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Preliminary communication

Synthesis of model glycolipids having two long alkyl chains

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Some transesterifications and hydrolyses have been successfully carried out in organic solvent with enzymes modified by the detergent didodecyl glucosyl glutamate. The stability and reaction activity of the enzymes used are strongly dependent on the type and structure of the detergents. Nonionic detergents were considered to be the most useful for modification of enzymes [1–5]. The present investigation has aimed at the synthesis of glycolipids having an amino acid residue interposed between the hydrophilic moiety and hydrophobic double-chain segment as a hydrogen-bonding component to constitute a morphologically stable bilayer membrane [6].

Generally, diethyl phosphocyanidate (DEPC) [7] is considered to be a good coupling reagent between an acid and amine and has been used for example to catalyze the formation of N-substituted lactobionamides from amines and lactobionic acid. However, DEPC was found to make a minor contribution to this condensation reaction, as well as *N*,*N*′-dicyclohexylcarbodiimide (DCC) [8].

Although lactobionic acid is readily converted into lactonolactone, the condensation of the lactonolactone with the amino groups of dialkyl L-glutamate is not possible, perhaps due to steric hindrance of two alkyl chains of dialkyl L-glutamate. We have selected *p*-aminomethylbenzoic acid in order to condense the oligosaccharide containing carboxyl group and the dialkyl L-glutamate under the action of DEPC in a final reaction

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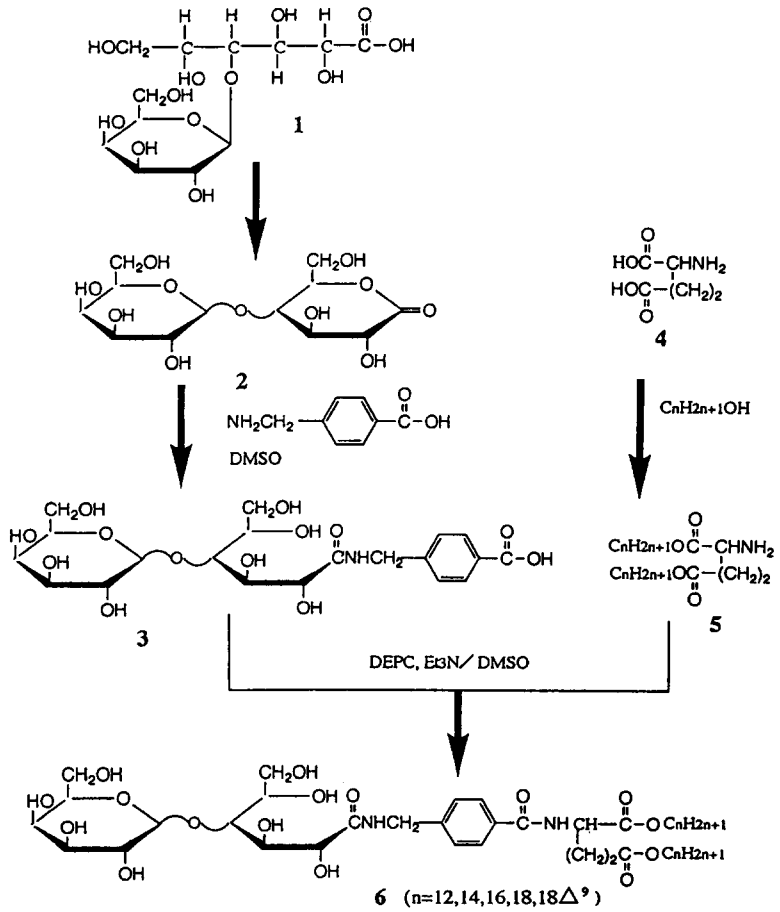

Scheme 1.

step, and found that aminolysis of lactonolactone with *p*-aminomethylbenzoic acid could proceed smoothly in quantitative yield. The synthetic route is shown in Scheme 1.

1. Experimental

N-*[*p-*(Dialkyl* L-*glutamate carbonyl)benzyl]lactobionamide* (**6**).—Lactobionic acid (25 g, 69.77 mmol) was dehydrated to lactonolactone (17.17 g, 50.48 mmol) [8–12] (**1** → **2**) in solvents 2-methoxyethanol and toluene, yield 72%, mp 195–196°C. Lactonolactone (4 g, 11.76 mmol), *p*-aminomethylbenzoic acid (1.76 g, 11.64 mmol) and 40 mL of dimethyl sulfoxide (Me_2SO) were mixed in a 100-mL flask. The reaction mixture was heated under stirring at 130–150°C for 3 h. Me_2SO was removed with a vacuum pump. The resultant lactoseamidemethylbenzoic acid (**2** → **3**) was precipitated from 200 mL of chloroform, yield 5.7 g, 100%, mp 95–97°C. L-Glutamic acid (20 g, 0.136 mol) and dodecyl alcohol (65 g, 0.349 mol) were esterified under catalysis of *p*-toluene-

sulfonic acid (32 g, 0.17 mol) [1,13] (**4** → **5**), didodecyl L-glutamate was formed, yield 74%. Didodecyl L-glutamate (5.43 g, 11.23 mmol), triethylamine (2.42 mL, 16.85 mmol) and lactoseamidemethylbenzoic acid were mixed and the coupling reagent DEPC (3.1 mL, 19.8 mmol) was added into the reaction system at 40–60°C. The reaction was carried out with stirring for 3 days. After the reaction, Me_2SO was completely removed with a vacuum pump. The resultant *N*-[*p*-(dialkyl L-glutamate carbonyl)benzyl]lactobionamide [14] (**3** + **5** → **6**) was recrystallized from acetone (100 mL) and then purified with treatment of silica chromatographic column using solvents of 1 : 3 methanol : chloroform (1 : 3 by vol), yield 4.31 g, 51%, mp 143–145°C.

Elemental analysis. $n = 12$, dodecyl, found: C, 61.27; H, 8.68; N, 2.70%. Calcd for ($C_{49}H_{84}O_{16}N_2$): C, 61.48; H, 8.85; N, 2.93%.

$n = 14$, tetradecyl, yield: 4.89 g (55%), mp 146–149°C. Found: C, 62.43; H, 9.11; N, 2.68%. Calcd for ($C_{53}H_{92}O_{16}N_2$): C, 62.82; H, 9.15; N, 2.77%.

$n = 16$, hexadecyl, yield: 5.79 g (61%), mp 150–152°C. Found: C, 64.31; H, 9.47; N, 2.71%. Calcd for ($C_{57}H_{100}O_{16}N_2$): C, 64.02; H, 9.43; N, 2.62%.

$n = 18$, octadecyl, yield: 6.20 g (62%), mp 154–158°C. Found: C, 65.30; H, 9.64; N, 2.54%. Calcd for ($C_{61}H_{108}O_{16}N_2$): C, 65.09; H, 9.67; N, 2.49%.

$n = 18\,\Delta^9$, oleyl, yield: 4.02 g (41%), mp 110–115°C. Found: C, 65.12; H, 9.29; N, 2.46%. Calcd for ($C_{61}H_{104}O_{16}N_2$): C, 65.33; H, 9.35; N, 2.50%.

A simple and effective synthetic method is presented for the synthesis of compounds **3** and **6** which can be conducted in Me_2SO without isolation of the intermediate formed in the reaction mixture. Synthesis and purification requires a few days and their large-scale preparation will be possible when necessary. Structures like compound **6**, which are similar to those mentioned in ref. [6], are expected to form morphologically stable bilayer membranes in aqueous media.

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