ELSEVIER

Carbohydrate Research 370 (1998) 77–81

CARBOHYDRATE RESEARCH

The synthesis of neoglycophospholipid conjugates via reductive amination of ω-oxoalkylglycosides and phosphatidylethanolamines

Lijun Sun, Elliot L. Chaikof *

Laboratory for Biomolecular Materials Research, Emory University School of Medicine, Department of Surgery, 1364 Clifton Road, N.E., Box M-11, Atlanta, GA 30322, USA

Received 28 October 1997; accepted 14 January 1998

Abstract

Phospholipid conjugates of mono- and disaccharides tethered with an *n*-decanyl spacer were efficiently synthesized via an improved reductive amination of deprotected ω-oxodecanyl β-glycosides and phosphatidylethanolamines with or without alkenyl groups. The ω-oxodecanyl β-glycosides were prepared by stereoselective glycosidation of glycosyl halides with 1,10-decanediol followed by pyridinium dichromate oxidation. The acetyl groups of the ω-oxodecanyl β-glycosides were removed with sodium methoxide prior to their conjugation with phosphatidylethanolamines.

Keywords: Neoglycophospholipid; Phospholipid; Reductive amination

1. Introduction

The development of new methodologies for the efficient synthesis of glycophospholipid conjugates is an area currently under intensive investigation [1–7]. As such, neoglycolipids hold significance in biological and biomaterials research as mimics of natural glycolipids, which are structurally more complex and available in limited quantities. Neoglycolipids have been widely used in the characterization of carbohydrate–protein interactions and in the identification and purification of lectins. In addition, they are invaluable as antigens for generating anti-carbohydrate antibodies, as artificial vaccines, and hold significant promise for receptor-targeted drug delivery, gene therapy, as well as in the study of cell–tissue interactions. Another potential application of glycolipids is in the formation of functionalized biomimetic membranes on solid supports [8–10].

Prior studies from our group and others on the synthesis of glycophospolipid conjugates have generally utilized a hydrogenation scheme to remove benzyl protecting groups from the carbohydrate moiety [11]. Thus, the method is not applicable to the synthesis of neoglycophospholipid conjugates with polymerizable functionalities such as

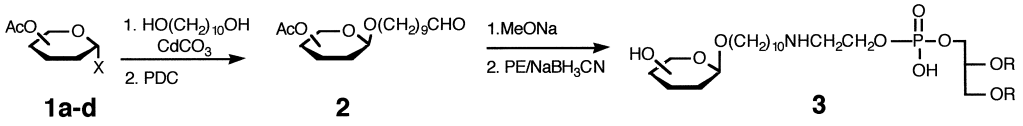
* Corresponding author. Tel: (404) 727-8413; Fax: (404) 727-3660; e-mail: echaikof@surgery.eushc.org

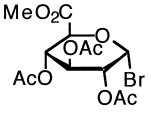
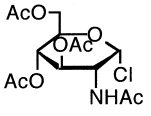
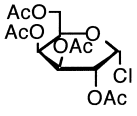
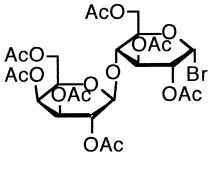
0008-6215/98/$19.00
PII S0008-6215(98)00032-9

acrylated or dienoyl phosphatidylethanolamines (PEs) [12,13]. Our interest in the polymerization of acrylated phospholipids and their conjugates at solid–liquid interfaces has led us to develop an alternative route to circumvent this problem. Herein we describe a method which permits carbohydrate conjugation to unsaturated phospholipids. In this case, the dioeloyl phosphatidylethanolamine (DOPE), as a model compound, is conjugated to carbohydrates possessing an ω-oxoalkyl functionality.

Summarized in Table 1 are the results for the synthesis of neoglycoconjugates via reductive amination of compounds **2** and phosphatidylethanolamine (PE). Glycosyl halides of mono (**1a–c**) and disaccharide (**1d**) derivatives, were treated with 5–10 equivalents of 1,10-decanediol by using $CdCO_3$ as the glycosidation promoter. After the reaction was completed as indicated by TLC monitoring, excess diol was precipitated with dichloromethane. The resulting crude products (contaminated by 10–15 mol% of 1,10-decanediol) were oxidized with pyridinium dichromate (PDC) to afford the requisite ω-oxodecanylglycosides (**2a–d**) in isolated yields of 40–62% over two steps, after flash chromatographic purification. The β-D-stereochemistry of the glycosylic bond, which was controlled by neighboring-group participation (OAc in **1a**, **1c** and **1d**, or NHAc in **1b**), was confirmed by a large coupling constant of $J = 7.8$–8.4 Hz of the anomeric protons having a chemical shift of 4.5–4.7 ppm. Methanolysis with MeONa in MeOH at room

Table 1
Synthesis of neoglycophospholipid conjugates



Entry	Glycosyl halides (1)	Carbohydrate	2 (yield %)	Compound 3	
				R	3 (yield %)
1	 **1a**	β-Glc*p*A	**2a** (55)	Stearoyl	**3a** (62)
2	 **1b**	β-Glc*p*NAc	**2b** (57)	Oleoyl	**3b** (67)
3	 **1c**	β-Gal*p*	**2c** (62)	Palmitoyl	**3c** (40)
4				Oleoyl	**3d** (46)
5	 **1d**	β-Lac	**2d** (41)	Palmitoyl	**3e** (55)
6				Oleoyl	**3f** (72)

temperature for 30 min was followed by neutralization with Dowex-50 (pyridinium form) complex. The MeOH solution of the deprotected ω-oxoalkylglycosides was then transferred to a mixture of $NaBH_3CN$ and PE in 1:1 MeOH–$CHCl_3$ (v/v) stirred at 50–60°C. Reductive amination proceeded for 30 min, and the reaction mixtures were concentrated and then subjected to flash chromatography or preparative TLC purification to afford the neoglycophospholipid conjugates (**3a–f**) in the yields indicated in Table 1. Both saturated (DPPE, DSPE) and unsaturated (DOPE) PEs could be conjugated to carbohydrates containing acetamido and carboxylic ester functionalities. Yields over two steps range from 40 to 72%.

In conclusion, we have developed an efficient method for the synthesis of neoglycophospholipid conjugates based on reductive amination of ω-oxoalkyl glycosides and PEs. The use of acetyl-protected carbohydrate derivatives not only provided high stereoselectivity for the glycosidation reaction, but also avoided the use of hydrogenation, thus providing a method for the synthesis of neoglycoconjugates with an unsaturated lipid moiety. The application of the method to the synthesis of polymerizable PE conjugates is currently under investigation and will be reported in due course.

2. Experimental

General methods.—^1H and ^{13}C NMR spectra were recorded on an Inova 400 (400 MHz ^1H, 100 MHz ^{13}C) spectrometer in either deuteriochloroform ($CDCl_3$) with chloroform (7.26 ppm ^1H, 77.00 ppm ^{13}C as an internal reference or a mixture of deuteriochloroform and deuteriomethanol (2:1 v/v) with methanol (3.10 ppm ^1H, 49.00 ppm ^{13}C) as an internal reference, unless otherwise stated. Data are reported in the following order: chemical shifts are given (δ ppm); multiplicity is indicated [s (singlet), d, (doublet), t (triplet), q (quartet), sx (sextet), sept (septet), m (multiplet)]; coupling constants, *J*, are reported (Hz); and integration is provided. Only the signals corresponding to the major anomers were reported, because most of the signals corresponding to the minor anomers were overlapped by the major ones. High-resolution mass spectra were recorded on a Jeol mass spectrometer. Analytical thin-layer chromatography (TLC) was performed on E. Merck silica gel plates with F-254 indicator.

Visualization was accomplished by one or more of the following methods: UV light, char with 10% H_2SO_4 in ethanol, and molybdenum blue. Solvents for extraction and chromatography were reagent grade and used as received. Flash column chromatography was conducted using 32–63 μm flash silica gel obtained from E. Merck. Solvents (chloroform, toluene, acetonitrile, THF, dichloromethane, dichloroethane) used as reaction media were dried over freshly regenerated 4Å molecular sieves before use. Methanol was dried over 3Å molecular sieves before use. Reagents purchased from commercial sources were used directly without further purification. All reactions, unless otherwise stated, were performed under a dry argon atmosphere in base-washed, oven-dried (230°C) glassware.

Starting materials.—Methyl α-D-glucopyranosyluronate bromide (**1a**); tetra-*O*-acetyl-α-D-galactopyranosyl chloride (**1b**); 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride, (**1c**) were purchased from Toronto Research Inc., Ontario, Canada. α-Lactosyl bromide (**1d**) was prepared according to a literature procedure [14]. Phosphatidylethanolamines (DOPE, DPPE, and DSPE) were purchased from Avanti Polar Lipids, Inc., Alabaster, Alabama. All other reagents and solvents were purchased from Aldrich Chemical Co., Milwaukee, MN and used as received.

Typical experimental procedure for the synthesis of ω-*oxo*-n-*decanyl* β-D-*glycosides* (**2**).—Synthesis of **2d**: ω-Oxodecanyl 2,3,4,6,2′,3′,4′-hepta-*O*-acetyl-β-lactopyranoside. A mixture of hepta-*O*-acetyllactosyl bromide (**1d**, 1.10 g, 1.57 mmol), 1,10-decanediol (1.50 g, 8.60 mmol) and $CdCO_3$ (0.27 g, 1.57 mmol) in CH_3CN (30 mL) was stirred at 65°C in the presence of 4Å molecular sieves (4.0 g) for 1.5 h. The reaction mixture was filtered and concentrated to a white solid, which was extracted with cold CH_2Cl_2 (2×30 mL). The organic solvent was removed to give a clear oil. The crude product was treated with pyridinium dichromate (PDC) (1.10 g, 2.93 mmol) in CH_2Cl_2 (30 mL) at rt for 16 h. The reaction mixture was diluted with ether (60 mL) and filtered through a pad of Celite and concentrated to a brown oil. Flash chromatographic purification (SiO_3, 50–75% EtOAc in hexanes) gave **2d** (0.51 g, 41%) as a white solid. R_f = 0.25 (50% EtOAc in hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ: 9.75 (s, 1 H), 4.47 (d, *J* 8.7 Hz, 1 H), 4.43 (d, *J* 8.1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.7 (CHO), 101.8, 100.6

(anomeric *C*s); FABMS: Calcd for $C_{36}H_{54}O_{19}$: 790.3; Found: 797.4 $(M+Li)^+$.

2a: *Methyl (ω-oxodecanyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate*. Yield: 55%. $R_f=0.40$ (50% EtOAc in hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ: 9.75 (t, *J* 2.0 Hz, 1 H; C*H*O), 4.52 (d, *J* 7.6 Hz, 1 H; anomeric *H*), 3.74 (s, 3 H; CO_2CH_3), 2.41 (dt, *J* 7.2, 1.6 Hz, 2 H; $OHCCH_2CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.9 (*C*HO), 100.8 (anomeric *C*); FABMS: Calcd for $C_{23}H_{36}O_{11}$: 488.2; Found: 495.3 $(M+Li)^+$.

2b: ω-*Oxodecanyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β-D-*glucopyranoside*. Yield: 57%. $R_f=0.30$ (75% EtOAc in hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ: 9.75 (t, *J* 1.6 Hz, 1 H; C*H*O), 4.68 (d, *J* 8.0 Hz, 1 H; anomeric *H*), 2.42 (dt, *J* 7.2, 1.6 Hz, 2 H; $OHCCH_2CH_2$), 1.93 (s, 3 H; $NHCOCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.0 (*C*HO), 100.7 (anomeric *C*); FABMS: Calcd for $C_{24}H_{39}NO_{10}$: 501.3; Found: 508.3 $(M+Li)^+$.

2c: ω-*Oxodecanyl 2,3,4,6-tetra-*O*-acetyl-*β-D-*galactopyranoside*. Yield: 62%. $R_f=0.62$ (10% MeOH in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ: 9.73 (t, *J* 1.5 Hz, 1 H; C*H*O), 4.42 (d, *J* 8.1 Hz, 1 H; anomeric *H*), 2.39 (dt, *J* 7.2, 1.5 Hz, 2 H; $CHOCH_2CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) 203.1 (*C*HO), 101.7 (anomeric *C*); FABMS: Calcd for $C_{24}H_{38}O_{11}$: 502.2; Found: 509.3 $(M+Li)^+$.

Typical experimental procedure for the synthesis of neoglycophospholipid conjugates (**3**).—*Synthesis of* **3f**.—*ω*-(1,2-Dioelyoyl-*sn*-glycero-3-phosphatidylethanolamino)decanyl *β*-D-lactopyranoside. A 1:1 MeOH–$CHCl_3$ (5 mL) solution of **2d** (140 mg) was treated with MeONa (30% in MeOH, 5 drops) at rt for 30 min. The reaction mixture was neutralized with Dowex-50 (pyridinium form) complex and then transferred to a solution of DOPE (120 mg) and $NaBH_3CN$ (40 mg) in 1:1 MeOH–$CHCl_3$ (10 mL) stirred at 58°C. After 30 min, the reaction mixture was concentrated and purified by flash chromatography (silica gel, $CHCl_3$–MeOH–H_2O of 125 mL:50 mL:2 mL) to afford 109 mg (55%) of **3f** as a white waxy solid. $R_f=0.22$ (SiO_2, 125:50:2 $CHCl_3$–MeOH–H_2O); ^1H NMR (400 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 5.28 (m, 4 H), 5.18 (m, 1 H), 4.24 (d, *J* 8.0 Hz, 1 H), 4.10 (dd, *J* 16.0, 6.8 Hz, 1H), 4.05 (m, 2 H), 3.93 (t, *J* 6.4 Hz, 2 H), 3.80 (m, 4 H), 3.78 (m, 2 H), 3.70 (m, 2 H), 3.6–3.4 (m, 8 H), 3.35 (m, 1 H), 3.24 (t, *J* 8.2 Hz, 1 H), 3.16 (br m, 2 H), 2.94 (br m, 2 H), 2.27 (q, *J* 7.6 Hz, 4 H), 1.96 (m, 8 H), 1.65 (m, 2 H), 1.56 (m, 6 H), 1.25 (s, 22 H), 1.21 (m, 36 H), 0.82 (t, *J* 6.8 Hz, 6 H); ^{13}C NMR (100 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 175.0, 174.6, 131.0, 130.6, 104.7, 103.6, 81.0, 76.4, 75.8, 75.7, 74.3, 74.2, 72.0, 70.2, 63.6, 62.6, 35.2, 35.0, 32.9, 30.7, 30.5, 30.3, 30.2, 30.1, 28.2, 27.3, 26.9, 26.6, 25.8, 25.7, 23.6, 14.9; FABMS: Calcd for $C_{63}H_{118}NO_{19}P$: 1223.8; Found: 1237.4 $(M+2Li-H)^+$.

3a: *Methyl* ω-*(1,2-distearoyl-*sn*-glycero-3-phosphatidylethanolamino)decanyl* β-D-*glucopyranosiduronate*. Yield: 62%; $R_f=0.62$ (SiO_2, 150:30:1 $CHCl_3$–MeOH–H_2O); ^1H NMR (400 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 5.16 (m, 1 H), 4.33 (dd, *J* 12.0, 3.2 Hz, 1 H), 4.24 (d, *J* 7.6 Hz, 1 H), 4.10 (dd, *J* 12.0, 6.8 Hz, 1 H), 4.03 (m, 2 H), 3.93 (t, *J* 5.6 Hz, 2 H), 3.8 (m, 2 H), 3.75 (s, 3 H), 3.56 (t, *J* 9.6 H, 1 H), 3.45 (q, *J* 9.6 Hz, 1 H), 3.39 (t, *J* 9.2 Hz, 1 H), 3.26 (dd, *J* 9.2, 8.0 Hz, 1 H), 3.11 (m, 2 H), 2.89 (dd, *J* 8.4, 7.6 Hz, 2H), 2.25 (q, *J* 7.6 Hz, 4H), 1.65 (m, 2 H), 1.55 (m, 6 H), 1.20 (s, 54 H), 0.82 (t, *J* 7.2 Hz, 6 H); ^{13}C NMR (100 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 174.9, 174.5, 170.9, 104.2, 76.9, 76.3, 74.2, 72.6, 71.3, 71.2, 64.8, 64.7, 63.5, 61.7, 61.6, 53.4, 35.2, 35.0, 32.9, 30.7, 30.6, 30.4, 30.2, 30.1, 30.0, 29.9, 27.5, 26.9, 26.8, 25.9, 25.8, 23.7, 15.0; FABMS: Calcd for $C_{58}H_{112}NO_{15}P$: 1093.8; Found: 1107.4 $(M+2Li-H)^+$.

3b: ω-*(1,2-Dioleoyl-*sn*-glycero-3-phosphatidylethanolamino)decanyl 2-acetoamido-2-deoxy-*β-D-*glucopyranoside*. Yield: 67%; $R_f=0.35$ (SiO_2, 150:50:2 $CHCl_3$–MeOH–H_2O); ^1H NMR (400 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 5.28 (m, 4 H), 5.17 (m, 1 H), 4.35 (dd, *J* 10.8, 2.4 Hz, 2 H), 4.10 (dd, *J* 10.8, 5.2 Hz, 1 H), 4.02 (m, 2 H), 3.94 (t, *J* 6.8 Hz, 2 H), 3.80 (m, 2 H), 3.70 (m, 1 H), 3.56 (t, *J* 8.0 Hz, 1 H), 3.4 (m, 3 H), 3.24 (m, 1 H), 3.10 (m, 2 H), 2.90 (t, *J* 8.0 Hz, 2 H), 2.27 (q, *J* 8.4 Hz, 4 H), 1.99 (m, 8 H), 1.95 (s, 3 H), 1.65 (m, 2 H), 1.55 (m, 4 H), 1.49 (m, 2 H), 1.25 (s, 36 H), 0.82 (t, *J* 6.8 Hz, 6 H); ^{13}C NMR (100 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 174.4, 174.1, 130.5, 130.2, 101.8, 76.5, 75.3, 71.3, 70.9, 70.8, 70.3, 64.4, 64.3, 63.1, 62.2, 56.7, 34.7, 32.5, 32.4, 30.2, 30.0, 29.9, 29.8, 29.5, 29.4, 27.7, 27.6, 26.9, 26.6, 26.2, 25.4, 25.3, 23.1, 14.4; FABMS: Calcd for $C_{59}H_{111}N_2O_{14}P$: 1102.8; Found: 1115.7 $(M+2Li-H)^+$.

3c: ω-*(1,2-Dipalmitoyl-*sn*-glycero-3-phosphatidylethanolamino)decanyl* β-D-*galactopyranoside*. Yield: 40%; $R_f=0.32$ (SiO_2, 125:25:1 $CHCl_3$–MeOH–H_2O); ^1H NMR (400 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 5.15 (m, 1 H), 4.33 (dd, *J* 12.0, 3.0 Hz, 2 H), 4.14 (d, *J* 6.9 Hz, 1 H), 4.08 (dd, *J* 12.0, 6.9 Hz, 1

H), 3.99 (m, 2 H), 3.91 (t, *J* 6.0 Hz, 2 H), 3.90 (m, 2 H), 3.69 (d, *J* 6.0 Hz, 2 H), 3.43 (m, 4 H), 3.10 (m, 2 H), 2.88 (t, *J* 7.8 Hz, 2 H), 2.50 (q, *J* 7.5 Hz, 4 H), 1.62 (m, 2 H), 1.53 (m, 6 H), 1.18 (s, 46 H), 0.79 (t, *J* 6.9 Hz, 6 H); ^{13}C NMR (100 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 174.5, 174.1, 103.9, 75.2, 74.1, 72.9, 70.9, 70.8, 70.4, 69.3, 64.3, 64.2, 63.0, 61.6, 61.1, 34.7, 34.6, 32.4, 30.2, 30.0, 29.8, 29.6, 29.5, 29.4, 26.9, 26.5, 26.2, 25.4, 25.3, 23.2, 14.1; FABMS: Calcd for $C_{53}H_{104}NO_{14}P$: 1009.7; Found: 1023.3 $(M+2Li-H)^+$.

3d: ω-*(1,2-Dileoyl*-sn-*glycero-3-phosphatidyleth-anolamino)decanyl* β-D-*galactopyranoside*. Yield: 46%; R_f = 0.30 (SiO_2, 150:30:1 $CHCl_3$–MeOH–H_2O); ^{1}H NMR (400 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 5.29 (m, 4 H), 5.20 (m, 1 H), 4.38 (dd, *J* 12.0, 3.2 Hz, 1 H), 4.18 (d, *J* 7.2 Hz, 1 H), 4.13 (dd, *J* 12.0, 7.8 Hz, 1 H), 4.05 (m, 2 H), 3.96 (t, *J* 7.8 Hz, 2 H), 3.85 (m, 1 H), 3.73 (d, *J* 7.4 Hz, 1 H), 3.47 (m, 2 H), 3.18 (m, 2 H), 2.96 (t, *J* 8.0 Hz, 2 H), 2.29 (q, *J* 8.0 Hz, 4 H),1.96 (m, 8 H), 1.67 (m, 2 H), 1.57 (m, 4 H), 1.25 (m, 36 H), 0.84 (t, *J* 7.8 Hz, 6 H); ^{13}C NMR (100 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 174.8, 174.4, 130.8, 130.5, 104.5, 75.9, 74.7, 72.3, 71.3, 70.8, 69.8, 64.7, 64.6, 63.5, 62.7, 62.0, 61.7, 41.5, 41.4, 35.1, 34.9, 32.9, 30.7, 30.3, 30.2, 30.1, 30.0, 29.9, 28.1, 27.4, 26.9, 26.8, 25.8, 23.6, 14.7; FABMS: Calcd for $C_{57}H_{108}NO_{14}$p 1061.8; Found: 1074.7 $(M+2Li-H)^+$.

3e: ω-*(1,2-Dipalmitoyl*-sn-*glycero-3-phosphatidyl-ethanolamino)decanyl* β-D-*lactopyranoside*. Yield: 55%; R_f = 0.32 (SiO_2, 150:50:2 $CHCl_3$–MeOH–H_2O); ^{1}H NMR (400 MHz, 2:1 CD_3OD–$CDCl_3$) δ (ppm): 5.18 (m, 1 H), 4.37 (dd, *J* 12.0, 3.2 Hz, 1 H), 4.31 (d, *J* 8.0 Hz, 1 H), 4.24 (d, *J* 8.0 Hz, 1 H), 4.13 (dd, *J* 12.0, 5.2 Hz, 1 H), 4.02 (m, 2 H), 3.95 (t, *J* 6.0 Hz, 2 H), 3.9–3.7 (m, 4 H), 3.6–3.4 (m, 4 H), 3.35 (m, 1 H), 3.24 (t, *J* 4.0 Hz, 1 H), 3.13 (m, 2 H), 2.93 (t, *J* 8.0 Hz, 2 H), 2.28 (q, *J* 7.2 Hz, 4 H), 1.65 (m, 2 H), 1.55 (m, 4 H), 1.20 (s, 46 H), 0.82 (t, *J* 7.2 Hz, 6H); ^{13}C NMR (100 MHz, CD_3OD–$CDCl_3$, v/v 2:1) δ (ppm): 174.6, 174.2, 104.3, 103.3, 80.5, 76.0, 75.4, 73.9, 71.6, 70.9, 70.7, 69.8, 64.5, 64.4, 63.2, 62.5, 62.1, 61.6, 61.4, 34.8, 34.6, 32.5, 30.2, 30.1, 29.9, 29.7, 27.0, 26.5, 25.5, 25.4, 23.2, 14.4; FABMS: Calcd for $C_{59}H_{114}NO_{19}P$: 1171.8; Found: 1178.8 $(M+Li)^+$.

Acknowledgements

The authors are grateful for the financial support provided by ONR, the Whitaker Foundation, and NIH HL56819. E.L.C. is a Clinician Scientist of the American Heart Association. NMR and MS facilities used in this study were purchased through grants from NIH and NSF.

References

[1] E.A.L. Biessen, D.M. Beuting, H.C.P. Rolen, G.A. van de Marel, J.H. van Boom, and T.J.C. van Berkel, *J. Med. Chem.*, 38 (1995) 1538–1546.
[2] T.B. Kuhlenschmidt and Y.C. Lee, *Biochemistry*, 23 (1983) 3569–3575.
[3] H.-J. Gabius, *Anal. Biochem.*, 189 (1990) 91–94.
[4] J. Haensler and F. Schuber, *Glycoconjugate J.*, 8 (1991) 116.
[5] S.A. Defrees, L. Phillips, L. Guo, and S. Zalipsky, *J. Am. Chem. Soc.*, 118 (1996) 6101–6104.
[6] P. Wang, M. Schuster, Y.-F. Wang, and C.-H. Wong. *J. Am. Chem. Soc.*, 115 (1993) 10487–10491.
[7] R.R. Schmidt, *Pure Appl. Chem.*, 61 (1989) 1257.
[8] A. Ulman, *Chem. Rev.*, 96 (1996) 1533–1544.
[9] E. Sackmann, *Science*, 271 (1996) 43–48.
[10] W. Muller, H. Ringsdorf, E. Rump, X. Zhang, L. Angermaier, W. Knoll, and J. Spinke, *J. Biomater. Sci., Polym. Edn.*, 6 (1994) 481–495.
[11] L. Sun and E.L. Chaikof, *Bioconjugate Chem.*, 8 (1997) 567–571.
[12] T.D. Sells and D.F. O'Brien, *Macromolecules*, 27 (1994) 226–233.
[13] W. Srisiri, Y.-S. Lee, and D.F. O'Brien, *Tetrahedron Lett.*, 36 (1995) 8945–8948.
[14] I. Farkas, R. Bognar, M.M. Menyhart, A.K. Tarnai, A. Bihari, and J. Tamas, *Acta Chim. Sci. Hung.*, 84 (1975) 325.