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## Preparation and Polymerization of 2-(Phthalimido)ethyl 10'-(Methacryloyloxy)decyl Hydrogen Phosphate

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### ABSTRACT

The preparation and polymerization of 2-(phthalimido)ethyl 10'-(methacryloyloxy)decyl hydrogen phosphate are described. This monomer was polymerized with 2,2'-azobisisobutyronitrile (AIBN). The properties of the resultant polymer are also described.

### INTRODUCTION

Considerable recent interest has centered about phospholipids because they are essential components of biological membranes [1-3]. It therefore seemed of particular interest to prepare vinyl monomers and polymers containing phospholipid analogs. We have made attempts [4-7] in the past few years to prepare such monomers and polymers. In the fourth paper of this series, we reported the synthesis and polymerization of 2-(phthalimido)ethyl 2'-(methacryloyloxy)ethyl

2'-(methacryloyloxy)ethyl hydrogen phosphate which is a valuable precursor for the synthesis of monomer containing a phospholipid analog. In order to provide an improved model compound closely resembling natural phospholipid, we have now prepared 2-(phthalimido)ethyl 10'-(methacryloyloxy)decyl hydrogen phosphate, in which the dimethylene chains of 2-(phthalimido)ethyl 2'-(methacryloyloxy)ethyl hydrogen phosphate are replaced by decamethylene chains to give a more hydrophobic character.

The present paper is concerned mainly with the synthesis and polymerization of 2-(phthalimido)ethyl 10'-(methacryloyloxy)decyl hydrogen phosphate. An attempted dephthaloylation of the resultant polymer with hydrazine hydrate is also described.

## EXPERIMENTAL

### Materials

Methacrylic acid, benzoyl chloride, sebacic acid, benzyl alcohol, phthalic anhydride, monoethanolamine, 2-chloroethanol, and 2,2'-azobisisobutyronitrile (AIBN) were obtained commercially and purified by distillation and recrystallization, respectively. Phosphorus tribromide, silver nitrate, sodium bicarbonate, sodium iodide, and sodium sulfate were reagent grade and used without further purification. Dry barium iodide was prepared by drying commercial  $\text{BaI}_2 \cdot 2\text{H}_2\text{O}$  in an oven at  $120^\circ\text{C}$  for 8 hr. Methacryloyl chloride was prepared by the reaction of methacrylic acid with benzoyl chloride [8]. Diethyl sebacate (I) was prepared by the reaction of sebacic acid with ethanol under acid-catalyzed conditions according to the method of Mićović [9]. The hydrogenation of I with sodium and ethanol gave 1,10-decandiol (II) according to the method of Manske [10]. 10-Hydroxydecyl chloride (III) was obtained by the reaction of II with hydrogen chloride in refluxing ligroin according to the method of Campbell and Sommers [11]. 10-Hydroxydecyl iodide (IV) was prepared by the reaction of III with sodium iodide in refluxing acetone by the usual method.

Silver dibenzyl phosphate, mp  $216^\circ\text{C}$  (lit. [12] mp  $216^\circ\text{C}$ ), was prepared by the reaction of Todd et al. [12]. 2-Bromoethyl phthalimide, mp  $80-82^\circ\text{C}$  (lit. [13] mp  $80-82^\circ\text{C}$ ), was prepared by the reaction of phthalic anhydride with monoethanolamine, followed by treatment with phosphorus tribromide [13]. 2-Iodoethyl phthalimide, mp  $100.5-101.5^\circ\text{C}$  (lit. [14] mp  $100.0-100.5^\circ\text{C}$ ), was prepared from 2-bromoethyl phthalimide and sodium iodide in refluxing acetone by

the method of de Hass and van Deenen [ 14]. Silver 2-(phthalimido) ethyl benzyl phosphate, mp 201-203° C (lit. [ 15] mp 198-203° C), was prepared by the method of van Deenen et al. [ 15]. All other reagents were commercially supplied and were purified by the usual methods.

### 10-Iododecyl Methacrylate (V)

In a four-necked round-bottomed flask (100 ml) equipped with a mechanical stirrer, a dropping funnel, a thermometer, and a reflux condenser were placed 10-hydroxydecyl iodide (IV) (28.4 g, 100 mmole), pyridine (9.5 g, 120 mmole), and chloroform (300 ml). The solution was cooled in an ice bath to 5° C, and methacryloyl chloride (10.4 g, 110 mmole) in chloroform (100 ml) was slowly added over a period of 1.5 hr under stirring, the temperature being held at 5° C. After being kept at this temperature for further 2 hr with stirring, the reaction mixture was allowed to stand overnight at this temperature. A 50-ml portion of water was added to the mixture. The organic layer was washed three times with H<sub>2</sub>O, dilute HCl, aqueous NaHCO<sub>3</sub>, H<sub>2</sub>O, and was then dried over anhydrous MgSO<sub>4</sub>. The dried organic layer was concentrated at reduced pressure, and the residue was distilled under reduced pressure to give 21.8 g (62%) of V, bp 150-152 C/1 Torr.

IR (neat) showed absorptions at 1710 (C=O) and 1630 cm<sup>-1</sup> (C=C).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) showed  $\delta$  = 1.30 (m, -CH<sub>2</sub>-, 16H), 1.95 (s, -CH<sub>3</sub>, 3H), 3.28 (t, -CH<sub>2</sub>I, 2H), 4.14 (t, -OCH<sub>2</sub>-, 2H), 5.55 (m, -CH=, 1H), and 6.11 ppm (s, -CH=, 1H).

Analysis: Calcd for C<sub>14</sub>H<sub>25</sub>O<sub>2</sub>I: C, 47.74%; H, 7.15%. Found: C, 48.39%; H, 7.15%.

### 2-(Phthalimido)ethyl 10'-Methacryloyloxydecyl Benzyl Phosphate (VI)

Silver 2-(phthalimido)ethyl benzyl phosphate (5.6 g, 12 mmole) and a Teflon-covered magnetic stirring bar were placed in a round-bottomed brown colored flask (300 ml) equipped with a reflux condenser and a dropping funnel. The mixture was vigorously stirred at room temperature for 15 min. To the stirred solution, 2-iodoethyl methacrylate (3.5 g, 10 mmole) in benzene (50 ml) was rapidly added in the dark. Thereaction mixture was refluxed for 8 hr and was then allowed to come to room temperature while protected from light. The silver iodide formed and unreacted silver 2-(phthalimido)ethyl benzyl phosphate were filtered off and washed with benzene (30 ml). The filtrate

and washing benzene were washed with water (50 ml). To the organic layer, small amounts of charcoal and anhydrous  $\text{Na}_2\text{SO}_4$  were added. The mixture was shaken for 10 min and was then allowed to stand overnight. It was filtered with a close filter paper to remove a small amount of silver iodide, charcoal, and  $\text{Na}_2\text{SO}_4$ . The filtrate was evaporated in vacuo with a stream of nitrogen for 10 hr to give 5.2 g (89%) of a colorless viscous liquid. By its IR and  $^1\text{H-NMR}$  spectra and its elemental analysis, it was identified as VI.

Analysis: Calcd for  $\text{C}_{31}\text{H}_{40}\text{O}_8\text{NP}$ : C, 63.58%; H, 6.88%; N, 2.39%. Found: C, 62.85%; H, 6.96%; N, 2.28%.

Barium 2-(Phthalimido)ethyl 10'-Methacryloyloxydecyl Phosphate (VIII)

2-(Phthalimido)ethyl 10'-methacryloyloxydecyl benzyl phosphate (VI) (5.0 g, 8.5 mmole), acetone (100 ml) and a Teflon-covered magnetic stirring bar were placed in a round-bottomed flask (300 ml) equipped with a reflux condenser and a dropping funnel. To the stirred solution, dry barium iodide (3.3 g, 8.5 mmole) in acetone (200 ml) was added under stirring at room temperature for 10 min. The mixture was refluxed with stirring for 7 hr, then being allowed to come to room temperature. The solution was evaporated in vacuo with a stream of nitrogen at room temperature. The residue was dissolved in hot water (300 ml) and was then allowed to come to room temperature. The solution was washed five times with diethyl ether (50 ml) to remove benzyl iodide. To the water layer, a small amount of charcoal was added. The mixture was shaken and was then allowed to stand overnight. The mixture was filtered with a tight filter paper. The filtrate was evaporated in vacuo with a stream of nitrogen at room temperature to give 2.3 g (48%) of VII as a pale yellow solid, mp  $181^\circ\text{C}$ .

IR (KBr) showed absorptions at 1770, 1700 (phthalimido  $\text{C}=\text{O}$ ), 1720 (ester  $\text{C}=\text{O}$ ), 1630 ( $\text{C}=\text{C}$ ), 1270, 1230, and  $1070\text{ cm}^{-1}$  ( $\text{O}=\text{P}-\text{O}^-$ ).

2-(Phthalimido)ethyl 10'-Methacryloyloxydecyl Hydrogen Phosphate (VIII)

Barium salt (VII) (2.0 g, 1.2 mmole) was dissolved in distilled water (100 ml) and methanol (100 ml). To the solution, a cation-exchange resin (Amberlite IR-120 B) (30.0 g) was added. The mixture was stirred at  $55^\circ\text{C}$  for 7 hr, and stirring was continued at room temperature for additional 12 hr. The resin was filtered off and washed with

distilled water (50 ml) and then methanol (50 ml). The filtrate and washing water and methanol were extracted with six 50-ml portions of chloroform. To the organic layer, a small amount of charcoal and anhydrous  $\text{Na}_2\text{SO}_4$  were added. After shaking for 10 min, the mixture was allowed to stand overnight. Then, the charcoal and  $\text{Na}_2\text{SO}_4$  were filtered out. The filtrate was evaporated in vacuo with a stream of nitrogen at room temperature to give 1.5 g (85%) of cloudy oil. By its IR and  $^1\text{H-NMR}$  spectra and its elemental analysis, it was identified as VIII.

Analysis: Calcd for  $\text{C}_{24}\text{H}_{34}\text{O}_8\text{NP}$ : N, 2.84%. Found: N, 2.47%.

#### Polymerization of 2-(Phthalimido)ethyl 10'-Methacryloyloxydecyl Hydrogen Phosphate (VIII)

The polymerization of 2-(phthalimido)ethyl 10'-methacryloyloxydecyl hydrogen phosphate (VIII) was carried out in DMF with AIBN as an initiator. A solution of VIII (0.81 g, 1.63 mmole), AIBN (3.03 mg, 0.185 mmole), and DMF (10 ml) were mixed in a glass tube which was flushed three times with nitrogen, sealed in vacuo, and then shaken at 60°C. After 4.5 hr, the contents of the tube were poured an excess of diethyl ether by which the polymer precipitated. It was purified by reprecipitation from chloroform solution with diethyl ether. The yield was 0.75 g (93%) of a white sticky polymer. It was soluble in DMF and chloroform, but almost insoluble in diethyl ether. Its infrared spectrum (Fig. 2) showed the disappearance of the absorption ( $1630\text{ cm}^{-1}$ ) due to the methacrylic double bond in the monomer.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) showed  $\delta = 0.98$  (s,  $-\text{CH}_3$ , 3H), 1.28 (m,  $-\text{CH}_2-$ , 18H), 3.70-4.40 (m,  $-\text{OCH}_2-$ ,  $=\text{NCH}_2-$ , 8H), 7.83-7.85 (m, phthalimido ring protons, 4H), and 11.5 ppm (s,  $-\text{OH}$ , 1H).

#### Hydrazinolysis of the Polymer Obtained

Poly(VIII) (0.70 g) was dissolved in dry chloroform (10 ml) and absolute ethanol (40 ml). To this solution, hydrazine hydrate was added slowly until the solution was adjusted to pH 8. The solution was refluxed for 4 hr, by which procedure a white precipitate was formed from the solution, and was then allowed to come to room temperature. The reaction mixture was acidified to about pH 6 by the addition of 37% formic acid, by which procedure an additional precipitate was formed. The white mass was washed successively with water, methanol, and chloroform by decantation. Then, the mass

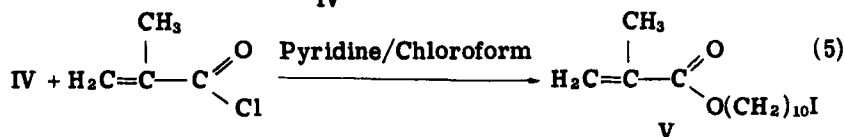
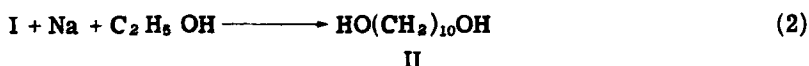
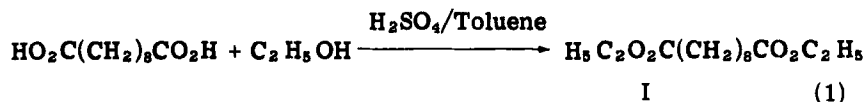
was extracted with acetic acid (20 ml), leaving a pale yellow gum. The acetic acid was removed under reduced pressure. The residue was crystallized from acetic acid to separate 0.2 g of diketophthaladine as white crystals, sublimating at about 200°C (lit. [16], sublimation point 200°C), identified with an authentic sample by comparison of IR spectra. The gummy polymeric material was almost insoluble in water as well as common organic solvents such as ethanol, benzene, acetone, chloroform, THF, DMF, and DMSO. Its IR spectrum (KBr) showed no absorption band (1770 cm<sup>-1</sup>) due to phthalimido group. Attempts to characterize it otherwise were unsuccessful.

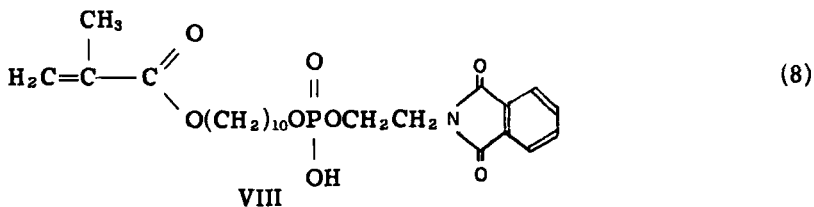
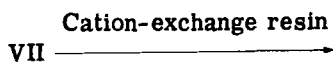
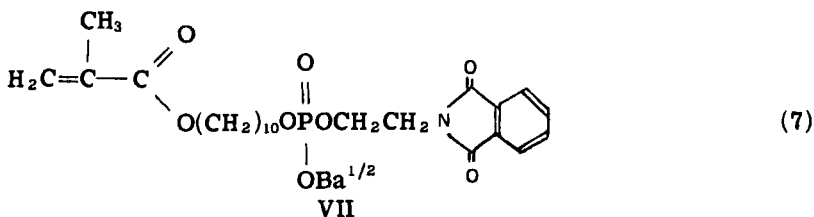
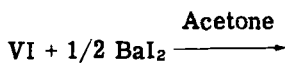
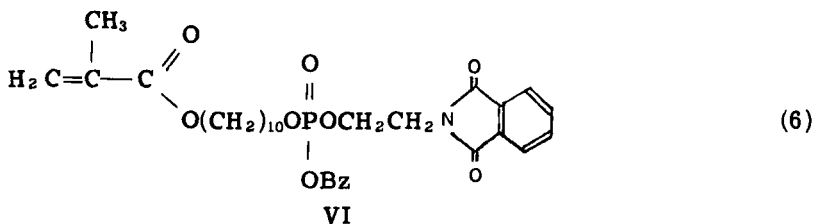
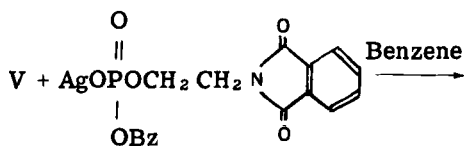
### Physical Measurements

The <sup>1</sup>H-NMR and IR spectra were recorded on a 60 MHz Hitachi-Perkin Elmer Model R-20 NMR spectrometer and a Jasco Model IR-G IR spectrometer, respectively. The <sup>1</sup>H-NMR chemical shifts were expressed in δ values in ppm downfield relative to TMS as internal standard.

## RESULTS AND DISCUSSION

The synthesis of 2-(phthalimido)ethyl 10'-methacryloyloxydecyl hydrogen phosphate (VIII) was performed through the steps shown in Eqs. (1)-(8).





Acid-catalyzed esterification of commercially available sebacic acid with ethanol gave diethyl sebacate (I) according to the procedure of Mićović [9]. The ester was readily reduced to 1,10-decanediol (II) with sodium and ethanol according to the method of Manske [10]. The treatment of the diol with hydrogen chloride in ligroin afforded



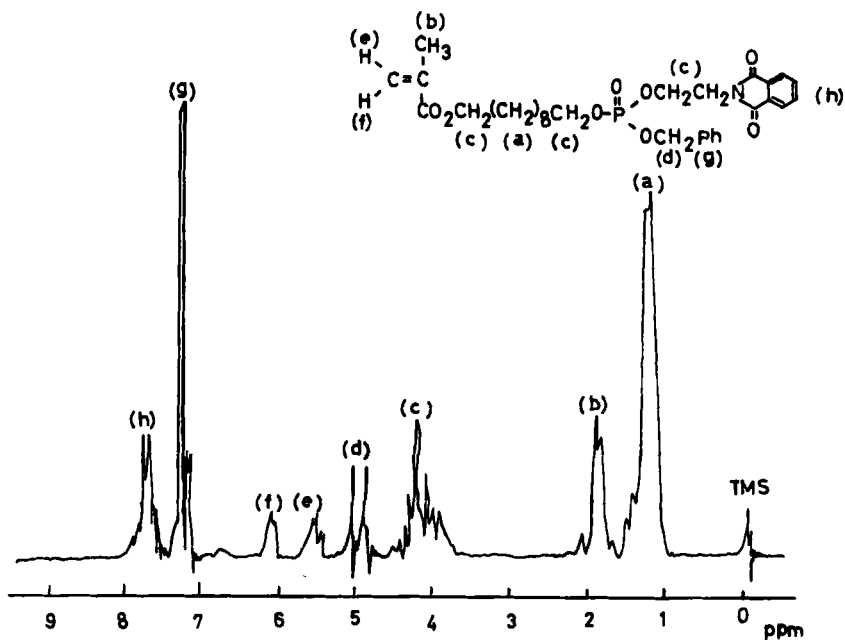


FIG. 1.  $^1\text{H-NMR}$  spectrum of 2-(phthalimido)ethyl 10'-methacryloyloxydecyl benzyl phosphate (VI) in  $\text{CDCl}_3$ ; TMS (tetramethylsilane) as internal standard.

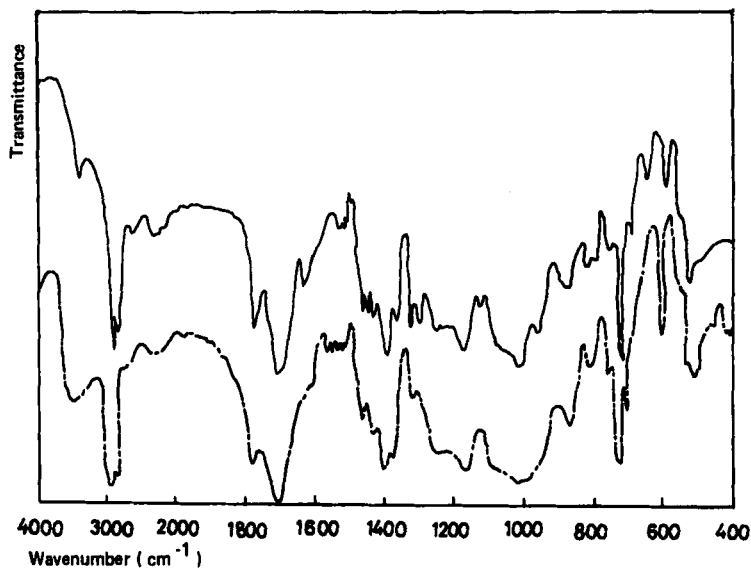


FIG. 2. Infrared spectra of (—) 2-(phthalimido)ethyl 10'-methacryloyloxydecyl hydrogen phosphate (VIII) (neat) and (---) poly(VIII) (film).

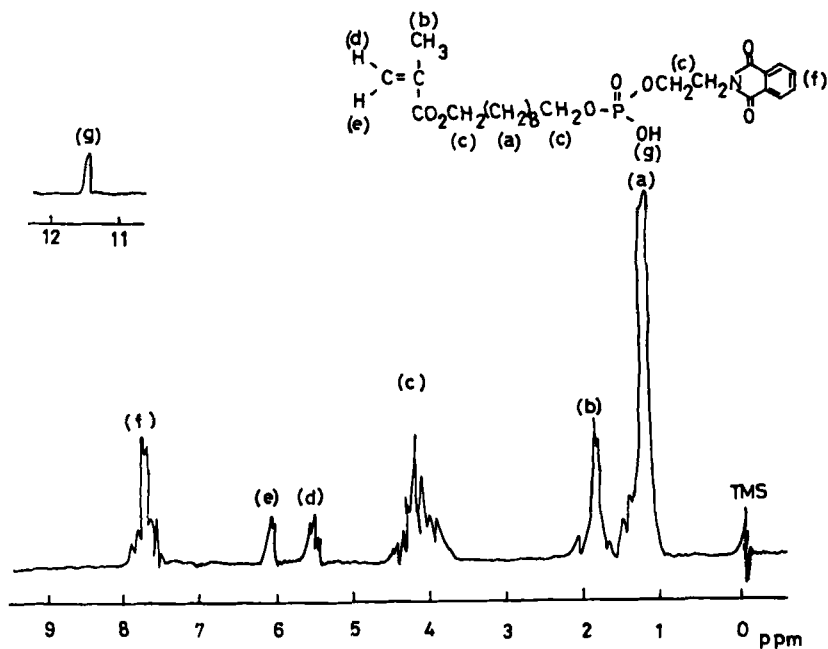


FIG. 3. <sup>1</sup>H-NMR spectrum of 2-(phthalimido)ethyl 10'-methacryloyloxydecyl hydrogen phosphate (VIII) in CDCl<sub>3</sub>; TMS (tetramethylsilane) as internal standard.

10-hydroxydecyl chloride (III) following the method of Campbell and Sommers [11]. III was subsequently converted into 10-hydroxydecyl iodide (IV) by reacting with sodium iodide in refluxing acetone. 10-Iododecyl methacrylate (V) was obtained in 62% yield by the reaction of IV with methacryloyl chloride in chloroform in the presence of pyridine and characterized by IR and <sup>1</sup>H-NMR spectroscopy and elemental analysis. The synthesis of 2-(phthalimido)ethyl 10'-methacryloyloxydecyl benzyl phosphate (VI) was carried out by using essentially the same experimental conditions and was described previously [7]. Thus, VI was prepared from V and silver 2-(phthalimido)ethyl benzyl phosphate [15] in 89% yield and characterized by its IR and <sup>1</sup>H-NMR (Fig. 1) spectra.

The reaction of VI with barium iodide in refluxing acetone afforded the corresponding barium 2-(phthalimido)ethyl 10'-methacryloyloxydecyl phosphate (VII) in 48% yield as a pale yellow solid, which was soluble in hot ethanol and slightly soluble in water. The subsequent treatment of the barium salt with a cation-exchange resin (Amberlite

IR-120 B) gave 2-(phthalimido)ethyl 10'-methacryloyloxydecyl hydrogen phosphate (VIII) in 85% yield as a cloudy oil. The characterization of VIII was based on its IR (Fig. 2) and  $^1\text{H-NMR}$  (Fig. 3) spectra and elemental analysis.

VIII was polymerized in DMF at  $60^\circ\text{C}$  for 4.5 hr by AIBN to give a white polymer in good yield. Its IR spectrum (Fig. 2) showed the disappearance of the absorption bands ( $940$  and  $1640\text{ cm}^{-1}$ ) due to the methacrylic double bond in the monomer, but the spectrum was otherwise unchanged. In its  $^1\text{H-NMR}$  spectrum, the absorptions ( $\delta = 5.50$  and  $6.10$  ppm) due to the terminal vinyl methylene protons in the monomer disappeared. The polymer was soluble in DMF and chloroform, but insoluble in diethyl ether.

Dephthaloylation of the polymer was attempted by heating with hydrazine hydrate in ethanolic chloroform followed by treatment with 37% formic acid to afford diketophthalazine and a gummy polymeric material, which was identified.

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