimethoxypropane (0.7 g, 6.8 mmol) and camphorsulfonic acid (10 mg). The mixture was stirred for 3 h at 20°C, when TLC (97:3 CH_2Cl_2–MeOH) showed the disappearance of **15**. The mixture was diluted with CH_2Cl_2 (10 mL), and the organic layer was washed with water and 0.9 M $NaHCO_3$ (10 mL), dried ($MgSO_4$), and concentrated. Column chromatography (99:1 CH_2Cl_2–MeOH) of the residue gave **16** (470 mg, 79% based on **14**); $[\alpha]_D$ −34° (*c* 1, $CHCl_3$). NMR data ($CDCl_3$): ^1H, δ 1.20 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6,6,6), 1.37 and 1.51 (2 s, 6 H, CMe_2), 1.79 (m, 2 H, H-2 spacer), 3.30 (t, 2 H, $J_{2,3}$ 5.7 Hz, H-3 spacer), 3.53 (dt, 1 H, $J_{1a,1b}$ 10.0, $J_{1a,2}$ 5.1 Hz, H-1a spacer), 3.69 (dd, 1 H, $J_{1,2}$ 6.3, $J_{2,3}$ 3.0 Hz, H-2), 3.77 (dq, 1 H, $J_{4,5}$ 1.8 Hz, H-5), 3.86 (dt, 1 H, $J_{1b,2}$ 5.0 Hz, H-1b spacer), 4.11 (dd, 1 H, $J_{3,4}$ 7.7 Hz, H-4), 4.52 (dd, 1 H, H-3), 4.69 (d, 1 H,

H-1), 5.08 (s, 2 H, CH_2Ph), and 7.12–7.48 (m, 5 H, Ph); ^{13}C, δ 15.4 (C-6), 24.8 and 25.8 [$C(CH_3)_2$], 29.3 (C-2 spacer), 37.8 (C-3 spacer), 65.0 (C-1, spacer), 65.3 (C-5), 66.3 (CH_2Ph), 68.6, 73.8, and 76.2 (C-2,3,4), 100.5 (C-1), 109.6 [$C(CH_3)_2$], 127.7–132.8 ($CH_{aromatic}$ and $C_{aromatic}$), and 156.4 (NHCO). Anal. Calcd for $C_{19}H_{26}NO_7$: C, 60.00; H, 6.84. Found: C, 60.09; H, 6.74.

*Ethyl 4-O-methyl-1-thio-α-*L*-rhamnopyranoside* (**18**).—To a stirred solution of ethyl 2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside[15] (1.8 g, 7.2 mmol) in DMF (30 mL) were added NaH (0.3 g, 80%, 1.3 equiv) and MeI (0.6 mL, 1.2 equiv). The mixture was stirred for 4 h at 20°C, MeOH was added, and the mixture was concentrated. A solution of the residue in CH_2Cl_2 (50 mL) was washed twice with water, and dried ($MgSO_4$) to give crude **17**, a solution of which in 9:1 acetic acid–water (50 mL) was stirred for 17 h at 50°C. The mixture was concentrated and toluene (2 × 25 mL) was evaporated from the residue. Column chromatography (99:1 → 97:3 CH_2Cl_2–MeOH) then gave **18** (1.2 g, 73% based on ethyl 2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside); $[\alpha]_D$ −235° (*c* 1, $CHCl_3$). NMR data ($CDCl_3$): ^1H, δ 1.29 (t, 3 H, *J* 7.5 Hz, SCH_2CH_3), 1.33 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6,6), 2.60 (ABq, 2 H, SCH_2CH_3), 3.12 (t, 1 H, $J_{3,4} = J_{4,5} = 9.3$ Hz, H-4), 3.57 (s, 3 H, OMe), 3.82 (dd, 1 H, $J_{2,3}$ 3.3 Hz, H-3), 3.95 (m, 1 H, H-5), 4.04 (dd, 1 H, $J_{1,2}$ 1.5 Hz, H-2), and 5.23 (d, 1 H, H-1); ^{13}C, δ 14.8 (SCH_2CH_3), 17.8 (C-6), 25.0 (SCH_2CH_3), 60.5 (OCH_3), 67.6, 71.5, 72.5 and 83.4 (C-2,3,4), and 83.8 (C-1). Anal. Calcd for $C_9H_{18}O_4S$: C, 48.64; H, 8.16. Found: C, 48.32; H, 8.21.

*Ethyl 2,3-di-O-benzoyl-4-O-methyl-1-thio-α-*L*-rhamnopyranoside* (**19**).—To a cooled (0°C) solution of **18** (160 mg, 0.7 mmol) in dry pyridine (10 mL) was added dropwise a mixture of benzoyl chloride (220 mg, 1.4 mmol) and pyridine (2 mL). The mixture was stirred for 2 h at room temperature, the reaction was quenched by the addition of water (2 mL), and the mixture was concentrated under reduced pressure. A solution of the residue in CH_2Cl_2 (20 mL) was washed with water (10 mL) and 0.9 M $NaHCO_3$ (10 mL), dried ($MgSO_4$), and concentrated, and toluene (2 × 10 mL) was evaporated from the residue. Column chromatography [1:0 → 0:1 light petroleum (bp 40–60°C)–CH_2Cl_2] afforded **19** (280 mg, 92%); $[\alpha]_D$ +15° (*c* 1, $CHCl_3$). NMR data ($CDCl_3$): ^1H, δ 1.33 (t, 3 H, *J* 7.5 Hz, SCH_2CH_3), 1.43 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6,6), 2.75 (ABq, 2 H, SCH_2CH_3), 3.60 (t, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz), 3.77 (s, 3 H, OMe), 4.23 (m, 1 H, H-5), 5.23 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 5.35 (dd, 1 H, $J_{3,2}$ 3.3 Hz, H-3), 5.68 (dd, 1 H, H-2), and 7.26–8.07 (m, 10 H, 2 Ph); ^{13}C, δ 14.9 (SCH_2CH_3), 17.8 (C-6), 25.5 (SCH_2CH_3), 60.7 (OCH_3), 68.3, 72.5, 72.8, and 81.1 (C-2,3,4,5), 81.9 (C-1), 128.3–133.3 ($CH_{aromatic}$ and $C_{aromatic}$), and 165.3, 166.2 (PhCOO). Anal. Calcd for $C_{23}H_{26}O_6S$: C, 64.17; H, 6.09. Found: C, 64.43; H, 6.17.

*3-Benzyloxycarbonylaminopropyl 6-deoxy-2-O-[2,4-di-O-benzoyl-3-O-(3-O-benzyl-4-O-chloroacetyl-2-O-methyl-α-*L*-fucopyranosyl)-α-*L*-rhamnopyranosyl]-3,4-O-isopropylidene-α-*L*-talopyranoside* (**20**).—A solution of *N*-iodosuccinimide (52 mg, 0.23 mmol) and trifluoromethanesulfonic acid (2 μL, 23 μmol) in 1:1 1,2-dichloroethane–ether (2.3 mL) was added dropwise to a cooled (0°C) and stirred mixture

of **6** (171 mg, 0.23 mmol), **13** (71 mg, 0.18 mmol), and 4A molecular sieves (0.5 g) in 1,2-dichloroethane (5 mL). The mixture was stirred for 10 min, then filtered, diluted with CH_2Cl_2 (10 mL), washed with M sodium thiosulfate (5 mL) and 0.9 M $NaHCO_3$ (10 mL), dried ($MgSO_4$), and concentrated. Column chromatography (99:1 CH_2Cl_2–MeOH) of the residue gave **20** (136 mg, 70%); $[\alpha]_D$ −12° (*c* 1, $CHCl_3$). For the ^1H NMR data, see Table I. Anal. Calcd for $C_{56}H_{66}ClNO_{18}$: C, 62.48; H, 6.18. Found: C, 62.34; H, 6.25.

3-Benzyloxycarbonylaminopropyl 6-deoxy-2-O-[2,4-di-O-benzoyl-3-O-(3-O-benzyl-2-O-methyl-α-L-fucopyranosyl)-α-L-rhamnopyranosyl]-3,4-O-isopropylidene-α-L-talopyranoside (**21**).—To solution of **20** (120 mg, 0.11 mmol) in MeOH (1 mL) and EtOAc (1 mL) were added acetic acid (66 mg, 1.1 mmol) and hydrazine monohydrate (55 mg, 1.1 mmol). The mixture was stirred for 17 h at 40°C, then concentrated, and a solution of the residue in CH_2Cl_2 (10 mL) was washed with water (5 mL), dried ($MgSO_4$), and concentrated. Column chromatography (99:1 CH_2Cl_2–MeOH) of the residue gave **21** (93 mg, 79%); $[\alpha]_D$ −18° (*c* 1, $CHCl_3$). ^{13}C NMR data ($CDCl_3$): δ 15.4, 15.8, and 17.4 (C-6^T, 6^F, 6^R), 25.4 and 26.2 [$C(CH_3)_2$], 29.8 (C-2 spacer), 38.3 (C-3 spacer), 58.6 (OCH_3), 65.2 (C-1 spacer), 66.4 (CH_2Ph), 65.9, 66.3, 66.9, 70.1, and 72.3 (C-2^T, 3^T, 4^T, 5^T, C-2^F, 3^F, 4^F, 5^F, and C-2^R, 3^R, 4^R, 5^R), 72.3 (CH_2Ph), 95.5, 98.9, and 99.3 (C-1^T, 1^F, 1^R), 110.4 [$C(CH_3)_2$], 127.6–133.4 ($CH_{aromatic}$ and $C_{aromatic}$), 156.2 (NHCO), 165.4 and 165.9 (PhCOO). Anal. Calcd for $C_{54}H_{65}NO_{17}$: C, 64.85; H, 6.55. Found: C, 64.76; H, 6.67.

3-Benzyloxycarbonylaminopropyl 6-deoxy-2-O-{2,4-di-O-benzoyl-3-O-[3-O-benzyl-4-O-(2,3-di-O-benzoyl-4-O-methyl-α-L-rhamnopyranosyl)-2-O-methyl-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-3,4-O-isopropylidene-α-L-talopyranoside (**22**).—To a cooled (0°C) and stirred mixture of **21** (80 mg, 0.08 mmol), ethyl 2,3-di-*O*-benzoyl-4-*O*-methyl-1-thio-α-L-rhamnopyranoside (**19**; 52 mg, 0.12 mmol), and powdered 4A molecular sieves (0.5 g) in 1,2-dichloroethane (3 mL) was added a solution of *N*-iodosuccinimide (27 mg, 0.12 mmol) and trifluoromethanesulfonic acid (1.1 μL, 1.2 μL) in 1:1 1,2-dichloroethane–ether (1.2 mL). The mixture was stirred for 5 min, then filtered, diluted with CH_2Cl_2 (5 mL), washed with M sodium thiosulfate (5 mL) and 0.9 M $NaHCO_3$ (5 mL), dried ($MgSO_4$), and concentrated. Column chromatography (99:1 CH_2Cl_2–MeOH) of the residue gave **22** (92 mg, 84%); $[\alpha]_D$ −2° (*c* 1, $CHCl_3$). For the ^1H and ^{13}C NMR data, see Tables I and II. Anal. Calcd for $C_{75}H_{84}NO_{23}$: C, 65.87; H, 6.19. Found: C, 65.73; H, 6.30.

3-Aminopropyl 6-deoxy-2-O-{3-O-[2-O-methyl-(4-O-methyl-α-L-rhamnopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-talopyranoside (**1**).—A mixture of **22** (92 mg, 0.07 mmol), acetic acid (3 mL), and water (0.5 mL) was heated at 50°C for 3 h, then concentrated, and toluene (3 × 5 mL) was evaporated from the residue. Column chromatography (99:1 CH_2Cl_2–MeOH) then gave the diol **23**, to a solution of which in MeOH (3 mL) was added potassium *tert*-butoxide (10 mg). The mixture was stirred for 16 h at 20°C, then neutralised with Dowex (H^+) resin, filtered, and concentrated. Column chromatography (MeOH) of the residue on Sephadex LH 20 afforded **24**, a solution of which in 3:1:1 2-propanol–water–acetic

acid (5 mL) was hydrogenated over 10% Pd–C (100 mg) for 48 h at 20°C. The catalyst was removed and the filtrate was concentrated to give **1** (31 mg, 66% based on **21**); $[\alpha]_D$ −2° (*c* 1, H_2O). LC–MS: *m/z* 688 ($M^+ + 1$). For the ^1H and ^{13}C NMR data, see Tables I and II. Anal. Calcd for $C_{29}H_{53}NO_{17}$: C, 50.65; H, 7.71. Found: C, 50.78; H, 7.75.

ACKNOWLEDGMENTS

We thank R.A.M. van der Hoeven for the LC–MS analysis of **1** and A.W.M. Lefeber and C. Erkelens for recording the ^1H and ^{13}C NMR spectra.

REFERENCES

1 E. Wolinsky, *Am. Rev. Respir. Dis.*, 119 (1979) 107–159.
2 L.S. Young, *J. Infect. Dis.*, 157 (1988) 863–867.
3 M.McNeil, A.Y. Tsang, and P.J. Brennan, *J. Biol. Chem.*, 262 (1987) 2630–2635.
4 M. Bozic, M. McNeil, D. Chatterjee, I. Jardine, and P.J. Brennan, *J. Biol. Chem.*, 263 (1988) 14984–14991.
5 H.M. Zuurmond, S.C. van der Laan, G.A. van der Marel, and J.H. van Boom, *Carbohydr. Res.*, 215 (1991) c1–c3.
6 P.J. Garegg and T. Norberg, *Acta Chem. Scand., Ser. B*, 33 (1979) 116–118; P.J. Garegg, P. Konradson, I. Kvarnstrom, T. Norberg, S.C.T. Svensson, and B. Wigilius, *ibid.*, 39 (1985) 569–577.
7 P. Smid, G.A. de Ruiter, G.A. van der Marel, F.M. Rombouts, and J.H. van Boom, *J. Carbohydr. Chem.*, 10 (1991) 833–84.
8 N. Nagashima and M. Ohno, *Chem. Lett.*, (1987) 141–144.
9 G.J.F. Chittenden and H. Regeling, *Recl. Trav. Chim. Pays-Bas*, 106 (1987) 44–47.
10 F.I. Auzanneau and D.R. Bundle, *Carbohydr. Res.*, 212 (1991) 13–24.
11 P. Bernston, A. Brändström, H. Jungren, L. Palme, S.E. Sjöstrand, and G. Sundell, *Acta Pharm. Suec.*, 14 (1977) 229–236.
12 G.H. Veeneman, S.H. van Leeuwen, and J.H. van Boom, *Tetrahedron Lett.*, 31 (1990) 1331–1334.
13 W.P. Griffith, S.V. Ley, G.P. Whitcombe, and A.D. White, *J. Chem. Soc., Chem. Commun.*, (1987) 1625–1627.
14 G.O. Aspinall and K. Takeo, *Carbohydr. Res.*, 121 (1983) 61–77.
15 G.H. Veeneman, L.J.F. Gomes, and J.H. van Boom, *Tetrahedron*, 45 (1989) 7433–7448.
16 C.A.A. van Boeckel and T. Beetz, *Tetrahedron Lett.*, (1983) 3775–3778.
17 M. Nilsson and T. Norberg, *J. Carbohydr. Chem.*, 8 (1989) 613–627.
18 D. Marion and K. Wutrich, *Biochem. Biophys. Res. Commun.*, 113 (1983) 967–974.
19 A. Bax and D.G. Davis, *J. Magn. Reson.*, 65 (1965) 355–360.