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3-BROMO-2-BROMOMETHYLPROPYL GLYCOSIDES IN THE PREPARATION OF DOUBLE-CHAIN BIS-SULFIDE NEO-GLYCOLIPIDS*

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ABSTRACT

Boron trifluoride etherate-induced glycosidation of 3-bromo-2-bromomethylpropan-1-ol with sugar acetates gave the title glycosides of the following sugars of the D series: Glc*p*, Gal*p*, Glc*p*A, GlcNPhth*p*, Xyl*p*, β-Gal*p*-(1→4)-Glc*p*, and α-Gal*p*-(1→4)-Gal*p*. Treatment of the fully acetylated glycosides with alkanethiols and cesium carbonate in *N,N*-dimethylformamide followed by deacetylation gave the corresponding bis-sulfide glycolipids.

INTRODUCTION

Glycolipids are localised in the outer half of cell-surface membrane bilayers where, *inter alia*, they exert different biological receptor functions[1–3]. Although unnatural synthetic glycolipids (neo-glycolipids) have been prepared[4], apparently there has been no report on the synthesis of neo-glycolipids that mimic the structure and amphiphilic properties of the naturally occurring compounds. We now describe the synthesis of some such neo-glycolipids related to **1–3**.

Neo-glycolipids are useful in biological receptor studies for coating of thin-layer plates, microtiter wells and cells, and for forming such aggregates as micelles and liposomes for agglutination studies[2]. The aglycon portion of glycolipids greatly influences the type of aggregates that are formed in aqueous solution; single-chain glycolipids give rise to spherical micelles, whereas double-chain glycolipids form double-layer liposomes[5]. In addition, neo-glycolipids would generally show increased stability against enzymic breakdown. Finally, it is desirable to be able to transform (or synthesise) oligosaccharides that are present uniquely on glycoproteins into the corresponding neo-glycolipids for use in receptor studies and coating experiments.

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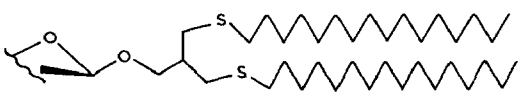
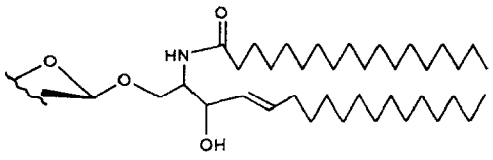


1 neo-glycolipid



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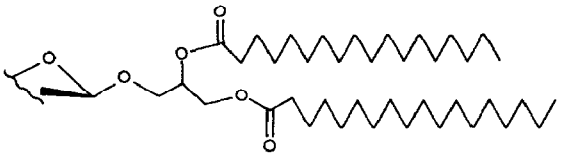


3 glycoglycerolipid

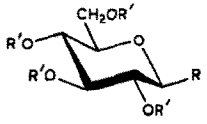
The stepwise synthesis[6a] of neo-glycolipids allows variation of, for example, the unsaturation and length of the hydrocarbon chains, and glycoside synthesis steps need to be performed only once. Also, 2-bromoethyl glycosides can be used to alkylate alkanethiols, thereby, *inter alia*, giving access to single-chain glycolipids with various chain-lengths[6].

RESULTS AND DISCUSSION

We have synthesised glycosphingolipid- and glycoglycerolipid-like double-chain neo-glycolipids by alkylation of thiols with 3-bromo-2-bromomethylpropyl glycosides [or dibromoisobutyl (DIB) glycosides]. Boron trifluoride etherate-mediated glycosidation[7] of 3-bromo-2-bromomethylpropan-1-ol (dibromoisobutyl alcohol, DIBol; **26**) with sugar acetates gave the DIB glycosides **4–10**. The method works best with primary alcohols and sugar 1,2-*trans* acetates[8] which can be prepared in near-quantitative yields and with a *trans*/*cis* ratio of >20:1 by treatment of acetylated 2-trimethylsilylethyl glycosides with boron trifluoride etherate in the presence of 1 equiv. of acetic anhydride[9].

Treatment of the DIB glycosides **4–10** with alkanethiols of various chain-lengths in *N*,*N*-dimethylformamide–cesium carbonate[6] gave the acetylated compounds **11–19**. Deacetylation in methanolic sodium methoxide–dichloromethane gave the neo-glycolipids **20–24**. The utilisation of these glycolipids will be reported elsewhere.

Surprisingly, DIBol (**26**) appears to be a novel compound, and was prepared



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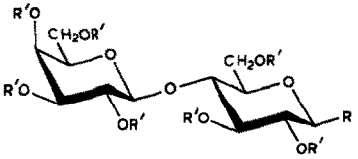

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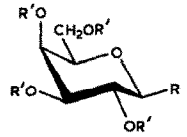

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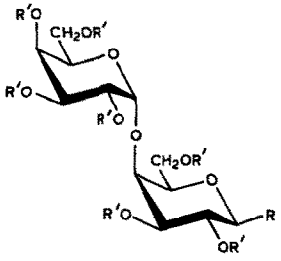

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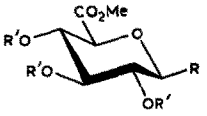

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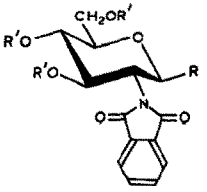

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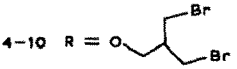
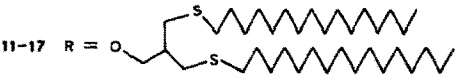
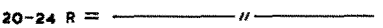
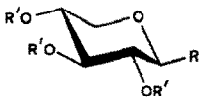
4–10 R =  , R′ = Ac

11–17 R =  , R′ = Ac

20–24 R =  , R′ = H



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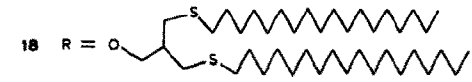
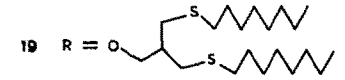
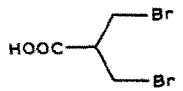
18 R =  , R′ = Ac

19 R =  , R′ = Ac



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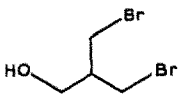

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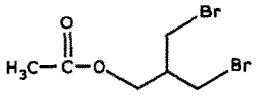

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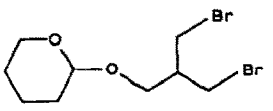

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by borane reduction of the known[10] acid **25**. The hydroxyl group of DIBol could be protected by acetylation (→**27**) or tetrahydropyranylation (→**28**) to give useful synthons.

EXPERIMENTAL

General. — Optical rotations were measured on solutions in $CDCl_3$ with a Perkin–Elmer 141 polarimeter. N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) or $CDCl_3$–CD_3OD–D_2O (CMD, 75:45:10) with Varian XL-300 and Nicolet WB 360 spectrometers. Solvents were removed at <0.1 Torr.

3-Bromo-2-bromomethylpropan-1-ol (*DIBol;* **26**). — To a stirred solution of 3-bromo-2-bromomethylpropanoic acid[10] (**25**; 15.3 g, 62.3 mmol) in dichloromethane (400 mL) at 0° under nitrogen was added diborane (M BH_3 in tetrahydrofuran; 187 mL) dropwise during ~10 min. After 1 h, the mixture was stirred overnight at room temperature, M hydrochloric acid (200 mL) was then added dropwise, the mixture was stirred for ~30 min, the aqueous phase was extracted with dichloromethane (3 × 50 mL), and the combined extracts were dried (Na_2SO_4) and concentrated. The resulting oil that was eluted from a column (200 × 45 mm) of silica gel with CH_2Cl_2 gave DIBol (**26**; 13.8 g, 96%), b.p. ~45°/0.1 Torr), n_D^{23} 1.5439; ν_{max} 3340 cm^{-1}. N.m.r. data ($CDCl_3$) ^1H, δ 3.79 (d, 2 H, J 5.7 Hz, CH_2O), 3.58 and 3.57 (2 ABq, each 2 H, J_{AB} 10.0 and J 5.5 Hz, CH_2Br), 2.27 [septet, 1 H, $CH(CH_2)_3$]; ^{13}C, δ 62.4 (CH_2OH), 44.4 (CH), 32.8 (CH_2Br).

Anal. Calc. for $C_4H_8Br_2O$: C, 20.7; H, 3.5. Found: C, 21.0; H, 3.7.

3-Bromo-2-bromomethylpropyl glycosides (**4–10**). — To a solution of the acetylated sugar (1.5 mmol) and DIBol (**26**, 2 mmol) in dry dichloromethane (10 mL) at room temperature was added boron trifluoride etherate (10 mmol). The reaction was monitored by t.l.c. (SiO_2; ethyl acetate–hexane). The sugar acetate was normally consumed within 1–4 h. The mixture was washed with water and saturated aqueous sodium hydrogencarbonate, dried (Na_2SO_4), and concentrated. Column chromatography (SiO_2; ethyl acetate–heptane) gave the following glycosides.

3-Bromo-2-bromomethylpropyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**4**, 54% from 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose), $[\alpha]_D^{23}$ −5° (*c* 0.6). ^1H-N.m.r. data ($CDCl_3$): δ 5.22 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.7 Hz, H-3), 5.1 (t, 1 H, $J_{4,5}$ 9.4 Hz, H-4), 4.99 (t, 1 H, H-2), 4.51 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 4.27 and 4.15 (ABq with further coupling, each 1 H, J_{AB} 12.6, $J_{5,6}$ 4.0 Hz, H-6,6'), 3.71 (m, 1 H, H-5), 2.34 [m, 1 H, $CH(CH_2)_3$].

Anal. Calc. for $C_{18}H_{26}Br_2O_{10}$: C, 38.5; H, 4.7. Found: C, 38.4; H, 4.7.

3-Bromo-2-bromomethylpropyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (**5**, 50% from 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose), $[\alpha]_D^{23}$ +1° (*c* 0.7). ^1H-N.m.r. data ($CDCl_3$): δ 5.40 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-4), 5.19 (dd, 1 H, $J_{2,3}$ 10.4 Hz, H-2), 5.03 (dd, 1 H, H-3), 4.47 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.19 and 4.13 (ABq

with further coupling, each 1 H, J_{AB} 11.2, $J_{5,6} = J_{5,6'} = 6.5$ Hz, H-6,6'), 3.92 (t, 1 H, $J_{4,5}$ 0.4 Hz, H-5), 2.35 [septet, 1 H, J 5.8 Hz, C*H*$(CH_2)_3$].

Anal. Calc. for $C_{18}H_{26}Br_2O_{10}$: C, 38.5; H, 4.7. Found: C, 39.3; H, 4.4.

Methyl (3-bromo-2-bromomethylpropyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate (**6**, 26% from methyl 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranuronate), $[\alpha]_D^{23}$ +3° (*c* 1.1). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.33–5.16 (m, 2 H, H-3,4), 5.01 (m, 1 H, H-2), 4.55 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.04 (d, 1 H, $J_{4,5}$ 9.4 Hz, H-5), 3.77 (s, 3 H, OMe), 2.34 [septet, 1 H, J 6.1 Hz, C*H*$(CH_2)_3$].

Anal. Calc. for $C_{17}H_{24}Br_2O_{10}$: C, 37.2; H, 4.6. Found: C, 37.5; H, 4.6.

3-Bromo-2-bromomethylpropyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**7**, 52% from 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranose[6d,11], αβ-ratio 1:1), $[\alpha]_D^{23}$ +20° (*c* 1). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.82 (t, 1 H, $J_{3,4}$ 10.1 Hz, H-3), 5.36 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 5.17 (t, 1 H, $J_{4,5}$ 10.1 Hz, H-4), 4.32 (dd, 1 H, $J_{2,3}$ 10.4 Hz, H-2), 4.33 and 4.19 (ABq with further coupling, each 1 H, J_{AB} 12.2, $J_{5,6}$ 5.0, $J_{5,6'}$ 2.2 Hz, H-6,6'), 3.89 (m, 1 H, H-5), 2.24 [m, 1 H, J 5.8 Hz, C*H*$(CH_2)_3$].

Anal. Calc. for $C_{24}H_{27}Br_2NO_{10}$: C, 44.4; H, 4.2. Found: C, 44.9; H, 4.3.

3-Bromo-2-bromomethylpropyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside (**8**, 50% from 1,2,3,4-tetra-*O*-acetyl-α,β-D-xylopyranose; αβ-ratio, 1:1), $[\alpha]_D^{23}$ −25° (*c* 0.9). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.18 (t, 1 H, $J_{2,3} = J_{3,4} = 8.3$ Hz, H-3), 4.98–4.89 (m, 2 H, H-2,4), 4.49 (d, 1 H, $J_{1,2}$ 6.7 Hz, H-1), 4.14 and 3.39 (ABq with further coupling, J_{AB} 11.5, $J_{4,5}$ 5.0, $J_{4,5'}$ 9.0 Hz, H-5,5'), 2.34 [septet, J 5.6 Hz, CH$(CH_2)_3$].

Anal. Calc. for $C_{15}H_{22}Br_2O_8$: C, 36.8; H, 4.5. Found: C, 37.3; H, 4.7.

3-Bromo-2-bromomethylpropyl 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside [**9**, 60% from 1,2,3,6-tetra-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranose], $[\alpha]_D^{23}$ −6° (*c* 0.7). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.35 (d, 1 H, $J_{3',4'}$ 2.9 Hz, H-4'), 5.20 (t, 1 H, $J_{2,3}$ 9.0 Hz, H-2), 5.11 (dd, 1 H, $J_{1',2'}$ 7.9, $J_{2',3'}$ 10.1 Hz, H-2'), 4.95 (dd, 1 H, H-3'), 4.89 (t, 1 H, $J_{3,4}$ 9.0 Hz, H-3), 4.50, 4.47 (2 d, each 1 H, J 7.9 Hz, H-1,1'), 2.32 [septet, 1 H, J 5.8 Hz, C*H*$(CH_2)_3$].

Anal. Calc. for $C_{30}H_{42}Br_2O_{18}$: C, 42.4; H, 5.0. Found: C, 42.4; H, 4.9.

3-Bromo-2-bromomethylpropyl 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-β-D-galactopyranoside [**10**, 43% from 1,2,3,6-tetra-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-α-D-galactopyranose[12]], $[\alpha]_D^{23}$ +69° (*c* 1.5). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.58 (dd, 1 H, $J_{4',5'}$ 1.0 Hz, H-4'), 5.39 (dd, 1 H, $J_{2',3'}$ 10.8 Hz, H-2'), 5.20 (dd, 1 H, $J_{3',4'}$ 3.6 Hz, H-3'), 5.17 (dd, 1 H, $J_{2,3}$ 10.8 Hz, H-2), 5.01 (d, 1 H, $J_{1',2'}$ 3.2 Hz, H-1'), 4.82 (dd, 1 H, $J_{3,4}$ 2.9 Hz, H-3), 4.47 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 2.37 [septet, 1 H, J 5.8 Hz, C*H*$(CH_2)_3$].

Anal. Calc. for $C_{30}H_{42}Br_2O_{18}$: C, 42.4; H, 5.0. Found: C, 43.1; H, 5.0.

Acetylated bis-sulfide glycolipids (**11–19**). — A mixture of the 3-bromo-2-bromomethylpropyl glycoside (**4–10**, 0.37 mmol), an alkanethiol (1 mmol), cesium carbonate (0.6 mmol), and *N,N*-dimethylformamide (2 mL) was stirred at room temperature for 24–48 h. The reaction was monitored by t.l.c. (SiO_2; ethyl acetate–

heptane). When the starting glycoside had been consumed, dichloromethane (30 mL) was added and the solution was washed with water (15 mL). The rate of phase separation could be increased by the addition of a small amount of aqueous sodium chloride. The organic phase was dried (Na_2SO_4) and concentrated, and the residue was subjected to chromatography on a column (300 × 15 mm) of silica gel with ethyl acetate–heptane, to give the following bis-sulfide glycolipids.

3-Hexadecylthio-2-hexadecylthiomethylpropyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**11**, 70% from **4** and hexadecanethiol), $[\alpha]_D^{23}$ −2° (*c* 1.1). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.20 (t, 1 H, $J_{2,3}$ 9.3 Hz, H-3), 5.06 (t, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 4.98 (dd, 1 H, H-2), 4.48 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 2.26 and 2.11 (ABq with further coupling, each 1 H, J_{AB} 12.4, $J_{5,6}$ 4.8, $J_{5,6'}$ 2.5 Hz, H-6,6'), 2.6-2.4 (m, 8 H, 4 CH_2S).

Anal. Calc. for $C_{50}H_{92}O_{10}S_2$: C, 65.5; H, 10.1. Found: C, 65.7; H, 10.2.

3-Hexadecylthio-2-hexadecylthiomethylpropyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (**12**, 79% from **5** and hexadecanethiol), $[\alpha]_D^{23}$ +1° (*c* 1.6). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.37 (dd, 1 H, $J_{4,5}$ 0.8 Hz, H-4), 5.17 (dd, 1 H, $J_{2,3}$ 10.3 Hz, H-2), 4.99 (dd, 1 H, $J_{3,4}$ 3.4 Hz, H-3), 4.44 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 2.7–2.4 (m, 8 H, 4 CH_2S).

Anal. Calc. for $C_{50}H_{92}O_{10}S_2$: C, 65.5; H, 10.1. Found: C, 65.3; H, 10.2.

Methyl (3-hexadecylthio-2-hexadecylthiomethylpropyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate (**13**, 68% from **6** and hexadecanethiol), $[\alpha]_D^{23}$ −2° (*c* 0.9). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.25 (t, 1 H, $J_{3,4}$ 9.0 Hz, H-3), 5.20 (t, 1 H, $J_{4,5}$ 9.4 Hz, H-4), 5.01 (dd, 1 H, $J_{2,3}$ 9.0 Hz, H-2), 4.54 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.03 (d, 1 H, H-5), 3.76 (s, 3 H, OMe), 2.60–2.45 (m, 8 H, 4 CH_2S).

Anal. Calc. for $C_{49}H_{90}O_{10}S_2$: C, 64.7; H, 10.2. Found: C, 64.9; H, 10.2.

3-Hexadecylthio-2-hexadecylthiomethylpropyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**14**, 81% from **7** and hexadecanethiol), $[\alpha]_D^{23}$ +12° (*c* 1.1). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.80 (dd, 1 H, $J_{2,3}$ 10.7 Hz, H-3), 5.32 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 5.16 (t, 1 H, $J_{3,4} = J_{4,5} = 9.2$ Hz, H-4), 2.5–2.2 (m, 8 H, 4 CH_2S).

Anal. Calc. for $C_{55}H_{93}NO_{10}S_2$: C, 67.0; H, 9.3; N, 1.4. Found: C, 67.0; H, 9.5; N, 1.4.

3-Hexadecylthio-2-hexadecylthiomethylpropyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside (**15**, 61% from **8** and hexadecanethiol), $[\alpha]_D^{23}$ −18° (*c* 1.1). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.15 (t, 1 H, $J_{2,3} = J_{3,4} = 8.5$ Hz, H-3), 4.98–4.85 (m, 2 H, H-2,4), 4.45 (d, 1 H, $J_{1,2}$ 6.7 Hz, H-1), 4.10 and 3.34 (ABq with further coupling, each 1 H, J_{AB} 12.0, $J_{4,5}$ 5.0, $J_{4,5'}$ 8.8 Hz, H-5,5'), 2.7–2.4 (m, 8 H, 4 CH_2S).

Anal. Calc. for $C_{47}H_{88}O_8S_2$: C, 66.8; H, 10.5. Found: C, 66.7; H, 10.6.

3-Hexadecylthio-2-hexadecylthiomethylpropyl 2,3,4-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**16**, 88% from **9** and hexadecanethiol), $[\alpha]_D^{23}$ −4° (*c* 0.8). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.34 (d, 1 H, $J_{4',5'}$ 2.5 Hz, H-4'), 5.19 (t, 1 H, $J_{2,3}$ 9.0 Hz, H-2), 5.10 (dd, 1 H, $J_{2',3'}$ 10.4 Hz,

H-2'), 4.95 (dd, 1 H, $J_{3',4'}$ 3.6 Hz, H-3'), 4.89 (dd, 1 H, $J_{3,4}$ 7.9 Hz, H-3), 4.47 and 4.45 (2 d, each 1 H, J 7.6 and 7.9 Hz, H-1,1'), 2.6–2.45 (m, 8 H, 4 CH_2S).

Anal. Calc. for $C_{62}H_{108}O_{18}S_2$: C, 61.8; H, 9.0. Found: C, 62.0; H, 9.3.

3-Hexadecylthio-2-hexadecylthiomethylpropyl 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-β-D-galactopyranoside (**17**, 51% from **10** and hexadecanethiol), $[\alpha]_D^{23}$ +52° (*c* 0.6). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.57 (dd, 1 H, $J_{4',5'}$ 0.8 Hz, H-4'), 5.38 (dd, 1 H, $J_{2',3'}$ 11.0 Hz, H-2'), 5.18 (dd, 1 H, $J_{3',4'}$ 3.7 Hz, H-3'), 5.16 (dd, 1 H, $J_{2,3}$ 11.0 Hz, H-2), 4.99 (d, 1 H, $J_{1',2'}$ 3.3 Hz, H-1'), 4.79 (dd, 1 H, $J_{3,4}$ 2.8 Hz, H-3), 4.44 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 2.7–2.45 (m, 8 H, 4 CH_2S).

Anal. Calc. for $C_{62}H_{108}O_{18}S_2$: C, 61.8; H, 9.0. Found: C, 60.7; H, 9.0.

3-Octadecylthio-2-octadecylthiomethylpropyl 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**18**, 67% from **9** and octadecanethiol), $[\alpha]_D^{23}$ −3° (*c* 0.8). ^{1}H-N.m.r. data ($CDCl_3$): the signals for the sugar moiety were practically identical with those of the spectra of **16** and **19**.

Anal. Calc. for $C_{66}H_{116}O_{18}S_2$: C, 62.8; H, 9.3. Found: C, 62.1; H, 9.1.

3-Octylthio-2-octylthiomethylpropyl 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**19**, 73% from **9** and octanethiol), $[\alpha]_D^{23}$ −5° (*c* 0.8). ^{1}H-N.m.r. data ($CDCl_3$): the signals for the sugar moiety were practically identical with those of the spectra of **16** and **18**.

Anal. Calc. for $C_{46}H_{76}O_{18}S_2$: C, 56.3; H, 7.8. Found: C, 57.1; H, 7.5.

Bis-sulfide glycolipids (**20–24**). — To a solution of each acetylated glycolipid (**11, 12, 15–17**; 0.2 mmol) in dichloromethane (15 mL) was added methanolic sodium methoxide (10 mL; from ~1 mg of sodium). The reaction was monitored by t.l.c. (chloroform–methanol–water, 65:35:10). One drop of acetic acid was added, the mixture was concentrated, filtered through silica gel (solvent as in t.l.c. above), and concentrated, and the residue was suspended in water (10 mL) and freeze-dried to give a quantitative yield of the glycolipid. Carbon analyses were outside normally accepted limits, probably due to remaining traces of water that could not be removed by freeze-drying. The following compounds were prepared in this way.

3-Hexadecylthio-2-hexadecylthiomethylpropyl β-D-glucopyranoside (**20**, from **11**), $[\alpha]_D^{23}$ −7° (*c* 0.9, CMD). ^{1}H-N.m.r. data (CMD, 50°): δ 4.29 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 2.70 [d, 4 H, J 6.4 Hz, $CH(CH_2S)_2$], 2.53 (t, 4 H, J 7.3 Hz, SCH_2CH_2).

Anal. Calc. for $C_{42}H_{84}O_6S_2$: C, 67.3; H, 11.3. Found: C, 65.9; H, 11.3.

3-Hexadecylthio-2-hexadecylthiomethylpropyl β-D-galactopyranoside (**21**, from **12**), $[\alpha]_D^{23}$ −3° (*c* 0.5, CMD). ^{1}H-N.m.r. data (CMD, 20°): δ 4.24 (virtual coupling[13], $J_{1,2}$ 7.6 Hz, H-1), 2.71 [d, 4 H, J 6.7 Hz, $CH(CH_2S)_2$], 2.53 (t, 4 H, J 7.2 Hz, SCH_2CH_2).

Anal. Calc. for $C_{42}H_{84}O_6S_2$: C, 67.3; H, 11.3. Found: C, 65.6; H, 11.1.

3-Hexadecylthio-2-hexadecylthiomethylpropyl β-D-xylopyranoside (**22**, from

15), $[\alpha]_D^{23}$ −6° (*c* 0.5, CMD). ^{1}H-N.m.r. data (CMD, 50°): δ 4.25 (d, 1 H, *J* 7.1 Hz, H-1), 2.69 [d, 4 H, *J* 6.4 Hz, CH(C*H*$_2$S)$_2$], 2.53 (t, 4 H, *J* 7.5 Hz, SC*H*$_2$CH$_2$).

Anal. Calc. for $C_{41}H_{82}O_5S_2$: C, 68.5; H, 11.5. Found: C, 66.3; H, 10.4.

3-Hexadecylthio-2-hexadecylthiomethylpropyl 4-*O*-β-D-galactopyranosyl-β-D-glucopyranoside (**23**, from **16**), $[\alpha]_D^{23}$ −3.5° (*c* 1.6, CMD). ^{1}H-N.m.r. data (CMD, 40°): δ 4.31 (d, 2 H, *J* 7.8 Hz, H-1,1'), 2.71 [d, 4 H, *J* 6.6 Hz, CH(C*H*$_2$S)$_2$], 2.53 (t, 4 H, *J* 7.3 Hz, SC*H*$_2$CH$_2$).

Anal. Calc. for $C_{48}H_{94}O_{11}S_2$: C, 63.3; H, 10.4. Found: C, 62.6; H, 10.6.

3-Hexadecylthio-2-hexadecylthiomethylpropyl 4-*O*-α-D-galactopyranosyl-β-D-galactopyranoside (**24**, from **17**), $[\alpha]_D^{23}$ +28° (*c* 0.6, CMD). ^{1}H-N.m.r. data (CMD, 50°): δ 5.01 (m, 1 H, H-4'), 4.27 (d, 1 H, $J_{1,2}$ 7.2 Hz, H-1), 2.72 [d, 4 H, *J* 6.3 Hz, CH(C*H*$_2$S)$_2$], 2.53 (t, 4 H, *J* 7.4 Hz, SC*H*$_2$CH$_2$).

Anal. Calc. for $C_{48}H_{94}O_{11}S_2$: C, 63.3; H, 10.4. Found: C, 61.6; H, 10.6.

3-Bromo-2-bromomethylpropyl acetate (**27**). — A mixture of 3-bromo-2-bromomethylpropan-1-ol (**26**; 512 mg, 2.21 mmol), pyridine (10 mL), and acetic anhydride (10 mL) was stirred at room temperature for 17 h and then co-concentrated with toluene, ethyl acetate (20 mL) was added, and the solution was washed with water (2 × 10 mL). The aqueous phase was extracted with ethyl acetate (10 mL), and the combined organic phases were dried (Na_2SO_4) and concentrated. The residue was eluted from silica gel with heptane–ethyl acetate (4:1) to give **27** (483 mg, 81%); ν_{max} 1752, 1230, and 1050 cm^{-1}. ^{1}H-N.m.r. data ($CDCl_3$): δ 4.18 (d, 2 H, *J* 6.4 Hz, AcOC*H*$_2$), 3.58 and 3.53 (dABq, 4 H, J_{AB} 10.6, *J* 5.3, *J* 6.2 Hz, C*H*$_2$Br), 2.41 (septet, 1 H, CH), 2.09 (s, 3 H, Me).

Anal. Calc. for $C_6H_{10}Br_2O_2$: C, 26.3; H, 3.7. Found: C, 26.8; H, 4.0.

3-Bromo-2-bromomethyl-1-(tetrahydropyran-2-yloxy)propane (**28**). — To a solution of 3-bromo-2-bromomethylpropan-1-ol (**26**; 1.0 g, 4.3 mmol) and dihydropyran (1.81 g, 21.6 mmol) in dry dichloromethane (20 mL) at 0° was added a solution of toluene-*p*-sulfonic acid (10 mg) in dichloromethane (2 mL). After 4 h, the mixture was left at room temperature for 5.5 h and then cooled to 0°, and more (10 mg, 2 mL) of the toluene-*p*-sulfonic acid solution was added. After 7 h, toluene (30 mL) and ether (20 mL) were added, and the mixture was washed with saturated aqueous sodium hydrogencarbonate (50 mL) and saturated aqueous sodium chloride (50 mL). The aqueous phases were extracted with toluene (50 mL), and the combined organic phases were dried (Na_2SO_4) and concentrated. The residue was distilled to give **28** (1.07 g, 79%), b.p. 85–105°/0.08 mmHg. Chromatography on a column of silica gel, using ethyl acetate–heptane (1:10), gave pure **28** (0.88 g, 65%), n_D^{23} 1.5120; ν_{max} 1130, 1060 cm^{-1}. Mass spectrum: *m/z* 85 (C_5H_9O, 100%), 133, 135 (C_3H_2OBr; 7 and 9%). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.62 (t, 1 H, *J* 3 Hz, OCHO), 3.75–3.90 (m, 2 H), 3.40–3.70 (m, 6 H), 2.35 (septet, 1 H, *J* ~5 Hz, BrCH$_2$C*H*).

Anal. Calc. for $C_9H_{16}Br_2O_2$: C, 34.2; H, 5.1. Found: C, 34.7; H, 5.1.

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