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Preliminary communication

Synthesis of 2-O-hexadecanoyl-1-O-hexadecyl- $[\alpha$ -Glc-6S0₃ Na- $(1\rightarrow 6)$ - α -Glc- $(1\rightarrow 6)$ - α -Glc- $(1\rightarrow 3)$]-sn-glycerol: a proposed structure for the glycero-glucolipids of human gastric secretion and of the mucous barrier of rat-stomach antrum*

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In 1977, Slomiany and his co-workers² proposed structure 1 for the glyceroglucolipid of human gastric secretion. As part of a project on the synthesis of cell-surface glycolipids, we describe here, for 1, an unambiguous, total synthesis having high regioand stereo-control. Based on retrosynthetic considerations, structure 1 was divided into two key intermediates, 2 and 3, each of which was then synthesized, as follows.



^{*}Synthetic Studies on Cell-Surface Glycans, Part XXIII. For Part XXII, see ref. 1. **To whom enquiries should be addressed.

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Allyl 2,3,4-tri-O-benzyl- β -D-glucopyranoside (4) was treated with monochloroacetic anhydride in pyridine, to give a quantitative yield of 5, $[\alpha]_D$ +38.2°*, which was deallylated with¹ PdCl₂ in aq. AcOH-AcONa for 2 h at 60°, to give a 71.2% yield of 6. Treatment of 6 with the complex $[Me_2N^+=CHOSOCI]$ Cl⁻, formed *in situ* from SOCl₂ in the presence of a trace³ of HCONMe₂ (DMF) in Cl(CH₂)₂Cl gave a quantitative yield of 7, which reacted with 4 in the presence of Hg(CN)₂ HgBr₂ powdered molecular sieves⁴ 4A in Cl(CH₂)₂Cl for 6 h at 60° to give, in 95% yield, a mixture of 8 and 10 in the ratio of 10:1; compound 8: $[\alpha]_D$ +44.6°, δ_C : 96.93 (C-1b, ¹/_{CH} 168.6 Hz) and 102.67 (C-1a, ¹/_{CH} 157.5 Hz); compound 10: δ_C : 103.92 (C-1b) and 102.73 (C-1a). Deacylation of 8 afforded a quantitative yield of 9; m.p. 95.-98° (iPr₂O), $[\alpha]_D$ +43.4°: δ_C : 97.09 (C-1b, ¹/_{CH} 168.5 Hz) and 102.73 (C-1a, ¹/_{CH} 157.5 Hz).

Glycosidation of 9 with 7 under the same conditions as before afforded an 83% yield of 11; $\delta_{\rm C}$: 102.73 (C-1a, ${}^{17}_{\rm CH}$ 157.5 Hz), 97.03 (${}^{17}_{\rm CH}$ 168.5 Hz), and 96.93 (${}^{17}_{\rm CH}$ 168.5 Hz) for C-1b and C-1c, Deallylation of 11 to give 12, and chlorination of 12, afforded a 75% yield of the key intermediate 2; $\delta_{\rm H}$: 5.98 (d, H-1a, J 4.0 Hz); $\delta_{\rm C}$: 93.41 (${}^{17}_{\rm CH}$ 175.8 Hz for C-1a).

The other key intermediate, 3, was synthesized in the following way. 3-O-Benzyl-sn-glycerol⁵ 13 was treated with⁶ Bu₂SnO in 10:1 toluene – methanol under reflux, to give 14, which was alkylated with hexadecyl bromide in DMF for 2 h at 90 110°, to give a 71% yield of 15, $[\alpha]_D$ +38.2°. Acylation of 15 with palmitoyl chloride in pyridine to give 16, $[\alpha]_D$ +0.6°, δ_H : 5.16 (m, 1 H, H-2), and hydrogenolysis of 16 in the presence of 5% Pd - C in EtOH, afforded a 98% yield of the key intermediate 3; $[\alpha]_D$ -1.2°; δ_H : 4.99 (m, 1 H, H-2); δ_C : 72.91 (C-2).



*Values of $[\alpha]_D$ were measured for CHCl₃ solutions at 25°, unless noted otherwise. Compounds having $[\alpha]_D$ recorded gave satisfactory data for elemental analyses.



Scheme 3

Glycosidation of 3 with 2 in the presence of $AgOSO_2CF_3$ -powdered molecular sieves 4A in $Cl(CH_2)_2Cl$ afforded an 84% yield of 17, $[\alpha]_D$ +60.4°, R_F 0.65 in 6:1 toluene-EtOAc, which was refluxed with thiourea⁷ in EtOH, to give an 87.5% yield of 18, $[\alpha]_D$ +51.3°; R_F 0.40 in 6:1 toluene--EtOAc; δ_C : 97.42 (two anometic carbon atoms, ${}^{1}J_{CH}$ 168.5 Hz) and 97.14 (one anometic carbon atom, ${}^{1}J_{CH}$ 168.5 Hz). Treatment of 18 with the sulfur trioxide-pyridine complex in pyridine for 3 h at 50-60° gave a 94.1% yield of 19, $[\alpha]_D$ +45.0°, R_F 0.78 in 65:25:4 CHCl₃--MeOH--H₂O. Debenzylation of 19 by catalytic transfer of hydrogen with 10% Pd-C in⁸ 10:1 MeOH-HCO₂ H gave the target compound 1: $[\alpha]_D$ +64.2° (1:1 MeOH-THF); R_F 0.15 in 65:25:4 CHCl₃-MeOH-H₂O; δ_H (400 MHz. Me₂SO d₆, 20°): 5.062 (m, 1 H, H-2), 4.660 (d, 1 H, J 4.0 Hz), 4.630 (d, 1 H, J 4.0 Hz), 4.619 (d, 1H, J 4.0 Hz) for H-1a, H-1b and H-1c, 3.904 (q, 1 H, J 2, 12 Hz, H-6c), and 3.802 (q, 1 H, J 6, 12 Hz, H-6c). It is to be noted that comparison of the 400-MHz, 1 H-n.m.r. data for the synthetic and the natural sample* showed their nonidentity. Because the structure of the synthetic sample was firmly supported both by the synthetic sequence and by the n.m.r. data, the structure assigned to the natural sample must be reconsidered.

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