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POLYMERIC PHOSPHOLIPID ANALOGS. XXV. PREPARATION AND POLYMERIZATION OF *p*-VINYLBENZYL-2-(TRIMETHYLAMMONIUM) ETHYL PHOSPHATE

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ABSTRACT

The preparation and polymerization of *p*-vinylbenzyl-2-(trimethylammonium)ethyl phosphate are described. This monomer was polymerized with 2,2′-azobisisobutyronitrile (AIBN). The properties of the resultant polymer are described.

INTRODUCTION

Considerable attention has recently been paid to the phospholipids because they are known to be important building units of biological membranes [1, 2]. From this point of view, it seemed attractive to investigate the behavior of polymeric phospholipid analogs. In recent years, numerous reports [3-8] have appeared concerning the synthesis and properties of vinyl polymers having phosphatidylethanolamine and choline analogs in the side chains and poly-

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acrylate backbones. The polyacrylate backbones are weak toward acid or base. Thus, it appeared desirable to prepare such vinyl polymers with polystyrene backbones. The present paper is mainly concerned with the synthesis and polymerization of *p*-vinylbenzyl-2-(trimethylammonium)ethyl phosphate.

EXPERIMENTAL

Materials

Triethylamine, ethylene glycol, phosphorus trichloride, and phenylethyl alcohol were commercially obtained and purified by distillation. Methanol and ethanol were distilled in the presence of magnesium methoxide and magnesium ethoxide to ensure dryness. Benzene, dichloromethane, and acetonitrile were dried by distillation from phosphorus pentoxide. Diethyl ether was distilled from lithium aluminum hydride to ensure dryness. All solvents were dried over Molecular Sieves (Nakarai Chemicals, M4M7034). AIBN was purified by two recrystallizations from 1:1 ethanol-water.

2-Chloro-1,3,2-dioxaphospholane, bp 45.5-46.5°C/15 torr (Ref. 12, 45.5-47.0°C/torr), was prepared in 66% yield by reaction of ethylene glycol with phosphorus trichloride in dichloromethane, according to the method of Lucas et al. [12]. 2-Chloro-2-oxo-1,3,2-dioxaphospholane, bp 103.5-105.0°C/1 torr (Ref. 13, bp 79°C/0.4 torr), was prepared in 90% yield by oxidation of 2-chloro-1,3,2-dioxaphospholane with oxygen, according to the method of Edmundson [13].

Phenylethylbromide (II), bp 94-96°C/11 torr (Ref. 9, bp 95-97°C/11 torr), was prepared by heating phenylethyl alcohol (I) with 37% hydrobromic acid, according to the method of Kondo et al. [9]. The chloromethylation of II by use of paraformaldehyde and hydrogen chloride in carbon disulfide in the presence of zinc chloride gave a mixture of *ortho* and *para* isomers, of which two recrystallizations from petroleum ether gave the pure *para* isomer (III), mp 48.0-50.5°C (Ref. 9, mp 48-50°C), following the method of Kondo et al. [9].

p-(β-Bromoethyl)benzyl acetate (IV), bp 138-139°C/2 torr, was prepared in 85% yield by reaction of II with potassium acetate in refluxing acetic acid for 11 h, according to the procedure of Abramo et al. [10]. *p*-Vinylbenzyl alcohol (V), mp 24-25°C (Ref. 10, mp 24°C), was prepared by reaction of IV with sodium hydroxide in refluxing ethanol in the presence of a small amount of hydroquinone, according to the procedure of Abramo et al. [10].

Oxygen, potassium acetate, and trimethylamine hydrochloride were commercially obtained and used without further purification. Trimethylamine was prepared by the reaction of trimethylamine hydrochloride with 40% sodium hydroxide by the procedure of Adams et al. [14].

2-(*p*-Vinylbenzyl)-2-oxo-1,3,2-dioxaphospholane (VI)

Into a dried 300-mL three-necked round-bottom flask, equipped with a mechanical stirrer, a dropping funnel, and a condenser attached to a calcium chloride drying tube, was placed 12.0 g (0.09 mol) V and 9.0 g (0.09 mol) triethylamine in 150 mL dry ethyl ether. After cooling the solution in a Dry Ice/methanol bath (-20°C), 12.8 g (0.09 mol) 2-chloro-2-oxo-1,3,2-dioxaphospholane was added slowly to the stirred solution over a period of 0.5 h, by which procedure triethylamine hydrochloride began to precipitate from the solution. The reaction mixture was maintained at -15 to -5°C during the addition and then allowed to warm up to 5-15°C. After being kept at this temperature for 1.5 h, the precipitate formed was filtered off and washed with 50 mL dry diethyl ether. The filtrate was evaporated *in vacuo* in a stream of nitrogen for 1 h to give Product VI as a white viscous liquid in quantitative yield.

IR (neat) showed absorptions at 2970 (CH_2), 1630 (C=C), 1610, 1510 (phenyl), 1290, 1030 (P=O), and 925 cm^{-1} (P–OCH_2–).

^{1}H-NMR ($CDCl_3$) showed δ = 4.00-4.55 (m; –CH_2–, 4H), 5.05-5.25 (d; –CH_2–, 2H), 5.23-5.90 (q; =CH_2, 2H), 6.50-7.00 (q; –CH=, 1H), and 7.15-7.45 (d; aromatic ring protons, 4H).

p-Vinylbenzyl-2-(trimethylammonium)ethyl Phosphate (VII)

Into a 300-mL glass pressure bottle (Top Model E 1435, Type E) were placed 21.5 g (0.089 mol) VI and 100 mL acetonitrile. After the pressure bottle was cooled in cold water, 5.3 g (0.089 mol) of trimethylamine was rapidly added to the cold solution. The pressure bottle was closed and then shaken in a thermostat maintained at 50°C for 17 h. After the reaction, it was cooled down in cold water to 10°C. After it was opened, its contents were rapidly filtered through a filter paper. The filtrate was evaporated *in vacuo* with a stream of nitrogen for 1 h to afford a white solid. The solid residue was dissolved in methanol and reprecipitated from THF. This procedure was repeated three times to afford a pure product as a white hygroscopic solid. Yield: 20.0 g (74.7%).

IR (neat) showed absorptions at 1630 (C=C), 1608, 1510 (phenyl), 1230, and 1090 cm^{-1} (PO–O^-).

The ^{1}H NMR ($CDCl_3$) is shown in Fig. 1.

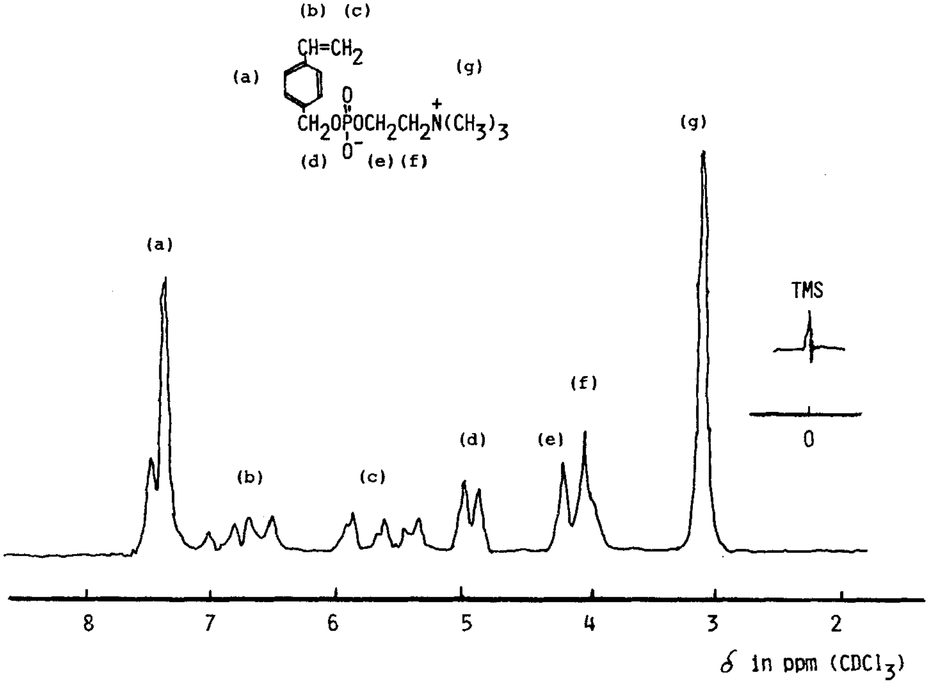


FIG. 1. ^{1}H-NMR spectrum of *p*-vinylbenzyl-2-(trimethylammonium)ethyl phosphate.

Analysis: Calculated for $C_{14}H_{22}O_4NP\cdot 2H_2O$: C, 48.65; H, 7.53; N, 4.05%. Found: C, 48.27; H, 7.43; N, 4.39%.

Polymerization of VII

The polymerization of VII was carried out in methanol with AIBN as initiator. A solution of 1.974 g (7.3 mmol) VII, 12 mg (0.073 mmol) AIBN, and 12.5 mL dry methanol were placed in a glass tube, which was flushed nine times with nitrogen, sealed *in vacuo*, and then shaken at 60°C for 5 h. After the polymerization, the contents of the tube were poured into an excess of acetone and the polymer precipitated. The mixture was allowed to stand for some time, the precipitate was collected, and it was washed successively with 50 mL acetone. The crude product was purified by reprecipitation from methanol solution with acetone to give 0.888 g (45.8%) of pure polymer as a white solid. It was hydroscopic and soluble in methanol, but almost insoluble in acetone and diethyl ether. The polymer decomposed at 230-235°C.

Its IR spectrum (KBr) showed the disappearance of the absorption band due to the vinyl double bond (1630 cm^{-1}) in the monomer, but otherwise the spectrum was unchanged.

Viscosity Measurements

Measurements were carried out with a Ubbelohde viscometer

Spectroscopic Measurements

The ^{1}H-NMR and IR measurements were carried out on a 60 MHz Hitachi-Perkin Elmer Model R-20 spectrometer and a Jasco Model IR spectrometer.

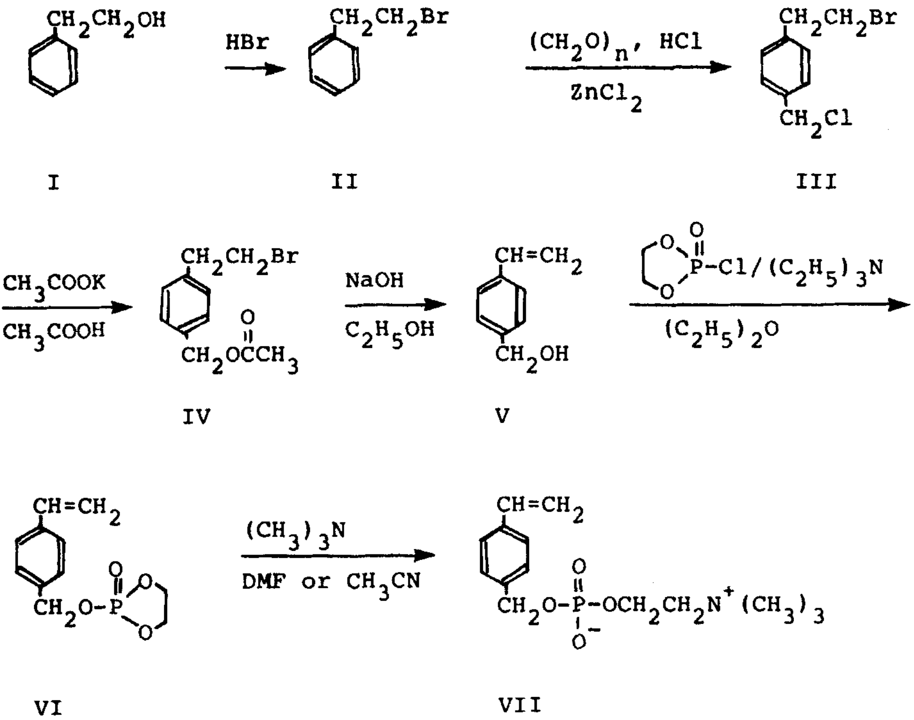
RESULTS AND DISCUSSION

The monomer, *p*-vinylbenzyl-2-(trimethylammonium)ethyl phosphate (VII), was prepared by Scheme 1.

β-Phenylethyl bromide (II) was obtained by reaction of β-phenylethyl alcohol (I) with hydrobromic acid. The chloromethylation of II by use of paraformaldehyde and hydrogen chloride in carbon disulfide in the presence of zinc chloride gave a mixture of *ortho* and *para* isomers of β-bromoethylbenzyl chloride [9, 10]. Two recrystallizations of the isomers from petroleum gave the pure *para* isomer (III). The subsequent reaction of III with potassium acetate in refluxing acetic acid gave β-bromoethylbenzyl acetate (IV). *p*-Vinylbenzyl alcohol (V) [10] was prepared by the reaction of IV with sodium hydroxide in refluxing ethanol.

The synthesis of 1-(*p*-vinylbenzyl)-2-oxo-1,3,2-dioxaphospholane (VI) was achieved by the reaction of V with 2-chloro-2-oxo-1,3,2-dioxaphospholane in diethyl ether in the presence of triethylamine [6]. The Product VI was obtained as a viscous liquid in nearly quantitative yield and characterized by its IR and ^{1}H-NMR spectroscopy. According to the method of Thoung and Chabrier [11], the Resultant VI was reacted with trimethylamine in acetonitrile to give the corresponding VII as a viscous liquid in 75% yield. The monomer was very hygroscopic and soluble in acetone, but insoluble in diethyl ether and carbon tetrachloride.

The monomer was polymerized in methanol at 60°C for 5 h with AIBN to give the corresponding poly(VII) in 46% yield as a white powder, which



SCHEME 1.

was hygroscopic and soluble in methanol, but insoluble in diethyl ether and carbon tetrachloride. The IR spectrum showed the disappearance of the absorption band due to the vinyl double bond (1635 cm^{-1}) in the monomer, but otherwise the spectrum was unchanged.

REFERENCES

[1] J. B. Finean, in *Form and Function of Phospholipids* (G. B. Ansell, J. N. Hawthorn, and R. M. Dawson, eds.) Elsevier, New York, 1973, p. 171.

[2] J. H. Fendler, *Membrane Mimetic Chemistry,* Wiley, New York, 1982, Chap. 6.

[3] S. Nakai, T. Nakaya, and M. Imoto, *Makromol. Chem., 178,* 2963 (1977).

[4] S. Nakai, T. Nakaya, and M. Imoto, *Ibid.*, *179,* 2349 (1978).
[5] H. H. Hub, H. Hupfer, A. Koch, and H. Ringsdorf, *J. Macromol. Sci.–Chem.*, *A15,* 701 (1981).
[6] T. Umeda, T. Nakaya, and M. Imoto, *Makromol. Chem. Rapid Commun.*, *3,* 457 (1982).
[7] S. L. Regen, A. Singh, G. Oehme, and M. Singh, *J. Am. Chem. Soc.*, *104,* 791 (1982).
[8] M. Yasuzawa, T. Nakaya, and M. Imoto, *J. Macromol. Sci.–Chem.*, *A23,* 963 (1986).
[9] S. Kondo, T. Ohtuka, K. Ogura, and K. Tsuda, *Ibid.*, *A13,* 767 (1979).
[10] J. G. Abramo and E. C. Chapin, *J. Org. Chem.*, *26,* 2571 (1961).
[11] N. T. Thoung and P. Chabrier, *Bull. Sci. Chim. Fr.*, p. 667 (1974).
[12] H. Lucas, F. W. Mitchell, and C. N. Scully, *J. Am. Chem. Soc.*, *72,* 5491 (1950).
[13] R. E. Edmundson, *Chem. Ind.*, p. 1828 (1962).
[14] R. Adams and T. K. Brown, *Org. Synth. Collect. Vol. I,* p. 528 (1943).

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