

Well-defined poly(2-hydroxyethyl methacrylate) and its amphiphilic block copolymers via acidolysis of anionically synthesized poly(2-vinyloxyethyl methacrylate)

Eli Ruckenstein, Hongmin Zhang

Chemical Engineering Department, State University of New York at Buffalo, Amherst, NY 14260, USA

Received: 22 June 2001/Revised version: 15 August 2001/Accepted: 15 August 2001

Summary

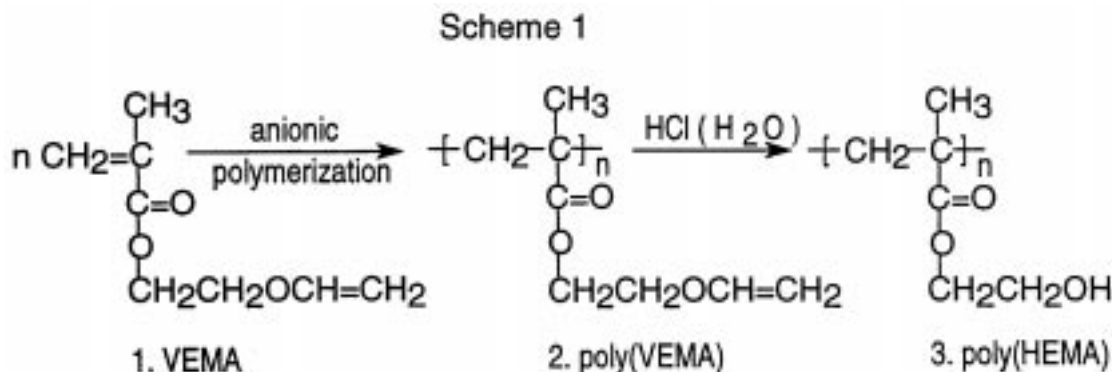
A novel approach to a well-defined poly(2-hydroxyethyl methacrylate) [poly(HEMA)] and to its amphiphilic block copolymers was developed. The selective living anionic polymerization of the methacryloyl group of the bifunctional monomer 2-vinyloxyethyl methacrylate (VEMA) generated a functional polymer with a controlled molecular weight and a narrow molecular weight distribution ($M_w/M_n = 1.05-1.09$). This polymer is very stable under normal conditions. Being soluble in the common organic solvents, its characterization could be carried out easily. The unreacted vinyl groups in the side chains of the resulting polymer were further reacted with hydrochloric acid. This acidolysis changed poly(VEMA) to a well-defined poly(HEMA). In addition, the anionic block copolymerization of VEMA with styrene or methyl methacrylate also proceeded smoothly, generating the corresponding block copolymers. After acidolysis, these copolymers were turned into amphiphilic block copolymers containing a hydrophilic poly(HEMA) block.

Introduction

Poly(2-hydroxyethyl methacrylate) [poly(HEMA)] has become one of the most important biomaterials, due to its biocompatibility, transparency and hydrophilicity (1). Because of its usefulness, the development of techniques for its synthesis has received great attention. In addition to the nonliving radical polymerization which produces poly(HEMA) with uncontrolled molecular weight and broad molecular weight distribution (MWD), several living polymerization techniques have also been applied to this monomer. Although the group transfer polymerization (2) and the recently-developed atom transfer radical polymerization (3) can provide a narrow MWD poly(HEMA), the living anionic polymerization is still the best way to prepare, not only a well-defined homopoly(HEMA), but block and graft copolymers with other monomers as well (4).

Before being subjected to anionic polymerization, the hydroxyl group of HEMA must be protected. Otherwise, it deactivates the anionic initiator instantaneously. For this purpose, the silyl group (5) and the acetoxyethyl group (6) have been used as protecting

groups, and both are sufficiently stable to allow the anionic polymerization to proceed smoothly. However, after polymerization, the protecting groups detach by themselves easily, and this makes the characterization of the (co)polymers difficult, because poly(HEMA) is insoluble in the common solvents, such as toluene, chloroform, THF, etc. Therefore, the ideal way is to obtain a stable and soluble polymer first, which after characterization can be easily changed into poly(HEMA).



Such an approach to poly(HEMA) and to its block copolymers with styrene (St) and methyl methacrylate (MMA) was developed in the present paper. As shown in Scheme 1, the methacryloyl group of 2-vinyloxyethyl methacrylate (VEMA; 1 in Scheme 1) could be selectively polymerized anionically to generate a stable functional polymer, poly(VEMA) (2 in Scheme 1). Poly(HEMA) could be obtained by eliminating the vinyl groups present in the side chains of poly(VEMA) via the reaction with hydrochloric acid. Amphiphilic block copolymers, poly(St-b-HEMA) and poly(MMA-b-HEMA) were also synthesized by the block copolymerization of VEMA with St or MMA, followed by acidolysis.

Experimental

Materials

Tetrahydrofuran (THF), toluene, MMA (Aldrich, 99%), St (Aldrich, 99%), 1,1-diphenylethylene (DPE, Aldrich, 97%) and lithium chloride (Aldrich, 99.99%) were purified as reported previously (7). 2-Vinyloxyethyl methacrylate (VEMA) was synthesized through the reaction between 2-chloroethyl vinyl ether (CEVE, Aldrich, 99%) and sodium methacrylate (SMA, Aldrich, 99%) (8), in the presence of tetrabutylammonium iodide as a phase transfer catalyst and 4-tert-butylcatechol as inhibitor. To increase the monomer yield, an improved synthetic method was used, in which SMA was added twice and the product was distilled directly without any working up. CEVE (125 g, 1.17 mol), SMA (32.5 g, 0.30 mol), tetrabutylammonium iodide (1.0 g) and 4-tert-butylcatechol (0.8 g) were added to a 500 mL round-bottom flask equipped with a condenser, a thermometer and a paddle stirrer. Under nitrogen, this mixture was stirred at 115°C for 5 h. Then, SMA (15.0 g, 0.14 mol) was added again and the reaction allowed to proceed for an additional 10 h. After the byproduct NaCl was removed by filtration, the filtrate was directly distilled under reduced pressure (b.p. 45°C/1 mm Hg). In this manner, a pure VEMA was obtained with a high yield (65.0 g, 95%, based on the amount of SMA added twice).

Polymerization

For the anionic homopolymerization of VEMA, the initiator 1,1-diphenylhexyllithium (DPHL) was first prepared by reacting DPE with n-BuLi ($[DPE]/[n-BuLi]_0 = 1.2$), in THF, at -40°C , for 20 min. Then, the polymerization was carried out at -70°C by adding VEMA to the above initiator solution. After a selected time interval, the reaction was terminated by adding a small amount of methanol. The polymer was precipitated in water and vacuum-dried overnight at 40°C . The anionic block copolymerization of VEMA and MMA was carried out using the polymerization sequence of VEMA followed by MMA or vice versa, under conditions similar to those for the homopolymerization. For the preparation of poly(St-b-VEMA), St was first polymerized anionically, using n-BuLi as initiator, in a mixture of toluene and THF (3:1 by volume), at -55°C . Then, a THF solution of DPE ($[DPE]/[n-BuLi]_0 = 1.3$) and LiCl ($[LiCl]/[n-BuLi]_0 = 3$) was added. After 20 min, VEMA was polymerized at -70°C by adding the monomer to the above initiator solution. The block copolymers thus obtained were purified in a manner similar to that used for the homopolymer.

Acidolysis

The acidolysis was carried out by using either an immediate or a delayed process. In the former case, the polymerized solution was diluted to 3g/100 mL with THF and the resulted solution (30 mL) was reacted with hydrochloric acid (6 M, 2 mL) at room temperature. As the reaction proceeded, the system became cloudy, because of the poor solubility of the resulting poly(HEMA) in THF. To keep the reaction going homogeneously, a few drops of methanol were gradually added. After about 1 h, the polymer was precipitated in hexane, washed with water and vacuum-dried at 35°C overnight. In the delayed process, the purified poly(VEMA) or the block copolymer was re-dissolved in THF (3g/100 mL) and the acidolysis was performed in the same way.

Measurements

^1H NMR spectra were recorded in CDCl_3 or CD_3OD on an Inova-400 spectrometer. M_n and M_w/M_n of the (co)polymer were determined by gel permeation chromatography (GPC) on the basis of a polystyrene calibration curve. The GPC measurements were carried out using THF as solvent, at 30°C , with a 1.0mL/min flow rate and a 1.0cm/min chart speed. FT-IR spectra were recorded using KBr pellets on a Perkin-Elmer 1760-X spectrometer.

Results and Discussion

Homopolymerization of VEMA

VEMA possesses both a vinyloxy type and a methacryloyl type polymerizable C=C bond. Because the former can undergo only cationic polymerization (8), it does not affect the anionic polymerization of the latter. The anionic polymerization of VEMA was carried out using DPHL as initiator, in THF, in the presence of LiCl ($[LiCl]/[n-BuLi]_0 = 3$) (9), at -70°C . As shown in Table 1, the monomer conversion was 100% in each case, the molecular weight of the resulting polymer could be well controlled by the concentration ratio of the monomer and initiator, and its MWD was very narrow ($M_w/M_n = 1.05-1.09$). As illustrated in Fig. 1a, the GPC chromatogram of poly(VEMA) exhibited a very sharp, symmetrical peak. The above results indicate that the anionic polymerization of VEMA proceeded smoothly without any side reaction. The resulting

poly(VEMA) was very stable. Even after being stored in a vinyl bag for two months, no change in its molecular weight or molecular structure was detected by GPC and NMR. In addition, because it is soluble in most common solvents, such as toluene, benzene, chloroform, THF, 1,4-dioxane, acetone, etc., its characterization could be performed easily.

Table 1. Anionic polymerization of VEMA^a

Run	[VEMA] ₀ /M	[n-BuLi] ₀ /mM	Time/min	10 ⁻⁴ M _n ^b	M _w /M _n ^b
PVEMA-1	0.427	11.1	30	0.60(0.62)	1.05
PVEMA-1	0.427	6.6	40	1.05(1.03)	1.05
PVEMA-1	0.427	4.0	50	1.78(1.69)	1.07
PVEMA-1	0.382	2.6	60	2.25(2.32)	1.05
PVEMA-1	0.592	3.0	80	3.40(3.10)	1.08
PVEMA-1	0.427	1.7	90	4.10(4.00)	1.09

^a Before the monomer addition, n-BuLi was reacted with DPE ([DPE]/[n-BuLi]₀ = 1.2) at -40°C for 20 min and the resulting adduct DPHL was used as the initiator directly. The polymerization was carried out in THF, in the presence of LiCl ([LiCl]/[n-BuLi]₀ = 3), at -70°C. The monomer conversion was 100% in each case.

^b Determined by GPC. The data in the brackets are the calculated M_n.

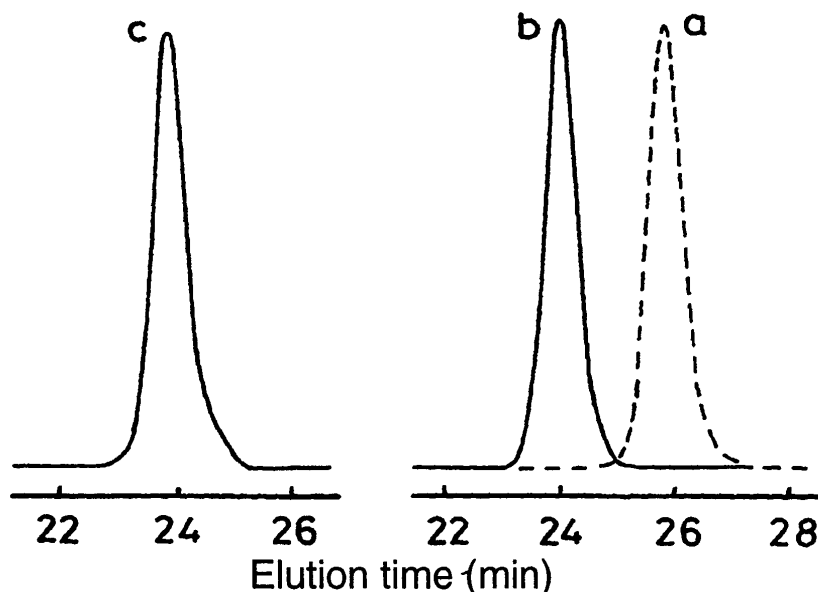


Figure 1. GPC traces of living poly(VEMA) (peak a, M_n = 4810, M_w/M_n = 1.05), poly(VEMA-*b*-MMA) (peak b, M_n = 19100, M_w/M_n = 1.04) prepared via the block copolymerization of MMA from the living end of the above poly(VEMA), and the re-protected poly(HEMA-*b*-MMA) (peak c, M_n = 21800, M_w/M_n = 1.07).

Block copolymerization of VEMA with MMA or St

The block copolymerization of VEMA with MMA was carried out under conditions similar to those used for the homopolymerization of VEMA. As shown in Table 2, regardless of the polymerization sequence (VEMA→MMA or MMA→VEMA), the block copolymerization proceeded smoothly in each case. The determined molecular weights and the copolymer compositions were consistent with those calculated and the

resulting copolymers possessed very narrow MWDs ($M_w/M_n = 1.04-1.12$). Figures 1b and 1a present the GPC chromatograms of a block copolymer, poly(VEMA-*b*-MMA), and of its precursor, poly(VEMA), respectively. After the block copolymerization of MMA from the living end of poly(VEMA) (peak a), a new single, sharp peak (peak b) corresponding to the resulting block copolymer appeared in the high molecular range, indicating that a pure block copolymer, free of its precursor polymer, was obtained.

Table 2. Anionic block copolymerization of VEMA with MMA or St ^a

Run	Polymerization Sequence	n-BuLi mmol	M ₁ g	M ₂ g	10 ⁻⁴ M _n ^b	M _w /M _n ^b	M ₁ /M ₂ ^c
VM-1	VEMA-MMA	0.20	2.0	2.0	2.30(2.02)	1.11	52/48(50/50)
VM-2	VEMA-MMA	0.20	1.0	3.0	1.91(2.02)	1.04	25/75(25/75)
MV-1	MMA-VEMA	0.20	2.0	2.0	2.20(2.02)	1.09	49/51(50/50)
MV-2	MMA-VEMA	0.20	1.0	3.0	1.96(2.00)	1.05	26/74(25/75)
SV-1	St-VEMA ^d	0.20	1.0	3.0	1.92(2.00)	1.05	27/73(25/75)
SV-2	St-VEMA ^d	0.25	2.0	2.0	1.64(1.60)	1.09	51/49(50/50)
SV-3	St-VEMA ^d	0.10	2.0	2.0	4.38(4.00)	1.12	48/52(50/50)

^a The block copolymerization of VEMA and MMA was carried out using a sequential monomer addition of VEMA followed by MMA or vice versa, in THF, in the presence of LiCl ([LiCl]/[n-BuLi]₀ = 3), at -70°C. The polymerization times for VEMA and MMA were 40 and 20 min, respectively. The polymer yield was quantitative in each case.

^b Determined by GPC. The data in the brackets are the calculated M_n.

^c The weight ratio of the two components in the copolymer was determined by ¹H NMR. The data in the brackets are the calculated weight ratios of the two monomers.

^d See Experimental section.

The block copolymer of St and HEMA is a typical amphiphilic block copolymer. Its precursor block copolymer, poly(St-*b*-VEMA), was prepared using the polymerization sequence of St followed by VEMA. After the polymerization of St was performed using n-BuLi as initiator, in a mixture of toluene and THF (3:1 by volume), at -55°C, a THF solution of DPE ([DPE]/[n-BuLi]₀ = 1.3) and LiCl ([LiCl]/[n-BuLi]₀ = 3) was added and this was followed by the block copolymerization of VEMA. As shown in Table 2, as for the block copolymerization of VEMA and MMA, the block copolymers of St and VEMA possessed controlled molecular weights and compositions, as well as narrow MWDs ($M_w/M_n = 1.05-1.12$). All the above block copolymers of VEMA with MMA or with St could be changed to the corresponding amphiphilic block copolymers by acidolysis.

Acidolysis

The acidolysis of (co)polymers was carried out at room temperature by reacting the (co)polymer with hydrochloric acid. This reaction could be accomplished either immediately or via a delayed process. In the former case, a polymerized solution containing a certain amount of homopoly(VEMA) or a block copolymer was subjected to acidolysis. In the latter case, the purified (co)polymer was re-dissolved in THF, and was reacted with hydrochloric acid after some time. The same results were obtained in both

cases.

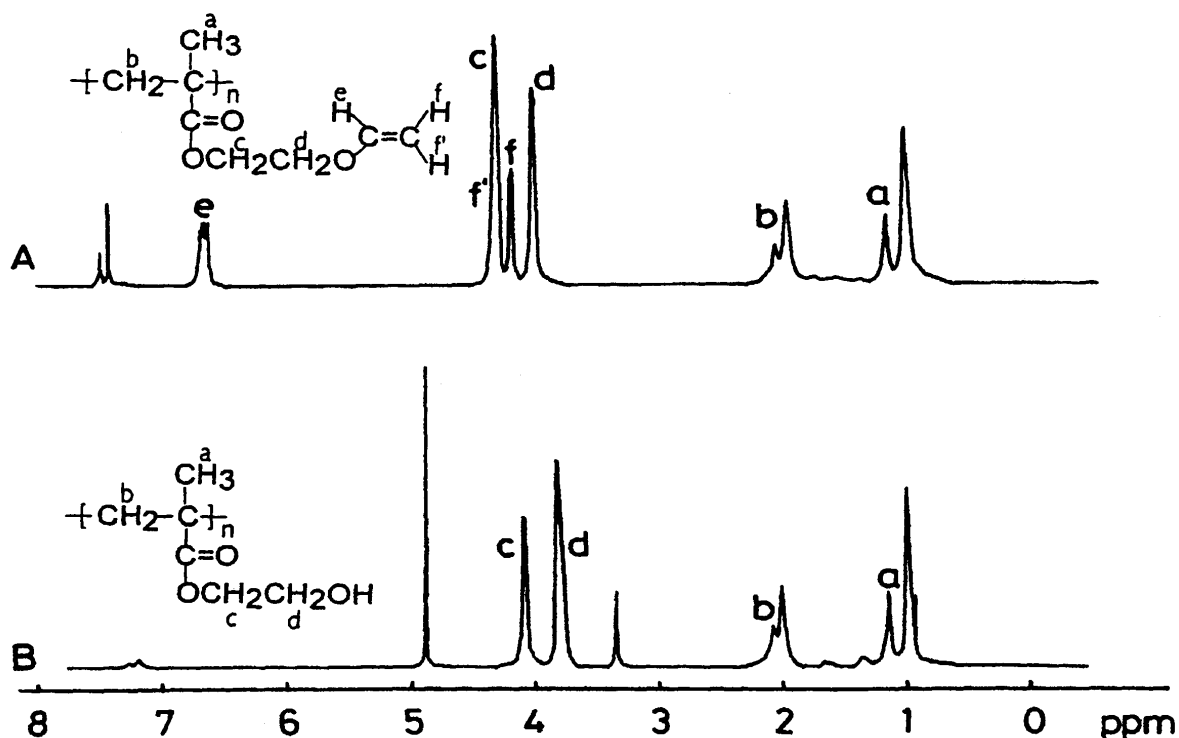


Figure 2. ^1H NMR spectra of poly(VEMA) (A, in CDCl_3) and poly(HEMA) (B, in CD_3OD) obtained via acidolysis of the above poly(VEMA).

Figures 2A and 2B present the ^1H NMR spectra of poly(VEMA) and its product of acidolysis, respectively. After acidolysis, the peaks e, f and f' corresponding to the vinyl groups disappeared completely and the spectrum (Figure 2B) of the product coincided with that of poly(HEMA). The FT-IR measurements also indicated that the absorption due to the vinyl group at 1620 cm^{-1} completely disappeared after acidolysis and a broad band due to the formed hydroxyl groups emerged between $3200\text{--}3700\text{ cm}^{-1}$. The solubility of the resulting product is quite different from that of its precursor, poly(VEMA). It is soluble in alcohols, such as methanol, ethanol, etc., but insoluble in the solvents mentioned above for poly(VEMA). The poly(HEMA) and poly(MMA-b-HEMA) were re-protected by their reaction with acetic anhydride to perform the GPC measurements. As shown in Figure 1c, the GPC chromatogram of the resulting product is almost the same as that of its precursor (Figure 1b), indicating that no crosslinking and/or chain fracture took place during the acidolysis process.

References

1. (a) Castner DG, Ratner BD, Grainger DW, Kim SW, Okano T, Suzuki K, Briggs D, Nakahama S (1992) *J Biomater Sci, Polym Ed* 3:462 (b) Lewis KB, Ratner BD (1993) 159: 77
2. Sogah DY, Hertler WR, Webster OW, Cohen GM (1987) *Macromolecules* 20:1473
3. (a) Beers KL, Boo S, Gaynor SG, Matyjaszewski K. (1999) *Macromolecules* 32:5772 (b) Robinson KL, Khan MA, de Paz Banez MV, Wang XS, Armes SP (2001) *Macromolecules* 34:3155

4. Senshu K, Yamashita S, Ito M, Hirao A, Nakahama S. (1995) *Langmuir* 11:2293
5. Hirao A, Kato H, Yamaguchi K, Nakahama S (1986) *Macromolecules* 19:1294
6. Zhang HM, Ruckenstein E (1998) *J Polym Sci, Polym Chem* 36:1865
7. Zhang HM, Ruckenstein E (2001) *Macromolecules* 34:3587
8. Aoshima S, Hasegawa O, Higashimura T (1985) *Polym Bull* 13:229
9. Fayt R, Forte R, Jacobs C, Jerome R, Ouhadi T, Teyssie Ph, Varshney SK (1987) *Macromolecules* 20:1442