Studies on the Synthesis and Properties of Novel Phospholipid Analogous Polymers

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SYNOPSIS

Two kinds of phospholipid analogous compounds, methacrylate monomers (**4a–b**) and acrylamide monomers (**5a–b**), were prepared and polymerized with a radical initiator in water at room temperature. The viscosity behavior of these charged polymers were investigated in the presence or absence of inorganic salts, and the found inherent viscosity [η] of amide polymer (**poly7a**) is higher than those of ester polymers (**poly6a1 and poly6b**). On the other hand, the radical copolymerization of monomer **5b** with acrylamide (**AAm**) was also carried out in water. Based on the x-ray analyses, it is proposed that some of the obtained polymers show ordered bilayer structures in condensed phase. Furthermore, the thermal properties were studied by DSC and TG-DTA measurements. © 1996 John Wiley & Sons, Inc.

INTRODUCTION

Although present in body fluids such as plasma and bile, the phospholipids are found in highest concentration in the various cellular membranes where they perform many different functions, such as to serve as structural components of membranes.[1] Nearly one-half of the mass of the erythrocyte membrane is composed of various phospholipids. In addition, phospholipids also play many physiological actions, and they are well studied in the fields of biochemistry and pharmaceutics.[2,3] From these points of view, it has seemed attractive to investigate the behaviors of monomeric and polymeric phospholipid analogs.

On the other hand, there has been considerable interest in the synthesis of "polysoaps," which behave analogously to low molecular weight surfactants.[4,5] This is because polysoaps have found increasing use in science and in technology, ranging from enzyme models to additives in tertiary oil recovery. Polysoaps can be prepared by three methods: by polymerization of reactive surfactants;[5,6] by copolymerization of hydrophilic and hydrophobic monomers; or by appropriate modification of preformed polymers, such as grafting hydrophobic chains onto hydrophilic polymers.[7] Among of them, the first method produces polymers with the best-defined molecular structures.

Many studies concerning the synthesis and properties of polymeric phospholipid analogs containing phosphatidylethanolamines, phosphatidylcholines, or their analogous moieties in polymers' back bones or in the side chains have been performed over the past almost 20 years.[8–15] However, to our knowledge, all these polymers were obtained with radical polymerizations in organic solvents, and no study has been reported for the preparation of a phospholipid analogous polymer by radical solution polymerization in water at room temperature. Therefore, in this work, amphiphilic, water-soluble, or partly water-soluble methacrylate monomers (**4**) and acrylamide monomers (**5**) containing both phosphatidylcholine analogs and alkyl groups were newly prepared and characterized, respectively. These monomers were homopolymerized and copolymerized by radical polymerization in water with am-

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monium peroxodisulfate as an initiator at room temperature. Furthermore, the properties of these obtained polymers are also described, as well as those of the monomers.

EXPERIMENTAL

Materials

Acetonitrile, chloroform, and benzene were distilled over phosphorus pentoxide. Tetrahydrofuran (THF) was distilled from lithium aluminium hydride. Anhydrous methanol was obtained by distillation in the presence of magnesium and iodine. Acetone was dried by distillation from anhydrous potassium carbonate. *N,N*-Dimethylaminoethyl methacrylate was purchased from Tokyo Kasei Co., Ltd., Japan. *N,N*-Dimethylaminopropyl acrylamide was obtained from Kohjin Co., Japan. 2-Chloro-2-oxo-1,3,2-dioxaphospholane (**1**), b.p. (1.0 mbar) 102.5°C ~ 105.0°C, was prepared according to the methods of Lucas[16] and Edmundson.[17] All other solvents and chemicals are extra pure grade reagent and are used without further purification. All reagents are purchased from Nacalai Chemical Co. unless otherwise noted.

Methods

Proton (^{1}H) NMR spectra were recorded on a JEOL α-400 FT-NMR spectrometer (400 MHz). Proton chemical shifts, reported in parts per million, were referenced to tetramethylsilane directly as an internal standard. Multiplicities of resonance peaks are indicated as singlet s, triplet t, broad singlet bs, double doublet dd, multiplet m. Infrared (IR) spectra (KBr disks) were obtained using a Jasco A-202 spectrometer and were reported in wave numbers (cm^{-1}). In the IR data presentation, bracketed s and vs indicate the extent of absorption as strong and very strong. Column chromatography was carried out on silica gel (Wakogel C-200). The melting points of obtained polymers were measured by a micro melting point apparatus (Yanaco MP-J3). The viscosity measurements were performed with a Ubbelohde-type viscometer at 25 ± 0.1°C. For an x-ray diffraction measurement, the specimen was completely sealed with mica in the sample holder. The specimen was stable during x-ray diffraction measurement as judged from the reproducibility of the diffraction pattern. The x-ray powder diagram was photographed with nickel-filtered Cu Kα radiation (37.5 kV, 20 mA), using a flat-plate camera of 39.2 mm passage at room temperature. Thermal properties were determined by differential scanning calorimetry (DSC), using a Rigaku Thermoflex apparatus DSC-8230B. The sample quantity was 10 mg with a 10°C/min rate of heating. Pyrolysis was carried out with a Rigaku TG-DSC instrument standard type CN8076 E1.

2-Hexoxy-2-oxo-1,3,2-dioxaphospholane (3a)

In detail, into a thoroughly dry 500 mL three-necked round-bottomed flask equipped with a mechanical stirrer, a drying tube, and a dropping funnel were placed 10.22 g (0.10 mol) of 1-hexanol (**2a**) and 11.13 g (0.11 mol) of triethylamine in 200 mL of dry THF. After cooling with dry-ice/methanol bath (−20°C), 14.25 g (0.10 mol) of **1** were slowly added to the stirred solution by dropwise over a period of 1 h. During the dropping, the mixture was maintained at −20 ~ −15°C, and triethylamine hydrochloride as a white solid was precipitated. After being dropped, the reaction mixture was then allowed to warm up to 0°C and stirred for further 2 h. The precipitate was filtered off and washed with 30 mL of THF. The filtrate was concentrated on a rotary evaporator under reduced pressure to obtain pure **3a** as a pale yellow liquid. Yield: 20.40 g (98.0 %).

2-Octoxy-2-oxo-1,3,2-dioxaphospholane (3b)

Using the same method for preparing **3a**, **3b** was also prepared as a pale yellow liquid from the reaction of 1-octanol (**2b**) [13.03 g (0.10 mol)] with **1** [14.25 g (0.10 mol)]. The reaction was performed at −10°C as dropping temperature and 0 ~ 10°C as maintaining temperature. Yield: 22.87 g (96.8 %). IR (KBr): 2910 and 2850 (vs: $-(CH_2)_{n+2}CH_3$, ν_{C-H}); 1460 (s: $-(CH_2)_{n+2}CH_3$, δ_{C-H}); 1275 (s: O—P=O, ν_{P-O}), and 1050 cm^{-1} (vs: P—O—C, ν_{C-O}). ^{1}H-NMR ($CDCl_3$): δ = 0.88 (t: 3H, $-CH_3$); 1.20 ~ 1.42 (m: xH, $-CH_2CH_2(CH_2)_nCH_3$); 1.57 (bm: 2H, $-OCH_2CH_2-(CH_2)_n-$) and 4.13 ~ 4.30 ppm (m: 6H, $-OCH_2CH_2O-$ and $-POCH_2CH_2(CH_2)_n-$). **3a**: n = 3, x = 6; **3b**: n = 5, x = 10.

2-[2-(Methacryloyl ethyl)dimethyl ammonio]ethyl Hexyl Phosphate (4a)

After 18.74 g (0.09 mol) of **3a** and 60 mL of dry acetonitrile were placed into a 300 mL glass pressure bottle, 18.86 g (0.12 mol) of *N,N*-dimethylaminoethyl methacrylate dissolved in 60 mL of dry ace-

tonitrile was quickly added into the same bottle. The pressure bottle was closed and then shacken in a thermostat at 60°C for 40 h. After the reaction it was cooled to room temperature. The pressure bottle was opened, then the solution was concentrated to give crude product as a yellow liquid. The crude product was refined by column chromatography on absorption silica gel (elution with methanol/acetone; 20:1; v/v) to give pure **4a** as a pale yellow viscous liquid. Yield: 25.56 g (77.7 %).

2-[2-(Methacryloyl ethyl)dimethyl ammonio]ethyl Octyl Phosphate (4b)

With the similar procedure for preparing **4a**, crude compound **4b** as a yellow liquid was also prepared from the reaction of **3b** [21.26 g (0.09 mol)] with *N,N*-dimethylaminoethyl methacrylate [18.86 g (0.12 mol)]. The crude product was purified by column chromatography on silica gel (methanol/acetone; 10:1; v/v) to give **4b** as a pale yellow viscous liquid. Yield: 27.59 g (78.1 %). IR (KBr): 2910 and 2850 (vs: $-(CH_2)_{n+2}CH_3$, ν_{C-H}); 1460 (s: $-(CH_2)_{n+2}CH_3$, δ_{C-H}); 1710 (vs: —COO—, $\nu_{C=O}$); 1630 (vs: $CH_2=C-$, $\nu_{C=C}$); 1230 (vs: $O^-—P=O$, ν_{P-O}), and 1050 ~ 1080 cm^{-1} (vs: P—O—C, ν_{C-O}). ^{1}H-NMR (CD_3OD): δ = 0.88 (t: 3H, $-CH_3$); 1.19 ~ 1.42 (m: xH, $-CH_2CH_2(CH_2)_n-$); 1.62 (m: 2H, $-OCH_2CH_2(CH_2)_n-$); 1.95 (s: 3H, $=C(CH_3)-$); 3.25 (s: 6H, $-N^+(CH_3)_2-$); 3.58 (m: 2H, $-N^+CH_2CH_2OP-$); 3.90 (m: 2H, $-COOCH_2-CH_2N^+-$); 4.15 ~ 4.25 (m: 4H, $-CH_2OPOCH_2-$); 4.60 (m: 2H, $-COOCH_2-$); 5.65 (s: 1H, HC=C COO—, *trans*); 6.13 ppm (s: 1H, HC=CCOO—, *cis*). **4a**: n = 3, x = 6; **4b**: n = 5, x = 10.

4a: $C_{16}H_{32}O_6NP \cdot H_2O$ (383.48)	Calc.(%)	C 50.11	H 9.48	N 3.65
	Found(%)	C 50.01	H 9.23	N 3.44
4b: $C_{18}H_{36}O_6NP \cdot H_2O$ (411.54)	Calc.(%)	C 52.53	H 9.82	N 3.40
	Found(%)	C 52.37	H 9.71	N 3.56

2-[3-(Acrylamide propyl)dimethyl ammonio]ethyl Hexyl Phosphate (5a)

Into a 300 mL glass pressure bottle, 18.74 g (0.09 mol) of **3a**, 18.75 g (0.12 mol) of *N,N*-dimethylaminopropyl acrylamide and 60 mL of acetonitrile were placed, and then the bottle was shaken for 40 h at 60°C. After concentrating the solution, the crude product as a yellow liquid was purified by column chromatography eluting with the mixture of methanol and water (1:2; v/v) to afford pure **5a** as a pale yellow viscous liquid. Yield: 24.74 g (70.4 %).

2-{3-(Acrylamide propyl)dimethyl ammonio}ethyl Octyl Phosphate (5b)

With the same operation for preparing **5a**, **5b** was also prepared from the reaction of **3b** [21.26 g (0.09 mol)] with *N,N*-dimethylaminopropyl acrylamide [18.75 g (0.12 mol)]. The crude product was purified by column chromatography on silica gel (methanol/water; 1:1; v/v) to obtain pure **5b** as a pale yellow viscous liquid. Yield: 26.86 g (71.3 %). IR(KBr): 2910 and 2850 (vs: $-(CH_2)_{n+2}CH_3$, ν_{C-H}); 1460 (s: $-(CH_2)_{n+2}CH_3$, δ_{C-H}); 1660 (vs: CONH, $\nu_{C=O}$); 1625 (vs: $CH_2=CH-$, $\nu_{C=C}$); 1230 (vs: $O^-—P=O$, ν_{P-O}), and 1050 ~ 1080 cm^{-1} (vs: P—O—C, ν_{C-O}). ^{1}H-NMR (CD_3OD): δ = 0.88 (t: 3H, $-CH_3$); 1.20 ~ 1.39 (m: xH, $-CH_2CH_2(CH_2)_nCH_3$); 1.57 (m: 2H, $-OCH_2CH_2(CH_2)_n-$); 2.08 (bm: 2H, $-CONHCH_2CH_2-$); 3.27 (s: 6H, $-N^+(CH_3)_2-$); 3.40 (bs: 2H, $-CONHCH_2-$); 3.55 ~ 3.75 (4H, $-CH_2^+NCH_2-$); 4.13 ~ 4.24 (bm: 4H, $-CH_2OPOCH_2-$); 5.55 (dd: 1H, $CH=CCONH-$, *trans*); 6.24 (dd: 1H, $C=CHCONH-$), and 6.42 ppm (dd: 1H, $CH=CCONH-$, *cis*). **5a**: n = 3, x = 6; **5b**: n = 5, x = 10.

5a: $C_{18}H_{35}O_5N_2P \cdot H_2O$ (408.54)	Calc.(%)	C 52.92	H 9.15	N 6.86
	Found(%)	C 52.67	H 9.07	N 6.94
5b: $C_{20}H_{39}O_5N_2P \cdot H_2O$ (436.60)	Calc.(%)	C 55.00	H 9.48	N 6.42
	Found(%)	C 55.21	H 9.53	N 6.21

Table I Conditions of Polymerization for Homopolymers and Copolymer

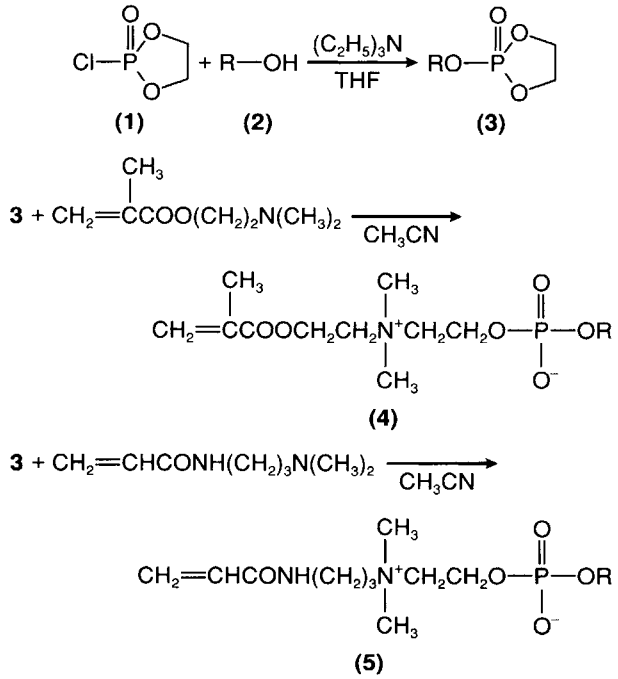
Polymer	Corresponding Monomer	Monomer Weight (g)	Solvent (mL)		$(NH_4)_2S_2O_8$ (mg)	$NaHSO_3$ (mg)	Time (h)
			H_2O	CH_3OH			
poly6a1	**4a**	1.0	3.0	0	0.50	0.25	16
poly6a2	**4a**	1.0	3.0	0	0.25	0.13	18
poly6b	**4b**	1.0	2.0	1.0	0.50	0.25	20
poly7a	**5a**	1.0	9.0	0	0.50	0.25	6
poly7b	**5b**	1.0	9.0	0	0.50	0.25	8
poly8	**5b, AAm**[a]	0.1, 1.0	9.0	0	0.50	0.25	6

[a] AAm: acrylamide.

Polymerization of Monomers

The homopolymerizations of monomers **4a–b** and **5a–b** were carried out under nitrogen atmosphere in a two-necked 50 mL flask fixed with nitrogen inlet, electromagnetic stirrer, and nitrogen outlet. The monomers and ammonium peroxodisulfate [$(NH_4)_2S_2O_8$] were dissolved with a certain concentration (see Table I) in pure water or a mixture of water and methanol, which were replaced by nitrogen for 1 h. Then, sodium hydrogen sulfite ($NaHSO_3$) as a promoter was rapidly introduced to the same flask. These solutions were stirred at room temperature for 6 ~ 20 h corresponding to different monomers (see Table I). In the process of polymerization, white solid was precipitated only for monomer **5b**, and the other polymer solutions were still kept clear. After the polymerizations, the solutions were poured into excess acetone to give crude polymers. The soluble polymers (**poly6a1, poly6a2, poly6b,** and **poly7a**) were purified two times by dissolving in methanol and then reprecipitation in acetone, while the insoluble polymer (**poly7b**) was washed by methanol three times. The obtained precipitates were dried in vacuum to give the corresponding polymers (**poly6a1, poly6a2, poly6b, poly7a,** and **poly7b**) as white solids.

Using the same method, the copolymerization of monomer **5b** with acrylamide (**AAm**) was also carried out, and the white solid was precipitated as well as the homopolymerization of monomer **5b**. The crude product was purified by washing three times with water and methanol to give copolymer (**poly8**) as a white solid. Elemental analysis was found as: C, 54.01; H, 8.40; N, 12.53.



Monomer	a	b
R	$-(CH_2)_5CH_3$	$-(CH_2)_7CH_3$
4	**4a**	**4b**
5	**5a**	**5b**

Scheme 1 Synthesis for monomers **4a–b** and **5a–b**.

RESULTS AND DISCUSSION

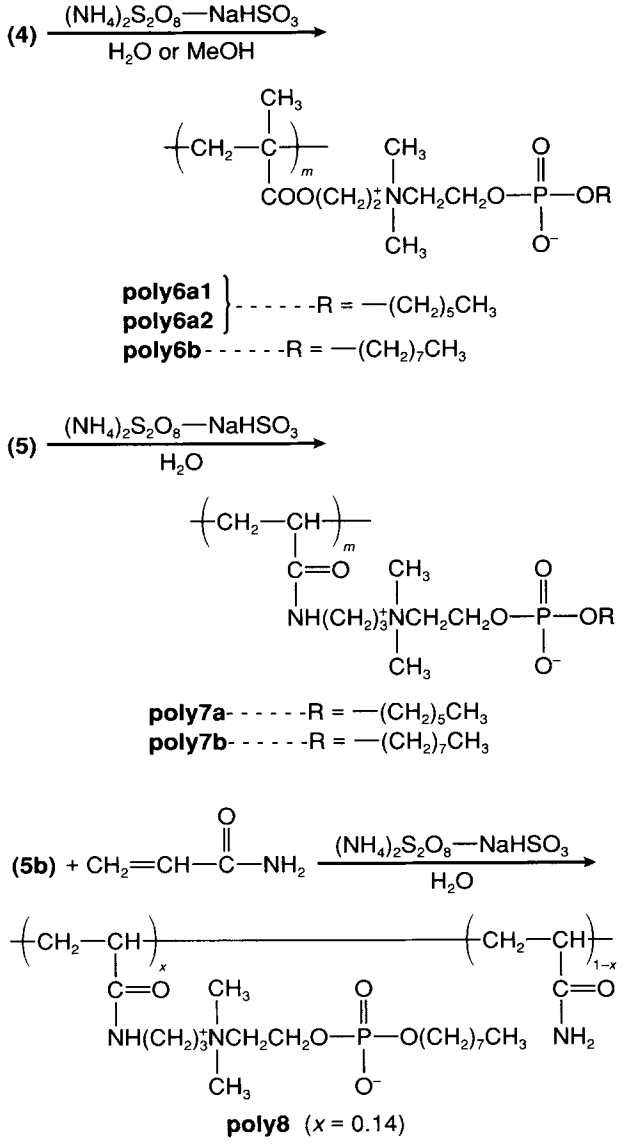
Phospholipid analogous methacrylate monomers (**4a–b**) and acrylamide monomers (**5a–b**) containing both phosphatidylcholine analogs and alkyl groups were synthesized according to the reaction Scheme 1.

2-Chloro-2-oxo-1,3,2-dioxaphospholane (**1**) was prepared according to the procedure described by

Lucas[16] and Edmundson.[17] 2-Alkoxy-2-oxo-1,3,2-dioxaphospholane (**3**) was obtained by the reaction of **1** with alkyl alcohols (**2**). According to the method of Thoung and Chabrier,[18] the reaction of **3** with *N,N*-dimethylaminoethyl methacrylate or *N,N*-dimethylaminopropyl acrylamide was carried out in anhydrous acetonitrile at 60°C for 40 h to give 2-[2-(methacryloyl ethyl)dimethyl ammonio]ethyl alkyl phosphates (**4a–b**) or 2-[3-(acrylamide propyl)dimethyl ammonio]ethyl alkyl phosphates (**5a–b**) in good yields. The monomers were confirmed by IR, ^{1}H-NMR, and elemental analysis, respectively. All the monomers are pale yellow viscous liquids. They are hygroscopic and easily soluble in methanol but almost insoluble in acetone, diethylether, or benzene. Furthermore, the monomer **4a**, **5a**, and **5b** are soluble in water, while the monomer **4b** is partially soluble in water.

Under nitrogen atmosphere, the homopolymerizations of monomers **4a–b** and **5a–b** were carried out in pure water or in a mixture of water and methanol with $(NH_4)_2S_2O_8$ as an initiator at room temperature. With different polymerization time and different ratio of the initiator, **poly6a1**, **poly6a2**, **poly6b**, **poly7a**, and **poly7b** were obtained, respectively (see Table I). Using the same method, **poly8** was also obtained by the copolymerization of monomer **5b** with **AAm**. All the soluble homopolymers (**poly6a1**, **poly6a2**, **poly6b**, and **poly7a**) were purified by reprecipitation in acetone two times. The insoluble homopolymer **poly7b** was washed by methanol, and insoluble copolymer **poly8** was washed by water and methanol three times. The polymerization procedures were shown in Scheme 2.

All the polymers are white hygroscopic solids. No melting points were observed until the polymers were heated up to 250°C. Their yields are found to be about 70 ~ 75%, and the solubilities in various solvents are listed in Table II. **Poly6a1**, **poly6a2**, **poly6b**, and **poly7a** are soluble in water or methanol, while **poly7b** is almost insoluble in any solvent. In order to improve the solubility of **poly7b**, monomer **5b** was copolymerized with **AAm**; however, the obtained copolymer (**poly8**) is also almost insoluble in any solvent. Furthermore, we confirmed these polymers by IR and ^{1}H-NMR, respectively. The IR spectra of homopolymers and copolymer showed that the absorption bands of acrylic C=C double bonds are absent, while the absorption bonds of other groups appear as well as corresponding monomers. In the ^{1}H-NMR spectra, only the peaks of C=C double



Scheme 2 The homopolymerizations of monomers **4a–b** and **5a–b** and copolymerization of monomer **5b** with AAm.

bonds disappeared, while the other peaks remained similar to those of monomers.

The IR spectra of monomer **5b**, homopolymer **poly7b**, and copolymer **poly8** are shown in Figure 1. The monomer and homopolymer show two strong absorption bands, and the **poly8** shows two weak absorption bands around 1230 and 1080 cm^{-1}, which can be attributed to the stretching vibration of O$^-$—P=O and P—O—C groups. The characteristic absorption peak of C=C appears clearly at 1625 cm^{-1} in the IR spectrum of monomer **5b**; however, it does not exist in the IR spectra of **poly7b** and **poly8**.

Table II Solubilities of Homopolymers and Copolymer in Various Solvents

	Solvents[a]						
Polymer	Water	Methanol	Acetone	Benzene	Chloroform	THF	DMF
poly6a1	+−	+	−	−	+−	−	+
poly6a2	+−	+	−	−	+−	−	+
poly6b	+−	+	−	−	+−	−	+
poly7a	+	+	−	−	+−	−	+
poly7b	+−	+−	−	−	+−	−	+−
poly8	+−	+−	−	−	+−	−	+−

+: soluble at room temperature; −: insoluble; +−: partially soluble or swelling.
[a] THF: tetrahydrofuran; DMF: *N,N*-dimethylformamide.

The characteristic absorption band of amide group is shown at 1660 cm^{-1} for monomer **5b**, owing to the stretching vibration of C=CCONH— group, while it is shown at 1650 cm^{-1} for **poly7b** due to the stretching vibration of C—CCONH— group. Furthermore, two peaks at 1650 and 1640 cm^{-1} corresponding to the stretching vibration of C—CCONH— group and C—$CCONH_2$ group, respectively, are shown in the IR spectrum of **poly8**. These spectral data convinced that the homopolymerization of monomer **5b** and the copolymerization of monomer **5b** with **AAm** were achieved, indeed.

In previous work[19] we have found that vinyl polymers having phosphatidylcholine groups or analogous groups in the side chains show the properties of polyelectrolytes in their viscosity behavior in aqueous solution. It is because that the $-PO_4^-$— group dissociates as a weak acid, while the $-N^+(CH_3)_3$ group dissociates as a strong base.[20] We, therefore, studied the viscosity behavior of these homopolymers in the presence or absence of sodium chloride at 25°C by using a Ubbelodhe-type viscometer. Figure 2 shows the plots of reduced viscosity (η_{sp}/C) vs. polymer concentration (C) for **poly6a1** and **poly6b** in the presence of sodium chloride, respectively. They are measured in the mixture of water and methanol (2:1, v/v) because both the polymers are partially soluble in pure water. These η_{sp}/C were found to decrease with the dilution of polymer concentrations, and their inherent viscosity [η] was found to be 0.25 and 0.17 dL/g, respectively.

In order to increase the molecular weight of **poly6a1**, the monomer **4a** was polymerized with lower ratio of the initiator to give **poly6a2**. The **poly6a2** is partially soluble in pure water or the mixture of water and methanol; therefore, its viscosity behavior was examined in methanol without sodium chloride (Fig. 3). The η_{sp}/C of **poly6a2** was found to increase rapidly with the reduce of concentration. It was revealed that **poly6a2** shows the viscosity behavior similar to the usual polyelectrolytes in polar solvent. This phenomena may result from the mutual repulsion between N^+ and N^+, particularly the possible chain expansion at low concentration.

As **poly7a** is easily soluble in water at room temperature, its viscosity measurement was carried out at 25°C in NaCl aqueous solution (Fig. 2). As well as **poly6a1** and **poly6b**, the η_{sp}/C of **poly7a** was also found to reduce upon the dilution of the polymer concentration, and the inherent viscosity [η] was found to be 0.36 dL/g. Comparing this inherent viscosity with that of **poly6a1** that contains the same alkyl group in side chains, it could be considered that the molecular weight of polyacrylamide (**poly7a**) is larger than that of polymethacrylate (**poly6a1**) when they were polymerized in pure water.

The viscosity measurements of **poly7b** and **poly8** could not be carried out, because they are almost insoluble in water and methanol. The poor solubilities may be contributed to the existence of longer alkyl chains in their side chains (octyl group), and by their bigger molecular weight.

The structures of condensed phases of **poly7b** and **poly8** were investigated by x-ray diffraction (XRD) method at room temperature. In the XRD pattern of **poly7b**, a strong ring with spacing of 28.8 Å in small-angle region, and a diffuse ring with spacing of 4.4 Å in wide-angle region were observed as shown in Figure 4. From the results of XRD, a structure is proposed for condensed phase of **poly7b**, which is basically constructed from alternately stacked bilayers with hydrophilic and hydrophobic regions of the side chains. The main chain is arranged in the middle of hydrophilic region where

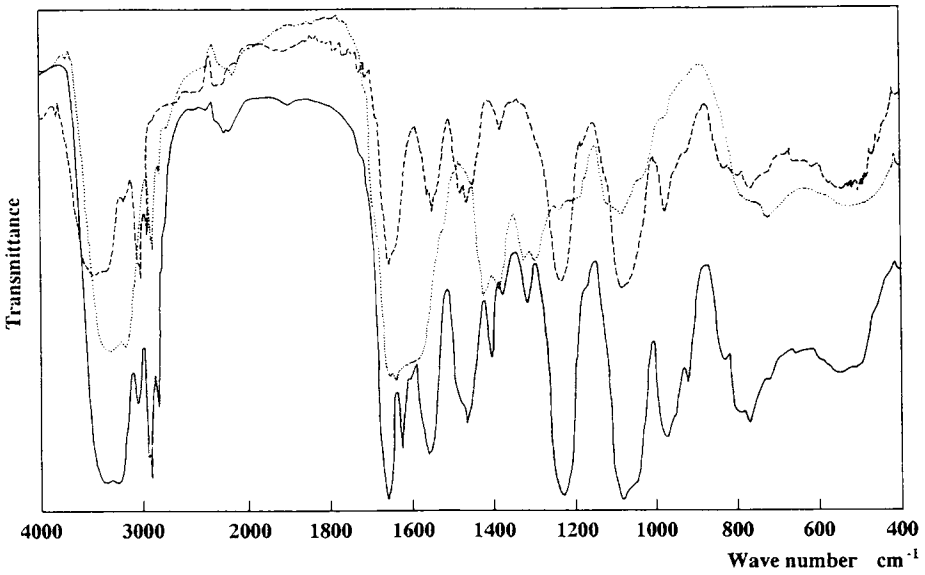


Figure 1 Comparison of the IR spectra of monomer **5b** (—), **poly7b** (---), and **poly8** (· · ·).

polar head groups of side chains are stood out alternately towards opposite direction from the main chain (Fig. 5). Side-by-side packing of hydrocarbon chains of side chains in the bilayer is in a disordered state, judging from the observed diffuse ring in wide angle region of XRD measurement.

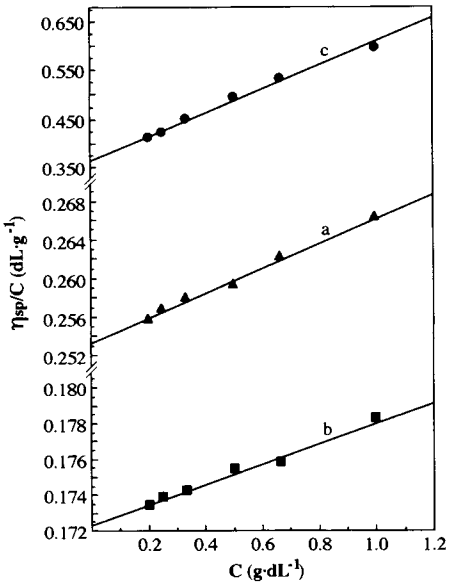


Figure 2 Reduced viscosities of polymers in the presence of 0.1 *M* NaCl at 25°C. (a) **poly6a1** and (b) **poly6b** in the mixture of water and methanol (2:1, v/v); (c) **poly7a** in water.

The side chain of **poly7b** has only one hydrocarbon chain for one bulky polar head group. The lengh of extended polar head group of side chain and that of the planar zig-zag hydrocarbon chain are estimated as about 13 Å and about 10 Å, respectively. The resulting total length of a side chain, i.e., 23 Å (= 13 Å + 10 Å), is too small to explain the observed value of the long period, and 46 Å (23 Å × 2) is too large. Therefore, in the proposed model, hydrocarbon chains standing out from two adjacent main chains are arranged toe-to-toe interdigitated with each other, and whole side chains are slightly tilted against the layer normal, giving a stable bilayer structure with thickness of about 30 Å. The diffuse

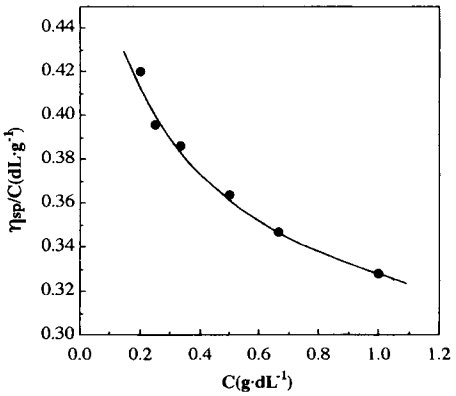
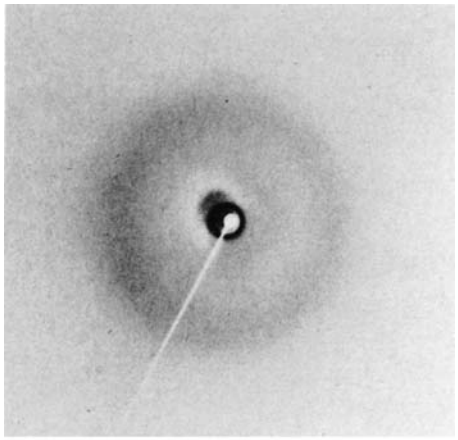
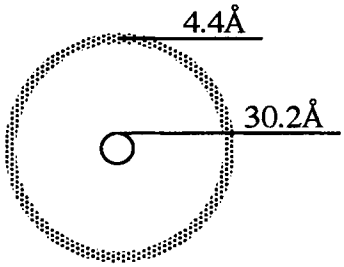
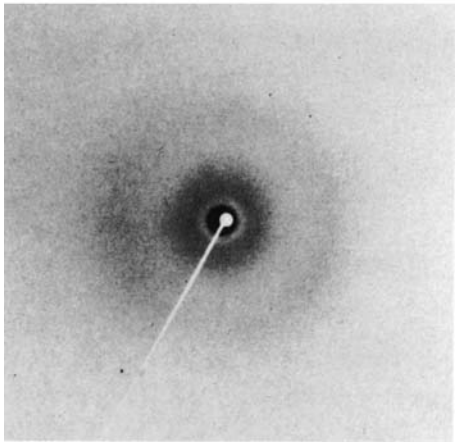


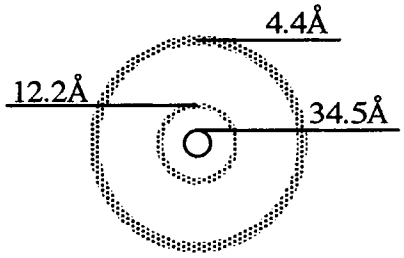
Figure 3 Reduced viscosity of **poly6a2** in methanol in the absence of sodium chloride at 25°C.





(a) Homopolymer **poly7b**





(b) Copolymer **poly8**

Figure 4 X-ray diffraction patterns for **poly7b** and **poly8** obtained with a flat camera by Ni-filtered x-rays of Cu Kα (camera length = 39.2 mm).

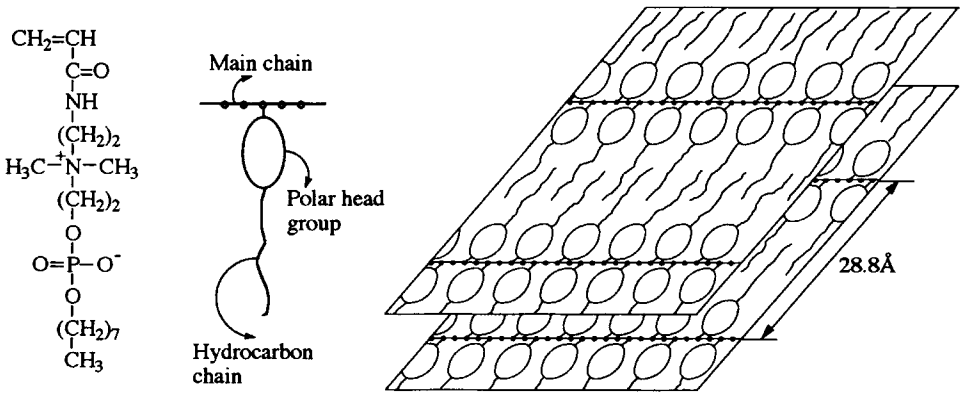


Figure 5 Schematic representation of the two-dimensional packing for a proposed structure of **poly7b** at room temperature.

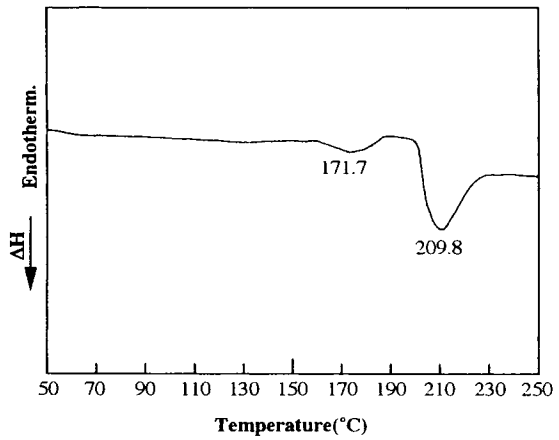


Figure 6 DSC thermogram of **poly8**.

ring with spacing of 4.4 Å indicates that the arrangement of hydrocarbon chains is in a disordered state.

For copolymer **poly8**, a strong ring with spacing of 34.5 Å in small-angle region, and two diffuse rings with spacing of 12.2 Å and 4.4 Å in wide-angle region were observed by XRD method (Fig. 4). The XRD result implies that the longer side chains, which are the same side chains as those of **poly7b**, exist as many clusters and show nearly the same structure as that of **poly7b**. In this case, one such cluster is estimated to be composed of under several 10 side chains, taking the sharpness of diffraction profile into consideration. Therefore, the arrangement of the side chains should be somewhat different from that shown in **poly7b**. The observed value of the bilayer thickness for **poly8**, 34.5 Å, is larger than that of **poly7b**, implying that the side chains of **poly 8** are nearly parallel to the layer normal. The diffuse ring at $(12.2Å)^{-1}$ may come from the region of the shorter side chains, i.e., amide group ($-CONH_2$). Thus, XRD results imply that this polymer **poly8** is a block copolymer.

The thermal properties of **poly8** were studied by DSC as well as TG-DTA measurements. Under nitrogen, the DSC measurement was carried out from 0 to 250°C with heating at 10°C/min. As shown in Figure 6, two broad endothermic peaks around 171.7°C and 209.8°C were observed. They may correspond to the decomposition of the phosphates in the side chains and the pyrolysis of copolymer, respectively. There is no indication for premature decomposition of the polymer due to the quaternary ammonium groups. Furthermore, in the temperature range between 0 to 160°C, no thermal transition could be detected, in agreement with other studies on polyzwitterions.[5,21] Obviously, the ionic groups of the polymer either shift the glass transition above the decomposition temperature or give rise to such a substantial broadening of the transition that it cannot be detected.

The thermal stability of **poly8** in air was further evaluated from TG-DTA thermogram obtained with a heating rate of 10°C/min. **Poly8** began to degrade at around 83.8°C, through a multistep degradation as shown in Figure 7. The first step of weight loss for **poly8** corresponds to the evaporation of water because it is very hygroscopic. According to the results of Kishore,[22,23] the second step can be considered to the pyrolysis of the formation for the phosphates, and its temperature is nearly consistent with the observed result by DSC measurement.

CONCLUSION

2-[2-(Methacryloyl ethyl)dimethyl ammonio]ethyl alkyl phosphates and 2-[3-(acrylamide propyl) dimethyl ammonio]ethyl alkyl phosphates have been prepared and characterized. They are found to be useful as polymeric phospholipid analogs. Using $(NH_4)_2S_2O_8$ as an initiator, and with pure water or the mixture of water and methanol as a solvent, the phospholipid analogous polymers have been obtained by free radical homopolymerization and copolymerization at room temperature. It has been demonstrated that the molecular weight of polyacrylamides is higher than that of polymethacrylates. Furthermore, the polymers show the properties of polyelectrolytes in polar solvent, and show thermostabilities until they are heated up to about 170°C. On the other hand, the polymers **poly7b**

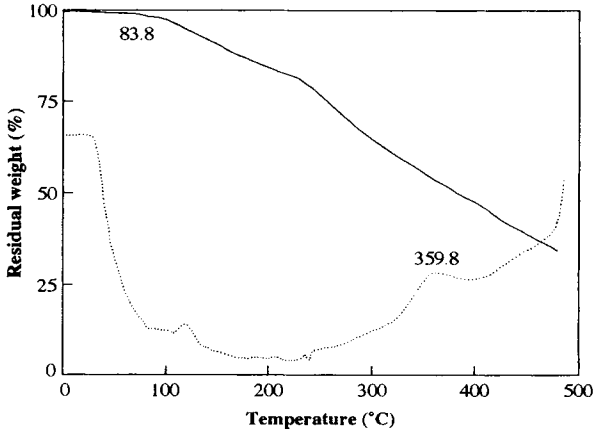


Figure 7 TG-DTA thermogram of **poly8**.

and **poly8** containing longer alkyl groups in their side chains exist stacked bilayer structures in condensed phases. All the polymers obtained by polymerizations in water could be applied widely in pharmaceutical chemistry such as delivery of drugs and physiological activators, especially **poly7b** and **poly8**, which are insoluble but swelling in water may be used as synthetic vitreous body.

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