Synthesis, Polymerization, and Copolymerization of Aliphatic Vinyl Azide

Nirmala R. James, A. Jayakrishnan

Polymer Chemistry Division, Biomedical Technology Wing, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Satelmond Palace Campus, Trivandrum 695 012, India

ABSTRACT: The synthesis and characterization of a fully aliphatic polymeric azide by polymerization of its vinyl monomer 1,3-diazidoisopropyl methacrylate (DAIPM) is reported. DAIPM was prepared by azidation of epichlorohydrin followed by coupling with methacrylic acid. Homopolymer and copolymers with methyl methacrylate were prepared and characterized by IR, GPC, TGA, DTA, and elemental analyses. These polymers are freely soluble in organic solvents like dichloromethane, tetrahydrofuran, dimethyl formamide, acetone, and so forth and do not crosslink on storing. The polymers show decreased thermal stability with an increase in azide content and undergo exothermic decomposition on heating. © 2003 Wiley Periodicals, Inc. J Appl Polym Sci 87: 1852–1857, 2003

Key words: azide polymers; epichlorohydrin; copolymerization; vinyl azide; diazidoisopropyl methacrylate

INTRODUCTION

Organoazides are versatile intermediates in synthetic organic chemistry, because the azide moiety can subsequently be converted into several other types of substituent groups.[1,2] Azides find extensive application in the field of lithography as photosensitive components.[3–6] Quinone diazide sulfonates of compounds with phenolic groups or aromatic azides, such as 1-azidopyrene, phenylene bisazide, 4,4′-diazidobiphenyl, 4,4′-diazidobiphenyl methane, and 2-anilino-5-azidobenzoic acid, have been used for this purpose. Naphthaquinone diazide along with copolymers of methyl methacrylate (MMA) and methacrylic acid (MA) were used to obtain photoresist coatings on Si wafers.[4] Copolymers of MMA and poly(p-azido styrene) were also used.[5] A reaction of poly(3-chloromethyl-2,6-dimethyl phenylene oxide) with sodium azide to prepare the corresponding polymeric azide was reported by Daly.[7] Azide catalysts such as phenacyl azide, azidonitrobenzene, and 2-azidonitroaniline were employed for a peroxyoxalate chemiluminescence reaction.[8] Aryl azides with an azidophenyl moiety have proved to be useful in photoimmobilization of dipyridamole onto a polyurethane surface to improve hemocompatibility.[9] Polymerization of an ester of 2-hydroxyethyl methacrylate and p-azidobenzoic acid yielded a polymeric dye for nonlinear optics.[10,11]

Usually aliphatic polymeric azides are prepared by converting poly(vinyl chloride)[12,13]; poly(epichlorohydrin)[14]; halohydrins from poly(glycidyl methacrylate) and polybutadiene; and polymeric haloethyl acrylates, methacrylates, and methacrylamides[15–17] into the corresponding azides by treatment with sodium azide. To the best of our knowledge, the synthesis and polymerization of vinyl azides to prepare their corresponding polymers are not reported in the literature. A major drawback of the polymeric azides from acrylic polymers is that they undergo rapid crosslinking on storage. However, these polymers were reacted with acetylenic and olefinic derivatives to attain triazole derivatives[15,16] and with triphenylphosphine to yield phosphine imines that act as intermediates for the preparation of amines, imines, carbodiimides, and so forth.[17] Tanaka et al.[18] reported the conversion of the chloroethyl ester of poly(L-glutamic acid) into an azidoethyl ester by a reaction with sodium azide.

Our interest in polymeric azides springs from the observation that a covalently bound azide moiety on a polymer surface can still exert potential antibacterial properties against both Gram positive and Gram negative organisms. In a recent communication[19] we showed that azidated poly(vinyl chloride) resists bacterial adhesion of both *Staphylococcus aureus and Escherichia coli.* Even though sodium azide has been used an antibacterial agent for many years, it was surprising to observe that the covalently bound azide resists bacterial adhesion and colonization on the polymer surface. It was therefore of interest to synthesize aliphatic vinyl azides that could be polymerized and copolymerized with other vinyl monomers in small
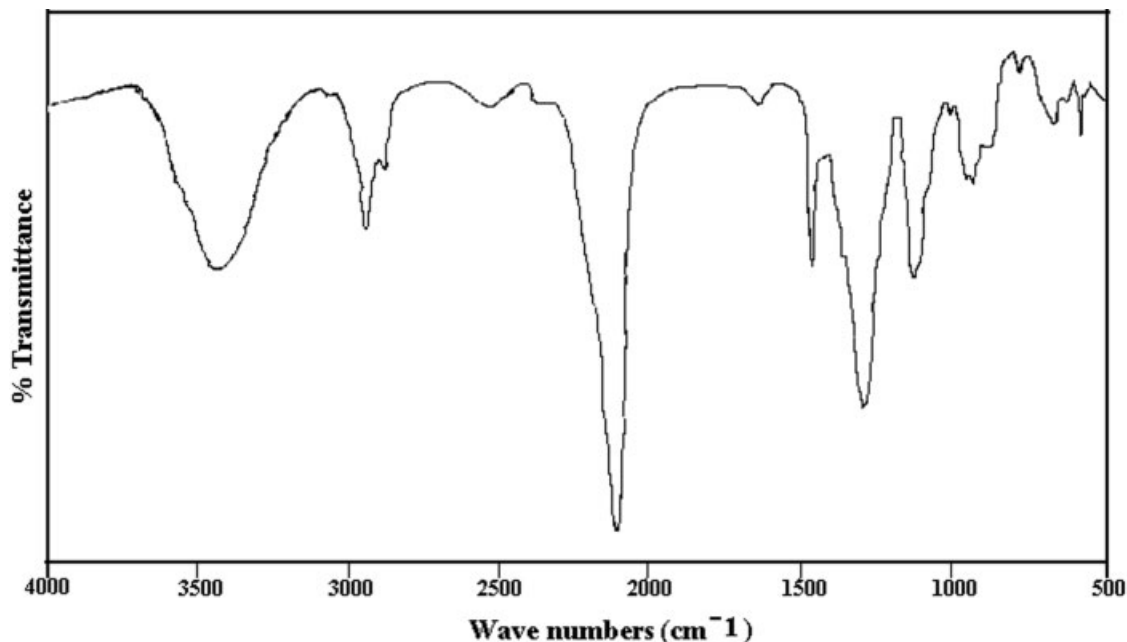
Figure 1 The IR spectrum of 1,3-diazidopropan-2-ol.

quantities and to examine their antibacterial properties.

The present work thus deals with the synthesis, characterization, polymerization, and copolymerization of an aliphatic vinyl azide. It is significant that the prepared polymers did not undergo crosslinking when stored and were freely soluble in solvents for acrylic polymers.

EXPERIMENTAL

Materials

Epichlorohydrin and sodium azide obtained from S.D. Fine Chemicals Ltd. (Bombay, India) were used without further purification. While *tert*-butylammonium bromide (TBAB, Spectrochem, Bombay, India) dicyclohexyl carbodiimide (DCC, Sigma), and dimethylamino pyridine (DMAP, Sigma) were used as received; 2,2′-azobis isobutyronitrile (AIBN, BDH) was recrystallized from methanol and used. MA (Aldrich) was purified by distillation under reduced pressure. MMA (Merck) was freed of inhibitor by washing with sodium hydroxide solution followed by water; then it was dried over anhydrous sodium sulfate and distilled under reduced pressure prior to use. Solvents such as dichloromethane (DCM), dimethyl formamide (DMF), and methanol were distilled and used.

Methods

The NMR spectra were recorded using a Bruker 200-MHz instrument (AC-200, Bruker) with tetramethyl silane (TMS) as the internal standard and CDCl$_3$ as the

solvent. The IR spectra were recorded using a FTIR spectrometer (model 410, Nicolet). Thermal analyses were performed using a TA thermal analyzer (model SDT-2960, TA Instruments Inc.) in a nitrogen atmosphere at a heating rate of 10 or 20°C/min. The number- and weight-average molecular weights and molecular weight distributions were determined by GPC using a Waters HPLC system with a 510 pump, a 7725 Rheodyne injector, Styragel HR columns, Millenium 32 software, and an R401 differential refractometer. Tetrahydrofuran (THF) was used as the mobile phase at a flow rate of 1 mL/min. The instrument was calibrated using polystyrene standards (Polysciences). The elemental analyses of the copolymers were carried out using a Perkin–Elmer CHNS analyzer (series II, model 2400).
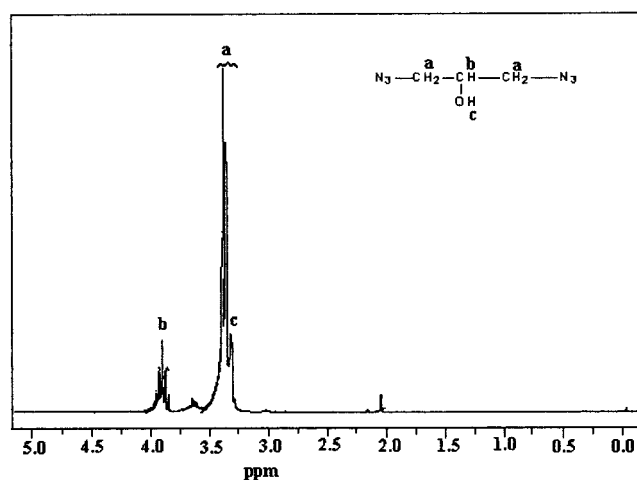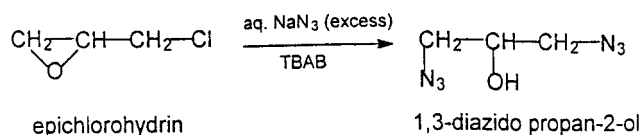

Figure 2 The ^{1}H-NMR spectrum of 1,3-diazidopropan-2-ol.

epichlorohydrin   1,3-diazido propan-2-ol

Scheme 1 The preparation of 1,3-diazidopropan-2-ol.

Scheme 2 The formation of 1,3-diazidopropan-2-ol from epichlorohydrin.

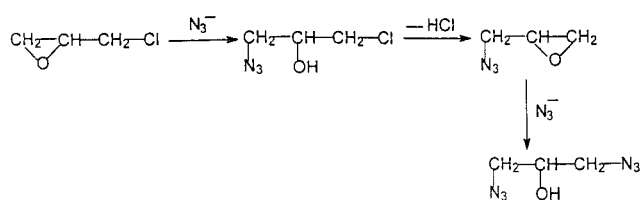## Synthesis of 1,3-diazidopropan-2-ol

1,3-Diazidopropan-2-ol was prepared by azidation of epichlorohydrin. Sodium azide (40 g, 0.61 mol) was dissolved in 50 mL of water; 0.312 g (0.001 mol) of TBAB and 20 mL (23.6 g, 0.25 mol) of epichlorohydrin were added and stirred in the dark for 24 h at room temperature. After diluting the reaction mixture with DCM, the organic layer was separated and evaporated off in a rotavapor at room temperature. Thin layer chromatography (TLC, Silicagel 60 TLC plates, Merck) of the product obtained using ethyl acetate/hexane (2:3) as the eluent showed two components, and the major component with an RF value of 0.66 was isolated by column chromatography on a silicagel column (60–200 mesh, SD Fine Chem Ltd.). Elution was performed using an ethyl acetate/hexane mixture. Yield: ~60%. IR (neat, cm^{-1}): 3417 (ν_{OH}), 2101 ($\nu_{C-N3)_3}$ ^{1}H-NMR (200 MHz, CDCl$_3$, TMS, ppm): δ 3.91 (m, 1H, —CH$_2$—CHN$_3$—CH$_2$—), 3.38 (d, 4H, —CH_2—CHN$_3$—CH$_2$—), 3.33 (s, 1H, —OH)

Determination of epoxy value

The presence of any unreacted epichlorohydrin in the product was checked by the determination of the epoxy value via the hydrochlorination method.[20] Into an Erlenmeyer flask was introduced 0.5 g of the product and 25 mL of the hydrochlorination reagent (6.5 mL of concentrated HCl, made up to 250 mL with dioxane), and the flask was stoppered and shaken well. The contents were allowed to stand at room temperature for 15 min. At the end of the reaction period, the contents were titrated against 0.1N methanolic NaOH using phenolphthalein as an indicator. A blank was also carried out. For comparison, the experiment was also performed with an equal quantity of epichlorohydrin.

Synthesis of 1,3-diazidoisopropyl methacrylate (DAIPM)

1,3-Diazidopropan-2-ol (5 g, 0.0358 mol) was dissolved in 25 mL of DCM and the reaction mixture was cooled to 0°C. To this was added 0.43 g (0.00358 mol) of DMAP, 3.08 g (0.0358 mol) of MA, and 7.37 g (0.0358 mol) of DCC. Dicyclohexyl urea started precipitating immediately. The reaction was allowed to continue for 12 h with magnetic stirring at room temperature. The product was filtered to remove the di-

cyclohexyl urea and the solvent was evaporated in a rotavapor under reduced pressure. TLC showed three components (ethyl acetate/hexane 2:3). The major component with an RF value of 0.76 was isolated by column chromatography using ethyl acetate/hexane (2:3) as the eluent. Yield: ~80%. IR (neat, cm^{-1}): 2100 ($\nu_{C-N3)_3}$ 1720 ($\nu_{C=O}$), 1635 ($\nu_{C=C}$).

Preparation of homopolymer and copolymers

DAIPM (4 g) was placed in 20 mL of dry DMF in a 100-mL round-bottomed flask fitted with an overhead stirrer, 0.004 g (0.1 wt %) of AIBN was added, and polymerization was performed at 75°C for 5 h with stirring under a stream of nitrogen. The reaction mixture was poured into methanol and the precipitated polymer was filtered and dried under reduced pressure and stored at 4°C in the dark. Copolymers of DAIPM with MMA were also prepared in a similar fashion at different molar compositions of DAIPM.

RESULTS AND DISCUSSION

Epichlorohydrin was azidated using sodium azide in the presence of TBAB as the phase transfer catalyst. The determination of the epoxy content of the product showed that the epoxy content was virtually nil because the hydrochlorination reagent that was added remained unconsumed, which was indicated by a titer value that was almost equal to that of the blank. When the titration was performed with an equal quantity of epichlorohydrin, only a very small quantity of the hydrochlorination reagent was left unconsumed. Sodium azide is one of the main nucleophilic azide sources in organo azide preparation.[1] It is known that sodium azide reacts with epoxides to give azido alcohols.[21–23] The IR spectrum of the purified product obtained after the reaction of DAIPM with sodium

1,3-diazido propan-2-ol   methacrylic acid   1,3-diazido isopropyl methacrylate
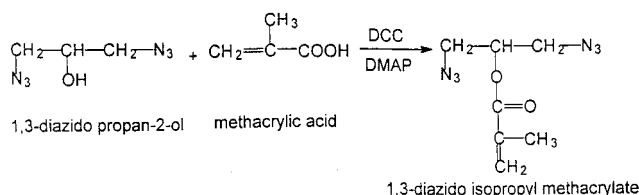
Scheme 3 The preparation of DAIPM.

TABLE I
Compositions and Yields of Polymers

Polymer Code	Feed Composition (mol %)		Copolymer Composition (mol %)		Yield %
	MMA	DAIPM	MMA	DAIPM	
P1	80	20	84	16	60
P2	50	50	61	39	70
P3	20	80	35	65	60
P4	0	100	0	100	62

azide given in Figure 1 clearly shows the presence of a hydroxyl group at 3417 cm^{-1} and azide at 2100 cm^{-1}.

The NMR spectrum (Fig. 2) of the product shows a multiplet centered at 3.91 ppm, corresponding to a single proton, a doublet at 3.38 ppm, corresponding to four protons, and singlet at 3.33 ppm, corresponding to a single proton due to a hydroxyl proton. Epichlorohydrin can undergo two separate nucleophilic epoxide ring opening reactions, because of the feasibility of the initial product to readily reform an oxirane ring, and generate an intermediate glycidyl adduct. The two ring opening reactions occur almost exclusively by attack of the nucleophile on the primary carbon atom.[22] It seems that under the reaction conditions, wherein the concentration of the azide is more than twice the molar concentration of epichlorohydrin, the azide ion has also replaced the chlorine atom in the epichlorohydrin. Thus, the product formed is 1,3-diazidopropan-2-ol (Scheme 1). The possible reaction pathway is depicted Scheme 2.

MA was reacted with 1,3-diazidopropan-2-ol in DCM in the presence of DCC and DMAP to attain DAIPM (Scheme 3). An IR spectrum of the product showed an intense peak corresponding to azide at 2100 cm^{-1} and the ester group at 1720 cm^{-1}.

A homopolymer and copolymers with MMA were prepared from the above monomer. Polymerizations were performed in DMF at 75°C for 5 h. Monomer feed compositions, the percentage of yield, and copolymer compositions determined by elemental analyses are given in Table I. All the polymers were freely soluble in DCM, DMF, THF, acetone, and so forth. The polymers obtained were characterized by IR, TGA, GPC, and elemental analysis.

TABLE II
Molecular Weight of Polymers Determined by GPC

| Polymer Code	M_n (Dal)	M_w (Dal)	Polydispersity
P1	23,472	41,480	1.767
P2	14,453	36,918	2.554
P3	11,831	24,443	2.066
P4	12,568	32,475	2.584
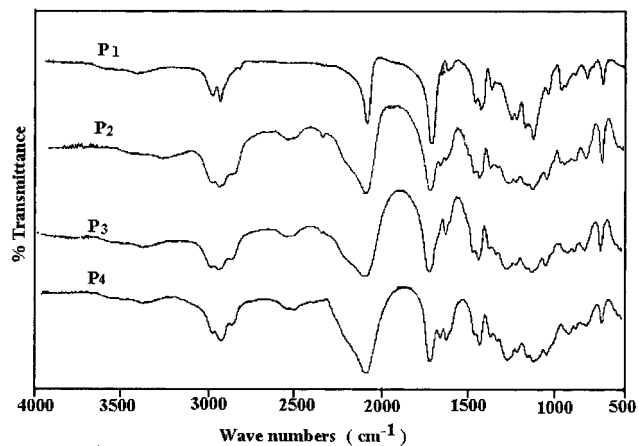
Figure 3 IR spectra of polymers and their molar compositions: P1, 80:20 MMA/DAIPM; P2, 50:50 MMA/DAIPM; P3, 20:80 MMA/DAIPM; P4, 0:100 MMA/DAIPM.

The molecular weights of the polymers determined by GPC are given in Table II. Note that with an increasing amount of the azide monomer DAIPM in the feed, there is a gradual decrease in the molecular weight of the polymer formed. The IR spectra of the samples are given in Figure 3. We found that as the concentration of the azide component increases, the intensity of the peak at 2100 cm^{-1}, which is due to azide, increases with respect to the peak at 1730 cm^{-1}, which is due to the ester group. TG traces of poly(diazido isopropyl methacrylate) and copolymers obtained at a heating rate of 10°C/min are given in Figure 4. The thermal stability of the copolymers decreases with the increase in the azide component. A similar observation was made by Jayakrishnan et al. in the case of azide substituted poly(vinyl chloride).[12] The copolymer with the lower azide component (P1) showed better thermal stability and 50% weight loss occurred at 393°C; for copolymers with higher concen-
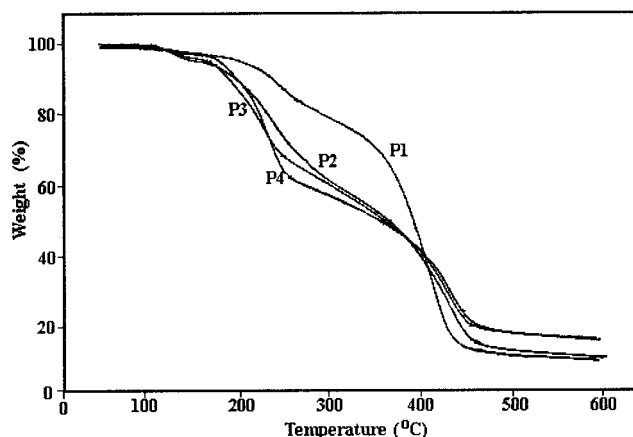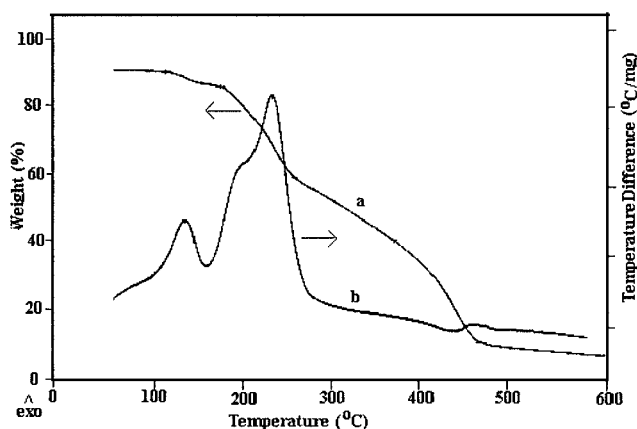

Figure 4 TGA traces of polymers (heating rate 10°C/min) and their molar compositions: P1, 80:20 MMA/DAIPM; P2, 50:50 MMA/DAIPM; P3, 20:80 MMA/DAIPM; P4, 0:100 MMA/DAIPM.
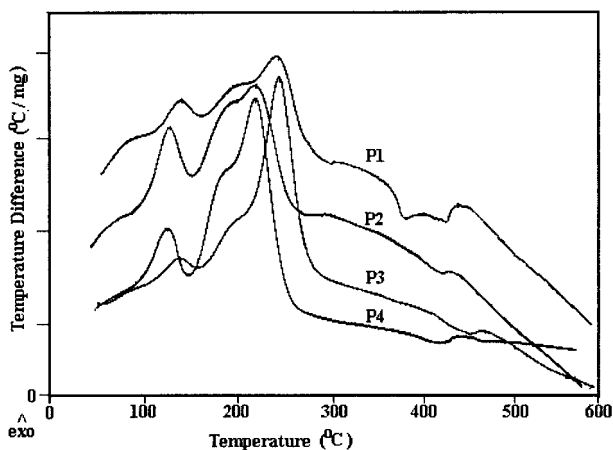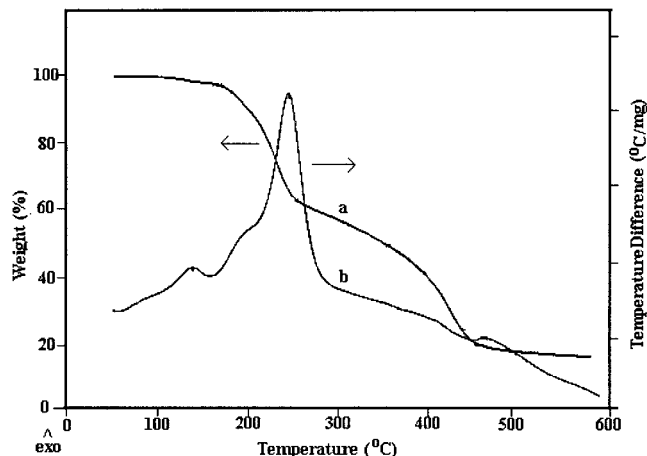
Figure 5 DTA traces of polymers (heating rate 10°C/min) and their molar compositions: P1, 80:20 MMA/DAIPM; P2, 50:50 MMA/DAIPM; P3, 20:80 MMA/DAIPM; P4, 0:100 MMA/DAIPM.

Figure 7 (a) TGA and (b) DTA traces of P4 (heating rate 10°C/min) with a molar composition of 0:100 MMA/DAIPM.

trations of the azide component, 50% weight loss occurred at 360°C.

DTA traces of the samples are given in Figure 5. All the samples show peaks attributable to exothermic decomposition. Azides are known to be explosives[24] and undergo reactions with the evolution of hot gases on heating. The temperature at which this exothermic reaction takes place varies with the azide content. Decomposition takes place mainly in two stages. This behavior becomes predominant in the case of copolymers with higher azide content. This is clear from Figures 6 and 7 in which DTA traces of P3 and P4 along with a TGA are given. Sample P1 shows a major exothermic peak at 244°C, followed by a broad endothermic region, corresponding to the gradual decomposition, as seen from the TGA. Samples P2 and P3 show the major exothermic peak at 230°C, and P4 has a similar peak at 245°C. It is seen from Figure 5 that the peaks due to the exothermic decomposition be-
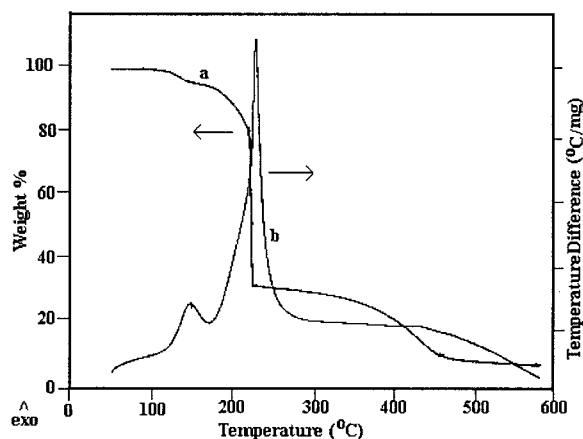
come narrow and well defined as the azide content in the copolymer increases. The decrease in weight percentage roughly matches the nitrogen contents of the copolymers. Thus, the exothermic decomposition corresponds to decomposition of the azide component with the evolution of nitrogen. The low intensity exothermic peak seen with all samples in the DTA at around 135°C, corresponding to a weight loss of not more than 4%, is presumably due to the presence of very small molecular weight oligomers in the polymers. Thermograms were also taken at a heating rate of 20°C/min for P3 (Fig. 8). The TGA showed a rapid decrease in weight starting at around 200°C with nearly 70% weight loss, but a sharp exotherm with a peak at 226°C was observed in the corresponding DTA. It has been reported that for explosives like lead azide and barium azide, when higher heating rates were employed, 100% weight loss occurred at 200°C with a very sharp exotherm in the DTA, which was

Figure 6 (a) TGA and (b) DTA traces of P3 (heating rate 10°C/min) with a molar composition of 20:80 MMA/DAIPM.

Figure 8 (a) TGA and (b) DTA traces of P3 (heating rate 20°C/min) with a molar composition of 20:80 MMA/DAIPM.

attributed to detonation (explosive decomposition) taking place at that temperature.[25] Comparing the thermograms taken at 10°C/min with those at 20°C/min, it can safely be assumed that these copolymers are susceptible to detonation at higher heating rates.

A homopolymer and copolymers of DAIPM with MMA were not found to undergo crosslinking, even after a storage period of 4 months, because they were freely soluble in common solvents for acrylic polymers. A preliminary toxicological evaluation of these polymers by cell culture showed that they were not cytotoxic. This was important from the point of view of their intended use in the biomedical field. The bacterial resistance of these polymers is presently being evaluated and will be reported elsewhere. Apart from their possible application in the biomedical field, the thermal properties of these polymers point to their possible use as explosives also.

CONCLUSIONS

A novel vinyl azide monomer (DAIPM), which is capable of undergoing free-radical homopolymerization and copolymerization with other vinyl monomers, was prepared starting from epichlorohydrin and MA. Epichlorohydrin could be conveniently azidated by sodium azide in the presence of a phase transfer catalyst that was then coupled with MA to obtain an azide group containing an acrylic monomer. A homopolymer and copolymers with MMA with different azide contents could be prepared from the monomer. These polymers were found to be soluble in common organic solvents even after prolonged storage, a feature that is not normally seen with aliphatic polymeric azides because they are known to undergo crosslinking on storage. The copolymers show reduced thermal stability with an increase in the azide content. The copolymers and the homopolymer undergo exothermic decomposition.

References

1. Turnbull, K. In Encyclopedia of Reagents for Organic Synthesis; Paquette, L. A., Ed.; Wiley: New York, 1995; Vol. 7, p 4509.
2. Petite, H.; Frei, V.; Huc, A.; Herbage, D. J Biomed Mater Res 1994, 28, 159.
3. Uetani, Y.; Takemoto, I. U.S. Pat. 6,245,478 (2001).
4. Okino, T.; Asakawa, K.; Shida, N.; Ushirogouchi, T.; Nakase, M. U.S. Pat. 6,228,552 (2001).
5. Conley, W. E.; Fahey, J. T.; Moreau, W. M.; Sooriya, K. R.; Welsh, K. M. U.S. Pat. 5,795,701 (1998).
6. Conley, W. E.; Fahey, J. T.; Moreau, W. M.; Sooriya, K. R.; Welsh, K. M. U.S. Pat. 5,783,361 (1998).
7. Daly, W. H. Polym Prepr Am Chem Soc Div Polym Chem 1979, 20, 835.
8. Oh, S. K.; Cha S. H. U.S. Pat. 5,494,827 (1996).
9. Aldenhoff, Y. B. J.; Koole, L. H. J Biomed Mater Res 1995, 29, 917.
10. Hayesh, A.; Goto, Y.; Nakayama, M.; Sato, H.; Watanabe, T.; Miyata, S. Macromolecules 1992, 25, 5094.
11. Kato, M.; Hirayama, T.; Matsuda H.; Minami, N.; Okada, S.; Nakanishi, H. Makromol Chem Rapid Commun 1994, 15, 741.
12. Jayakrishnan, A.; Sunny, M. C.; Rajan, M. N. J Appl Polym Sci 1995, 56, 1187.
13. Takeshi, M.; Okawara, M. J Polym Sci Polym Lett Ed 1969, 7, 201.
14. Vanderberg, E. J. U.S. Pat. 3,654,917 (1972).
15. Cohen, H. L. J Polym Sci Polym Chem Ed 1981, 19, 1337.
16. Cohen, H. L. J Polym Sci Polym Chem Ed 1981, 19, 3269.
17. Cohen, H. L. J Polym Sci Polym Chem Ed 1985, 23, 1671.
18. Tanaka, H.; Endo, T.; Okawara, M. Nippon Kagaku Kaishi 1973, 1775.
19. Lakshmi, S.; Pradeep Kumar, S. S.; Jayakrishnan, A. J Biomed Mater Res 2002, 61, 26.
20. Jahn, H.; Goetzky, P. In Epoxy Resins, Chemistry and Technology; May, C. A., Tanaka, Y., Eds.; Marcel Dekker : New York, 1973; p 663.
21. March, J. Advanced Organic Chemistry, 3rd ed.; Wiley Eastern: New Delhi, 1978; p 306.
22. Lenz, R. W. Organic Chemistry of Synthetic Polymers; Wiley: New York, 1967; p 161.
23. Huber, J. E. In Encyclopedia of Reagents for Organic Synthesis; Paquette, L. A., Ed.; Wiley: New York, 1995; Vol. 4, p 2326.
24. Lindner, V. In Kirk–Othmer Encyclopedia of Chemical Technology, 3rd ed.; Wiley: New York, 1978; Vol. 9, p 561.
25. Maycock, J. N.; Pai, V. R. In Thermal Analysis; Schwenker, R. F., Jr., Garn, P. D., Eds.; Academic: New York, 1969; Vol. 1, p 243.