Carbohydrate Research, 163 (1987) 189–208
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

TOTAL SYNTHESIS OF GLOBOTRIAOSYL-*E* AND *Z*-CERAMIDES AND ISOGLOBOTRIAOSYL-*E*-CERAMIDE*

KATSUYA KOIKE, MAMORU SUGIMOTO, SUSUMU SATO, YUKISHIGE ITO, YOSHIAKI NAKAHARA, AND TOMOYA OGAWA**

RIKEN (The Institute of Physical and Chemical Research), Wako-shi, Saitama, 351-01 (Japan)

(Received June 2nd, 1986; accepted for publication in revised form, November 28th, 1986)

ABSTRACT

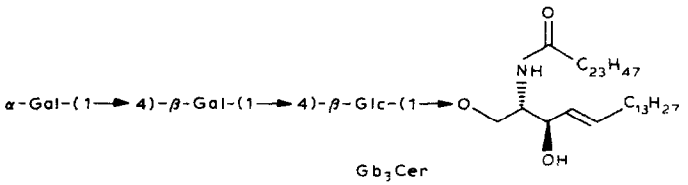
Stereoselective, total synthesis of *O*-α-D-galactopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→1)-*N*-tetracosanoyl-[2*S*,3*R*,4*E* (and 4*Z*)]-sphingenine and *O*-α-D-galactopyranosyl-(1→3)-*O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→1)-*N*-tetracosanoyl-(2*S*,3*R*,4*E*)-sphingenine was achieved by using *O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate, *O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α (and β)-D-glucopyranosyl fluoride, and *O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate.

INTRODUCTION

Globotriaosylceramide (Gb_3Cer; **1**) has been isolated from various tissues[2], and the complete structure was finally assigned[3] by enzymic and ^1H-n.m.r. spectral study. Gb_3Cer (**1**) has been identified[4] as P^k antigen in the P blood-group system, and is also regarded as a glycolipid antigen associated with Burkitt lymphoma[5]. Recently, the α-Gal-(1→4)-Gal sequence of **1** and related globosides was shown to act as a receptor for the binding of uropathogenic *E. coli* to human uroepithelial cells[6]. On the other hand, the isomeric globotriaosylceramide **3** ($isoGb_3Cer$) has been isolated only from rat-spleen tissues[7], rat-mammary tumor[8], and dog intestine[9], and the structure was assigned from methylation analysis and enzymic hydrolysis[8]. As part of a project on the synthesis of glycosphingolipids, we now describe a total synthesis of Gb_3Cer (**1**), Gb_3Cer (*Z* isomer) (**2**), and $isoGb_3Cer$ (**3**).

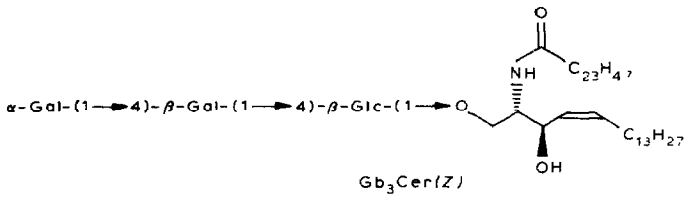
*Part 43 in the series "Synthetic Studies on Cell-surface Glycans". For Part 42, see ref. 1.
**To whom enquiries should be addressed.

0008-6215/87/$ 03.50



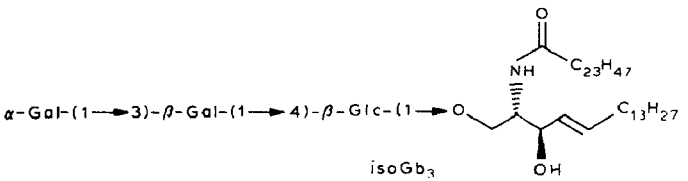
Gb_3Cer

1



$Gb_3Cer(Z)$

2



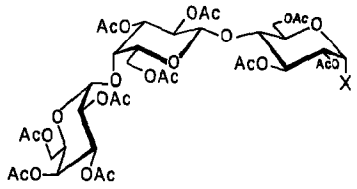
$isoGb_3$

3

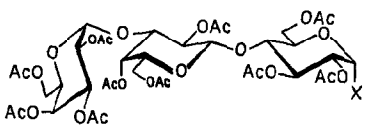
In connection with the project, syntheses of alkyl *O*-α-D-galactopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-(1→4)-β-D-glucopyranosides had been reported by Cox *et al.*[10], Garegg and Hultberg[11], and Dahmén *et al.*[12]. Completely protected trisaccharide corresponding to the glycan part of Gb_3Cer (**1**) had been synthesized by Paulsen and Bünsch[13] as part of their study on the synthesis of the glycan part of Forssman antigen. Jacquinet and Sinaÿ[14] reported a synthesis of free trisaccharide α-Gal-(1→4)-β-Gal-(1→4)-Glc, starting from *O*-(2,3,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-D-glucopyranosyl benzoate according to the route of Garegg and Hultberg[11]. A total synthesis of globotriaosylceramide was reported for the first time in 1978 by Shapiro and Acher[15]; stereochemical aspects of the synthetic sequence were, however, not discussed. Development of a stereoselective and unambiguous route for the total synthesis of globotriaosylceramide and related glycosphingolipids still remained to be achieved.

RESULTS AND DISCUSSION

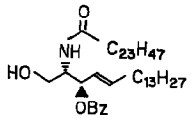
Because we had already developed[16], starting from D-glucose, an efficient route for the synthesis of the *E*- and *Z*-ceramide parts **6** and **7** of glycosphingolipids, other key intermediates for the synthesis of globotriaosylceramides **1** and **2** and iso-



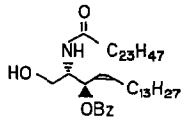
4



5



6



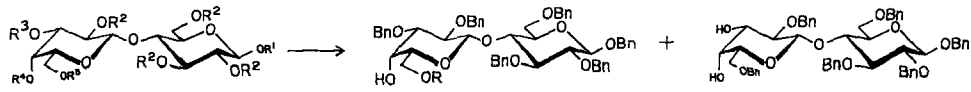
7

globotriaosylceramide **3** should be the corresponding glycosyl donors **4** and **5**, respectively. The trisaccharide derivatives **4** and **5** may be synthesized from such adequately protected lactose derivatives as **16** and **17**, respectively, by use of either glycosyl donor **24** or **30**.

Benzyl *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside[17] (**9**), readily obtainable from lactose octaacetate[18] (**8**) by a stannyl method of glycosylation[19], was transformed into benzyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-isopropylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**13**) and benzyl *O*-(2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**14**) in 62 and 16% yield, respectively, in three steps *via* compounds **11** and **12**: (*i*) NaOMe–MeOH, (*ii*) $(MeO)_2CMe_2$–TsOH·H_2O–DMF, (*iii*) NaH–BnBr–DMF. The structure of **13** (and of **14**) was assigned from the ^{13}C-n.m.r. spectra, which respectively contained a signal characteristic[20] for acetal carbon atoms of isopropylidene acetals having a six-membered and a five-membered ring, at 98.8 and 109.7 p.p.m.

Hydrolysis of compound **13** in aq. acetic acid provided compound **15**, and site-selective benzylation of **15** by a stannyl method[21] afforded an 86% yield of benzyl *O*-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**16**), a useful glycosyl acceptor for the synthesis of the glycan part of the globo series of glycosphingolipids. Lipták *et al.*[22] had reported the synthesis of compound **16** as a minor product of the reductive ring-opening of the benzylidene group of benzyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside with $LiAlH_4$ and $AlCl_3$. However, they reported an $[\alpha]_D$ value ($CHCl_3$) of +4°, which is not in agreement with our value of +22°.

Treatment of **14** with aq. acetic acid afforded benzyl *O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**17**), which is a

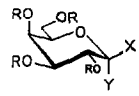


	R^1	R^2	R^3	R^4	R^5
8	Ac	Ac	Ac	Ac	Ac
9	Bn	Ac	Ac	Ac	Ac
10	Bn	H	H	H	H
11	Bn	H	H	(CMe_2)	
12	Bn	H	(CMe_2)		H
13	Bn	Bn	Bn	(CMe_2)	
14	Bn	Bn	(CMe_2)		Bn

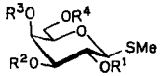
Bn = $PhCH_2$

15 R=H
16 R=Bn

17



	X	Y	R
18	OAc	H	Ac
19	SMe	H	Ac
20	H	SMe	Ac
21	SMe	H	H
22	SMe	H	Bn
23	H	OH	Bn
24	H	Cl	Bn



	R^1	R^2	R^3	R^4
25	H	(CMe_2)		H
26	H	H	(CMe_2)	
27	Bn	(CMe_2)		Bn
28	Bn	Bn	(CMe_2)	
29	Bn	H	H	Bn
30	Bn	Ac	Ac	Bn

suitable glycosyl acceptor for the synthesis of the glycan part of the isoglobo, lacto, and ganglio series[23] of glycosphingolipids.

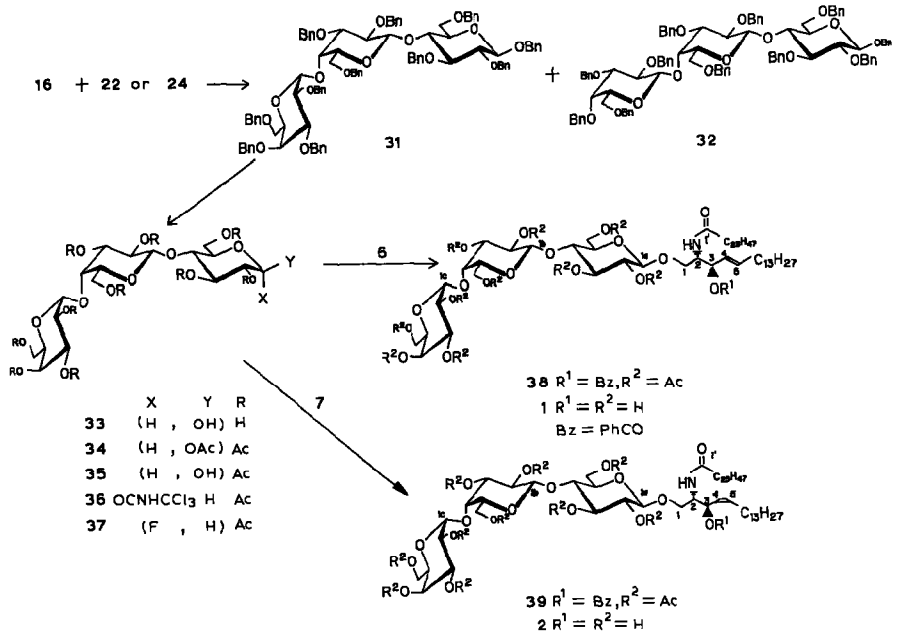
Having prepared the glycosyl acceptors **16** and **17** for the synthesis of trisaccharide derivatives **4** and **5**, respectively, synthesis of the corresponding glycosyl donors is now discussed. In addition to the use of well established galactopyranosyl chloride **24**, we intended to examine the use of methyl 1-thioglycosides **22** and **30** in the presence of cupric bromide[24]. Methyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (**19**), readily obtainable[25], together with the α anomer **20**, by the reaction of penta-*O*-acetyl-β-D-galactose (**18**) with methyl tributyltin sulfide, was transformed in 70% yield into the known[26] D-galactosyl chloride **24** in 3 steps *via* compound **21**, methyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-galactopyranoside (**22**), and compound **23** in the conventional way. Isopropylidenation of compound **21** afforded the isomers **25** and **26**, and benzylation thereof gave methyl 2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside (**27**) and its 4,6-*O*-isopropylidene isomer **28** in 83 and 16% yield, respectively. Acid hydrolysis of compound **27** afforded compound **29**, and acetylation of **29** gave diacetate **30**.

Glycosylation of benzyl *O*-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**16**) with 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl chloride (**24**) in the presence of silver triflate and molecular sieves 4A afforded a mixture of perbenzylated trisaccharides **31** and **32** in 63 and 19% yield, respectively. The stereochemistry of **31** and **32** was determined by ^{13}C-n.m.r.

data: in the case of **31**, two signals for two anomeric carbon atoms with the β-D-configuration, at δ 102.9 and 102.5, and one signal for an anomeric carbon atom with the α-D-configuration, at δ 100.8, were observed; for **32**, three signals for three β-D-anomeric carbon atoms were at δ 102.8, 102.6, and 102.5.

Use of the methyl 1-thio-D-glucoside **22** as the glycosyl donor was examined as follows. Treatment of the glycosyl acceptor **16** with **22** in the presence of cupric bromide–silver triflate in 1,2-dichloroethane afforded, in 94% yield, a mixture of **31** and **32** in the ratio of 3.4:1. The same glycosylation in the presence of cupric bromide and mercuric bromide was found to give a 90% yield of a mixture of **31** and **32** in the ratio of 1.4:1 when nitromethane was used as the solvent, and an 89% yield of a mixture of **31** and **32** in the ratio of 1:1.7 when 1,2-dichloroethane was the solvent. These experiments clearly showed that, in the synthesis of the trisaccharide **31** using perbenzylated D-galactopyranosyl donors and perbenzylated lactose derivative **16** as the acceptor, methyl 1-thioglycoside **22** when used in combination with an adequate Lewis acid, gave a better result than the well known chloride **24**. Hydrogenolysis of compound **31** gave free trisaccharide **33**. The ^{1}H-n.m.r. spectrum of **33** was in good agreement with the date reported[14] by Jacquinet and Sinaÿ. Without further purifiation, free trisaccharide **33** was acetylated to a 1:1 mixture of α- and β-peracetate **34**, which was site-selectively deacylated with hydrazine and acetic acid[27] to give an 85% yield of a mixture of the α and β anomer of hemiacetal **35** in the ratio of 5:2, judged from the ^{13}C-n.m.r. spectrum.

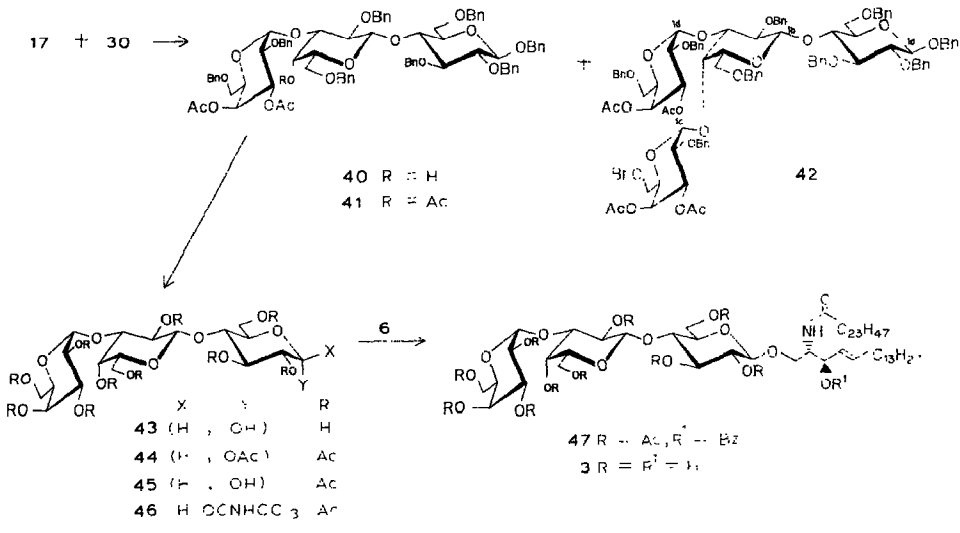
Compound **35** was then transformed into two kinds of glycosyl donor. Treatment of **35** with 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) and trichloroacetonitrile[28] afforded α-D-trichloroacetimidate **36** in 79% yield. Reaction of **35** with diethylaminosulfur trifluoride[29] in dichloromethane afforded a 1:10 mixture of α- and β-fluoride **37** in 94% yield. In the ^{1}H-n.m.r. spectrum of **37**, a signal for H-1aβ was observed, with the intensity of one proton, at δ 5.411, as a double doublet with



J 5.1 and 53.0 Hz, while only a lower-field pair as the signal for H-1aα, with the intensity of 0.09 proton, at δ 5.740, was observed as a doublet with *J* 3.3 Hz.

Glycosylation of the properly protected *E*-sphingenine[16] **6** with trichloroacetimidate **36** in the presence[28] of $BF_3 \cdot Et_2O$ afforded the desired product **38** in 13% yield (64% yield based on the trichloroacetimidate **36** consumed). Similarly, glycosylation of acceptor **6** with fluoride **37** in the presence of silver perchlorate and stannous chloride[30] afforded the same compound **38** in 29% yield. The stereochemistry of the glycosylation product was assigned as β-D from the ^{1}H-n.m.r. spectrum of **38**, which showed a signal for H-1a at δ 4.461, as a doublet with *J* 7.8 Hz. Deacetylation of **38** afforded globotriaosylceramide **1**, the ^{1}H-n.m.r. spectrum of which was found quite reasonable on comparison with that of the related, natural glycolipid, globotetraosylceramide, reported by Dabrowski *et al.*[31]. By use of the (*Z*)-sphingenine derivative **7** as a glycosyl acceptor for glycosylation with trichloroacetimidate **36**, compound **39** was obtained in 34% yield. Again, the stereochemistry of the glycosylation product was assigned as β-D by use of the ^{1}H-n.m.r. data, which contained a signal for H-1a and H-1b at δ 4.478, as a doublet with *J* 7.5 Hz. Deacylation of **39** gave the *Z* isomer of globotriaosylceramide (**2**), whose ^{1}H-n.m.r. spectrum agreed with the assigned structure.

In order to synthesize the trisaccharide part of isoglobotriaosylceramide, glycosylation of benzyl *O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**17**) with methyl 3,4-di-*O*-acetyl-2,6-di-*O*-benzyl-1-thio-β-D-galactopyranoside (**30**) in the presence of cupric bromide[23] and silver triflate was examined; it afforded a 41% yield of the desired, protected trisaccharide **40**, as well as a 35% yield of the diglycosylated product **42**. The structure of **40** was assigned from the ^{13}C-n.m.r. spectrum, which contained a signal for C-1c at δ 94.5, in agreement with the α-D configuration, along with a deshielded signal for C-3b at



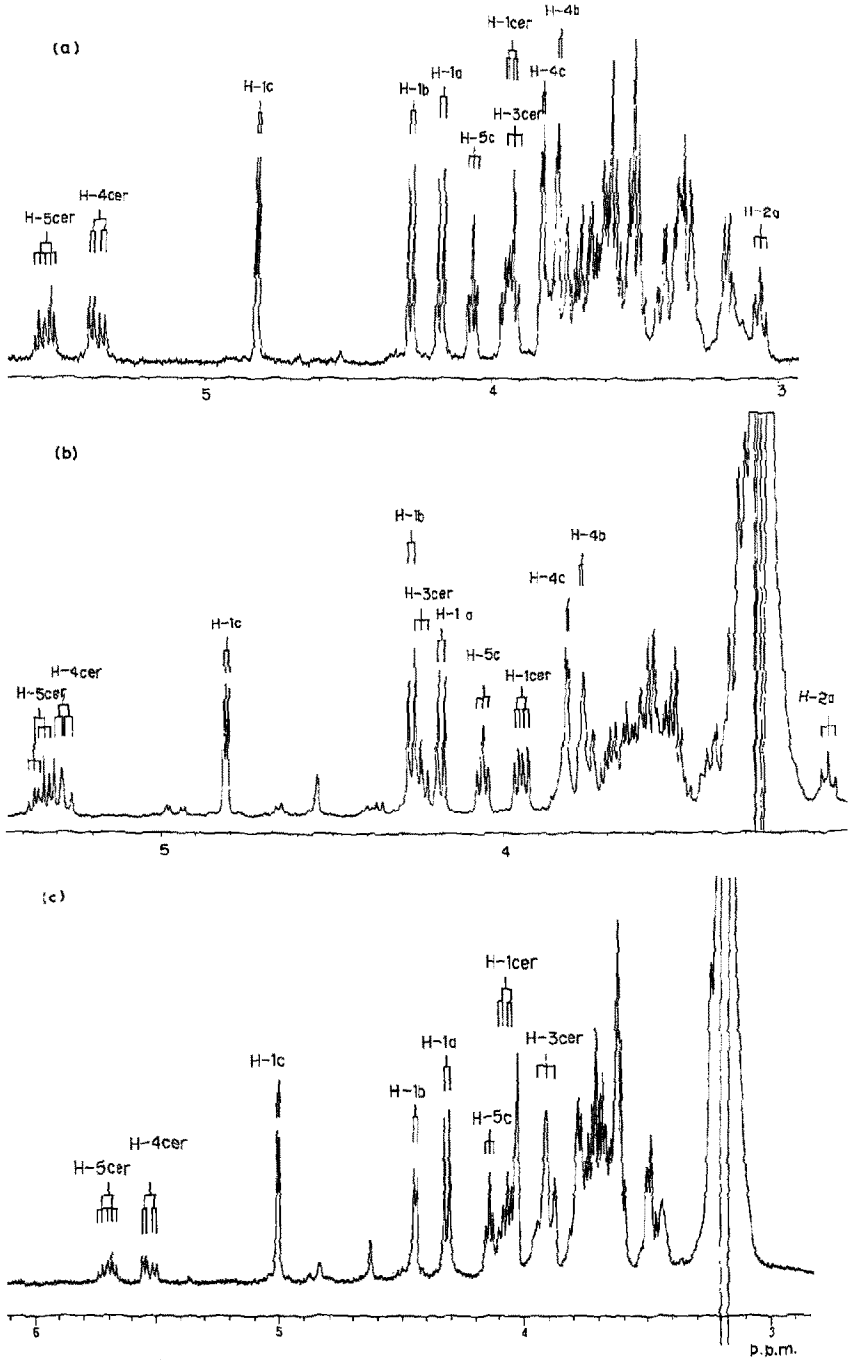


Fig. 1. 400-MHz, ^{1}H-n.m.r. spectra of (a) synthetic α-Gal-(1→4)-β-Gal-(1→4)-β-Glc-(1→Cer (*E*) (**1**) at 60°, (b) synthetic α-Gal-(1→4)-β-Gal-(1→4)-β-Glc-(1→Cer (*Z*) (**2**) at 60°, and (c) synthetic α-Gal-(1→3)-β-Gal-(1→4)-β-Glc-(1→Cer (*E*) (**3**) at 95°. The spectra were recorded in 49:1 Me_2SO-d_6–D_2O, for the sample after exchanging several times with Me_2SO–D_2O. Values of δ_H are expressed in p.p.m. downward from Me_4Si, by reference to an internal standard of Me_2CO (2.225).

δ 82.9. The site of glycosylation in compound **40** was further evidenced by transformation into acetate **41**; its ^{1}H-n.m.r. spectrum showed two deshielded signals for H-4b and H-4c, at δ 5.156 and 5.353.

Hydrogenolysis of compound **40** in AcOH at 80° gave **43**, and acetylation of **43** gave a 3:2 mixture of the α and the β anomer of peracetate **44**. Transformation of compound **44** into trichloroacetimidate **46** in 60% yield was performed as described for compound **34**. Crucial glycosylation of the (*E*)-sphingenine derivative **6** with trichloroacetimidate **46** was achieved in the presence[28] of $BF_3 \cdot Et_2O$, to give a 33% yield of completely protected isoglobotriaosylceramide **47**. The stereochemistry of the glycosylation product was assigned as β-D by observing in its ^{1}H-n.m.r. spectrum a signal for H-1a at δ 4.376, as a doublet with J 7.8 Hz. Finally, deacylation of compound **47** afforded the target isoglobotriaosylceramide **3**, the structure of which was in full agreement with the ^{1}H-n.m.r. data.

In conclusion, by use of the key intermediates (*E*)- and (*Z*)-sphingenine derivatives **6** and **7** as glycosyl acceptors, and glycotriaosyl trichloroacetimidate or fluoride **36, 37**, and **46** as glycosyl donors, total synthesis of globotriaosyl- and isoglobotriaosyl-ceramide was achieved in a stereocontrolled way.

EXPERIMENTAL

General. — Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were determined with a Perkin–Elmer Model 241 MC polarimeter, for solutions in $CHCl_3$ at 25°, unless noted otherwise. Column chromatography was performed on columns of Silica Gel Merck (70–230 mesh; E. Merck, Darmstadt, Germany). Flash chromatography was conducted on columns of Wako gel C-300 (200–300 mesh; Wako Pure Chemicals, Osaka, Japan). Thin-layer chromatography (t.l.c.) was performed on plates (layer thickness, 0.25 mm) precoated with Silica Gel 60 F_{254} (E. Merck, Darmstadt, Germany). High-performance thin-layer chromatography (h.p.t.l.c.) was performed on plates (layer thickness, 0.20 mm) precoated with Silica Gel 60 F_{254} (E. Merck, Darmstadt, Germany). I.r. spectra were recorded with an EPI-G2 Hitachi spectrophotometer, using KBr pellets for the crystalline samples, and neat films for the liquid samples. ^{1}H-N.m.r. spectra were recorded with either a JNM-GX400 or a JNM-FX90Q n.m.r. spectrometer, using tetramethylsilane as the internal standard. ^{13}C-N.m.r. spectra were recorded with a JNM-FX 100FT n.m.r. spectrometer operated at 25.05 MHz. The ^{1}H and ^{13}C signal assignments cited with an asterisk may have to be interchanged. The values of δ_C and δ_H are expressed in p.p.m. downwards from the internal standard, for solutions in $CDCl_3$, unless noted otherwise.

Benzyl O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (**9**). — To a solution of benzyl tributyltin oxide (4.4 g, 11 mmol) and $SnCl_4$ (1.4 mL, 12 mmol) in $Cl(CH_2)_2Cl$ (30 mL) was added dropwise a solution of compound **8** (6.8 g, 10 mmol) in $Cl(CH_2)_2Cl$ (35 mL) at 0–5°. The

mixture was stirred for 16 h at 20°, poured into aq. $NaHCO_3$–KF, stirred for 1 h, and filtered through Celite. The aqueous layer was extracted with EtOAc, and the extracts were combined, successively washed with aq. KF and H_2O, dried ($MgSO_4$), and evaporated *in vacuo*. The residue crystallized from EtOAc–pet. ether, to give **9** (6.59 g, 90.5%); m.p. 148–150°, $[\alpha]_D$ −33.7° (*c* 1.03); lit.[32] m.p. 145–146°, $[\alpha]_D$ −34.4° (*c* 2); R_F 0.43 in 1:1 toluene–EtOAc; n.m.r. data: δ_H 2.14 (s, 6 H, 2 Ac), 2.05 (s, 9 H, 3 Ac), 2.00 (s, 3 H, Ac), and 1.96 (s, 3 H, Ac); δ_C 101.0 ($^1J_{CH}$ 162 Hz, C-1b) and 99.2 ($^1J_{CH}$ 161 Hz, C-1a).

Benzyl O-*(2,3-di*-O-*benzyl-4,6*-O-*isopropylidene-β*-D-*galactopyranosyl-(1→4)-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**13**) *and benzyl* O-*(2,6-di*-O-*benzyl-(1→4)-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**13**) *and benzyl*-O-*(2,6-di*-O-*benzyl-3,4*-O-*isopropylidene-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**14**). — A solution of compound **9** (21.7 g, 30 mmol) in MeOH (200 mL)–0.1M NaOMe (20 mL) was stirred for 16 h at 20°, made neutral with Amberlyst 15, and filtered. The filtrate was evaporated *in vacuo*, to give compound **10** (13 g, quantitative) which was used for the next step without purification. A solution of compound **10** (12.4 g, 28.7 mmol), 2,2-dimethoxypropane (17.6 mL, 143.4 mmol), and *p*-TsOH·H_2O (0.55 g) in DMF (100 mL) was stirred for 5 h at 20°, made neutral with Et_3N (5 mL), and evaporated *in vacuo* below 40°. The residue was chromatographed on SiO_2 in 13:2 CH_2Cl_2–MeOH, to give a mixture (13.2 g, 97.4%) of compounds **11** (R_F 0.49 in 6:1 $CHCl_3$–MeOH) and **12** (R_F 0.57) which was used for the next step without separation.

To a suspension of NaH (50% oil dispension, 9.97 g, 208 mmol) in DMF (100 mL) was added a mixture (13.1 g, 27.7 mmol) of compounds **11** and **12**, and the mixture was stirred for 30 min at 0–5°; then benzyl bromide (25 mL, 208 mmol) was added dropwise at −5 to 0°, and the mixture was stirred for 16 h at 20°. The excess of NaH was decomposed with MeOH, and the mixture was evaporated *in vacuo*. The residue was partitioned between EtOAc and H_2O, and the organic layer washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 4:1 toluene–EtOAc afforded compounds **13** (15.9 g, 62.2%) and **14** (4.2 g, 16.4%).

Compound **13**: $[\alpha]_D$ +1.7° (*c* 0.35); R_F 0.47 in 4:1 toluene–EtOAc; n.m.r. data: δ_H: 1.47 and 1.40 (two s, CMe_2); δ_C 102.6 ($^1J_{CH}$ 160 Hz, C-1a and C-1b), 98.8 (CMe_2), 29.0 (CMe_2), and 21.4 (CMe_2).

Anal. Calc. for $C_{57}H_{62}O_{11}$: C, 74.17; H, 6.77. Found: C, 74.19; H, 6.81.

Compound **14**: $[\alpha]_D$ +9.4° (*c* 1.49); lit.[33] $[\alpha]_D$ +6° (*c* 1); R_F 0.60 in 4:1 toluene–EtOAc; n.m.r. data: δ_C 109.7 (CMe_2), 102.5 ($^1J_{CH}$ 160 Hz, C-1b), 101.9 ($^1J_{CH}$ 160 Hz, C-1a), 28.0 (CMe_2), and 26.4 (CMe_2).

Anal. Calc. for $C_{57}H_{62}O_{11}$: C, 74.17; H, 6.77. Found: C, 74.02; H, 6.67.

Benzyl O-*(2,3-di*-O-*benzyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**15**). — A solution of compound **13** (2.03 g, 2.2 mmol) in AcOH (20 mL)–H_2O (4 mL) was stirred for 1 h at 60–70°, and evaporated *in vacuo*. The trace of solvents in the residue was co-evaporated with EtOH and toluene.

The residue (1.89 g, 97%) crystallized from MeOH to give **15** (1.23 g, 63%); m.p. 148–150°, $[\alpha]_D$ +15.0° (*c*, 0.58); lit.[22] m.p. 146–147°, $[\alpha]_D$ +13° (*c* 0.67, acetone); R_F 0.39 in 2:1 toluene–EtOAc; n.m.r. data: δ_C 102.6 ($^1J_{CH}$ 159 Hz, C-1a and C-1b) and 62.3 (C-6b).

Anal. Calc. for $C_{54}H_{58}O_{11}$: C, 73.45; H, 6.62. Found: C, 73.48; H, 6.60.

Benzyl O-(2,3,6-tri-O-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside (**16**). — A mixture of compound **15** (10.6 g, 12 mmol) and $(Bu_3Sn)_2O$ (5.4 g, 9 mmol) in toluene (50 mL) was stirred under reflux, with azeotropic removal of water, for 4 h, and toluene (40 mL) was distilled off. To the residual solution were added benzyl bromide (50 mL) and Bu_4NBr (1.9 g, 6 mmol), and the mixture was stirred for 16 h at 90°. After evaporation *in vacuo*, a solution of the residue in EtOAc (200 mL) was stirred with aq. KF for 1 h, and the suspension filtered through Celite. The organic layer was dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 9:1 toluene–EtOAc gave **16** (10.4 g, 89%); $[\alpha]_D$ +22.1° (*c* 0.53); lit.[22] $[\alpha]_D$ +4° (*c* 0.6); R_F 0.73 in 2:1 toluene–EtOAc; n.m.r. data: δ_C 102.6 ($^1J_{CH}$ 159 Hz, C-1a and C-1b).

Anal. Calc. for $C_{61}H_{64}O_{11}$: C, 75.29; H, 6.63. Found: C, 75.14; H, 6.66.

Benzyl O-(2,6-di-O-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside (**17**). — A solution of compound **14** (76 mg, 0.08 mmol) in AcOH (0.5 mL) and H_2O (0.1 mL) was stirred for 1 h at 70–80°, cooled and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 5:1 toluene–EtOAc afforded **17** (49 mg, 68%) which crystallized from MeOH; m.p. 81–88°, $[\alpha]_D$ +19.5° (*c* 1.2); lit.[33] m.p. 105°, $[\alpha]_D$ +5.4° (*c* 0.5); R_F 0.36 in 8:3 toluene–EtOAc; n.m.r. data: δ_C 102.6 ($^1J_{CH}$ 159 Hz, C-1a and C-1b).

Anal. Calc. for $C_{54}H_{58}O_{11}$: C, 73.45; H, 6.62. Found: C, 73.52; H, 6.50.

Methyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-galactopyranoside (**19**) *and methyl 2,3,4,6-tetra-O-acetyl-1-thio-α-D-galactopyranoside* (**20**). — To a solution of compound **18** (37.7 g, 96.6 mmol) and Bu_3SnSMe (36.9 g, 109 mmol) in $Cl(CH_2)_2Cl$ (600 mL) was added dropwise a solution of $SnCl_4$ (17 mL, 146 mmol) in $Cl(CH_2)Cl$ (200 mL) at 0–5° under stirring. The mixture was stirred for 3 h at 20°, poured into aq. KF–$NaHCO_3$ with vigorous stirring, and filtered through Celite. The filtrate was diluted with EtOAc (1 L), washed successively with aq. $NaHCO_3$ and H_2O, dried ($MgSO_4$), and evaporated *in vacuo*. The residue crystallized from MeOH, to give **19** (24.2 g). The mother liquor was evaporated, and the residue chromatographed on SiO_2 in 9:1 toluene–EtOAc, to give **19** (28.0 g, 80%) and **20** (1.0 g, 2.8%).

Compound **19**: m.p. 113–115°, $[\alpha]_D$ +2.0° (*c* 0.94); lit.[34] m.p. 108°, $[\alpha]_D$ +2.9°; R_F 0.30 in 2:1 toluene–EtOAc; n.m.r. data: δ_H 5.440 (dd, 1 H, *J* 0.3 and 3.4 Hz, H-4), 5.270 (t, 1 H, *J* 10.0 Hz, H-2), 5.060 (dd, 1 H, *J* 3.4 and 10.0 Hz, H-3), 4.400 (d, 1 H, *J* 10.0 Hz, H-1), 4.169 (dd, 1 H, *J* 6.6 and 11.2 Hz, H-6), 4.122 (dd, 1 H, *J* 6.6 and 11.5 Hz, H-6'), 3.965 (dt, 1 H, *J* 0.3 and 6.6 Hz, H-5), 2.202 (s, 3 H, S*Me*), 2.162 (s, 3 H, Ac), 2.084 (s, 3 H, Ac), 2.054 (s, 3 H, Ac), and 1.994 (s, 3 H, Ac); δ_C 83.4 ($^1J_{CH}$ 151 Hz, C-1) and 11.4 (S*Me*).

Anal. Calc. for $C_{15}H_{22}O_9S$: C, 47.61; H, 5.86; S, 8.47. Found: C, 47.56; H, 5.85; S, 8.44.

Compound **20**: $[\alpha]_D$ +200° (*c* 0.32); R_F 0.35 in 9:1 toluene–EtOAc; n.m.r. data: δ_H 5.622 (d, 1 H, *J* 5.1 Hz, H-1), 5.456 (d, 1 H, *J* 3.2 Hz, H-4), 5.300 (dd, 1 H, *J* 5.3 and 10.7 Hz, H-2), 5.239 (dd, 1 H, *J* 3.2 and 10.7 Hz, H-3), 4.551 (t, 1 H, *J* 6.6 Hz, H-5), 4.139 (dd, 1 H, *J* 6.3 and 14.8 Hz, H-6), 4.106 (dd, 1 H, *J* 6.3 and 12.5 Hz, H-6'), 2.153 (s, 3 H, S*Me*), 2.079 (s, 3 H, Ac), 2.062 (s, 3 H, Ac), 2.054 (s, 3 H, Ac), and 1.996 (s, 3 H, Ac); δ_C 83.0 ($^1J_{CH}$ 171 Hz, C-1) and 12.2 (S*Me*).

Anal. Calc. for $C_{15}H_{22}O_9S$: C, 47.61; H, 5.86; S, 8.47. Found: C, 47.64; H, 5.80; S, 8.06.

*Methyl 1-thio-β-*D*-galactopyranoside* (**21**). — A solution of compound **19** (1.17 g, 3.1 mmol) in MeOH (30 mL)–0.1M NaOMe (2 mL) was stirred for 16 h at 20°, made neutral with Amberlyst 15, and the suspension filtered. The filtrate was evaporated *in vacuo*, and the residue (646 mg, quantitative) crystallized from EtOH, to give **21**; m.p. 132–133°, $[\alpha]_D$ −5.1° (*c* 0.56, MeOH); lit.[34] m.p. 174–175°, $[\alpha]_D$ +10.7° (H_2O); R_F 0.35 in 7:3 $CHCl_3$–MeOH; n.m.r. data: δ_H (CD_3OD) 4.212 (d, 1 H, *J* 9.5 Hz, H-1), 3.882 (dd, 1 H, *J* 1.2 and 3.4 Hz, H-4), 3.747 (dd, 1 H, *J* 6.8 and 11.5 Hz, H-6), 3.679 (dd, 1 H, *J* 5.4 and 11.5 Hz, H-6'), 3.577 (t, 1 H, *J* 9.3 Hz, H-2), 3.529 (ddd, 1 H, *J* 1.2, 5.4, and 6.6 Hz, H-5), 4.464 (dd, 1 H, *J* 3.4 and 9.3 Hz, H-3), and 2.194 (s, 3 H, S*Me*); δ_C 87.2 ($^1J_{CH}$ 154 Hz, C-1) and 11.5 (S*Me*).

Anal. Calc. for $C_7H_{14}O_5S$: C, 39.99; H, 6.71; S, 15.25. Found: C, 39.86; H, 6.71; S, 15.22.

*Methyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-*D*-galactopyranoside* (**22**). — To a suspension of NaH (60%; 3.2 g, 80 mmol) in DMF (80 mL) was added dropwise a solution of compound **21** (2.1 g, 10 mmol) in DMF (30 mL) at −5 to 0° and the mixture was stirred for 30 min at −5 to 0°. To this mixture was added dropwise benzyl bromide (9.6 mL, 80 mmol) and the mixture was stirred for 3 h at 10–20°. The excess of NaH was decomposed by the dropwise addition of MeOH, and the mixture was evaporated *in vacuo*. A solution of the residue in EtOAc (100 mL) was successively washed with water and satd. aq. NaCl, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 4:1 hexane–EtOAc afforded **22** (5.22 g, 91.5%); $[\alpha]_D$ +1.6° (*c* 2.3); R_F 0.41 in 4:1 toluene–EtOAc; n.m.r. data: δ_H 2.205 (s, 3 H, S*Me*); δ_C 85.6 ($^1J_{CH}$ 154 Hz, C-1), 84.0 (C-3), and 12.7 (S*Me*).

Anal. Calc. for $C_{35}H_{38}O_5S \cdot 0.25\ C_6H_5CH_3$: C, 74.02; H, 7.06; S, 5.41. Found: C, 74.45; H, 6.77; S, 5.43.

*2,3,4,6-Tetra-*O*-benzyl-*D*-galactopyranose* (**23**). — A mixture of compound **22** (740 mg, 1.3 mmol), $HgCl_2$ (775 mg, 2.9 mmol), and $CaCO_3$ (286 mg, 2.9 mmol) in 80% aq. MeCN was stirred under reflux for 16 h, and filtered through Celite. The filtrate was evaporated *in vacuo*, and a solution of the residue in EtOAc (100 mL) was washed successively with H_2O and satd. aq. NaCl, dried ($MgSO_4$), and evaporated *in vacuo*; the residue was chromatographed on SiO_2 in 4:1 toluene–EtOAc, to give **23** (579 mg, 82.6%); $[\alpha]_D$ +13.1° (*c* 1.6); lit.[26a] m.p. 66–68°, $[\alpha]_D$

+74° (pyridine–phenol); R_F 0.13 in 9:1 toluene–EtOAc; n.m.r. data: δ_C 99.0 (C-1β) and 93.0 (C-1α).

Anal. Calc. for $C_{34}H_{36}O_6 \cdot H_2O$: C, 73.10; H, 6.86. Found: C, 72.79; H, 6.49.

2,3,4,6-Tetra-O-benzyl-α-D-galactopyranosyl chloride (**24**). — To a solution of compound **23** (579 mg, 1.07 mmol) in $Cl(CH_2)_2Cl$ (4 mL) were added $SOCl_2$ (1 mL, 13.7 mmol) and DMF (0.05 mL). The mixture was stirred for 16 h at 20°, filtered through a thin layer of SiO_2, and the filtrate evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 9:1 hexane–EtOAc gave **24** (558 mg, 93%); $[\alpha]_D$ +55.6° (*c* 0.63); lit.[26a] $[\alpha]_D$ +147° (benzene); R_F 0.23 in 9:1 toluene–EtOAc; n.m.r. data: δ_H 6.139 (d, 1 H, *J* 3.6 Hz, H-1); δ_C 94.9 ($^1J_{CH}$ 181 Hz, C-1).

Methyl 2,6-di-O-benzyl-3,4-O-isopropylidene-1-thio-β-D-galactopyranoside (**27**) *and methyl 2,3-di-O-benzyl-4,6-O-isopropylidene-1-thio-β-D-galactopyranoside* (**28**). — A solution of compound **21** (2.8 g, 13.3 mmol), 2,2-dimethoxypropane (2.45 mL, 20.0 mmol), and $TsOH \cdot H_2O$ (255 mg) was stirred for 16 h at 20°, made neutral with Et_3N (5 mL), and evaporated *in vacuo*. A solution of the residue in EtOAc (100 mL) was washed with aq. $NaHCO_3$, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 9:1 $CHCl_3$–MeOH gave a mixture (3.04 g, 91%) of **25** and **26** which was used for the next step. The mixture (3.04 g, 12.2 mmol) was benzylated as described for compound **22**. Chromatography on SiO_2 in 10:1 toluene–EtOAc afforded **27** (4.32 g, 82.6%) and **28** (0.85 g, 16.3%).

Compound **27**: $[\alpha]_D$ −15.7° (*c* 1.00); R_F 0.45 in 9:1 toluene–EtOAc; n.m.r. data: δ_H 4.847 (d, 1 H, *J* 11.5 Hz, OC*H*$_2$Ph), 4.743 (d, 1 H, *J* 11.2 Hz, OC*H*$_2$Ph), 4.635 (d, 1 H, *J* 12.0 Hz, OC*H*$_2$Ph), 4.544 (d, 1 H, *J* 12.0 Hz, OC*H*$_2$Ph), 4.328 (d, 1 H, *J* 9.8 Hz, H-1), 4.241–4.200 (m, 2 H, H-3,4), 3.916 (t, 1 H, *J* 6.1 Hz, H-5), 3.82–3.73 (2 H, H-6,6'), 3.48–3.43 (m, 1 H, H-2), 2.202 (s, 3 H, S*Me*), 1.441 (s, 3 H, C*Me*$_2$), and 1.354 (s, 3 H, C*Me*$_2$); δ_C 109.9 (*C*Me$_2$), 84.4 (C-1), 27.9 (C*Me*$_2$), 26.4 (C*Me*$_2$), and 12.9 (S*Me*).

Anal. Calc. for $C_{24}H_{30}O_5S$: C, 66.95; H, 7.02; S, 7.45. Found: C, 66.99; H, 7.01; S, 7.26.

Compound **28**: m.p. 129–130°, $[\alpha]_D$ −24.0° (*c* 0.60); R_F 0.28 in 9:1 toluene–EtOAc; n.m.r. data: δ_H 4.873 (s, 2 H, OC*H*$_2$Ph), 4.771 (d, 1 H, *J* 12.5 Hz, OC*H*$_2$Ph), 4.697 (d, 1 H, *J* 12.5 Hz, OC*H*$_2$Ph), 4.285 (d, 1 H, *J* 9.5 Hz, H-1), 4.109 (d, 1 H, *J* 2.9 Hz, H-4), 3.850 (t, 1 H, *J* 9.5 Hz, H-2), 3.517 (dd, 1 H, *J* 3.4 Hz and 9.3 Hz, H-3), 3.29–3.19 (m, H-5), 2.233 (s, 3 H, S*Me*), 1.505 (s, 3 H, C*Me*$_2$), and 1.428 (s, 3 H, C*Me*$_2$); δ_C 98.9 (*C*Me$_2$), 84.2 ($^1J_{CH}$ 151 Hz, C-1), 81.0 (C-3), 63.0 (C-6), 29.1 (C*Me*$_2$), 18.7 (C*Me*$_2$), and 11.6 (S*Me*).

Anal. Calc. for $C_{24}H_{30}O_5S$: C, 66.95; H, 7.02; S, 7.45. Found: C, 67.18; H, 7.03; S, 7.53.

Methyl 2,6-di-O-benzyl-1-thio-β-D-galactopyranoside (**29**). — A solution of compound **27** (4.18 g, 9.7 mmol) in CF_3CO_2H (10 mL)–MeOH (1 mL) was stirred for 15 min at −10 to −5°, and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 9:1 toluene–EtOAc gave **29** (3.40 g, 90.0%); m.p. 91–92°, $[\alpha]_D$ +6.3° (*c*

0.60); R_F 0.32 in 7:3 toluene–EtOAc; n.m.r. data: 4.946 (d, 1 H, *J* 11.0 Hz, OC*H*$_2$Ph), 4.709 (d, 1 H, *J* 11.0 Hz, OC*H*$_2$Ph), 4.573 (s, 2 H, OC*H*$_2$Ph), 4.319 (d, 1 H, *J* 9.3 Hz, H-1), 4.024 (t, 1 H, *J* 2.9 Hz, H-4), 3.771 (dd, 1 H, *J* 5.4 and 10.0 Hz, H-6), 3.733 (dd, 1 H, *J* 5.1 and 10.0 Hz, H-6'), 3.601 (t, 1 H, *J* 5.4 Hz, H-5), 3.546 (t, 1 H, *J* 9.3 Hz, H-2), 2.817 (d, 1 H, *J* 3.7 Hz, OH-4), 2.627 (d, 1 H, *J* 5.4 Hz, OH-3), and 2.250 (s, 3 H, SMe); δ_C 85.3 ($^1J_{CH}$ 153 Hz, C-1) and 12.9 (SMe).

Anal. Calc. for $C_{22}H_{26}O_5S$: C, 64.59; H, 6.71; S, 8.21. Found: C, 64.47; H, 6.68; S, 8.07.

*Methyl 3,4-di-*O*-acetyl-2,6-di-*O*-benzyl-1-thio-β-*D*-galactopyranoside* (**30**). — A solution of compound **29** (1.68 g, 4.3 mmol) in pyridine (10 mL) and Ac_2O (8.1 mL, 86 mmol) was stirred for 16 h at 20° and then evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 9:1 toluene–EtOAc gave **30** (2.06 g, 98.6%) which crystallized from toluene–EtOAc; m.p. 76–77°, $[\alpha]_D$ −2.9° (*c* 1.1); R_F 0.68 in 9:1 toluene–EtOAc; n.m.r. data: δ_H 5.482 (d, 1 H, *J* 3.2 Hz, H-4), 5.019 (dd, 1 H, *J* 3.4 and 9.8 Hz, H-3), 4.839 (d, 1 H, *J* 10.7 Hz, OC*H*$_2$Ph), 4.609 (d, 1 H, *J* 11.0, OC*H*$_2$Ph), 4.553 (d, 1 H, *J* 12.0 Hz, OC*H*$_2$Ph), 4.460 (d, 1 H, *J* 9.8 Hz, H-1), 4.409 (d, 1 H, *J* 12.0 Hz, OC*H*$_2$Ph), 3.845 (t, 1 H, *J* 6.8 Hz, H-5), 3.645 (t, 1 H, *J* 9.5 Hz, H-2), 3.560 (dd, 1 H, *J* 5.9 and 9.5 Hz, H-6), 3.455 (dd, 1 H, *J* 6.8 and 9.5 Hz, H-6'), 2.267 (s, 3 H, S*Me*), 2.035 (s, 3 H, Ac), and 1.943 (s, 3 H, Ac); δ_C 86.0 ($^1J_{CH}$ 153 Hz, C-1), 20.7 (2 CO*Me*), and 13.3 (S*Me*).

Anal. Calc. for $C_{26}H_{30}O_7S$: C, 64.18; H, 6.21; S, 6.59. Found: C, 63.86; H, 6.39; S, 6.61.

Benzyl O-*(2,3,4,6-tetra-*O*-benzyl-α-*D*-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**31**) *and benzyl* O-*(2,3,4,6-tetra-*O*-benzyl-β-*D*-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**32**). — (*A*) A mixture of compound **16** (108 mg, 0.11 mmol), compound **22** (89 mg, 156 μmol), $AgOSO_2CF_3$ (86 mg, 334 μmol), $CuBr_2$ (55 mg, 208 μmol), and powdered molecular sieves 4A (800 mg) in $Cl(CH_2)_2Cl$ (4 mL) was stirred for 3 h at 20°, diluted with EtOAc (20 mL), and filtered through Celite. The filtrate was successively washed with aq. $NaHCO_3$ and H_2O, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 15:1 toluene–EtOAc gave **31** (121 mg, 73%) and **32** (35 mg, 21%).

(*B*) A mixture of compound **16** (103 mg, 106 μmol), compound **22** (84 mg, 148 μmol), $HgBr_2$ (80 mg, 317 μmol), $CuBr_2$ (52 mg, 232 μmol), and powdered molecular sieves 4A (800 mg) in $MeNO_2$ (4 mL) was stirred for 3 h at 20°, diluted with EtOAc (20 mL), and filtered through Celite. Processing as in (*A*) afforded **31** (84 mg, 53%) and **32** (46 mg, 37%).

(*C*) A mixture of compound **16** (97 mg, 100 μmol), compound **22** (80 mg, 140 μmol), $HgBr_2$ (76 mg, 30 μmol), $CuBr_2$ (49 mg, 220 μmol), and powdered molecular sieves 4A (800 mg) in $Cl(CH_2)_2Cl$ (4 mL) was stirred for 3 h at 20°, diluted with EtOAc (20 mL), and filtered through Celite. Processing as in (*A*) afforded **31** (50 mg, 33%) and **32** (83 mg, 56%).

(*D*) To a mixture of compound **16** (1.1 g, 1.13 mmol), $AgOSO_2CF_3$ (872 mg, 3.39 mmol), and powdered molecular sieves 4A (4 g) in $Cl(CH_2)_2Cl$ (10 mL) was added dropwise, with stirring under Ar, a solution of compound **24** (759 mg, 1.36 mmol) in $Cl(CH_2)_2Cl$ (10 mL) at 20°. The mixture was stirred for 16 h at 20°, diluted with EtOAc (50 mL) and filtered through Celite. Processing as described in (*A*) and chromatography on SiO_2 in 4:1 hexane–EtOAc afforded **31** (924 mg, 63%) and **32** (284 mg, 19%).

Compound **31**: $[\alpha]_D$ +24.1° (*c* 0.90); R_F 0.42 in 4:1 hexane–EtOAc; n.m.r. data: δ_C 102.9 ($^1J_{CH}$ 157 Hz, C-1b), 102.5 ($^1J_{CH}$ 157 Hz, C-1a), and 100.8 ($^1J_{CH}$ 165 Hz, C-1c).

Anal. Calc. for $C_{95}H_{98}O_{16}$: C, 76.28; H, 6.60. Found: C, 76.57; H, 6.61.

Compound **32**: $[\alpha]_D$ +18.6° (*c* 1.9); R_F 0.28 in 4:1 hexane–EtOAc; n.m.r. data: δ_C 102.8, 102.6, and 102.5 for C-1a, C-1b, and C-1c.

Anal. Calc. for $C_{95}H_{98}O_{16}$: C, 76.28; H, 6.60. Found: C, 76.59; H, 6.59.

O-*α*-D-*Galactopyranosyl*-(*1→4*)-O-*β*-D-*galactopyranosyl*-(*1→4*)-D-*glucopyranose* (**33**). — A mixture of compound **31** (907 mg, 0.61 mmol) and 10% Pd–C (450 mg) in AcOH (45 mL) was stirred for 2 h at 80° under H_2, and filtered through Celite. The filtrate was coevaporated with EtOH, to give **33** (305 mg, quantitative) which was used for the next step without purification; R_F 0.29 in 2:2:1 1-BuOH–EtOH–H_2O; n.m.r. data: δ_H (D_2O, 60°) 5.221 (d, 0.4 H, *J* 3.9 Hz, H-1a*α*), 4.970 (d, 1 H, *J* 3.4 Hz, H-1c), 4.656 (d, 0.6 H, *J* 8.1 Hz, H-1a*β*), 4.507 (d, 1 H, *J* 7.6 Hz, H-1b), 4.314 (t, 1 H, *J* 6.3 Hz, H-5c), and 3.284 (t, 0.6 H, *J* 8.3 Hz, H-2a*β*); lit.[14] δ_H (D_2O) 5.23 (d, *J* 3.6 Hz, H-1a*α*) and 4.67 (d, *J* 8.0 Hz, H-1a*β*); δ_C (D_2O, 20°, internal 1,4-dioxane) 104.0 (C-1b), 101.1 (C-1c), 96.5 (C-1a*β*), and 92.5 (C-1a*α*).

O-(*2,3,4,6-Tetra*-O-*acetyl*-*α*-D-*galactopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl*-*β*-D-*galactopyranosyl*)-(*1→4*)-*2,3,6-tri*-O-*acetyl*-*α*- *and* -*β*-D-*glucopyranosyl acetate* (**34**). — A solution of compound **33** (316 mg, 0.63 mmol) in pyridine (8 mL) and Ac_2O (6.5 mL) was stirred for 16 h at 20°, and then evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 2:3 toluene–EtOAc afforded **34** (342 mg, 68%) as a 1:1 mixture of the *α* and *β* anomer; R_f 0.47 and 0.43 in 1:2 toluene–EtOAc; n.m.r. data: δ_H 6.252 (d, 0.5 H, *J* 3.6 Hz, H-1a*α*), 5.690 (d, 0.5 H, *J* 8.3 Hz, H-1a*β*), and 5.591 (bs, 1 H, H-4c); δ_C 100.8, 100.6 (C-1b*α* and C-1b*β*), 99.3 (C-1c), 91.3 (C-1a*β*), and 88.7 (C-1a*α*).

Anal. Calc. for $C_{40}H_{54}O_{27}\cdot 0.5\ C_6H_5CH_3$: C, 51.58; H, 5.77. Found: C, 51.81; H, 5.83.

O-(*2,3,4,6-Tetra*-O-*acetyl*-*α*-D-*galactopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl*-*β*-D-*galactopyranosyl*)-(*1→4*)-*2,3,6-tri*-O-*acetyl*-D-*glucopyranose* (**35**). — A solution of compound **34** (326 mg, 0.34 mmol) and $H_2NNH_2\cdot AcOH$ (40 mg, 0.44 mmol) in DMF (1 mL) was stirred for 30 min at 50°, and then diluted with EtOAc (50 mL). The organic layer was washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 1:2 toluene–EtOAc afforded recovered **34** (28 mg, 8.6%) and **35** (243 mg; 85.1% based on **34** consumed); R_f 0.18 in 1:2 toluene–EtOAc; n.m.r. data: δ_H 5.590 (bs, 1 H, H-4c); δ_C 100.8 (C-1b),

99.3 (C-1c), 94.9 (C-1aβ), and 89.8 (C-1aα).

Anal. Calc. for $C_{38}H_{52}O_{26}$: C, 49.35; H, 5.67. Found: C, 49.51; H, 5.67.

Conversion of **35** *into the glycosyl trichloroacetimidate* (**36**) *and fluoride* (**37**). — A mixture of compound **35** (237 mg, 0.25 mmol), Cl_3CCN (100 μL, 1.01 mmol), and 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) (30 μL) in CH_2Cl_2 (1 mL) was stirred for 5 h at 0–5° under Ar, and then evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 1:1 hexane–THF gave O-*(2,3,4,6-tetra*-O-*acetyl-α*-D-*galacto-pyranosyl)-(1→4)*-O-*(2,3,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*acetyl-α*-D-*glucopyranosyl trichloroacetimidate* (**36**) (220 mg, 79%); R_F 0.35 in 1:1 hexane–THF; n.m.r. data: δ_H 8.648 (s, 1 H, C=NH), 6.482 (d, 1 H, *J* 3.8 Hz, H-1a), 2.132, 2.109, 2.096, 2.092, 2.074, 2.066, 2.063, 2.042, 2.011, and 1.987 (10 s, 30 H, 10 Ac).

To a solution of compound **35** (49 mg, 52 μmol) in CH_2Cl_2 (1 mL) was added DAST (Et_2NSF_3, 12 μL, 105 μmol) at 0°. After stirring for 16 h at 20°, the mixture was diluted with CH_2Cl_2. The organic layer was washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 1:1 hexane-THF afforded O-*(2,3,4,6-tetra*-O-*acetyl-α*-D-*galactopyranosyl)-(1→4)*-O-*(2,3,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*acetyl-α- (and β-)*D-*galactopyra-nosyl fluoride* (**37**) (46 mg, 94%) as a mixture of the α and β anomer in the ratio of 1:10; R_F 0.41 in 1:1 hexane–THF; n.m.r. data: 5.740 (d, 0.09 H, *J* 3.3 Hz, a lower-field pair of dd for H-1aα), 5.586 (d, 1 H, *J* 2.4 Hz, H-4c), 5.411 (dd, 1 H, *J* 5.1 and 53.0 Hz, H-1aβ), and 2.136 (s, 6 H), 2.132 (s, 3 H), 2.113 (s, 3 H), 2.085 (s, 3 H), 2.079 (s, 3 H), 2.075 (s, 3 H), 2.055 (s, 6 H), and 1.994 (s, 3 H) for 10 Ac.

O-*(2,3,4,6-Tetra*-O-*acetyl-α*-D-*galactopyranosyl)-(1→4)*-O-*(2,3,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)*-O-*(2,3,6-tri*-O-*acetyl-β*-D-*glucopyranosyl)-(1→1)-(2S,3R,4E)-3*-O-*benzoyl-2*-N-*tetracosanoylsphingenine* (**38**). — (*A*) To a mixture of compound **36** (50 mg, 46 μmol), compound **6** (35 mg, 46 μmol), and powdered molecular sieves AW 300 (100 mg) in $CHCl_3$ (1 mL) was added $BF_3 \cdot Et_2O$ (6 μL) at 0–5°. The mixture was stirred for 24 h at 20° under Ar, and filtered through Celite. The filtrate was washed with aq. $NaHCO_3$, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 1:1 toluene–EtOAc afforded **38** (10 mg, 13%; 64% based on consumed **36**), as well as recovered **35** (14 mg, 33%) and **36** (24 mg, 48%).

(*B*) To a mixture of $AgClO_4$ (9 mg, 42 μmol), $SnCl_2$ (8 mg, 43 μmol), and powdered molecular sieves 4A (300 mg) was added a solution of compound **37** (21 mg, 22.6 μmol) and compound **6** (14 mg, 19 μmol) in $CHCl_3$ (1 mL) at 0–5°. The mixture was stirred for 16 h at 15–20°, diluted with $CHCl_3$, and filtered. The filtrate was washed with aq. $NaHCO_3$, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 3:2 hexane–THF afforded **38** (9.2 mg, 29%).

Compound **38**: $[\alpha]_D$ +35.5° (*c* 0.5); R_F 0.62 in 1:2 toluene–EtOAc; n.m.r. data: 5.867 (dt, 1 H, *J* 6.9 and 15.4 Hz, H-5cer), 5.751 (d, 1 H, *J* 9.0 Hz, NH), 5.581 (d, H, *J* 2.4 Hz, H-4c), 5.540 (t, 1 H, *J* 7.3 Hz, H-3cer), 5.471 (dd, 1 H, *J* 7.8

and 15.1 Hz, H-4cer), 5.384 (dd, 1 H, *J* 3.2 and 11.0 Hz, H-3c), 4.979 (d, 1 H, *J* 3.7 Hz, H-1c), 4.480 (d, 1 H, *J* 8.1 Hz, H-1b), and 4.461 (d, 1 H, *J* 7.8 Hz, H-1a).

Anal. Calc. for $C_{87}H_{137}NO_{29}$: C, 62.91; H, 8.31; N, 0.84. Found: C, 62.77; H, 8.30; N, 0.84.

O-*(2,3,4,6-Tetra-O-acetyl-α-D-galactopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-β-D-galactopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-β-D-glucopyranosyl)-(1→1)-(2S,3R,4Z)-3-O-benzoyl-2-N-tetracosanoylsphingenine* (**39**). — To a mixture of compound **36** (35 mg, 32 μmol), compound **7** (24 mg, 32 μmol), and powdered molecular sieves AW 300 (100 mg) in $CHCl_3$ (0.7 mL) was added BF_3·ether (6 μL, 49 μmol) at 0–5°. The mixture was stirred for 16 h at 20°, diluted with $CHCl_3$, and filtered through Celite. The filtrate was washed with aq. $NaHCO_3$, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 1:1 toluene–EtOAc afforded **39** (18 mg, 34%); $[\alpha]_D$ +39.7° (*c* 0.85); R_F 0.63 in 1:2 toluene–EtOAc; n.m.r. data: δ_H 5.847 (dd, 1 H, *J* 7.3 and 8.3 Hz, H-3cer), 5.808 (d, 1 H, *J* 9.0 Hz, NH), 5.669 (td, 1 H, *J* 6.9 and 11.4 Hz, H-5cer), 5.582 (d, 1 H, *J* 2.4 Hz, H-4c), 5.392 (dd, 1 H, *J* 9.3 and 11.0 Hz, H-4cer), 4.979 (d, 1 H, *J* 3.7 Hz, H-1c), 4.478 (d, 2 H, *J* 7.5 Hz, H-1a,1b), and 2.131, 2.093, 2.083, 2.070, 2.062, 2.055, 2.021, 2.018, 1.985, and 1.943 (10 s, 30 H, 10 Ac).

Anal. Calc. for $C_{87}H_{137}NO_{29}·H_2O$: C, 62.24; H, 8.34; N, 0.83. Found: C, 62.13; H, 8.19; N, 0.97.

O-*α-D-Galactopyranosyl-(1→4)-O-β-D-galactopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→1)-(2S,3R,4E)-2-N-tetracosanoylsphingenine* (**1**) *and its* (Z) *isomer* (**2**). — A solution of compound **38** (10 mg, 6 μmol) in 1:1 MeOH–THF (1 mL) and 5% NaOMe–MeOH (10 μL) was stirred for 5 h at 20°, diluted with 1:1 MeOH–THF (10 mL), treated with Amberlyst 15, and the suspension filtered through Celite. The filtrate was evaporated *in vacuo*. Purification of the residue by Sephadex LH-20 in 26:13:2 $CHCl_3$–MeOH–H_2O afforded **1** (5.7 mg, 83%); $[\alpha]_D$ +19.0° (*c* 0.36, pyridine); R_F 0.64 in 26:13:2 $CHCl_3$–MeOH–H_2O; n.m.r. data: δ_H (49:1 Me_2SO-d_6–D_2O, 65°) 5.564 (td, 1 H, *J* 6.8 and 15.4 Hz, H-5cer), 5.385 (dd, 1 H, *J* 6.6 and 15.2 Hz, H-4cer), 4.825 (d, 1 H, *J* 3.9 Hz, H-1c), 4.284 (d, 1 H, *J* 7.3 Hz, H-1b), 4.179 (d, 1 H, *J* 7.8 Hz, H-1a), 4.068 (t, 1 H, *J* 6.8 Hz, H-5c), 3.944 (dd, 1 H, *J* 5.4 and 10.3 Hz, H-1cer), 3.925 (t, 1 H, *J* 7.3 Hz, H-3cer), 3.826 (d, 1 H, *J* 3.0 Hz, H-4c), 3.776 (d, 1 H, *J* 3.1 Hz, H-4b), and 3.063 (t, 1 H, *J* 8.1 Hz, H-2a).

Similarly, a solution of compound **39** (47 mg, 28 μmol) in 1:1 MeOH–THF (2 mL) and 5% NaOMe–MeOH (47 μL) was stirred for 2 h at 20°, diluted with 1:1 MeOH–THF, treated with Amberlyst 15, and the suspension filtered. The filtrate was evaporated *in vacuo*, and the residue was purified by use of Sephadex LH-20 in 26:13:2 $CHCl_3$–MeOH–H_2O, to give O-*α-D-galactopyranosyl-(1→4)-O-β-D-galactopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→1)-(2S,3R,4Z)-2-N-tetracosanoylsphingenine* (**2**; 28.6 mg, 89%); $[\alpha]_D$ +18.0° (*c* 1.4, pyridine); R_F 0.67 in 26:13:2 $CHCl_3$–MeOH–H_2O; n.m.r. data: δ_H (49:1 Me_2SO-d_6–D_2O, 60°) 7.323 (d, 1 H, *J* 8.8 Hz, NH), 5.356 (td, 1 H, *J* 7.3 and 10.7 Hz, H-5cer), 5.288 (dd, 1 H, *J*

8.3 and 10.9 Hz, H-4cer), 4.815 (d, 1 H, *J* 3.9 Hz, H-1c), 4.276 (d, 1 H, *J* 7.6 Hz, H-1b), 4.246 (t, 1 H, *J* 8.1 Hz, H-3cer), 4.186 (d, 1 H, *J* 7.8 Hz, H-1a), 4.065 (t, 1 H, *J* 6.1 Hz, H-5c), 3.950 (dd, 1 H, *J* 5.6 and 10.3 Hz, H-1cer), 3.820 (d, 1 H, *J* 2.7 Hz, H-4c), 3.776 (d, 1 H, *J* 2.8 Hz, H-4b), and 3.061 (t, 1 H, *J* 8.1 Hz, H-2a); δ_C (pyridine-d_5) 173.4 (C-1'cer), 132.4 (C-4cer), 132.2 (C-5cer), 105.7, 105.3 (C-1a and C-1b), 103.0 (C-1c), 81.9 (C-4a), 79.5 (C-4b), 62.6, 61.7, 60.4 (C-6a, C-6b, and C-6c), 55.0 (C-2cer), 36.8 (C-2'cer), 32.0 (C-6cer, C-16cer, C-22'cer), 26.3 (C-3'cer), 22.8 (C-17cer, C-23'cer), and 14.2 (C-18cer and C-24'cer).

Benzyl O-*(3,4-di-*O*-acetyl-2,6-di-*O*-benzyl-α-*D*-galactopyranosyl)-(1→3)-*O*-(2,6-di-*O*-benzyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**40**), *its 4'-acetate* (**41**), *and benzyl* O-*(3,4-di-*O*-acetyl-2,6-di-*O*-benzyl-α-*D*-galactopyranosyl)-(1→3)-*O*-[(3,4-di-*O*-acetyl-2,6-di-*O*-benzyl-α-*D*-galactopyranosyl)-(1→4)]-*O*-(2,6-di-*O*-benzyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**42**). — To a mixture of $AgOSO_2CF_3$ (436 mg, 1.7 mmol), $CuBr_2$ (395 mg, 1.8 mmol), and powdered molecular sieves 4A (2.0 g) was added a solution of compound **30** (386 mg, 0.79 mmol) and compound **17** (500 mg, 0.57 mmol) in $Cl(CH_2)_2Cl$ (10 mL). After stirring for 16 h at 20°, the mixture was diluted with $CHCl_3$ (50 mL), filtered through Celite, and the filtrate washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 4:1 hexane–THF afforded **40** (299 mg, 41%) and **42** (343 mg, 35%).

Compound **40**: $[\alpha]_D$ +22.5° (*c* 0.84); R_F 0.34 in 7:3 hexane–THF; n.m.r. data: δ_H 5.35–5.31 (m, 3 H, H-1c,3c,4c), and 2.003 (s, 3 H) and 1.982 (s, 3 H) for 2 Ac; δ_C 102.6 (C-1a,1b), 94.5 (C-1c), 82.9 (C-3b), and 81.9 (C-4a).

Anal. Calc. for $C_{78}H_{84}O_{18} \cdot C_6H_5CH_3$: C, 72.84; H, 6.62. Found: C, 72.97; H, 6.59.

A solution of compound **40** (11 mg, 8.5 μmol)in 1:1 pyridine–Ac_2O (0.5 mL) containing 4-(dimethylamino)pyridine (DMAP, 5 mg) was stirred for 15 min at 60° and evaporated *in vacuo*. Chromatography of the residue in 7:3 hexane–THF afforded *benzyl* O-*(3,4-di-*O*-acetyl-2,6-di-*O*-benzyl-α-*D*-galactopyranosyl)-(1→3)-*O*-(4-*O*-acetyl-2,6-di-*O*-benzyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* **41** (7.3 mg, 65%); R_F 0.27 in 7:3 hexane–THF; n.m.r. data: δ_H 5.552 (d, 1 H, *J* 3.1 Hz, H-4b*), 5.399 (dd, 1 H, *J* 3.1 and 10.5 Hz, H-3c), 5.353 (d, 1 H, *J* 3.4 Hz, H-1c), 5.156 (d, 1 H, *J* 2.2 Hz, H-4c*), and 1.971 (s, 3 H), 1.940 (s, 3 H), and 1.767 (s, 3 H) for 3 Ac.

Compound **42**: $[\alpha]_D$ +39.1° (*c* 0.66); R_F 0.26 in 7:3 hexane–THF; n.m.r. data: δ_H 5.732 (d, 1 H, *J* 2.6 Hz, H-4c), 5.498 (dd, 1 H, *J* 3.0 and 10.7 Hz, H-3c), 5.352 (d, 1 H, *J* 3.0 Hz, H-4d), 5.324 (dd, 1 H, *J* 3.4 and 10.5 Hz, H-3d), and 2.002, 1.997, 1.936, and 1.897 (4 s, 12 H, 4 Ac); δ_C 102.9 (C-1b), 102.5 (C-1a), and 97.7 and 97.0 (C-1c,1d).

Anal. Calc. for $C_{102}H_{110}O_{25}$: C, 70.57; H, 6.39. Found: C, 70.52; H, 6.41.

*O-(2,3,4,6-Tetra-*O*-acetyl-α-*D*-galactopyranosyl)-(1→3)-*O*-(2,3,6-tri-*O*-acetyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α (and β)-*D*-glucopyranosyl acetate* (**44**). — A mixture of compound **40** (280 mg, 0.22 mmol) and 10% Pd–C

(140 mg) in AcOH (14 mL) was stirred for 4 h at 80° under H_2, and filtered through Celite. The filtrate was evaporated *in vacuo* to give crude **43** (R_F 0.5 in 2:2:1 1-BuOH–EtOH–H_2O), which was dissolved in 1:1 pyridine–Ac_2O (6 mL) containing DMAP (5 mg). This solution was stirred for 16 h at 20° and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 11:9 hexane–THF afforded **44** (176 mg, 84%); R_F 0.46 in 1:1 hexane–THF; n.m.r. data: δ_H 6.254 (d, 0.6 H, *J* 3.7 Hz, H-1aα), 5.675 (d, 0.4 H, *J* 8.1 Hz, H-1aβ), and 4.414 (bd, 1 H, *J* 7.8 Hz, H-1b); δ_C 101.2 and 100.9 (C-1b), 93.7 (C-1c), 91.6 (C-1aβ), and 89.0 (C-1aα).

Anal. Calc. for $C_{40}H_{54}O_{27}$: C, 49.69; H, 5.63. Found: C, 50.21; H, 5.71.

O-(2,3,4,6-Tetra-O-acetyl-α-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-α (and β)-D-glucopyranose (**45**) *and its trichloroacetimidate* (**46**). — A solution of compound **44** (150 mg, 155 μmol) and $H_2NNH_2 \cdot AcOH$ (18.5 mg, 202 μmol) in DMF (1 mL) was stirred for 5 min at 60°, diluted with EtOAc (50 mL), washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 1:1 hexane–THF afforded **45** (121 mg, 85%) as a mixture of the α and the β anomer in the ratio of 2:1, based on the ^{13}C-n.m.r. spectrum; R_F 0.18 in 1:1 hexane–THF; n.m.r. data: δ_H 5.531 (t, 0.7 H, *J* 9.8 Hz, H-3aα), 5.452 (t, 1 H, *J* 1.5 Hz, H-4b*), 5.369 (d, 1 H, *J* 3.4 Hz, H-1c), 5.333 (d, 1 H, *J* 2.4 Hz, H-4c*), and 4.445 (d, 1 H, *J* 7.8 Hz, H-1b); δ_C 100.8 (C-1b), 94.9 (C-1aβ), 93.6 (C-1c), and 89.8 (C-1aα).

Anal. Calc. for $C_{38}H_{52}O_{26} \cdot 0.5\ H_2O$: C, 48.88; H, 5.72. Found: C, 48.81; H, 5.54.

To a solution of compound **45** (97 mg, 105 μmol) and CCl_3CN (105 μL, 1.1 mmol) in CH_2Cl_2 (1 mL) was added 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) (15 μL, 10 μmol) at 0–5°. The mixture was stirred for 2 h at 0–10° and evaporated *in vacuo*. Chromatography of the residue on SiO_2 in 1:1 hexane–THF afforded *O-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-α-D-glucopyranosyl trichloroacetimidate* **46** (81 mg, 71%); R_F 0.31 in 1:1 hexane–THF; n.m.r. data: δ_H 8.663 (s, 1 H, C=NH), 6.482 (d, 1 H, *J* 3.8 Hz, H-1a), 5.566 (t, 1 H, *J* 9.8 Hz, H-3a), 5.455 (d, 1 H, *J* 2.2 Hz, H-4b), 5.338 (d, 1 H, *J* 2.2 Hz, H-4c), 5.251 (s, 1 H, H-1c), and 4.466 (d, 1 H, *J* 7.8 Hz, H-1b); δ_C 161.0 (OC=N), 101.0 (C-1b), 93.6 (C-1c), and 93.0 (C-1a).

O-(2,3,4,6-Tetra-O-acetyl-α-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-β-D-glucopyranosyl)-(1→1)-(2S,3R,4E)-3-O-benzoyl-2-N-tetracosanoylsphingenine (**47**). — To a mixture of compound **46** (97 mg, 90 μmol), compound **6** (74 mg, 98 μmol), and powdered molecular sieves AW 300 (500 mg) in $CHCl_3$ (2.1 mL) was added a 10% solution of $BF_3 \cdot Et_2O$ in $CHCl_3$ (189 μL) at 0–5°. The mixture was stirred for 16 h at 20°, diluted with $CHCl_3$ (20 mL), and filtered through Celite. Evaporation of the filtrate *in vacuo* and chromatography of the residue on SiO_2 in 4:1 toluene–THF afforded **47** (54 mg, 33%); $[\alpha]_D$ +29.9° (*c* 0.8); R_F 0.49 in 1:1 hexane–THF; n.m.r. data: δ_H 5.865 (td, 1 H, *J* 6.6 and 15.4 Hz, H-5cer), 5.738 (d, 1 H, *J* 9.3 Hz, NH),

5.533 (t, 1 H, *J* 7.0 Hz, H-3cer), 5.457 (dd, 1 H, *J* 7.6 and 15.1 Hz, H-4cer), 5.443 (d, 1 H, *J* 2.9 Hz, H-4c*), 5.321 (d, 1 H, *J* 2.4 Hz, H-4b*), 4.444 (d, 1 H, *J* 7.8 Hz, H-1b), 4.376 (d, 1 H, *J* 7.8 Hz, H-1a), and 2.150, 2.135, 2.106, 2.074, 2.060, 2.055, 2.042, 2.024, 1.946, and 1.935 (10 s, 30 H, 10 Ac).

Anal. Calc. for $C_{87}H_{137}NO_{29} \cdot H_2O$: C, 62.24; H, 8.34; N, 0.83. Found: C, 62.43; H, 8.15; N, 0.81.

O-α-D-*Galactopyranosyl-(1→3)*-O-β-D-*galactopyranosyl-(1→4)*-O-β-D-*glucopyranosyl-(1→1)-(2S,3R,4E)-2*-N-*tetracosanosylsphingenine* (**3**). — A solution of compound **47** (37 mg, 22 μmol) in 2:1 THF–MeOH (1.6 mL) containing 5% NaOMe–MeOH (36 μL) was stirred for 16 h at 20°, diluted with 2:1 THF–MeOH (10 mL), treated with Amberlyst 15, and the suspension filtered through Celite. The filtrate was evaporated *in vacuo* and purification of the residue by means of Sephadex LH 20 in pyridine afforded **3** (24.5 mg, 97%); $[\alpha]_D$ +34.9° (*c* 1.1, pyridine); R_F 0.64 in 26:13:2 $CHCl_3$–MeOH–H_2O; n.m.r. data: δ_H (49:1 Me_2SO-d_6–D_2O, 95°) 7.251 (d, 1 H, *J* 8.1 Hz, NH), 5.707 (td, 1 H, *J* 7.1 and 15.6 Hz, H-5cer), 5.529 (dd, 1 H, *J* 6.6 and 15.4 Hz, H-4cer), 5.004 (d, 1 H, *J* 2.4 Hz, H-1c), 4.448 (d, 1 H, *J* 7.3 Hz, H-1b), 4.318 (d, 1 H, *J* 7.8 Hz, H-1a), 4.145 (t, 1 H, *J* 6.3 Hz, H-5c), and 4.077 (dd, 1 H, *J* 7.1 and 13.7 Hz, H-1cer).

ACKNOWLEDGMENTS

This work was partly supported by special coordination funds of the Science and Technology Agency of the Japanese Government. We thank Dr. J. Uzawa and Mrs. T. Chijimatsu for recording and measuring the n.m.r. spectra and Dr. H. Honma and his staff for the elemental analyses. We also thank A. Takahashi and K. Moriwaki for their technical assistance.

REFERENCES

1 K. KOIKE, M. SUGIMOTO, Y. NAKAHARA, AND T. OGAWA, *Carbohydr. Res.*, 162 (1987) 237–246.

2 S. HAKOMORI, in J. N. KANFER AND S. HAKOMORI (Eds.), *Handbook of Lipid Research, Vol. 3, Sphingolipid Biochemistry*, Plenum Press, New York, 1983, pp. 99–101; A. MAKITA AND N. TANIGUCHI, in H. WIEGANDT (Ed.), *New Comprehensive Biochemistry, Vol. 10, Glycolipids*, Elsevier, Amsterdam, 1985, pp. 20–23.

3 J. KAWANAMI, *J. Biochem. (Tokyo)*, 62 (1967) 105–117; S. HANDA, T. ARIGA, T. MIYATAKE, AND T. YAMAKAWA, *ibid.*, 69 (1971) 625–627; S. HAKOMORI, B. SIDDIQUI, Y.-T. LI, S.-C. LI, AND C. G. HELLERQVIST, *J. Biol. Chem.*, 246 (1971) 2271–2277; S.-C. LI AND Y.-T. LI, *ibid.*, 246 (1971) 3769–3771.

4 M. NAIKI AND D. M. MARCUS, *Biochem. Biophys. Res. Commun.*, 60 (1974) 1105–1111; *Biochemistry*, 14 (1975) 4837–4841; D. M. MARCUS, M. NAIKI, AND S. K. KUNDU, *Proc. Natl. Acad. Sci. U.S.A.*, 73 (1976) 3263–3267.

5 E. NUDELMAN, R. KANNAGI, S. HAKOMORI, M. PARSONS, M. LIPINSKI, J. WIELS, M. FELLOUS, AND T. TURSZ, *Science*, 220 (1983) 509–511; J. WIELS, E. H. HOLMES, N. COCHRAN, T. TURSZ, AND S. HAKOMORI, *J. Biol. Chem.*, 259 (1984) 14,783–14,787.

6 G. KÄLLENIUS, R. MÖLLBY, S. B. SVENSSON, J. WINBERG, A. LUNDBLAD, S. SVENSSON, AND B. CEDERGREN, *FEMS Microbiol. Lett.*, 7 (1980) 297–302; H. LEFFLER AND C. S. EDÉN, *ibid.*, 8 (1980) 127–134; K. BOCK, M. E. BREIMER, A. BRIGNOLE, G. C. HANSSON, K.-A. KARLSSON, G. LARSON, H. LEFFLER, B. E. SAMUELSSON, N. STRÖMBERG, AND C. S. EDÉN, *J. Biol. Chem.*, 260 (1985) 8545–8551.

7 P. STOFFYN, A. STOFFYN, AND G. HAUSER, *Biochim. Biophys. Acta*, 306 (1973) 283–286; H. ARITA AND J. KAWANAMI, *J. Biochem. (Tokyo)*, 81 (1977) 1661–1664.
8 H. ARITA AND J. KAWANAMI, *J. Biochem. (Tokyo)*, 76 (1974) 1067–1074.
9 S. S. SUNG AND C. C. SWEELEY, *Biochim. Biophys. Acta*, 575 (1979) 295–298.
10 D. D. COX, E. K. METZNER, AND E. J. REIST, *Carbohydr. Res.*, 63 (1978) 139–147.
11 P. J. GAREGG AND H. HULTBERG, *Carbohydr. Res.*, 110 (1982) 261–266.
12 J. DAHMÉN, T. FREJD, G. MAGNUSSON, G. NOORI, AND A.-S. CARLSTRÖM, *Carbohydr. Res.*, 127 (1984) 15–25.
13 H. PAULSEN AND A. BÜNSCH, *Carbohydr. Res.*, 100 (1982) 143–167.
14 J.-C. JACQUINET AND P. SINAY, *Carbohydr. Res.*, 143 (1985) 143–149.
15 D. SHAPIRO AND A. J. ACHER, *Chem. Phys. Lipids*, 22 (1978) 197–206.
16 K. KOIKE, Y. NAKAHARA, AND T. OGAWA, *Glycoconjugate J.*, 1 (1984) 107–109; K. KOIKE, M. SUGIMOTO, Y. NAKAHARA, AND T. OGAWA, *ibid.*, 2 (1985) 105–108.
17 D. BEITH-HALAHMI, H. M. FLOWERS, AND D. SHAPIRO, *Carbohydr. Res.*, 5 (1967) 25–30.
18 C. S. HUDSON AND J. M. JOHNSON, *J. Am. Chem. Soc.*, 37 (1915) 1270–1275.
19 T. OGAWA AND M. MATSUI, *Carbohydr. Res.*, 51 (1976) c13–c18.
20 J. P. CLAYTON, R. S. OLIVER, N. H. ROGERS, AND T. J. KING, *J. Chem. Soc., Perkin Trans. 1*, (1979) 838–846; J. G. BUCHANAN, M. E. CHACÓN-FUERTES, A. R. EDGAR, S. J. MOORHOUSE, D. I. RAWSON, AND R. H. WIGHTMAN, *Tetrahedron Lett.*, 21 (1980) 1793–1796.
21 T. OGAWA AND M. MATSUI, *Carbohydr. Res.*, 62 (1978) c1–c4; *Tetrahedron*, 37 (1981) 2363–2369; T. OGAWA, T. NUKADA, AND M. MATSUI, *Carbohydr. Res.*, 101 (1982) 263–270; T. OGAWA, Y. TAKAHASHI, AND M. MATSUI, *ibid.*, 102 (1982) 207–215; A. VEYRIÈRES, *J. Chem. Soc., Perkin Trans. 1*, (1981) 1626–1629.
22 A. LIPTÁK, I. JODÁL, AND P. NÁNÁSI, *Carbohydr. Res.*, 52 (1976) 17–22.
23 T. OGAWA AND M. SUGIMOTO, *Carbohydr. Res.*, 135 (1985) c5–c9; M. SUGIMOTO AND T. OGAWA, *Glycoconjugate J.*, 2 (1985) 5–9; M. SUGIMOTO, T. HORISAKI, AND T. OGAWA, *ibid.*, 2 (1985) 11–15.
24 S. SATO, K. KOIKE, Y. ITO, AND T. OGAWA, *Carbohydr. Res.*, 155 (1986) c6–c10.
25 T. OGAWA AND M. MATSUI, *Carbohydr. Res.*, 54 (1977) c17–c21.
26 (a) P. W. AUSTIN, F. E. HARDY, J. G. BUCHANAN, AND J. BADDILEY, *J. Chem. Soc.*, (1965) 1419–1424; (b) T. IVERSEN AND D. R. BUNDLE, *Carbohydr. Res.*, 103 (1982) 29–40.
27 G. EXCOFFIER, D. GAGNAIRE, AND J.-P. UTILLE, *Carbohydr. Res.*, 39 (1975) 368–373.
28 R. R. SCHMIDT AND J. MICHEL, *Angew. Chem., Int. Ed. Engl.*, 19 (1980) 731–732; R. R. SCHMIDT, J. MICHEL, AND M. ROOS, *Justus Liebigs Ann. Chem.*, (1984) 1343–1357.
29 W. M. ROSENBROOK, JR., D. A. RILEY, AND P. A. LARTEY, *Tetrahedron Lett.*, (1985) 3–4; G. H. POSNER AND S. R. HAINES, *ibid.*, (1985) 5–8.
30 T. MUKAIYAMA, Y. MURAI, AND S. SHODA, *Chem. Lett.*, (1981) 431–432.
31 J. DABROWSKI, P. HANFLAND, AND H. EGGE, *Biochemistry*, 19 (1980) 5652–5658.
32 N. K. RICHTMYER, *J. Am. Chem. Soc.*, 68 (1946) 1136–1137.
33 H. PAULSEN AND M. PAAL, *Carbohydr. Res.*, 137 (1985) 39–62.
34 B. HELFERICH, H. GRUNEWALD, AND F. LANGENHOFF, *Chem. Ber.*, 86 (1953) 873–875.