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Yeonho Seo[a]; Yu-Jun Li[a]; Tadao Nakaya[a]
[a] Department of Bioapplied Chemistry, Faculty of Engineering, Osaka City University, Osaka, Japan

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PREPARATION AND POLYMERIZATION OF 2-(ACRYLOYLOXY)ETHYL-2-(TRIMETHYLAMMONIUM)ETHYL PHOSPHATE AND 4-(ACRYLOYLOXY)BUTYL-2-(TRIMETHYLAMMONIUM)ETHYL PHOSPHATE

Yeonho Seo, Yu-Jun Li, and Tadao Nakaya*
Department of Bioapplied Chemistry, Faculty of Engineering, Osaka City University, 3-3-138 Sugimoto, Sumiyoshi-ku, Osaka 558, Japan.

ABSTRACT

2-(Acryloyloxyl)ethyl-2-(trimethylammonium)ethyl phosphate (**4a**) and 4-(acryloyloxyl)butyl-2-(trimethylammonium)ethyl phosphate (**4b**) were prepared and characterized by their IR and ^{1}H NMR spestral data and elemental analyses. **4a** was homopolymerized and compolymerized with 2-hydroxyethyl acrylate, stearyl acrylate, and 1,3-dioleylacylglycerol-2-acrylate using 2,2'-azoisobutyronitrile (AIBN) as initiator. Poly (**4a**) of the resultant polymers exhibited liquid crystalline behaviors from 118 up to 152 °C observed by a polarization microscopy. Moreover, the water-soluble polymer, Poly (**4a**), among the resulting polymers showed a polyelectrolyte behavior from its viscosity measurement.

INTRODUCTION

With the first synthesis of 2-(methacryloyloxy)ethyl-2-aminoethyl hydrogen phosphate by us [1], attention is now being focused on its potential application in various field of biomaterial research [2-4]. Our continuing interest in the monomer synthesis bearing phosphatidylethanolamine [1, 5] and phosphatidylcholine [6-9] analogs prompted

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*To whom correspondence should be addressed.

us to design two new simple monomers, 2-(acryloyloxy)ethyl-2-(trimethylammonium)ethyl phosphate (**4a**) and 4-(acryloyloxy)butyl-2-(trimethylammonium)ethyl phosphate (**4b**).

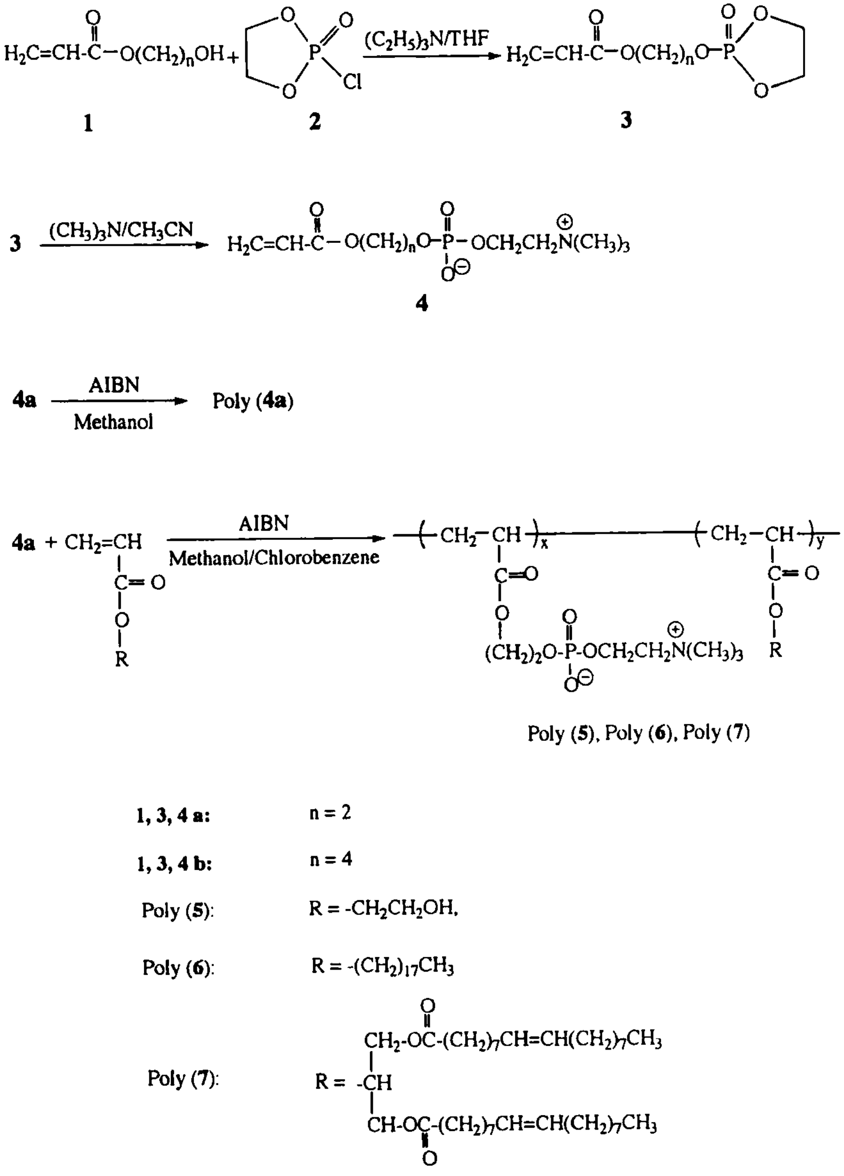
The present communication is mainly concerned with the preparation of **4a** and **4b**, polymerization and copolymerization of **4a**.

RESULTS AND DISCUSSION

The synthetic procedure is outlined in Scheme 1.

As starting materials, 2-hydroxyethyl acrylate (**1a**) was commercially obtained and 4-hydroxybutyl acrylate (**1b**) was obtained from Osaka Organic Chemical Company. 2-Chloro-2-oxo-1,3,2-dioxaphospholane (**2**) was prepared according to the method of Lucas and Edmundson et al. [10, 11]. The syntheses of 2-(2-oxo-1,3,2-dioxaphospholan-2-yloxy)ethyl acrylate (**3a**) and 4-(2-oxo-1,3,2-dioxaphospholan-2-yloxy)butyl acrylate (**3b**), which were not isolated, were achieved respectively by the reaction of **2** with **1a** or **1b** in THF in the presence of triethylamine at -20°C for 2h, according to the method of Nguyen Thanh and Chabrier [12]. Products **3a** and **3b** were obtained in nearly quantitative yield and characterized by their IR and ^{1}H NMR spectral data. **3a** and **3b** were reacted with trimethylamine in dry acetonitrile at 50-60°C for 20 h to afford 2-(acryloyloxy)ethyl-2-trimethylammonium)ethyl phosphate (**4a**) and 4-(acryloyloxy)butyl-2-trimethylammonium)ethyl phosphate (**4b**) as white crystalline solids in good yields, respectively. **4a** and **4b** were very hygroscopic and soluble in water, methanol, and DMF, but almost insoluble in acetone, THF, and benzene. The monomers **4a** and **4b** were characterized by their ^{1}H NMR and IR spectral data and elemental analyses.

The monomer **4a** was polymerized with AIBN (0.02 mol-% of the monomer) in methanol at 75°C for 18 h to give the corresponding Poly (**4a**) as a white powder in good yield. Using a procedure similar to that described for the homopolymerizaton of **4a**, the copolymerization of **4a** with some vinyl monomers including 2-hydroxyethyl acrylate, stearyl acrylate, and 1,3-dioleylacylglycerol-2-acrylate were carried out in methanol or a mixture of methanol and chlorobenzene (volume ratio 9/1) at 75°C for 18 h to give Poly (**5**), Poly (**6**) and Poly (**7**) in good yields, respectively. The resulting polymers were characterized by their IR and ^{1}H NMR spectra data. The IR spectra of the resulting polymers showed the disappearance of the absorption bands (1638 cm^{-1}) due to the vinyl double bond in the monomer **4a**. The ^{1}H NMR spectrum showed the absence of the absorption peaks δ = 5 .92 - 6.41 ppm (m; CH_2=CH-, 3H).



1, 3, 4 a: n = 2

1, 3, 4 b: n = 4

Poly (**5**): R = $-CH_2CH_2OH$,

Poly (**6**): R = $-(CH_2)_{17}CH_3$

Poly (**7**): R = $-CH(CH_2-OC(=O)-(CH_2)_7CH=CH(CH_2)_7CH_3)(CH-OC(=O)-(CH_2)_7CH=CH(CH_2)_7CH_3)$

SCHEME 1

The thermal properties of the resulting polymers were studied by polarizing microscopy. The polarization microscopy measurements were carried out with a polarizing microscope with a Yanaco Model MP heating stage. Poly (**4a**) was found to exhibit liquid crystalline behaviors from 118 up to 152°C and was soluble in water, methanol, and DMF, but insoluble in acetone, THF and benzene, whereas Poly (**5**), Poly (**6**) and Poly (**7**) were found to thermally stable up to 250 °C.

In previous works [9, 13,14], we have found that vinyl polymers having phosphatidylcholine in the side chains show the properties of polyelectrolytes in their viscosity behavior in aqueous solution. In contrast with these studies, we have also found that polymers containing phosphatedylcholine analogs in the polymer backbone do not show polyelectrolyte behavior, but show instead a linear increase of reduced viscosity vs. concentration of the polymer [15]. Accordingly, it is very interesting to determine whether the new polymers are polyelectrolytes or not. Therefore, viscosity measurements were performed at 25 °C in the presence and absence of sodium nitrate. Fig.1 shows plots of the reduced viscosity, η_{sp}/c, vs. c for Poly (**4a**) in aqueous solutions, where c is expressed in grams per 100 mL.

In pure water, η_{sp}/c was found to increase rapidly upon dilution, whereas the addition of sodium nitrate eliminates the increase. Thus, Poly (**4a**) shows polyelectrolyte behavior. However, Poly (**5**), Poly (**6**) and Poly (**7**) were unsoluble in water. The monomer **4b** and its homopolymerization and copolymerization are being in progress.

EXPERIMENTAL

Materials

Most of the reagents were commercially obtained and used without further purification. Trimethylamine was prepared by reaction of trimethylamine hydrochloride with 40% sodium hydroxide, following the procedure of Adams and Brown [16]. 2-Chloro-1,3,2-dioxaphospholane, bp 45.5-46.5°C/15 mbar (Ref. 10: bp 45.5-47.0°C/15 mbar, was prepared in 65% yield by the method of Lucas et al.[10]. 2-Chloro-2-oxo-1,3,2-dioxaphopholane (**2**), bp. 102.5-105.0°C/0.4 mbar (Ref. 11: bp 79°C/0.4 mbar), was prepared in 90% yield by oxidation of 2-chloro-1,3,2-dioxaphospholane with oxygen, following the method of Edmundson [11].

2-(2-oxo-1,3,2-dioxaphospholan-2-yloxy)ethyl acrylate (3a)

Into a dried 500 mL three-necked round bottom flask equipped with a mechanical stirrer, drying tube, and dropping funnel were placed 20.0 g (0.172 mol) of 2-hydroxy ethyl acrylate (**1a**) and 20.92 g (0.21 mol) of triethylamine in 300 mL of dry THF. After

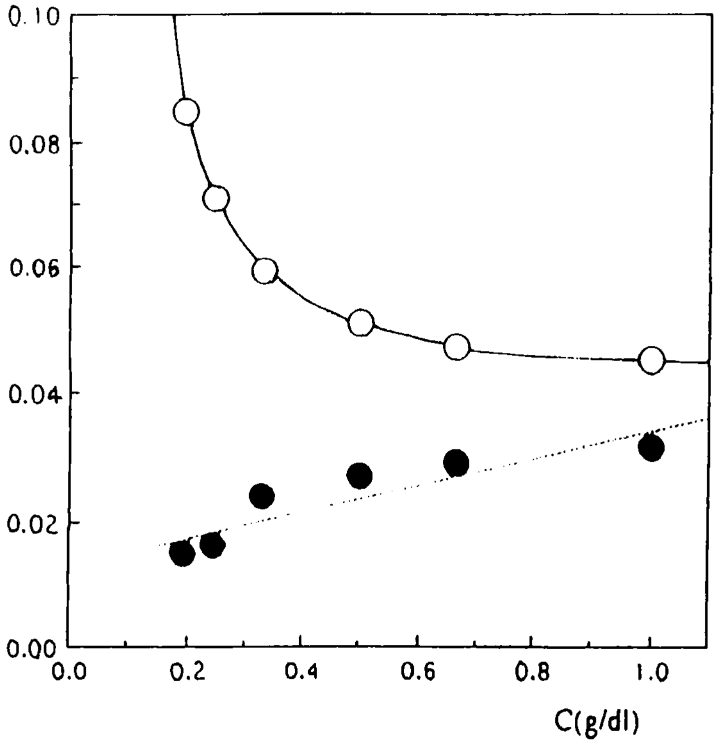


FIG. 1. Reduced viscosity of poly (**4a**) in aqueous solutions at 25 °C; (O) in pure water; (●) in 0.05 mol / L $NaNO_3$.

cooling the solution in a dry ice/methanol bath (-20 °C), 24.51 g (0.172 mol) of 2-chloro-2-oxo-1,3,2-dioxaphospholane (**2**) was slowly added to the stirred solution over a period of 1 h, triethylamine hydrochloride began to precipitate from the solution. The reaction mixture was maintained at -20 to -15 °C during the addition, After being kept at this temperature for 2 h, and then allowed to warm up to room temperature forl h. The precipitate formed was filtered off and washed with 30 mL of THF. The filtrate and the THF solutions were evaporated in vacuum in a stream of nitrogen for 2 h to give **3a** as colorless viscous liquid. Yield: 37.5 g (98%).

IR(neat) : 1720 (C=O), 1638 (C=C), 1240 (P=O), and 1080 cm^{-1} (-PO-CH_2-).

^{1}H NMR ($CDCl_3$) : δ = 3.80-4.50 (m; -CH_2-, 8H), 5.92, 6.12 and 6.38 ppm (m; CH_2=CH-, 3H).

4-(2-oxo-1,3,2-dioxaphospholan-2-yloxy)butyl acrylate (3b)

Using the similar procedure described for preparing **3a**, **3b** was prepared by the reaction of 4-hydroxy butyl acrylate (**1b**) with 2-chloro-2-oxo-1,3,2-dioxaphospholane (**2**) . Yield: (97%).

IR(neat) : 1720 (C=O), 1638 (C=C), 1240 (P=O), and 1080 cm^{-1} (-PO-CH$_2$-).

^{1}H NMR (CDCl$_3$) : δ = 1.72 (m; -CH$_2$CH$_2$-, 4H), 3.80-4.50 (m; -CH$_2$-, 8H), 5.92, 6.12 and 6.38 ppm (m; CH$_2$=CH-, 3H).

2-(acryloyloxy)ethyl-2-trimethylammonium)ethyl phosphate (4a)

Into a 300 mL glass pressure bottle (Top Model E 1435. Type A) were placed 30.0 g (0.13 mol) of **3a** and 100 mL of dry acetonitrile. 30.7 g (0.52 mol) of trimethylamine was rapidly added to the solution. The pressure bottle was closed and then shaken in a thermostat maintained at 50-60 °C for 20 h. After it had been allowed to cool to 0 °C, the pressure bottle was opened, and the solution was condensed to give a caramel product. The crude product was dissolved in methanol and reprecipitated from acetone, which crystallized on standing in a freezer for several days. Pure **4a** as a white solid; mp 20 °C, 25.6 g (70%).

IR(neat) : 1720 (C=O), 1638 (C=C), 1240 (P=O), and 1080 cm^{-1}(PO-CH$_2^-$).

^{1}H NMR (CDCl$_3$ and CD$_3$OD): δ = 3.12 [s; -N$^+$(CH$_3$)$_3$, 9H], 3.57(t; -CH$_2$N$^+$, 2H), 4.06-4.31(m; POCH$_2$-, OCH$_2$CH$_2$OP-, 6H), 5.92, 6.12, and 6.38 ppm (m; CH$_2$=CH-, 3H).

Analysis: Calculated for $C_{10}H_{20}NO_6P$ (281.3): C, 42.70; H, 7.17; N, 4.98%; Found: C, 42.58; H, 7.22; N, 4.57%

4-(acryloyloxy)butyl-2-trimethylammonium)ethyl phosphate (4b)

Using a similar procedure described for preparing **4a**, **4b** was prepared by the reaction of **3b** with trimethylamine. Yield: (72%).

IR(neat) : 1720 (C=O), 1638 (C=C), 1240 (P=O), and 1080 cm^{-1}(PO-CH$_2^-$).

^{1}H NMR (CDCl$_3$ and CD$_3$OD): δ = 1.72 (m; -CH$_2$CH$_2$-, 4H), 3.12 [s; -N$^+$(CH$_3$)$_3$, 9H], 3.57(t; -CH$_2$-N$^+$, 2H), 4.06-4.31(m; POCH$_2$-, OCH$_2$CH$_2$OP-, 6H), 5.92, 6.12, and 6.38 ppm (m; CH$_2$=CH-, 3H).

Analysis: Calculated for $C_{12}H_{24}NO_6P$ (309.3): C,46.60; H, 7.82; N, 4.53%; Found: C, 46.61; H, 7.36 N, 4.60%

Polymerization procedure

The homopolymerization of monomer **4a** and copolymerization of monomer **4a** with 2-hydroxyethyl acrylate in methanol, stearyl acrylate and 1,3-dioleylacylglycerol-2-

acrylate in a mixture of methanol and chlorobenzene (volume ratio 9:1) were carried out with AIBN (0.02 mol-% of the monomer) as initiator in a sealed ampoule with shaking at 75°C. After shaking for 18h, the ampoules were opened and the contents were poured into a large excess of acetone to give white products Poly(**4a**) and Poly(**5**), Poly(**6**), and Poly(**7**), respectively. The resulting polymers, Poly(**4a**), Poly(**6**), and Poly(**7**) were purified by reprecipitation from methanol solution with acetone. Poly(**5**) was washed with methanol. The IR spectra of the resulting polymers showed the disappearance of the absorption bands at 1630 cm^{-1} due to the acrylic C=C double bonds in the monomer **4a** but otherwise the spectra remained unchanged. ^{1}H-NMR spectra of polymers also showed the absence of chemical shift at 5.92, 6.15, and 6.41 owing to the C=C double bonds.

Physical measurements

The ^{1}H NMR and IR measurement were carried out on a 400 MHz alpha FT NMR α-400 and a Jasco A 202 spectrometers. The polarization microscopy measurements were carried out with a polarizing microscope with a Yanaco Model MP heating stage.

CONCLUSION

2-(Acryloyloxyl)ethyl-2-(trimethylammonium)ethyl phosphate (**4a**) and 4-(acryloyloxyl)butyl-2-(trimethylammonium)ethyl phosphate (**4b**) were prepared and characterized by their IR and ^{1}H NMR spestral data and elemental analyses. **4a** was homopolymerized and compolymerized with 2-hydroxyethyl acrylate, stearyl acrylate, and 1,3-dioleylacylglycerol-2-acrylate using 2,2'-azoisobutyronitrile (AIBN) as initiator. Poly (**4a**) of the resultant polymers exhibited liquid crystalline behaviors from 118 up to 152°C observed by a polarization microscopy. Moreover, the water-soluble polymer, poly (**4a**), among the resulting polymers showed a polyelectrolyte behavior from its viscosity measurement.

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