Polymerization via Zwitterion. 16. Alternating Copolymerization of Cyclic Phosphite with α-Keto Acid

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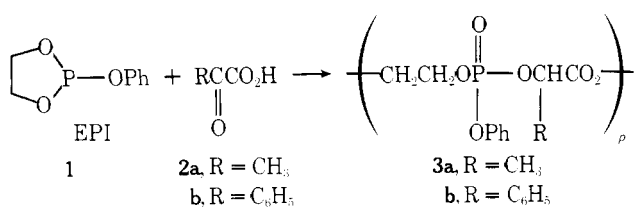
Received January 3, 1977

ABSTRACT: This paper describes a new spontaneous copolymerization between the cyclic phosphite of 2-phenoxy-1,3,2-dioxaphospholane and an α-keto acid such as pyruvic acid and phenylglyoxylic acid. The copolymerization occurred at temperatures above 100 °C without added catalyst to produce alternating copolymers. During copolymerization, the phosphite P^{III} in monomer was oxidized to phosphate P^{V} in the copolymer unit. Thus, it may well be termed "oxidation–reduction copolymerization". A scheme of polymerization involving a phosphonium zwitterion was presented.

Spontaneous alternating copolymerization, in which a nucleophilic monomer M_N and an electrophilic monomer M_E are mixed with each other to produce the key intermediate of "genetic zwitterion", $^{+}M_N\text{-}M_E^{-}$, has been developed by us.[1-16] M_N monomers which have hitherto been explored are cyclic imino ethers[2-10] (five- and six-membered), *N*-alkyliminotetrahydrofuran,[11] cyclic amine,[12] cyclic phosphonite,[13-15] and Schiff base,[16] and M_E monomers are β-propiolactone, cyclic anhydride of dibasic acid,[4,16] sulfo-lactone (sultone) of γ-hydroxypropanesulfonic acid,[5,14] acrylic acid,[6,10-13,16] acrylamide,[7,13] hydroxyalkyl acrylates,[8] and ethylenesulfonamide.[9,15] Many new copolymerizations have been developed by the combinations of the above M_N and M_E monomers. In addition, the alternating copolymerization of cyclic phosphonite with acrylates[17] as well as the 1:1:1 alternating terpolymerization of cyclic phosphonite, acrylate, and carbon dioxide[18] are known.

This paper describes the alternating copolymerization between the cyclic phosphite, 2-phenoxy-1,3,2-dioxaphospholane (ethylene phenyl phosphite) (EPI), **1**, with an α-keto acid such as pyruvic acid (PYA) **2a** (R=CH_3) or phenylglyoxylic acid (PhGA) **2b**.



EPI

1 **2a**, R = CH_3; **b**, R = C_6H_5 **3a**, R = CH_3; **b**, R = C_6H_5

The copolymerization occurred without any added catalyst to produce alternating copolymers **3**, which consist of a phosphate main chain. As will be seen in the above equation, the phosphorus atom in monomer **1** is trivalent, whereas that in the polymer unit of **3** is pentavalent. Thus, an oxidation from P^{III} to P^{V} takes place in the above copolymerization. On the other hand, the α-keto acid is reduced to a unit of α-hydroxy acid ester in the product. Thus, one monomer is oxidized and the other is reduced during copolymerization. It may be well termed "oxidation–reduction copolymerization". It is clearly distinguished from the so-called "redox polymerization", in which the redox reaction occurs between the two catalyst components to generate free radical. Therefore, it will be better to call the conventional redox polymerization "redox-initiated polymerization".

The product copolymers in the present study consist of a phosphate main chain. Elimination of the phenyl group of the copolymer was tried by hydrolysis and by hydrogenolysis in order to produce the polymeric diester of phosphoric acid, which is a biochemically interesting substance because it is a model of polynucleotides. Ring-opening polymerizations of five- and six-membered cyclic phosphate to produce polyphosphates have been reported.[19-21]

Results and Discussion

Alternating Copolymerizations of EPI with PYA and with PhGA. Without added catalyst, two copolymerizations, EPI–PYA and EPI–PhGA, occurred at 100–130 °C (Table I) to produce the respective alternating copolymers, **3a** and **3b**. Product copolymers are hygroscopic, white, resinous materials, although their molecular weights are not high.

The structures of the alternating copolymers have been established by ^1H NMR and IR spectroscopy as well as elemental analysis. Figure 1 shows an illustrative NMR spectrum of copolymer **3a** in $CDCl_3$ (sample No. 1 in Table I). Peak's assignment is as follows: peak A at δ 7.1–7.3 due to phenyl protons (5 H) of OPh, B at δ 4.8–5.3 due to methine proton (1 H) of P—O—CH, C at δ 4.1–4.5 assignable to two methylene groups (4 H) of $-OCH_2CH_2O-$,[13] and D at δ 1.3–1.7 ascribed to methyl protons (3 H) of P—O—C (CH_3). From the areas of the respective peaks, the molar ratio of 1:1 between two units was found. The IR spectrum of the same sample (Figure 2) shows characteristic absorptions, i.e., $\nu_{C=O}$ at 1760 cm^{-1}, $\nu_{P=O}$ at 1280 cm^{-1}, $\nu_{P\text{-}OPh}$ at 1200 cm^{-1}, and $\nu_{P\text{-}OCH}$ at 1100–980 cm^{-1}. Any absorption which was assignable to a carboxylic acid group was not observed. An example of elemental analysis is shown in Table II. The results may be taken to be acceptable when the highly hygroscopic property of polymer and possibility of partly hydrolytic cleavage of phenyl groups of copolymer are considered.

Similarly the structure of EPI–PhGA copolymer was also shown to be a 1:1 alternating copolymer **3b**. ^1H NMR ($CDCl_3$) shows three peaks, i.e., A at δ 3.8–4.5 ($-OCH_2CH_2O-$, 4 H), B at δ 5.7–6.0 (–OCH–, 1 H), C at δ 6.8–7.3 (two phenyl groups, 10 H). Characteristic absorptions of IR spectrum are $\nu_{C=O}$ at 1750 cm^{-1}, $\nu_{P=O}$ at 1280 cm^{-1}, $\nu_{P\text{-}OPh}$ at 1210 cm^{-1}, and $\nu_{P\text{-}OR}$ at 1070–950 cm^{-1}. Elemental analyses (Table II) are in agreement with the 1:1 composition of the two units. The structures of alternating copolymers, **3a** and **3b**, are supported also by the findings in the following sections.

Reaction Scheme of Alternating Copolymerization. On the basis of the general pattern of the spontaneous alternating copolymerization,[1] the following scheme is assumed to explain the course of the present alternating copolymerization. The initial step is the interaction between the two monomers, **1** and **2**, to form a transient zwitterion **4** by the bonding between the phosphorus atom of **1** and the carbonyl oxygen of **2**. Then, **4** is converted into the key species of zwitterion **5** by proton transfer. For this proton transfer, intermolecular and intramolecular mechanisms will possibly be considered. Elucidation of this problem requires further studies.

Then, the reaction between two molecules of **5** occurs, in which the phosphonium ring of one molecule is opened by a nucleophilic attack of the carboxylate group of the other molecule according to the reaction pattern of the Arbuzov reaction. The propagating species **7** is thus formed, which grows to **8** by the successive reaction with **5**. In addition, in-

Table I
Alternating Copolymerization of EPI with α-Keto Acids[a]

No.	M_E[b]	Solvent	Temp, °C	Time, h	Copolymer yield, %	Copolymer structure	Mol wt[c]
1	PYA	PhCN	130	40	80	**3a**	3870
2	PYA	$PhNO_2$	120	48	55	**3a**	
3	PYA	$PhCH_3$	120	48	55	**3a**	7500
4	PYA	PhCl	120	48	40	**3a**	3290
5	PhGA	PhCN	130	21	41	**3b**	1610
6	PhGA	$PhCH_3$	130	21	57	**3b**	3740
7	PhGA	$PhCH_3$	100	23	75	**3b**	2590
8	**6a**		120	24	100	**3a**	4100

[a] A mixture of EPI and an α-keto acid (each 3 mmol) in 1 mL of solvent was heated. [b] PYA: pyruvic acid. PhGA: phenylglyoxylic acid. [c] Determined by vapor pressure osmometry.

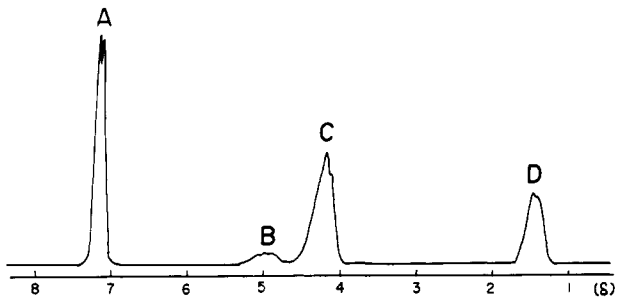


Figure 1. NMR spectrum of the alternating copolymer of EPI–PYA (in $CDCl_3$) (sample No. 1, Table I).

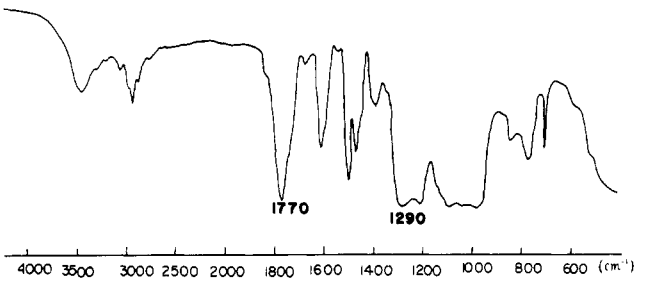
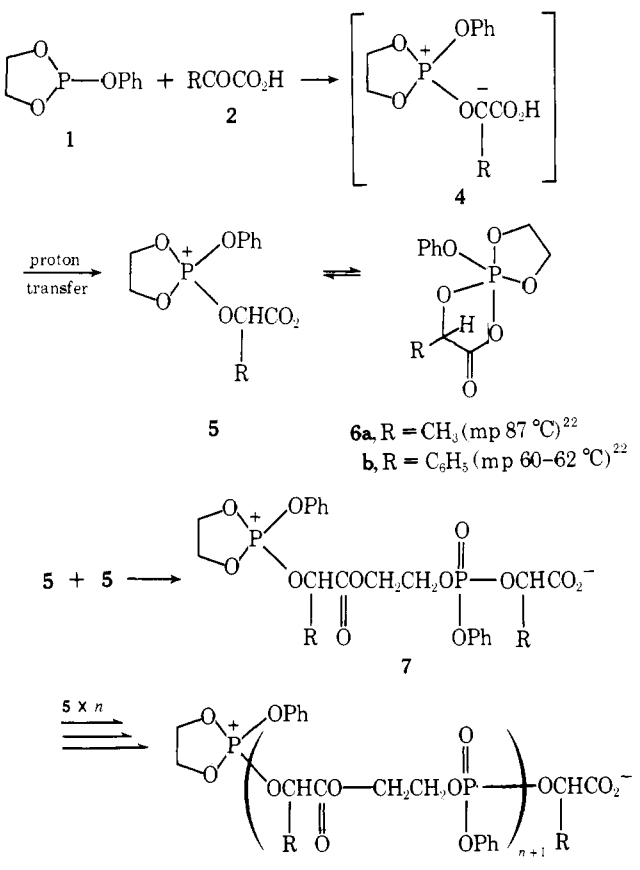


Figure 2. IR spectrum of the alternating copolymer of EPI–PYA (the same as in Figure 1).

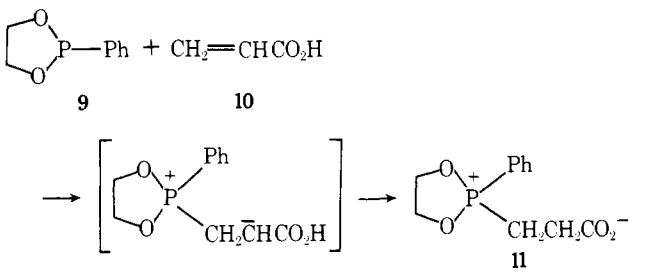


6a, R = CH_3 (mp 87 °C)[22]
b, R = C_6H_5 (mp 60–62 °C)[22]

termolecular reactions among the propagating species of **7** and **8** which will predominate at higher conversion stages of copolymerization take place.

The above scheme is supported by the isolation of a spiro compound of an pentaoxy phosphorane **6** from **1** and **2** at lower reaction temperatures, e.g., −20 °C.[22] The structure of **6** is easily derived from **5** by the intramolecular covalent bonding between the cationic site of phosphonium P^{IV} and the anionic site of carboxylate oxygen. When **6a** was heated in bulk at 120 °C, it was polymerized into **3a**. Formation of **6** at lower reaction temperature and its polymerization at temperatures above 120 °C are taken to suggest a reversible interconversion of **5** to **6**. At higher temperature, the P–OCO– bond is broken to produce **5**, the key intermediate of polymerization.

The above scheme of copolymerization is quite similar to that of the spontaneous alternating copolymerization of 2-phenyl-1,3,2-dioxaphospholane (**9**) with acrylic acid **10** in which a zwitterion **11** is produced by the nucleophilic addition of **9** to **10** followed by proton transfer.[13]



Hydrolysis of 3a. The product copolymer **3a** has the structure of a phosphoric acid triester. Some biopolymers such as polynucleotides are known to be composed of units of phosphoric acid diester. The conversion of **3a** into the corresponding polymers of phosphoric diester **12** was attempted by its hydrolysis and hydrogenolysis with platinum catalyst. The most important problem is to perform the selective

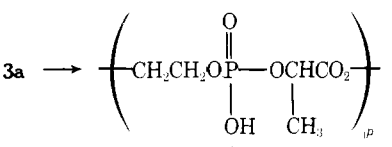


Table II
Elemental Analysis of Copolymers 3a and 3b

Copolymer (sample No. of Table I)	Formula	Anal. Calcd for 1:1 copolymer C	H	P	Found C	H	P
1a (No. 1)	$(C_{11}H_{13}O_6P)_n$	48.55	4.81	11.38	47.68	4.91	11.44
1b (No. 5)	$(C_{16}H_{15}O_6P)_n$	57.49	4.52	9.27	56.98	4.71	9.79

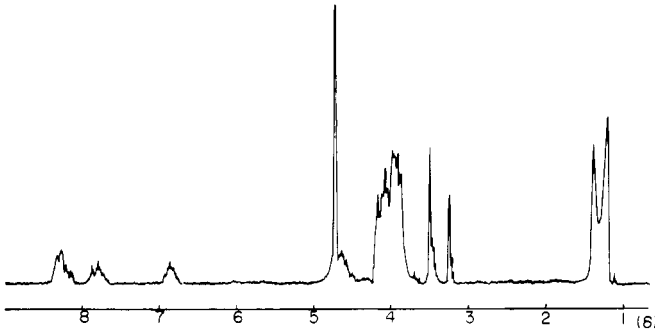


Figure 3. NMR spectrum (in D_2O) of the hydrolyzed sample of EPI–PYA alternating copolymer with CH_3CO_2H–pyridine (70 °C, 100 h).

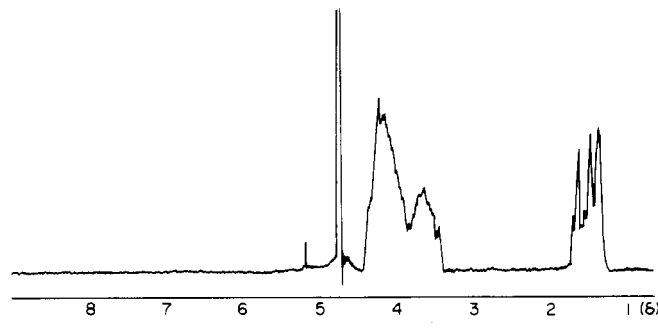


Figure 4. NMR spectrum (in D_2O) of the EPI–PYA alternating copolymer after hydrogenolysis (in CH_3CO_2H with Pt_2O catalyst, atmospheric pressure of H_2, room temperature for 6 h).

elimination of the phenyl group without the cleavage of the backbone phosphate group. First, alkaline and acid conditions were applied, i.e., NaOH (0.02 mol/L in MeOH/H_2O = 2/1), CH_3CO_2H–CH_3CO_2Na buffer (each 0.05 mol/L in MeOH/H_2O = 2/1), CH_3CO_2H (0.03 mol/L in MeOH), imidazole–CH_3CO_2H (each 0.1 mol/L in MeOH), and CH_3CO_2H–pyridine (each 0.1 mol/L in MeOH/H_2O = 2/1). In the cases with NaOH and imidazole–CH_3CO_2H systems, the hydrolytic cleavage of the phosphate backbone occurred considerably. This was indicated by the appearance of the characteristic singlet peak due to ethylene glycol, a hydrolysis product of the backbone, in the NMR spectrum of the hydrolysis mixture. The two systems of CH_3CO_2H and CH_3CO_2H–CH_3CO_2Na did not cause the hydrolysis. The CH_3CO_2H–pyridine system gave a better result. Figure 3 shows the NMR spectrum of the hydrolyzed polymer with this binary catalytic system (after 100 h at 70 °C). No peak assignable to phenyl protons was observed; instead the peak due to pyridinium (5 H) was observed at δ 6.8–8.5. Thus, the conversion of the phenyl phosphate group into pyridinium phosphate was indicated. Absence of the peak of phenyl protons shows the complete conversion after 100 h at 70 °C. Conversion after 4 h at the same temperature was about 50% and that after 12 h was 60%. With this catalytic system, however, the hydrolytic cleavage of the backbone phosphate could not be excluded, i.e., a small but clear peak due to ethylene glycol was observed in the NMR spectrum.

Hydrogenolysis of 3a. Selective cleavage of the aryl ester in aryl dialkyl phosphates by catalytic hydrogenation with platinum catalyst has been reported.[23] This method was applied to **3a.** In the literature procedure,[23] hydrogenation was carried out in ethanol. Hydrogenolysis of **3a** in ethanol, however, was very slow, i.e., the extent of the conversion determined by NMR spectroscopy was only 70% after 6 h at room temperature. In acetic acid, the hydrogenolysis rate was increased. Figure 4 shows the NMR spectrum of the hydrogenated polymer. No peak due to phenyl protons is seen, i.e., the phenyl phosphate group has been completely hydrolyzed. All peaks were reasonably assigned according to the structure **12,** i.e., δ 1.3–1.8 (3 H, P–O–CCH_3) δ 3.5–4.4 (4 H, –OCH_2CH_2–O–). Elemental analysis (see Experimental Section), however, showed 88% removal of the phenyl group. The discrepancy may probably be ascribed to the formation of a small number of cyclohexyl phosphate groups by the direct hydrogenation of the phenyl group. Detection of a small amount of cyclohexyl group by NMR spectroscopy was very difficult. The molecular weight of the sample of **3a** was 2870 which decreased to 1000 (the calculated value was 1960) by catalytic hydrogenolysis. Thus, selective cleavage of the phenyl phosphate group with a small fraction of backbone cleavage was realized.

Experimental Section

Materials. Solvents, benzonitrile, nitrobenzene, chlorobenzene, and toluene, were all purified as previously reported.[13] Pyruvic acid was a commercial reagent, which was purified by repeated distillation under nitrogen. Phenylglyoxylic acid was prepared by acid hydrolysis of commercially available benzoyl cyanide,[24] which was then purified by recrystallization from carbon tetrachloride, mp, 65–67 °C (lit.[24] 64–66 °C). EPI was prepared by the reaction of triphenylphosphite with ethylene glycol by a reported procedure,[25] bp 74 °C (0.2 mm) (lit. 70–76 (0.2 mm)), H^1 NMR ($CDCl_3$) δ 3.6–4.2 (m, 4 H, –OCH_2CH_2O–), δ 7.0–7.4 (m, 5 H, C_6H_5).

Measurements. The molecular weights of the copolymers were measured by vapor pressure osmometry (Hitachi Perkin-Elmer Model 115) in $CHCl_3$ at 34.6 °C. NMR spectrum was taken by a Hitachi NMR spectrometer R-20B (60 Mc).

Polymerization Procedure. A typical procedure was as follows. In a sealed tube 3 mmol each of EPI and PYA were dissolved in 1 mL of solvent at 0 °C. After an exothermic reaction ceased (usually in about 2 h), the reaction mixture was heated at 120 °C for 20 h. Then, the mixture was dissolved in 2 mL of chloroform and poured into 50 mL of diethyl ether to precipitate the polymeric product, which was then purified by reprecipitation by addition of a chloroform solution to a large amount of diethyl ether. The resulting copolymer was dried in vacuo and weighed. Results are shown in Table I.

Polymerization of 6a. According to a preparative method in our previous paper,[22] **6a** was prepared from 1 and **2a,** which was isolated in a crystalline form, mp 87 °C. The structure of **6a** was determined by IR and ^1H and ^{31}P NMR spectroscopy as well as elemental analysis. **6a** is very sensitive to moisture.[22] **6a** was heated in bulk at 120 °C under nitrogen for 20 h. The product polymer was purified by reprecipitation with a solvent/nonsolvent combination of chloroform and diethyl ether. The yield of polymer **3a** was almost quantitative

Hydrolysis of Copolymer 3a. To 0.36 g (1.32×10^{-3} molar unit) of copolymer **3a** (sample No. 1) was added 20 mL of methanol and 10 mL of water containing both 0.10 M acetic acid and pyridine (each 0.10 mol/L). The reaction mixture was refluxed at 70 °C for 100 h. The

solution was concentrated in vacuo to 5 mL and then poured into 50 mL of diethyl ether to give an oily product. It was dried in vacuo. The polymer thus isolated was about 0.10 g (28%).

Catalytic Hydrogenolysis of Copolymer 3a. To 0.37 g of copolymer (sample No. 1, Table I) dissolved in 25 mL of acetic acid 100 mg of PtO_2 was added. Hydrogenolysis was carried out at atmospheric pressure with vigorous shaking of a reaction flask. In 5 h, 150 mL of hydrogen gas was absorbed. Then, the catalyst was removed by filtration, and acetic acid was distilled out in vacuo. The distillation residue of polymer was washed thoroughly with diethyl ether and finally dried in vacuo to give 0.12 g of polymer. Anal. Found: C, 29.97; H, 4.73; P, 13.20.

References and Notes

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Copolymerization of Methyl α-*n*-Alkylacrylates (Alkyl = $C_{16}H_{33}$ and $C_{18}H_{37}$) with Methyl Methacrylate[1,2]

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Received April 13, 1977

ABSTRACT: Methyl α-*n*-alkylacrylates (alkyl = $C_{16}H_{33}$ and $C_{18}H_{37}$) were copolymerized with methyl methacrylate in bulk at 50 °C using a free-radical catalyst (AIBN) and anionically (sodium) in toluene at room temperature. Free-radical copolymerizations yielded polymers having $\overline{M}_n$ from 11 600 to 29 000 (22–83% yield). Homopolymerizations, with longer reaction periods, resulted in dimers and trimers (14–18% yield). Anionic copolymerizations of methyl α-*n*-hexadecylacrylate yielded $\overline{M}_n$ from 6 708 to 20 000 (17–43% yield). With twice the reaction time (2 weeks), homopolymerization yielded $\overline{M}_n$ = 1940 (42% yield). The rates of anionic and free-radical copolymerizations and homopolymerizations were low and approximately equal when the mol % methyl α-*n*-alkylacrylate in the initial monomer mix was >75. At <75 mol %, the rate of free-radical copolymerization increases rapidly with decreasing mol % methyl α-*n*-alkylacrylate in the initial monomer mix. The rate of anionic copolymerization increases slowly from 75 to 38 mol %. The long alkyl chain in the α position of the acrylic ester decreases markedly the polymerization rate. This is probably due to steric hindrance.

The behavior of methyl α-*n*-alkylacrylates (alkyl = $C_{16}H_{33}$ and $C_{18}H_{37}$) in copolymerization reactions with methyl methacrylate was investigated. This work is part of a study of polymers having long *n*-alkyl side chains attached directly to the polymer backbone.

In a previous paper,[3] the syntheses and homopolymerization reactions of methyl α-*n*-alkylacrylates (alkyl = $C_{12}H_{25}$, $C_{16}H_{33}$, and $C_{18}H_{37}$) were described. Monomers were prepared by a method which would yield an isomer free product. Anionic homopolymerizations were initiated with sodium metal or sodium naphthalene. The highest molecular weights and yields of polymer were obtained at 0 °C or above, using sodium metal as the catalyst. Yields and molecular weights, however, decreased with chain length (e.g., alkyl = $C_{12}H_{25}$, $\overline{M}_n$ = 15 000, 81% yield; alkyl = $C_{18}H_{37}$, $\overline{M}_n$ = 1380, 12% yield). Free-radical polymerizations, in emulsion or bulk, yielded only small percentages of oligomers. Experimental evidence indicated that the steric effect of the long-chain α-*n*-alkyl group considerably decreased the rate of anionic homopolymerization and resulted in the formation of dimers and trimers in free-radical polymerization.

Prior to this work, the only homopolymers of α-*n*-alkylacrylic esters (alkyl > CH_3) reported were those of methyl α-*n*-alkylacrylates (alkyl $\leq$ C_4H_9) prepared with anionic catalysts[4] or with diethylzinc–calcium complex[5] at −78 °C. The patent literature reports the polymerization of methyl α-*n*-alkylacrylates (alkyl = CH_3 to C_5H_{11}) initiated by heat (90–150 °C).[6]

It is well known,[7] however, that the copolymerization reactions of two olefinic monomers often show rate and mechanism characteristics considerably different from those of the homopolymerization reactions of either monomer alone. Copolymers, including monomers which would provide long alkyl side chains (in particular where the alkyl group is equal to or greater than $C_{16}H_{33}$), might, therefore, be accessible at higher polymerization rates and in yields sufficiently high for tech-