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Rapid Communication

Novel synthesis of D-*ribo*-[2*S*,3*S*,4*R*]-2-*N*-palmitoyl-2-aminoheptadecane-1,3,4-triol†

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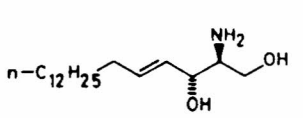
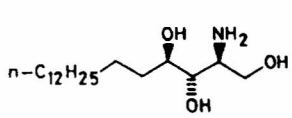
Novel synthesis of D-*ribo*-[2*S*,3*S*,4*R*]-2-*N*-palmitoyl-2-aminoheptadecane from D-mannose is described.

D-*erythro*-Sphingosine [(2*S*,3*R*,4*E*)-2-aminootadec-4-ene-1,3-diol] **1** and phytosphingosine-[(2*S*,3*S*,4*R*)-2-aminooctadecane-1,3,4-triol] **2** are the major backbone components of glycosphingolipids, which play important roles in biological processes on cell surfaces[1]. Phytosphingosine was first detected in fungi[2], plants[3], yeasts[4] and other organisms[5]. Later, phytosphingosine was also detected in vertebrate species[6] and sea organisms[7,8]. It is also present in mammalian tissues, for example in kidney[9], liver[10], uterus[11], intestine[12], skin[13], blood plasma[14] and thyrocytes[15]. Sphingosines have attracted considerable interest as potent inhibitors of protein kinase C, an essential enzyme in cell regulation and signal transduction[16]. Various synthetic approaches to optically active phytosphingosine have been reported[17]. In this communication we report the synthesis of a phytosphingosine analog from D-mannose.

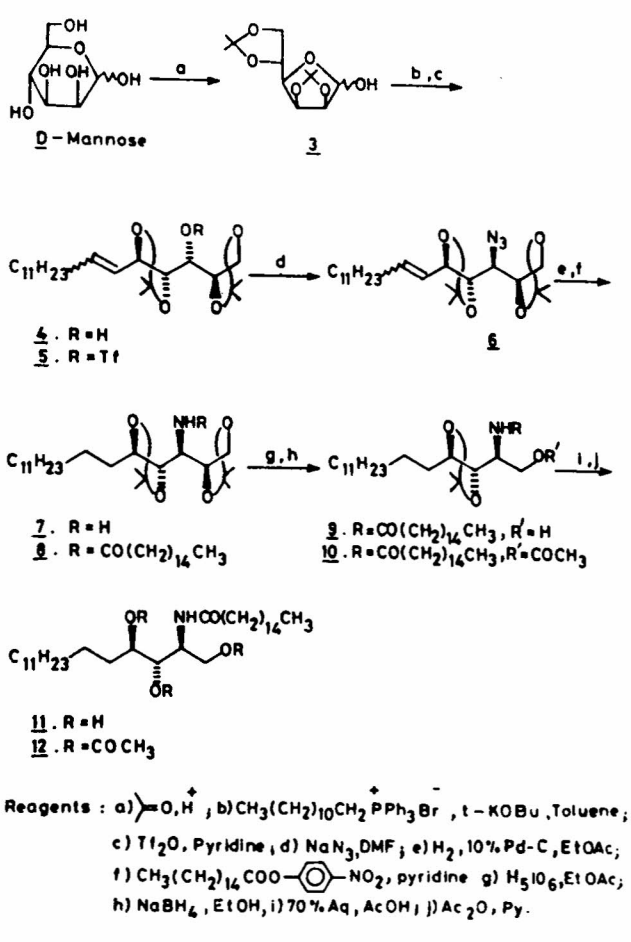
Diacetone mannose **3**, easily available from D-mannose on Wittig olefination with dodecyltriphenylphosphorane (dodecyltriphenylphosphonium bromide, KOBut, toluene, 16 hr) furnished **4** (cf. Scheme I) as an *E*/*Z* (40:60) mixture in 80% yield. Reaction of olefin **4** with 1.2 equivalents of Tf_2O and pyridine at 0 °C furnished the triflate **5**, which on further treat-ment with NaN_3 in DMF furnished azide **6** in 80% yield. IR absorption of **6** at 2100 cm^{-1} supported its assigned structure. Azide **6** on hydrogenation (H_2, 10% Pd-C, EtOAc at 50 psi) furnished the amine **7** in 65% yield, Palmitylation of amine **7** (*p*-nitrophenyl palmitate, Py, 80 °C) furnished the palmitate **8** in quantitative yield. The deprotec-tion/oxidation of terminal isopropylidene group in **8** with periodic acid in ethyl acetate followed by hydride reduction ($NaBH_4$, ethanol) furnished the ceramide **9** in 60% yield. Deprotection of **9** with 70% aqueous acetic acid furnished the



D-erythro-sphingosine **1**



Phytosphingosine **2**



Scheme I

† CDRI Communication No. 5769

ceramide 11[18] in quantitative yield. The ceramide 11 on acetylation (Ac_2O, Py) furnished the triacetate 12 (Scheme I) in quantitative yield.

In conclusion, the C-17 analog of phytoceramide has been efficiently synthesised from D-mannose.

Acknowledgement

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18 The elemental analysis and spectral data for the new compounds were in accordance with the structures assigned, and only selected data are listed.

12: IR (KBr, cm^{-1}): 3431, 3020, 2927, 1739, 1676; $[\alpha]_D^{20}$ +12.5 (*c* 1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, *J* = 6.00 Hz, 6H), 1.25 (s, 50H), 2.04 (s, 6H), 2.08(s, 3H), 2.20(m, 2H), 4.00(dd, *J* = 3.00, 12.00 Hz, 1H), 4.30 (dd, *J* =5.00, 10.00 Hz, 1H), 4.50(m, 1H), 4.92(dt, *J* = 3.00, 7.00 Hz, 1H), 5.12(dd, *J* = 4.00, 7.00 Hz, 1H), 5.95 (d, *J* = 10.00 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.99 (q), 28.61(q) 28.61(q), 28.89(q), 22.61(t), 25.49(t), 28.33(t), 29.29-21.63(t), 31.88(t), 36.73(t), 47.58(d), 62.69(t), 72.36(d), 72.99(d), 169.92(s), 170.68(s), 170.91(s), 172.74(s); MS: m/z 668 (M^++1), 608.