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Synthesis of Poly(iminocarbonates): Degradable Polymers with Potential Applications as Disposable Plastics and as Biomaterials

Chun Li and Joachim Kohn*

Department of Chemistry, Rutgers, The State University of New Jersey, New Brunswick, New Jersey 08903. *Received September 12, 1988*

ABSTRACT: The polymerization of diphenols with dicyanates leading to poly(iminocarbonates) has been investigated in detail. As a model system, the synthesis of poly(Bisphenol A–iminocarbonate) derived from Bisphenol A [2,2-bis(4′-hydroxyphenyl)propane] and Bisphenol A dicyanate [2,2-bis(4′-cyanatophenyl)propane] was systematically investigated. Bulk polycondensation was found to be unsuitable, contrary to a report in the literature. The solution polymerization of Bisphenol A and Bisphenol A dicyanate was optimized in terms of solvent, catalyst, and catalyst concentration. In THF with potassium *tert*-butoxide as the catalyst, molecular weights (M_w) up to 80 000 were obtained. In spite of the high sensitivity of cyanates toward hydrolysis, interfacial polymerization was found to be a feasible technique for the preparation of poly(iminocarbonates). In the presence of tetrabutylammonium bromide as a phase-transfer catalyst, molecular weights (M_w) in excess of 100 000 were achieved. The interfacial polymerization of Bisphenol A with cyanogen bromide rather than Bisphenol A dicyanate was also found to be feasible, eliminating the necessity to isolate and purify the reactive dicyanate. This finding is significant since the availability of a "one-pot" procedure could reduce the cost associated with the industrial-scale preparation of poly(iminocarbonates). In order to test the scope of the synthetic procedures, four structurally new poly(iminocarbonates) were prepared.

Poly(iminocarbonates) are little known polymers that are structurally related to the widely used poly(carbonates).[1,2] Formally, the iminocarbonate bond is derived by replacing the carbonyl oxygen of a carbonate by an imino group (Figure 1). This backbone modification imparts a high degree of hydrolytic instability to the polymer, apparently without significantly affecting the mechanical properties of the material.[3] Consequently, some poly(iminocarbonates), in particular poly(BPA–iminocarbonate), form biodegradable films and fibers that are in appearance and mechanical strength very similar to those made of poly(BPA–carbonate). (Abbreviations used: BPA, Bisphenol A; CTTH, (benzyloxy)carbonyl-L–tyrosyl-L-tyrosine hexyl ester; Dat–Tym, desaminotyrosyl–tyramine (see Table III for structure); DMF, dimethylformamide; GPC, gel permeation chromatography; THF, tetrahydrofuran; TDP, 4,4′-thiodiphenol.) Due to the combination of biodegradability, low toxicity, and mechanical strength, poly(BPA–iminocarbonate) may be suitable for a variety of industrial applications, including for example its use as a disposable material for food packaging. In view of the growing concern about the accumulation of nondegradable plastic materials in the environment, the development of such degradable polymers becomes increasingly important.

Poly(iminocarbonates) may also find medical applications. Recently, Kohn and Langer suggested the use of poly(BPA–iminocarbonate) as a biomaterial.[3] When polymers of low molecular weight ($M_w \sim 25\,000$) were used, it was found that poly(BPA–iminocarbonate) appears to be tissue compatible upon subcutaneous implantation and that various dyes physically entrapped within a polymeric device are slowly released over a prolonged period of time.[3] Replacement of BPA by tyrosine dipeptide derivatives as monomers yielded a backbone-modified poly(amino acid) consisting of tyrosine dipeptides linked together by iminocarbonate bonds.[4] This polymer was found to be immunologically active and has been used as an implantable antigen delivery device.[5]

Compared to poly(carbonates), little work has so far been published on the synthesis of poly(iminocarbonates). The first attempted synthesis of a poly(iminocarbonate) was reported by Hedayatullah,[6] who reacted aqueous solutions of various chlorinated diphenolate sodium salts with cyanogen bromide dissolved in methylene chloride. Unfortunately, Hedayatullah only reported the melting points and elemental analyses of the obtained products, which, according to Schminke,[7] were oligomers with molecular weights below 5000. After pure, aromatic dicyanates had become available,[8,9] a patent by Schminke et al.[7] described the synthesis of poly(iminocarbonates)

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* To whom correspondence should be addressed: Department of Chemistry, Rutgers, The State University of New Jersey, P.O. Box 939, Piscataway, NJ 08855-0939.

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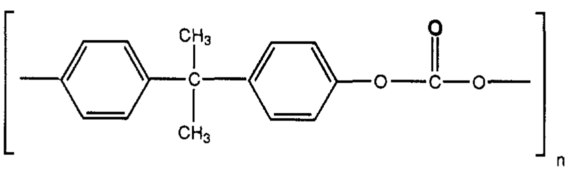
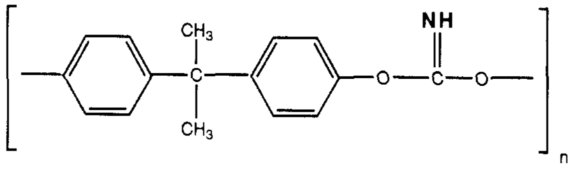


poly(BPA-carbonate)



poly(BPA-iminocarbonate)

Figure 1. Structures of poly(BPA–carbonate) (top) and poly(BPA–iminocarbonate) (bottom). The iminocarbonate bond is formally derived from the carbonate bond by replacing the carbonyl oxygen by an imino group.

with molecular weights of about 50 000 by the solution polymerization of a diphenol with a dicyanate. Bulk polymerization was also claimed to be possible.

Since the reactions leading to poly(iminocarbonates) had never been carefully studied, we investigated the synthesis of poly(iminocarbonates) in detail. For our studies BPA was chosen as a model monomer because BPA is reportedly one of the more reactive nucleophilic species among the commonly used diphenols[10] and because poly(BPA–iminocarbonate) can be directly compared to poly(BPA–carbonate), which is a well-characterized polymer.[1,2]

Experimental Section

Materials. Triethylenediamine was purchased from Air Products and Chemicals Inc. 4-(Dimethylamino)pyridine was obtained from Chemical Dynamics. Bisphenol A (polymer grade) was a gift from Shell Chemical Co. 4,4′-Thiodiphenol, 2,2′-dihydroxyazobenzene, tyramine, 3-(4-hydroxyphenyl)propionic acid, potassium *tert*-butoxide, tetrabutylammonium bromide, and cyanogen bromide were purchased from Aldrich Chemicals. BPA dicyanate[3] and *N*-(benzyloxy)carbonyl-L-tyrosyl-L-tyrosine hexyl ester[4] were prepared as described previously.

Solvents. All solvents were HPLC grade and were dried over 3-Å molecular sieves prior to use. THF was freshly distilled from sodium and benzophenone and transferred into the reaction vessel by syringe.

Measurements. ^{1}H NMR spectra were obtained on a Varian XL 200-MHz spectrometer, using $CDCl_3$ as solvent. FT-IR spectra were recorded on a Matson Lygnus 100 spectrometer. GPC data were obtained with a HPLC/GPC system consisting of a Perkin-Elmer Model 410 pump, Perkin-Elmer Model LC-235 diode array UV detector, a Waters Model 410 RI detector, and a Perkin-Elmer Model 3600 computerized data station. Two PL-gel GPC columns (300 mm × 7.7 mm, particle size 5 μm, pore size 10^3 and 10^5 Å, respectively) were placed in series and were operated at a flow rate 1.0 mL/min in THF or DMF (containing 0.1% of LiBr) at room temperature. Data were calculated either relative to polystyrene standards in THF or relative to poly(ethylene glycol) standards in DMF. Molecular weights are reported as weight averages. The barbituric acid reaction[11] was used for the quantitative determination of BPA dicyanate.

Microanalyses were performed by Robertson Laboratory, Inc., Madison, NJ.

Synthesis. Monomers. TDP dicyanate was prepared according to the procedure reported for BPA dicyanate.[3] After recrystallization from hexane (1 g in 150 mL) long needles were obtained; yield 77%. Mp: 97–98 °C. Dat–Tym was prepared according to the procedure reported for CTTH[4] by dicyclohexylcarbodiimide-mediated coupling of 3-(4-hydroxyphenyl)propionic acid and tyramine. After treatment with charcoal and recrystallization from acetic acid/water, colorless crystals were obtained; yield 69%. Mp: 173–175 °C.

Bulk Polymerization. Test tubes containing a magnetic stir bar were charged with approximately 1 g of a stoichiometric mixture of BPA and BPA dicyanate and 1 mol % of a catalyst. After flushing with argon, the tubes were tightly sealed and heated in an oil bath to either 80 or 135 °C for 12 h. The reaction products were analyzed by FT-IR, and the residual content of unreacted BPA dicyanate was determined spectrophotometrically using the barbituric acid reaction.[11] FT-IR (KBr pellet, cm^{-1}): 3338 (NH), 2966 (CH), 2872 (CH), 2275 (cyanate), 2237 (cyanate), 1678 (C=NH), 1598 (aromatic), 1563 (triazine), 1502 (aromatic), 1368 (triazine), 1301 (C=NH), 1200, 1167, 1072 (triazine), 1055, 1015, 988, 886, 829.

Solution Polymerizations. General Procedure. Under protection of argon, a 30–45% (w/v) solution of an exactly stoichiometric mixture of diphenol and dicyanate was prepared in various organic solvents, followed by the addition of catalyst as required. The conversion of dicyanate was monitored spectrophotometrically,[11] and the reaction was terminated when over 99% of the dicyanate had been consumed. After removal of the solvent, the polymer was extensively washed with an excess of acetone and dried in vacuum.

Optimized Solution Polymerization of BPA and BPA Dicyanate. Under argon, 1 g of BPA (4.381 mmol) and 1.219 g of BPA dicyanate (4.381 mmol) were dissolved in 5 mL of freshly distilled THF. A total of 10 μL of a 1 M solution of potassium *tert*-butoxide in THF was added, and the reaction was stirred for 4 h at 23 °C. Thereafter, poly(BPA–iminocarbonate) was precipitated as a gumlike material by the addition of 100 mL of acetone. After extensive washing with an excess of acetone, the crude polymer was dried in vacuo. A tough, transparent material was obtained (2.0 g, 90%). Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.86; H, 5.97; N, 5.53. Found: C, 75.46; H, 5.88; N, 5.33. FT-IR (film on NaCl, cm^{-1}): characteristic bands at 3341 (NH), 1675 (C=NH), 1601 (aromatic), 1502 (aromatic), 1301 (C=NH), 1056. ^{1}H NMR ($CDCl_3$): δ 7.11–7.31 (m, aromatic, 8 H), 5.73 (s, NH, 1 H), 1.68 (s, CH_3, 6 H). Molecular weight (relative to polystyrene standards by GPC): M_n 46 400; M_w 80 200; DP ~185.

Interfacial Polymerizations. General Procedure. A total of 4.5 mmol of a diphenol was dissolved in 45 mL of a 0.2 N aqueous solution of NaOH. Tetrabutylammonium bromide was added as needed. The required amount of dicyanate was dissolved in 45 mL of a water-insoluble, organic solvent. The two phases were vigorously mixed at 23 °C by an overhead stirrer operating at 2000 rpm. The disappearance of dicyanate from the organic phase was followed by the barbituric acid reaction.[11] The disappearance of BPA from the aqueous phase was followed by UV spectroscopy at 275 nm. If a polymeric product precipitated, it was collected on a Buchner funnel. Alternatively, the two phases were separated and the polymeric product was isolated by evaporation of the organic phase to dryness. For purification, the crude polymer was dissolved in a suitable, water-immiscible solvent, followed by washings with water, drying of the organic solution over magnesium sulfate, and reprecipitation with a suitable polymer nonsolvent.

BPA in the Presence of BPA Dicyanate (Optimized Procedure). The polymerization was conducted in a 250-mL three-necked flask equipped with an overhead stirrer. A total of 1.03 g of BPA (4.5 mmol) and 0.145 g of tetrabutylammonium bromide (10 mol %) were dissolved in 45 mL of a 0.2 N aqueous solution of NaOH and 1.51 g of BPA dicyanate (5.43 mmol) was dissolved in 45 mL of carbon tetrachloride. The two phases were vigorously mixed at 23 °C by an overhead stirrer operating at 2000 rpm. After 2 h, the precipitated polymer was collected on a Buchner funnel. For purification a solution of crude polymer in methylene chloride was washed with water and dried over magnesium sulfate, followed by reprecipitation of the polymer in acetone. FT-IR (film on NaCl, cm^{-1}): characteristic bands at 3341 (NH), 2968 (CH), 1678 (C=NH), 1601 (aromatic), 1502 (aromatic), 1301 (C=NH), 1056. ^{1}H NMR ($CDCl_3$): δ 7.10–7.25 (m, aromatic, 8 H), 5.80 (s, NH, 1 H), 1.66 (s, CH_3, 6 H). Molecular weight (relative to polystyrene standards by GPC): M_n 51 500; M_w 102 900; DP ~203.

BPA in the Presence of Cyanogen Bromide. The polymerization was conducted in a 250-mL three-necked flask equipped with overhead stirrer and dropping funnel. A total of 1.43 g cyanogen bromide (13.5 mmol) was dissolved in 45 mL of carbon

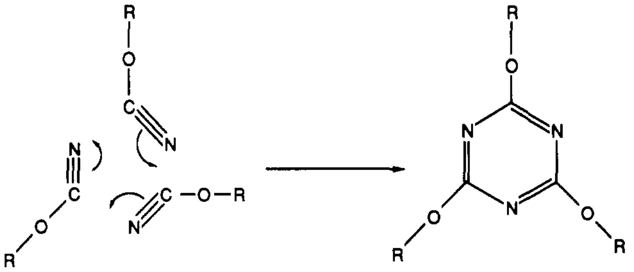


Figure 2. Structure of 1,3,5-triazine, formed by trimerization of cyanates. In the case of dicyanates, trimerization results in the formation of a highly cross-linked polymer.

tetrachloride and placed into the flask. With vigorous stirring at 2000 rpm, a solution of 2.05 g of BPA (9 mmol) and 0.29 g of tetrabutylammonium bromide (0.9 mmol) in 90 mL of 0.2 N aqueous NaOH was dropped into the flask over a period of 120 min. Thereafter, stirring was continued for an additional 120 min. A white precipitate formed, which was collected and washed with water. The polymer was further purified as described above; yield 0.73 g, 32%. Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.86; H, 5.97; N, 5.53. Found: C, 76.01; H, 5.78; N, 5.45. FT-IR (film on NaCl, cm^{-1}): characteristic bands at 3341 (NH), 2970 (CH), 2872 (CH), 1675 (C=NH), 1601 (aromatic), 1502 (aromatic), 1301 (C=NH), 1056. ^{1}H NMR ($CDCl_3$): δ 7.11–7.25 (m, aromatic, 8 H), 5.79 (s, NH, 1 H), 1.67 (s, CH_3, 6 H). Molecular weight (relative to polystyrene standards by GPC): M_n 31 700; M_w 52 900; DP ~125.

Results and Discussion

Bulk Polymerization. Reportedly, poly(iminocarbonates) can be prepared by the bulk polymerization of an equimolar mixture of an aromatic dicyanate and a diphenol.[7] Since for many industrial applications, polymerization in bulk is most economical, we investigated the polymerization of BPA and BPA dicyanate in bulk under various reaction conditions. An equimolar mixture of BPA and BPA dicyanate melted at 65–67 °C, which therefore is the lowest possible reaction temperature for a bulk polymerization. On the other hand, the finding that poly(BPA–iminocarbonate) decomposed at temperatures above 140 °C provided an upper temperature limit. Thus, bulk polymerizations were performed at 80 and 135 °C resulting in the formation of glassy, transparent polymers in all cases.

The known tendency of dicyanates to form 1,3,5-triazine rings (Figure 2) is a possible side reaction during the polymerization of BPA and BPA dicyanate. In order to investigate this possibility, we prepared an authentic sample of poly(BPA–triazine) by the bulk polymerization of pure BPA dicyanate according to the procedure of Schultheis.[12] Poly(BPA–triazine) showed characteristic IR absorption bands at 1562, 1368, and 1072 cm^{-1}.

When BPA was reacted with BPA dicyanate at 80 °C *in the absence of any catalyst* a polymeric product was obtained that showed all of the characteristic FT-IR absorptions of poly(BPA–triazine) (1562, 1368, and 1072 cm^{-1}) while none of the absorptions associated with the iminocarbonate bond (3320–3380, 1670–1680, and 1300–1305 cm^{-1}) could be detected. Thus, in the absence of a catalyst BPA did not add to the cyanate triple bond and self-condensation of BPA dicyanate to poly(BPA–triazine) was the only observable reaction. Only when basic catalysts such as 4-(dimethylamino)pyridine, triethylenediamine, or potassium *tert*-butoxide were added into the reaction mixture did the polymers obtained show the characteristic absorptions of poly(iminocarbonates) at 3320–3380, 1670–1680, and 1300–1305 cm^{-1} in addition to the triazine absorption bands at 1562, 1368, and 1072 cm^{-1}.

Semiquantitative analysis of the FT-IR peak ratios at 1670 cm^{-1} (iminocarbonate) and 1562 cm^{-1} (1,3,5-triazine) indicated that a higher proportion of iminocarbonate bonds was formed in the presence of the strongly basic potassium *tert*-butoxide than in the presence of tertiary amines. Similar results were obtained at 135 °C, except that all samples polymerized at 135 °C had a higher proportion of triazines than the corresponding samples polymerized at 80 °C. It seems that the thermal trimerization of dicyanates to 1,3,5-triazine rings (Figure 2) is an unavoidable side reaction during the bulk polymerization of BPA and BPA dicyanate. Consequently, linear chains of poly(BPA–iminocarbonate) will be cross-linked to a varying degree by interchain 1,3,5-triazine linkages, which were observed in the FT-IR spectra of all bulk polymerized materials. The insolubility of all bulk polymerized samples in all common solvents also indicated that cross-linking had occurred.

Solution Polymerization. Using the previously reported solution polymerization procedures,[3-5,7] we were able to obtain poly(iminocarbonates) with molecular weights (M_w) of about 25 000 Da. Since this is too low a value for most potential industrial or medical applications, we attempted to optimize the solution polymerization reaction by examining the influence of solvent, catalyst, and catalyst concentration on the molecular weight of the resulting polymers.

According to Schminke,[7] a wide variety of catalysts such as metal hydroxides, metal alkoxides, and tertiary or secondary amines can be used for the preparation of poly(iminocarbonates). For instance, the polymerization of hydroquinone and 1,4-dicyanatobenzene is effectively catalyzed by a variety of tertiary amines such as triethylamine.[3] It was therefore surprising that no polymerization occurred, when solutions containing BPA and BPA dicyanate were allowed to stand at 23 °C for over 24 h in the presence of up to 10% (by weight) of various amines such as triethylamine, *N*-ethylmorpholine, pyridine, triethylenediamine (DABCO), or 4-(dimethylamino)pyridine. The barbituric acid test[11] indicated no significant consumption of dicyanates under these conditions. Only in the presence of metal hydroxides or alkoxides, such as sodium hydroxide, sodium methoxide, or potassium *tert*-butoxide, was rapid and complete polymerization observed. Consequently, NaOH and potassium *tert*-butoxide were selected as model catalysts in the following experiments.

Next, we investigated the effect of various solvent systems on the polymerization reaction. Unfortunately, the choice of solvents is limited on one hand by the insolubility of BPA in highly nonpolar solvents, such as chlorinated hydrocarbons, toluene, or hexane, and on the other hand by the insolubility of BPA-dicyanate in polar solvents, such as alcohols. The necessity to prepare fairly concentrated solutions containing both BPA and BPA dicyanate dictated our selection of six solvent systems, ranging from DMF as the most polar medium to a mixture of ether/THF as the most nonpolar medium (Table I). The polymerizations were performed at 23 °C, in the presence of 1 mol % of either NaOH or potassium *tert*-butoxide (KOBu-*t*) as the catalyst, and allowed to proceed for 4 h at which time over 99% of all cyanates had been consumed.

Contrary to a previous report,[7] DMF consistently gave polymers of low molecular weight. One possible explanation is that DMF as a strongly polar, aprotic solvent may stabilize the electrodeficient cyanate function by solvation, thereby reducing its reactivity. Likewise, isopropanol was found to be a markedly inferior solvent for the polymerization reaction. Possibly, traces of isopropoxide anion

Table I
Solvent Effects on the Solution Polymerization of BPA and BPA Dicyanate[a]

solvent system	mol wt[b] obtained in presence of KOBu-*t*	mol wt[b] obtained in presence of NaOH	polymer solubility
ethyl ether/THF (4:1)	80 500	74 700	insoluble
acetone[c]	77 400	69 100	insoluble
isopropanol/THF (3:2)	28 800	25 100	insoluble
THF	82 200	55 800	soluble
dimethoxyethane	53 400	57 500	soluble
DMF	31 700	31 000	soluble

[a] Polymerizations were performed at 23 °C in the presence of 1 mol % of the indicated catalyst and allowed to proceed for 4 h. The initial concentration of monomer was 44% (w/v). [b] Weight average molecular weights were determined by GPC relative to polystyrene standards. Data are averages obtained from two repetitions. [c] A yellow color developed, which could not be removed from the polymer by extensive washings with fresh acetone.

could be formed that would react with cyanates, terminating the growing polymer chain. Also, acetone is probably not a good choice, since, among all tested solvents, only acetone led to the formation of a slightly yellow color, which was strongly adsorbed by the polymer and could not be removed by extensive washing.

In polymer nonsolvents such as ether/THF (4:1), isopropanol/THF (3:2), or acetone, the initially clear solution became turbid, and about 10–13 min after addition of the catalyst, a polymer gel separated from the reaction mixture. In neat THF, dimethoxyethane, and DMF the polymer was completely soluble, resulting in clear, viscous solutions. Interestingly, ether/THF (a polymer nonsolvent) yielded materials of high molecular weight, indicating that the rapid precipitation of poly(BPA–iminocarbonate) in ether/THF did not terminate the polymerization reaction. Our data (Table I) identified ether/THF (4:1) and neat THF as the best solvent systems and potassium *tert*-butoxide as the preferred catalyst. Best results were obtained with a catalyst concentration of about 0.2–1 mol %.

The polymerization reaction was monitored by removing aliquots of the reaction mixture at certain times for analysis by gel permeation chromatography. When the optimized procedure (23 °C, THF, 0.2 mol % of potassium *tert*-butoxide) was used, dimers were the predominant species after 5 min of reaction. At 15 min only traces of residual monomers were detectable, and at 30 min a single, smooth peak corresponding to a molecular weight (M_w) of 49 400 was obtained. At 60 min the molecular weight had increased to 65 200 (Figure 3). At this point the polymerization was virtually complete, and no further change was noticeable over the next 6 h.

Interfacial Polymerization. Schnell[13,14] reported the use of a two-phase system for the preparation of poly(carbonates) from BPA and phosgene. For the preparation of poly(iminocarbonates) analogous two-phase reaction systems are conceivable, containing BPA dicyanate in the organic phase and a mixture of BPA and NaOH in the aqueous phase. In most interfacial polymerizations, hydrolysis is a highly undesirable side reaction. For instance, in the interfacial formation of polyamides from acid chlorides and amines, hydrolysis of the water-sensitive acid chlorides, constitutes a wasteful loss of one of the reactants. On the other hand, the hydrolysis of BPA dicyanate generates BPA, which is a necessary reagent. This appears to be a unique feature of the interfacial synthesis of poly(BPA–iminocarbonate). It should therefore be possible to obtain poly(BPA–iminocarbonate) by simply hydrolyzing BPA dicyanate under phase-transfer conditions.

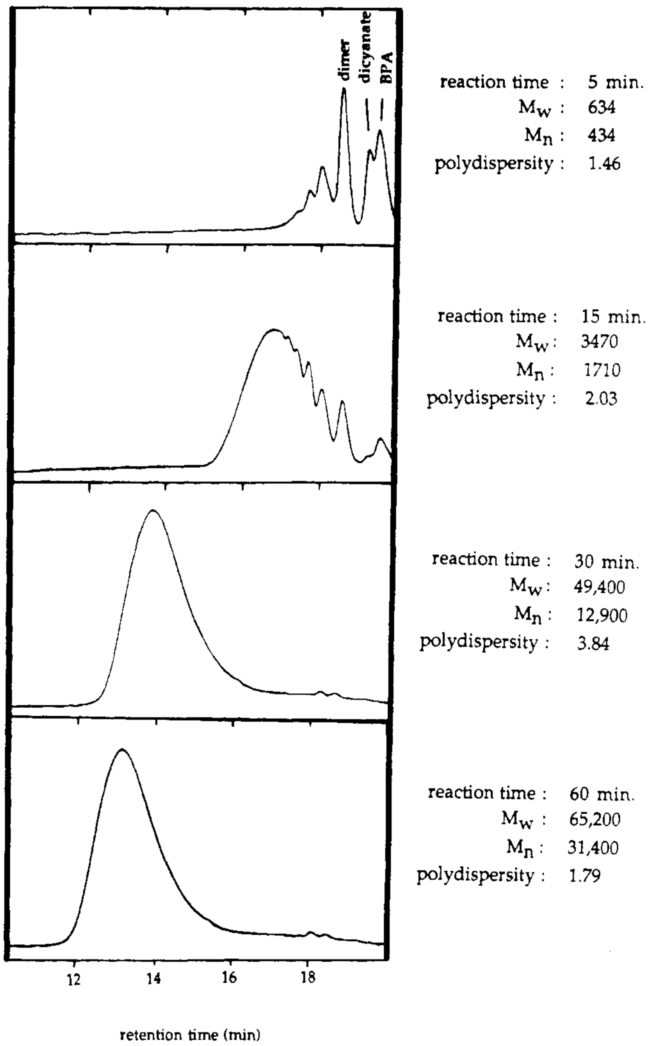


Figure 3. Solution polymerization of BPA and BPA dicyanate in THF at 23 °C in the presence of 0.2 mol % of potassium *tert*-butoxide as catalyst. At the indicated times, aliquots of the reaction mixture were withdrawn and analyzed by GPC relative to polystyrene standards.

In order to test this hypothesis, we exposed a solution of BPA dicyanate in carbon tetrachloride to a 0.2 N aqueous solution of NaOH containing 10 mol % of tetrabutylammonium bromide as a phase-transfer catalyst. Upon thorough mixing of the two phases, a white precipitate started to form within 100 min. This precipitate was a polymeric product having a molecular weight (M_w) of 35 500 relative to polystyrene standards. It was found by ^{1}H NMR, FT-IR, and elemental analysis to be identical with authentic poly(BPA–iminocarbonate) obtained by solution polymerization. Most notable was the complete absence of any indication of the formation of 1,3,5-triazine cross-links.

Since the initial ratio of BPA to BPA dicyanate in the reaction mixture could be expected to influence the obtained molecular weight, we performed a series of interfacial polymerization reactions in which the ratio of BPA to BPA dicyanate was varied while all other experimental conditions were kept constant. With carbon tetrachloride as the organic phase, the optimum ratio of BPA to BPA dicyanate was between 0.8 and 0.9. Under these conditions, polymers with very high molecular weight (M_w > 100 000) were obtained. In methylene chloride as the organic phase, the obtained molecular weights were consistently lower than in carbon tetrachloride and did not

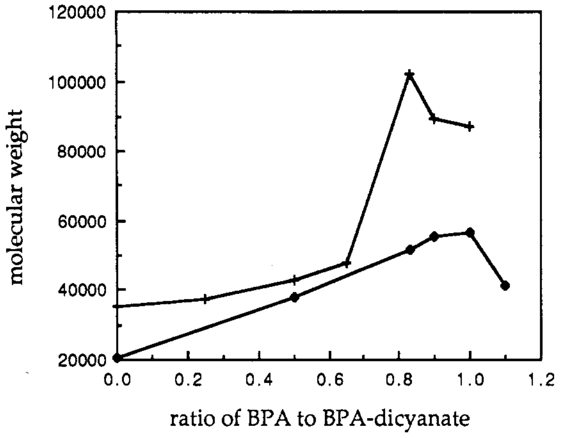


Figure 4. Molecular weights obtained by the interfacial polymerization of BPA and BPA dicyanate as function of the initial ratio of BPA to BPA dicyanate present in the reaction mixture: upper curve (+), reaction in carbon tetrachloride/water; lower curve (●), reaction in methylene chloride/water.

show the pronounced sensitivity to variations in the initial ratio of BPA to BPA dicyanate (Figure 4).

As a general rule, interfacial polymerizations yield higher molecular weights when a good polymer solvent is used as the organic phase. Since our data indicated that carbon tetrachloride (a polymer nonsolvent) is a better choice than methylene chloride (a polymer solvent), we investigated in more detail the effect of different solvents on the interfacial polymerization of BPA and BPA dicyanate. For our studies, we selected toluene as a model for a partial polymer solvent in addition to carbon tetrachloride and methylene chloride. In the methylene chloride/water system no precipitates formed at any time throughout the reaction and the phases separated readily whenever stirring was interrupted. With toluene, a milky, stable emulsion formed from which the polymer could be separated only with difficulty. Also with carbon tetrachloride as the organic phase a milky emulsion was initially formed. However, at a certain point an abrupt phase transition occurred: the milky emulsion broke up and polymer started to precipitate as a gumlike blob that tended to stick to the blades of the stirrer.

Considering the rapid precipitation of poly(BPA–iminocarbonate) in the carbon tetrachloride/water system, one would not usually expect this system to yield higher polymers than the methylene chloride/water system. In order to clarify this point we simultaneously monitored the concentration of BPA in the aqueous phase, the concentration of BPA dicyanate in the organic phase, and the polymer molecular weight throughout the interfacial polymerization reaction. We consistently found that while BPA dicyanate was rapidly consumed, the concentration of BPA in the aqueous phase remained constant or actually increased slightly during the initial phase of the polymerization reaction. Then, coinciding with the precipitation of the polymer, the concentration of BPA in the aqueous phase dropped abruptly, while the molecular weight of the polymer increased steadily, even after complete precipitation of the polymer had occurred (Figure 5).

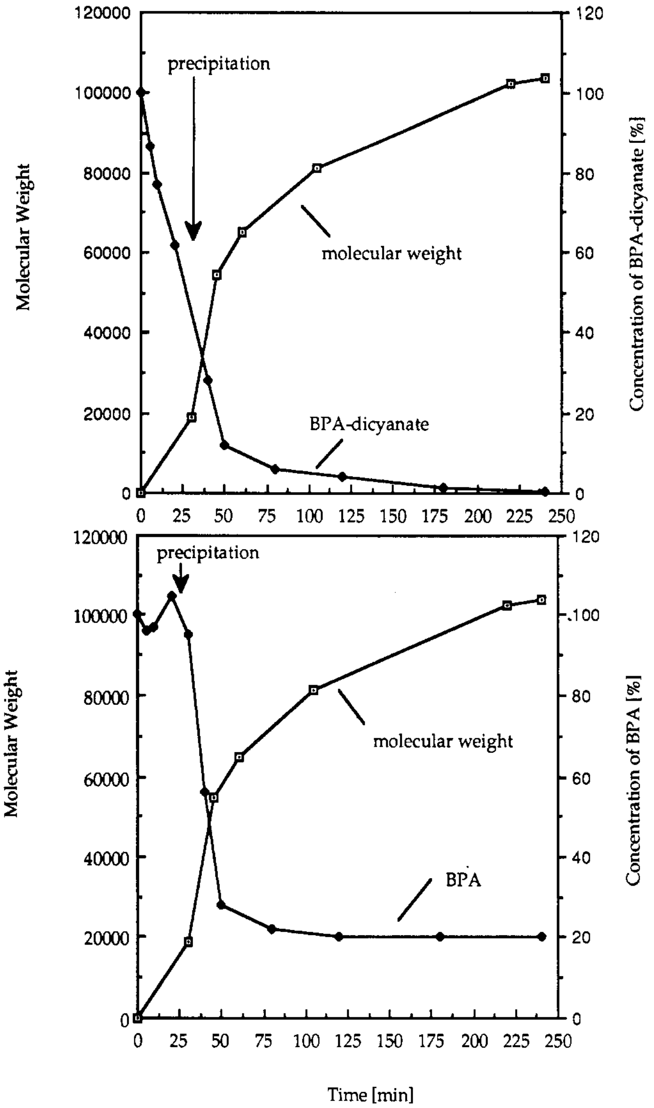


Figure 5. Relationship between (a) concentration of BPA dicyanate in the organic phase and the polymer molecular weight (upper graph), and (b) concentration of BPA in the aqueous phase and the polymer molecular weight (lower graph), during the interfacial polymerization of BPA and BPA dicyanate in carbon tetrachloride/water.

One possible way to interpret these data would be to assume that the concentration of BPA in the aqueous phase is kept nearly constant during the first 20 min of the reaction due to the rapid hydrolysis of BPA dicyanate to BPA monocyanate or BPA. Polymer starts to precipitate when the growing chains reach a critical length of about 15 000–20 000 Da. Our data indicate that, at this point, BPA is absorbed onto the precipitating polymer, facilitating the continuation of chain growth within the polymeric precipitate itself. Hence, the rapid precipitation of poly(BPA–iminocarbonate) in carbon tetrachloride actually seems to favor the formation of high polymers rather than impeding it.

BPA monocyanate must be assumed to be an intermediate in the hydrolysis of BPA dicyanate to BPA. BPA monocyanate may actually play an important role in the interfacial polymerization of BPA dicyanate and BPA. However, since our analytical techniques cannot distinguish between BPA monocyanate and an equimolar mixture of BPA dicyanate and BPA, the possible participation of BPA monocyanate in the polymerization reaction was not investigated.

Next we determined the optimum concentration of phase-transfer catalyst for the interfacial polymerization of BPA and BPA dicyanate in carbon tetrachloride, toluene, and methylene chloride. Tetrabutylammonium bromide was selected as the model catalyst. In order to obtain comparable results, the reaction conditions including the monomer ratio were kept constant in each case. The half-life of BPA dicyanate in the reaction mixture and the molecular weight of the resulting polymers were determined. The most pronounced rate enhancement was observed in methylene chloride, where the addition of only

Table II
Effect of Phase-Transfer Catalysis on Reaction Rate and Molecular Weight

solvent[a]	phase-transfer catalyst added, mol %	half-life of BPA dicyanate,[b] min	molecular weight[c]	isolated yield,[d] %
carbon tetrachloride	0	93	27 800	22
	5	26	63 000	68
	10	21	87 400	92
	20	20	65 800	98
	50	17	58 200	98
toluene	0	>600	69 000	29
	5	160	87 100	52
	10	100	62 300	60
	20	70	59 100	66
	50	17	38 100	80
methylene chloride	0	250	41 900	29
	5	10	53 100	84
	10	5	56 500	86
	20	~2	45 500	85
	50	<1	24 800	81

[a] Interfacial polymerizations were conducted at 23 °C by mixing an aqueous solution of BPA, sodium hydroxide, and tetrabutylammonium bromide with an organic solution of BPA dicyanate. See the Experimental Section for a detailed procedure. [b] Measured by monitoring the consumption of BPA dicyanate using the barbituric acid reaction. [c] Weight average molecular weight, determined by GPC relative to polystyrene standards. [d] Isolated yield of polymer after workup.

5% of tetrabutylammonium bromide reduced the half-life of BPA dicyanate about 25-fold, as compared to an only 4-fold reduction in carbon tetrachloride. In all tested solvents the optimum concentration of tetrabutylammonium bromide was about 5–10% (Table II).

Since dicyanates are prepared by the reaction of diphenols with cyanogen bromide,[8] it should in principle be possible to obtain high molecular weight poly(iminocarbonates) directly from the interfacial polymerization of a diphenol and cyanogen bromide. The use of cyanogen bromide as an in situ cyanylating agent would eliminate the need to prepare and purify the reactive dicyanates in a separate reaction step and could significantly reduce the cost associated with the industrial production of poly(iminocarbonates). The reaction of diphenols with cyanogen bromide would then be analogous to the preparation of poly(carbonates) from diphenols and phosgene. However, when Hedayatullah reacted aqueous solutions of diphenols with organic solutions of cyanogen bromide, no high polymers were obtained.[6]

Following Hedayatullah's procedure, we conducted interfacial polymerizations by adding an organic solution containing cyanogen bromide to an aqueous solution containing BPA, sodium hydroxide, and phase-transfer catalyst. The effect of factors such as organic solvent, ratio of cyanogen bromide to BPA, concentration of phase-transfer catalyst, volume ratio of the two phases, temperature, and reaction time was investigated. In each case, the final reaction mixture contained an excess of unreacted BPA and low molecular weight oligomers (Figure 6A).

Since cyanogen bromide is freely soluble in water while phosgene is only sparingly soluble, the failure to obtain poly(iminocarbonates) from diphenols and cyanogen bromide may be due to the marked tendency of cyanogen bromide to diffuse readily into the aqueous phase where it is rapidly hydrolyzed. Since Hedayatullah's procedure requires the addition of an organic solution of cyanogen bromide into an aqueous solution containing BPA and sodium hydroxide, cyanogen bromide is by necessity exposed to an excess of base, leading to preferential hydrolysis rather than reaction with diphenol. On the basis of this hypothesis, we reversed the order in which the reactants are brought into contact. Consequently, we added an aqueous solution of BPA, sodium hydroxide, and phase-transfer catalyst into a well-stirred solution of cyanogen bromide in carbon tetrachloride. Under these conditions a truly polymeric product was obtained (Figure 6B). As determined by the barbituric acid color reaction, the main reaction during the initial phase of the polymerization was the conversion of hydroxyl groups to cyanate groups. BPA mono- or dicyanates accumulated in the organic phase and then reacted with the remaining BPA in the usual way to form high polymers (M_w = 44 000–53 000). Poly(BPA–iminocarbonate) obtained from the interfacial polymerization of BPA and cyanogen bromide was analyzed by NMR, FT-IR, and elemental analysis and found to be identical in all aspects with an authentic sample of poly(BPA–iminocarbonate) obtained by solution polymerization.

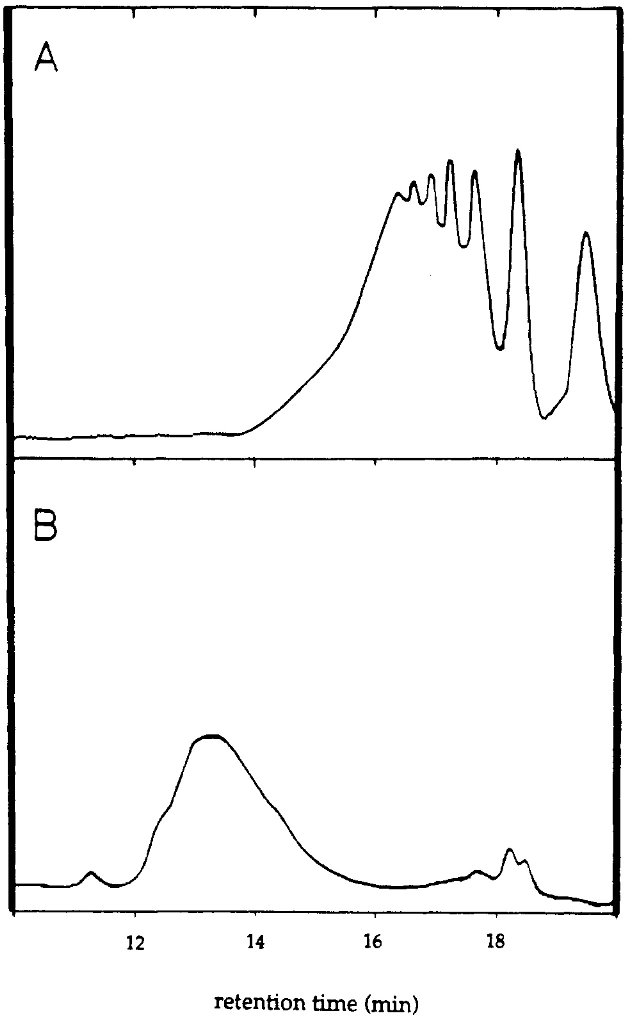
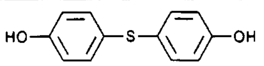
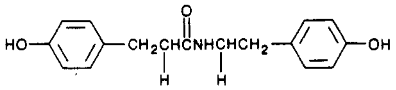
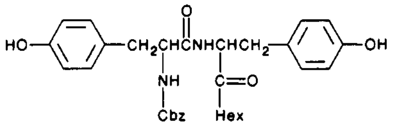
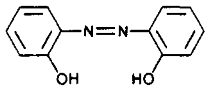


Figure 6. Products obtained from the interfacial polymerization of BPA in the presence of cyanogen bromide. A (upper graph): cyanogen bromide was added into a stirred solution of BPA, sodium hydroxide, and phase-transfer catalyst according to the procedure of Hedayatullah. Only oligomers of low molecular weight were obtained. B (lower graph): a solution of BPA, sodium hydroxide, and phase-transfer catalyst was added into a stirred solution of cyanogen bromide. High polymers were obtained.

Next, we replaced BPA by several other diphenols (Table III). Two of the tested diphenols are derivatives of L-tyrosine, a naturally occurring amino acid. Such monomers may give rise to biocompatible "specialty polymers" for medical applications.[4,5] First of all, we attempted the preparation of copolymers by reacting BPA

Table III
Monomers Used for the Synthesis of Copolymers[a]

chemical structure	name	mol wt
	4,4′-thiodiphenol (TDP)	66 000[b]
	desaminotyrosyl-tyramine (Dat–Tym)	45 000[c]
	*N*-Cbz-tyrosyltyrosine hexyl ester (CTTH)	31 500[b]
	2,2′-dihydroxyazobenzene (DAB)	polymerization failed

[a] Equimolar mixtures of BPA dicyanate and the indicated diphenol were polymerized in THF using the optimized procedure given in the Experimental Section. [b] Weight average molecular weight as determined by GPC in THF relative to polystyrene standards. [c] Weight average molecular weight as determined by GPC in DMF relative to poly(ethylene glycol) standards.

dicyanate with the diphenols listed in Table III, using the optimized *solution polymerization* procedure. With the exception of 2,2′-dihydroxyazobenzene, all diphenols polymerized readily and yielded high polymers. The failure of 2,2′-dihydroxyazobenzene to polymerize can possibly be attributed to the high degree of steric crowding in this ortho-substituted monomer. The copolymers of BPA dicyanate with CTTH, Dat–Tym, or TDP were soluble in chlorinated hydrocarbons, THF, and DMF and formed transparent, strong films by solvent casting. FT-IR spectroscopy (KBr pellet) revealed the characteristic absorption bands of poly(iminocarbonates) at 3320–3380, 1670–1680, and 1300–1305 cm^{-1}.

The copolymer of BPA dicyanate and TDP was also prepared by *interfacial polymerization*, by using an equimolar ratio of BPA dicyanate and TDP. However, since the hydrolysis of BPA dicyanate generates some free BPA, which then competes with TDP for incorporation into the polymer chain, the resulting copolymer should contain a certain excess of BPA repeat units. The ratio of BPA to TDP repeat units in the copolymer can be calculated from the sulfur content of the copolymer. For a strictly alternating copolymer (BPA/TDP = 1), the calculated sulfur content is 6.46%. On the basis of the experimentally determined sulfur content (elemental analysis found: C, 70.84; H, 5.13; S, 5.35), the actual ratio of BPA/TDP in the copolymer was found to be about 1.4, indicating that the interfacial polymerization technique indeed yields random copolymers rather than strictly alternating copolymers.

Finally, we used the optimized, interfacial polymerization procedure for the preparation of the homopolymer of TDP by reacting TDP dicyanate with TDP. The polymerization occurred readily as judged by the rapid consumption of TDP dicyanate. As in the case of poly(BPA–iminocarbonate) the polymer precipitated in the course of the reaction. However, contrary to poly(BPA–iminocarbonate) or the BPA/TDP copolymer, poly(TDP–iminocarbonate) was insoluble in all commonly used organic solvents, precluding the determination of its molecular weight. FT-IR spectroscopy (KBr pellet) showed the characteristic IR absorptions of poly(iminocarbonates).

We are presently studying the physical, mechanical, and biological properties of these structurally new poly(iminocarbonates) in more detail.

Conclusions

Since poly(iminocarbonates) may find applications ranging from disposable plastics to implantable, medical devices, we studied the reaction of diphenols with dicyanates in an attempt to develop reliable synthetic procedures for the preparation of poly(iminocarbonates) with weight average molecular weights in excess of 50 000 Da.

On the basis of the observation by FT-IR spectroscopy of 1,3,5-triazine cross-links in all bulk-polymerized samples, we concluded that bulk polymerization of diphenols and dicyanates appears to be unsuitable for the preparation of structurally well-defined, linear poly(iminocarbonates). However, the partially cross-linked polymers were glassy, transparent, and mechanically very strong materials that may find some applications as partially degradable, thermosetting resins.

Although the solution polymerization of diphenols with dicyanates reportedly resulted in poly(iminocarbonates) with molecular weights of about 50 000,[7] our attempts to reproduce these results failed to provide polymers with weight average molecular weights in excess of about 25 000 (GPC, relative to polystyrene standards).[3,4] We therefore studied the solution polymerization of BPA and BPA dicyanate in detail. An interesting result of our studies is the finding that both polymer solvents (e.g. THF) and polymer nonsolvents (e.g. ether/THF = 4/1) can yield equally high polymers, indicating that the rapid precipitation of polymer in the ether/THF mixture did not terminate the polymerization reaction. An optimized solution polymerization procedure, employing 0.2–1.0 mol % of potassium *tert*-butoxide as catalyst was developed and afforded poly(BPA–iminocarbonate) with a molecular weight (M_w) of about 80 000.

Interfacial polymerization was found to be a facile technique for the laboratory-scale preparation of poly(BPA–iminocarbonate), yielding molecular weights (M_w) in excess of 100 000. After purification narrow molecular weight distributions were obtained, as indicated by polydispersity values ranging from 1.5 to 2.0. Interestingly, the use of a polymer nonsolvent (carbon tetrachloride) as the organic phase was found to be particularly advantageous. On the basis of the data collected in Figure 5, we conclude that the polymerization reaction occurs within the precipitated polymer itself and not at the interface between the aqueous and organic phases.

Due to the partial hydrolysis of the dicyanate component, the interfacial polymerization technique gives rise to random copolymers when the diphenol component in the reaction mixture is not identical with the dicyanate. This is an important difference from the solution polymerization technique, which presumedly gives rise to strictly alternating copolymers.

Our finding that poly(BPA–iminocarbonate) can be prepared directly from BPA and cyanogen bromide is significant for the evaluation of poly(iminocarbonates) for possible large-scale industrial applications. Since the separate isolation and purification of the reactive dicyanates can be circumvented, the cost associated with the industrial-scale production of poly(BPA–iminocarbonate) should be comparable to the cost of the widely used poly(BPA–carbonate).

We prepared four structurally new poly(iminocarbonates), using polymerization procedures that had been optimized for BPA. All tested diphenols with the exception of the ortho-substituted 2,2′-dihydroxyazobenzene polymerized readily. Since the obtained polymers had lower molecular weights than poly(BPA–iminocarbonate), the synthetic procedures, although generally applicable, require careful optimization for each specific diphenol, in order to afford polymers with molecular weights above 50 000.

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Registry No. (BPA)(BPA dicyanate) (copolymer), 26025-74-1; (BPA)(BPA dicyanate) (SRU), 26101-32-6; (BPA)(cyanogen bromide) (copolymer), 118798-91-7; (TDP)(BPA dicyanate) (copolymer), 118798-92-8; (TDP)(BPA dicyanate) (SRU), 118798-96-2; (CTTH)(BPA dicyanate) (copolymer), 118798-95-1; (BPA dicyanate)(Dat-Tym) (copolymer), 118798-94-0; potassium *tert*-butoxide, 865-47-4; tetrabutylammonium bromide, 1643-19-2.

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Synthesis of Thermotropic Liquid Crystalline Side-Chain Polymers via Chemical Modification of Polymeric Carboxylic Acids

Y. F. Maa and S. H. Chen*

Department of Chemical Engineering and Laboratory for Laser Energetics, University of Rochester, Rochester, New York 14627.
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ABSTRACT: Esterification of poly(acrylic acid) and poly(methacrylic acid) with relatively bulky alkyl halides via the corresponding tetrabutylammonium salts in dimethylformamide was conducted by following three different procedures. The following observations were made: (1) the presence of methanol and water was detrimental to the desired reaction on the polymeric substrate, (2) the excess tetrabutylammonium hydroxide in the presence of a small amount of water caused the hydrolysis of base-sensitive alkylating agents, and (3) residual water accompanying polymeric carboxylate was conducive to the enhancement of the degree of substitution and product yield for alkylating agents that can survive the basic condition. For the base-sensitive alkylating agent, it is essential that residual tetrabutylammonium hydroxide be removed. The product showed liquid crystallinity with a degree of substitution as low as 25% for the polyacrylate backbone. For the stiffer polymethacrylate backbone, a degree of substitution of at least 40% is needed for mesophase formation.

I. Introduction

Since Finkelmann and Ringsdorf[1,2] first proposed the idea of inserting a flexible spacer between a polymer backbone and a mesogenic group to induce liquid crystal formation in a polymeric system, voluminous publications have appeared to date on the synthesis of liquid crystalline side-chain polymers. Of all the backbone structures that have been synthesized, polyacrylate and polymethacrylate are by far the most extensively studied.[3-7] Both acrylate- and methacrylate-based liquid crystalline polymers can, in principle, be synthesized either by direct polymerization of appropriate monomers or by chemically modifying poly(acrylic acid) and poly(methacrylic acid). The chemical modification approach has a distinctive advantage in that a wide range of narrowly defined chain lengths can be realized by the commercial availability of parent polymeric carboxylic acids. Moreover, liquid crystalline polymers with high stereochemical purity can be achieved.[8] These two features are particularly important in furnishing liquid crystalline polymers with well-defined structures for the elucidation of structure–property relationship.

There are several approaches to the synthesis of mesomorphic polyacrylate and polymethacrylate by way of

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* Author to whom correspondence should be addressed.