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SHORT COMMUNICATIONS

Synthesis and Polymerization of Macromonomer Having a Phospholipid Polar Group

Tsutomu OISHI,† Hirohito YAMASAKI,* Hiromi KADA,*
Kenjiro ONIMURA, Hiromori TSUTSUMI, and Akio HAYASHI**

Faculty of Engineering Yamaguchi University,
2-16-1 Tokiwadai, Ube, Yamaguchi 755-8611, Japan
**Ube National College of Technology,*
2-14-1 Tokiwadai, Ube, Yamaguchi 755-8555, Japan
***Tsukuba Research Laboratory, Nippon Oil & Fats Co. Ltd.,*
5-10 Tokodai, Tsukuba, Ibaraki 300-2635, Japan

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The excellent biocompatibility of a phosphorylcholine moiety has been confirmed.[1—7] The introduction of phosphorylcholine groups into a polymer surface is useful for improvement of protein adsorption-resistance properties. There are papers on the polymerization of 2-methacryloyloxyethyl phosphorylcholine (MPC), its derivatives and relative compounds.[1—9] In these papers the synthesis and polymerization of a macromonomer bearing oligo(MPC) have been reported by Ishihara and coworkers.[7]

To obtain more easily macromonomers bearing phospholipid polar groups, the authors adopted reaction of amino group terminated oligo(MPC) with a vinyl monomer bearing an isocyanate group instead of the reaction of carboxyl group with epoxy group. We obtained easily a macromonomer as follows.

A macromonomer bearing a phospholipid polar group was synthesized by a two-step reaction, as shown in Figure 1. MPC was polymerized in the presence of 2-aminoethanethiol ($NH_2CH_2CH_2SH$, AET) as a chain transfer agent to obtain amino group terminated oligo(MPC). The oligo(MPC) reacted with methacryloyloxyethyl isocyanate (MOI), supplied by SHOWA DENKO K. K., to convert an amino group to a polymerizable methacryloyl group in the presence of di-*n*-butyltin dilaurate (BTL) in water. The MPC macromonomer was radically copolymerized with butyl methacrylate (BMA) to obtain corresponding copolymers which were characterized by ^{1}H NMR and FT-IR analyses.

SYNTHESIS OF OLIGO(MPC)

Desired amounts of MPC and 2,2′-azobisisobutyronitrile (AIBN) were dissolved in ethanol, and AET was added to the solution. The mixture was put into a sealed test tube with a stirrer and degassed with dry nitrogen gas for three times to remove oxygen in the mixture. The polymerization was carried out at 60℃ for 6 h with stirring. The reaction mixture was poured into excess chloroform to precipitate oligo(MPC) prepared. The oligo(MPC) was purified by reprecipitation from the ethanol solution into excess chloroform twice. Oligo MPC was dried *in vacuo* at room temperature.

The molecular weights of products were determined by gel permeation chromatography (GPC). GPC (Tosoh system 8020 series with columns, Shodex OH pack SB 806 MHQ and Shodex OH pack SB802 5HQ) was used to estimate the number-average (M_n) and weight-average (M_w) molecular weights of the oligo(MPC) with poly(ethyleneglycol) standards in water. The synthetic results of oligo(MPC) are summarized in Table I. Oligo(MPC)s having different molecular weights were obtained. Molecular weight was controlled by concentrations of monomer, chain transfer reagent and initiator. The existence of amino group at the polymer end was confirmed by ^{1}H NMR measurement of the product obtained by reaction of amino group terminated oligo(MPC) with *p*-tolyl isocyanate. The product exhibited characteristic peaks assigned to aromatic protons of phenyl group around 7.2 ppm in the ^{1}H NMR spectrum.

SYNTHESIS OF MPC MACROMONOMER

A MPC macromonomer was synthesized by reaction of amino group terminated oligo(MPC) with an isocyanate group of MOI in the presence of BTL as catalyst. Organic synthesis reactions of (6-*O*-α-D-glucopyranosyl)-D-fructofuranose with MOI in water reported by Joachim Klein *et al.*[10] were carried out with this polymer reaction of oligo(MPC) with MOI in water. A typical reaction was as follows. The oligo(MPC) (2 g) having M_n of 19000 was dissolved in water (50 mL) at controlled pH 10.5 — 11 by NaOH aq. solution. The solution was put into a 100 mL egg-plant type flask with a magnetic stirrer and cooled to −3℃. After MOI (2 g) was added to the solution with a very small amount of BTL, the solution was kept below 0℃ for 24 h with vigorous stirring. The reaction mixture was raised to room temperature and poured into excess acetone to precipitate. The precipitate was stirred for 1 day in acetone to remove non-reacted MOI and the cata-

† To whom all correspondence should be addressed.

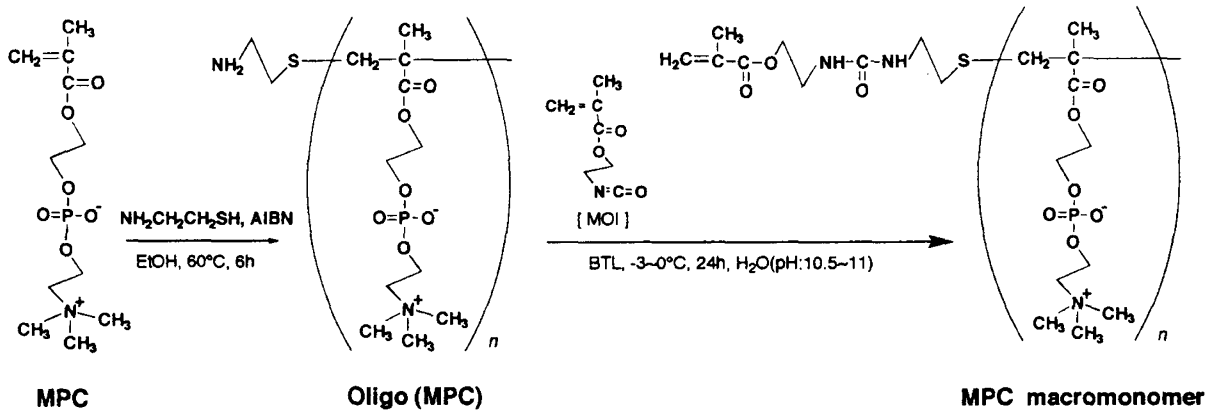

Figure 1. Synthetic pathway of MPC macromonomer.

Table I. *Synthetic results of oligo(MPC) for radical polymerization in ethanol for 6 h at 60℃*

run	Molar ratio in feed	Weight in feed			Yield			
	MPC : AET[a] : AIBN ($\times 10^3$ mol) : ($\times 10^4$ mol) : ($\times 10^4$ mol)	MPC (g)	AET[a] $\times 10^2$(g)	AIBN $\times 10^2$(g)	g (%)	M_n[b] $\times 10^{-4}$	M_w[b] $\times 10^{-4}$	M_w / M_n[b]
1	100 : 15 : 4 (3.4) : (5.1) : (1.4)	1.0	3.9	2.2	0.85 (85.3)	0.4	0.5	1.3
2	100 : 10 : 2 (17) : (17) : (3.4)	5.0	13	5.6	3.38 (67.6)	1.9	3.8	2.0
3	100 : 5 : 1 (3.4) : (1.7) : (0.3)	1.0	1.3	0.56	0.83 (83.3)	7.3	19.9	2.7
4	100 : 10 : 2 (3.4) : (3.4) : (0.7)	1.0	2.6	1.1	0.61 (60.5)	0.9	1.6	1.8

[a] AET : aminoethanethiol. [b] By GPC using poly(ethyleneglycol) standard in H_2O.

lyst. The MPC macromonomer was filtered off and lyophilized (yield 0.9 g, 46%).

Chemical structure of MPC macromonomer was confirmed by ^{1}H NMR (JEOL, EX-270). The ^{1}H NMR spectra of the macromonomer were measured in D_2O, as shown in Figure 2. Peaks assigned to olefinic protons (1′) and methyl protons (2′) of methacryloyl appeared at 5.72 and 6.15 ppm and about 1.88 ppm, respectively. Other peaks assigned to MPC units coincided with the integrated intensity.

SYNTHESIS OF COPOLYMER

To confirm the existence of reactive double bond group at the polymer end, we polymerized MPC macromonomer with a vinyl monomer. The MPC macromonomer was radically copolymerized with butyl methacrylate (BMA) to obtain the corresponding copolymer. MPC macromonomer (0.31 g), BMA (0.6 g) and AIBN (0.055 g) were dissolved in a mixture of ethanol (3 mL) and tetrahydrofuran (THF) (0.5 mL). The mixture was placed in a sealed tube with a stirrer and degassed with dry nitrogen gas three times. Copolymerization was carried out at 60℃ for 24 h. The reaction mixture was poured into excess acetone to precipitate copolymers. The precipitate was filtered off and stirred for 1 day in water to remove non-reacted MPC macromonomer. The residue was filtered off as the copolymer and dried *in vacuo* at 60℃ (yield 0.08 g, 9.0%). Chemical structure of the copolymer was confirmed by FT-IR (JEOL, Diamond-20) using by

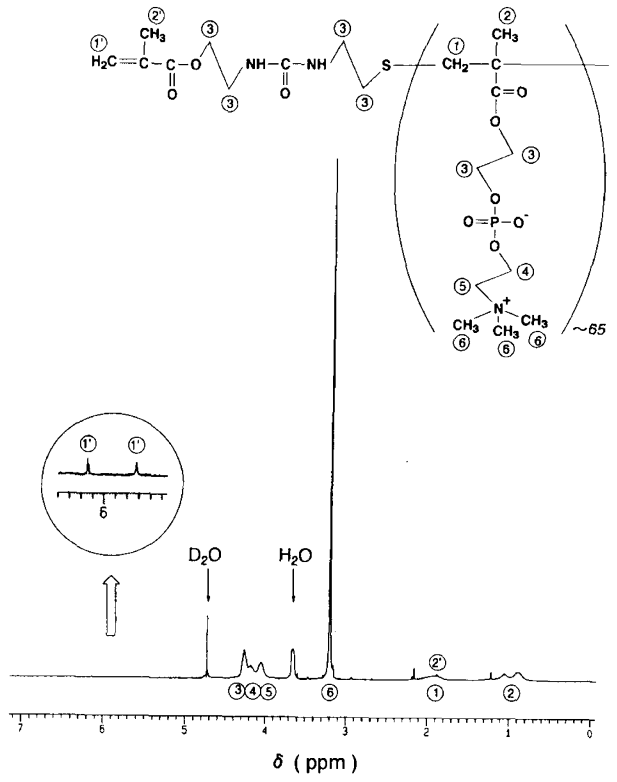

Figure 2. ^{1}H NMR spectrum of MPC macromonomer (run 2 in Table I) in D_2O.

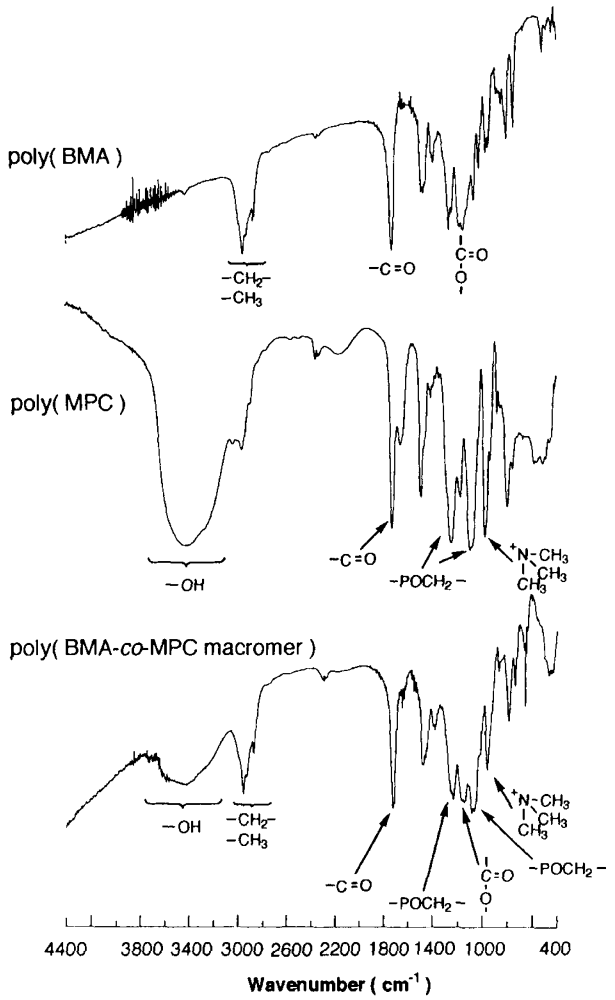

Figure 3. IR spectra of poly(BMA), poly(MPC) and poly(BMA-*co*-MPC macromonomer).

KBr and ^{1}H NMR measurement in CF_3COOD. FT-IR charts indicated the copolymer had characteristic peaks corresponding to poly(MPC) and poly(BMA), as shown in Figure 3. In the IR spectrum of the copolymer, the peaks assigned to -OH (3200—3700 cm^{-1}), $-POCH_2-$ (1240 and 1080), and $-N^+(CH_3)_3$ (970) for MPC, $-CH_3$ and $-CH_2-$ (2800—2950) for BMA, C=O (1730) for MPC and BMA were observed, suggesting that poly(BMA) segments exist in the copolymer. The ^{1}H NMR spectrum of the copolymer is shown in Figure 4. All peaks of the copolymer were assigned to MPC and BMA units. The composition of the copolymer was evaluated as (MPC units) / (BMA units) = 27 / 73 based on the integrated intensity of ^{1}H NMR peaks due to trimethyl groups (9H, 9 in Figure 4) of MPC and two methylene peaks (4H, 4 and 5 in Figure 4) of BMA units. The copolymer is thus clearly composed of MPC macromonomer and BMA units.

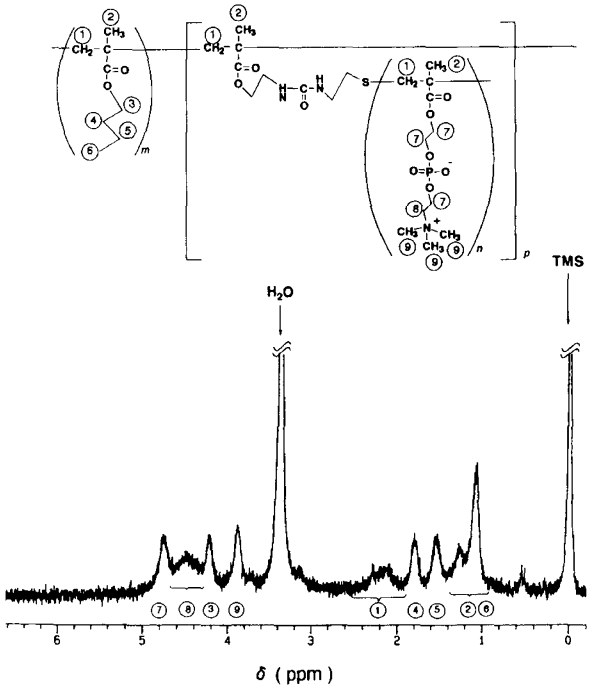

Figure 4. ^{1}H NMR spectrum of poly(BMA-*co*-MPC macromonomer) in CF_3COOD.

Biocompatibility of the copolymers obtained from the macromonomer are presently being examined.

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