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POLY[N-(2-HYDROXYPROPYL)METHACRYLAMIDE]—I

RADICAL POLYMERIZATION AND COPOLYMERIZATION

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Abstract—The radical polymerization of N-(2-hydroxypropyl)methacrylamide was investigated kinetically. The hydrophilic character of the polymerization medium was found to affect the rate of decomposition of the initiator [2,2′-azobis(methyl isobutyrate)] and the course of primary radical termination. The presence of the —OH group in the alkyl group attached to the nitrogen atom leads to an increase in the molecular weight of the polymer in comparison with polymers of N-alkyl methacrylamides. This phenomenon was interpreted in terms of the possibility of a polymer-analogous *trans*esteramidation and of an increased possibility of transfer to monomer and polymer. The copolymerization parameters of N-(2-hydroxypropyl)methacrylamide (M_1) with methyl methacrylate and styrene were determined; in the first case, $r_1 = 0{\cdot}84 \pm 0{\cdot}05$, $r_2 = 0{\cdot}66 \pm 0{\cdot}07$; in the second case, $r_1 = 0{\cdot}53 \pm 0{\cdot}08$, $r_2 = 1{\cdot}72 \pm 0{\cdot}19$.

INTRODUCTION

In our systematic investigation of hydrophilic polymers fulfilling the requirements for biomedical materials, we have studied hydrophilic esters of methacrylic acid,(1–5) N-substituted acrylamides,(6) and N-substituted methacrylamides.(7) After having determined the compatibility of these compounds toward living tissue, we investigated the effect of these structures on the blood system.(8) Of polymers suitable for the preparation of synthetic transfusion solutions, poly[N-(2-hydroxypropyl)methacrylamide] appeared to be the most interesting. The need for a detailed knowledge of the polymerization mechanism, of the possibilities of modification of the basic polymer backbone and of the structure of the polymer prompted this series of investigations. The present paper reports the kinetics of the radical polymerization of N-(2-hydroxypropyl)methacrylamide and the determination of the parameters for copolymerizations with methyl methacrylate and styrene.

EXPERIMENTAL

N-(2-hydroxypropyl)methacrylamide (N-HPMA) was prepared by reaction of methacryloyl chloride with 1-amino-2-propanol in acetonitrile at 0°. After separation of 1-amino-2-propanol hydrochloride and evaporation of acetonitrile, the monomer was purified by repeated crystallization from methanol. m.p. 67°. The compound was chromatographically pure.

Methyl methacrylate (MMA) and styrene (ST) (commercial products stabilized with hydroquinone) were first purified from inhibitor by means of 5 per cent NaOH solution and then rectified on a 40-plate column under reduced pressure. The absence of impurities was checked by gas chromatography.

2,2′-Azobis(methyl isobutyrate) (MADIB) was prepared by saponification of 2,2′-azobisisobutyronitrile with hydrogen chloride in methanol. The iminoether hydrochloride thus separated was hydrolysed with water at 35°. The crude product was purified by repeated crystallization from petroleum ether. m.p. 30°, in accordance with the literature.(15)

N-(2-hydroxypropyl) isobutyramide was obtained by reaction of isobutyroyl chloride with 1-amino-2-propanol similarly to N-(2-hydroxypropyl)methacrylamide. The product was first distilled (b.p.

143°/4 torr), then purified by repeated crystallization from the mixture acetone–petroleum ether (1:1). m.p. 41–42°.

Solvents were purified by rectification.

Polymerizations were performed in lens-shaped dilatometers at 60 ± 0·02°. After filling the dilatometers, the dissolved oxygen was removed by triple evacuation (pressure 5×10^{-5} torr, liquid nitrogen bath). The pressure between the individual cycles was balanced by catalytically purified nitrogen. Afterwards the dilatometers were sealed.

After reaching the required conversion, the polymerization was stopped by immersing the dilatometers in liquid nitrogen; the polymers were subsequently precipitated by pouring the reaction mixture into acetone containing traces of inhibitor. The conversion factor was determined gravimetrically from a series of 15 experiments. At 60°, 1 per cent conversion of 1 g monomer causes a contraction of 0·00136 cm^3.

The molecular weights were determined by light scattering (photogoniodiffusometer Wippler & Scheibling) in a 0·1 M aqueous KCl solution. The refractive index increment was determined with a Zeiss interferometer.

Copolymerizations also were performed in dilatometers. After about 5 per cent conversion, the reaction mixture was cooled in liquid nitrogen and polymer was precipitated in an excess of the precipitant. The copolymer composition was calculated from the nitrogen content in the copolymer; it had been confirmed$^{(9)}$ that loss of nitrogen due to the formation of imide bonds was negligible.

The decomposition of 2,2′-azobis(methyl isobutyrate) was followed in a series of ampoules filled with a solution of the azo compound in the mixed solvents described below and sealed after removal of oxygen. The ampoules were removed from the thermostat at intervals. The remaining azo compound was determined spectrometrically from the main absorption maximum on a Carry 14 apparatus.

RESULTS AND DISCUSSION

The determination of the reaction order with respect to the initiator for the polymerization of N-(2-hydroxypropyl)methacrylamide in water and in dimethyl formamide (DMF) is referred to Fig. 1. For a 60 per cent aqueous solution, the reaction order with respect to the initiator (MADIB) is 0·35 (curve 1), while in a 60 per cent dimethyl formamide solution, the reaction order with respect to the initiator is close to a half, i.e. 0·45 (curve 2). The composition of samples and the measured polymerization rates are given in Table 1.

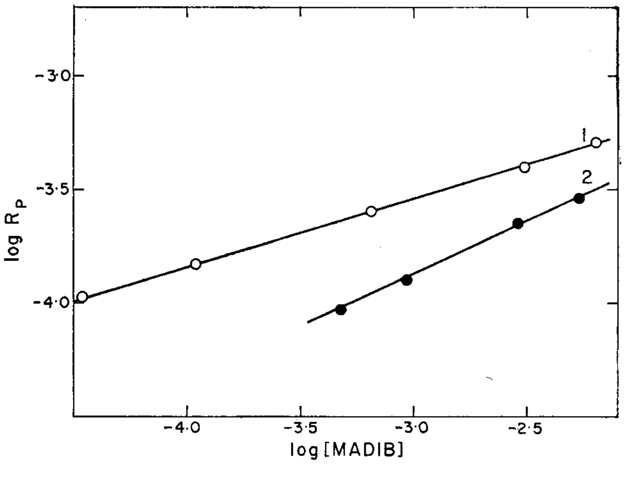


FIG. 1. Dependence of the polymerization rate of N-(2-hydroxypropyl)methacrylamide on the concentration of initiator (MADIB): ○ polymerization in H_2O; ● polymerization in DMF.

TABLE 1. DEPENDENCE OF THE POLYMERIZATION RATE AND MOLECULAR WEIGHT OF POLY[N-(2-HYDROXYPROPYL)METHACRYLAMIDE] ON THE COMPOSITION OF THE INITIAL MIXTURE

	Composition of the initial mixture					
Sample number	[N-HPMA] (mol/l)	[H_2O] (mol/l)	[DMF] (mol/l)	[MADIB] (mol/l)	$R_p \times 10^4$ (mol/l sec)	$\bar{M}_w \times 10^{-5}$
K 1	4·223	22·078	—	$6\cdot45 \times 10^{-4}$	2·532	—
K 3	4·210	22·191	—	$3\cdot03 \times 10^{-3}$	3·922	31·30
K 4	4·225	22·079	—	$6\cdot35 \times 10^{-3}$	5·128	35·50
K 7	4·199	22·277	—	$3\cdot43 \times 10^{-5}$	1·067	47·50
K 13	4·241	21·933	—	$1\cdot09 \times 10^{-4}$	1·482	38·00
K 9	4·938	16·591	—	$6\cdot62 \times 10^{-4}$	2·222	43·50
K 10	3·481	27·797	—	$6\cdot51 \times 10^{-4}$	1·569	44·50
K 11	2·771	33·260	—	$6\cdot37 \times 10^{-4}$	1·190	39·00
K 12	1·369	44·049	—	$6\cdot46 \times 10^{-4}$	4·902	—
K 52	4·087	—	5·509	$4\cdot68 \times 10^{-4}$	0·917	—
K 53	4·081	—	5·519	$9\cdot24 \times 10^{-4}$	1·233	33·30
K 54	4·037	—	5·600	$2\cdot86 \times 10^{-3}$	2·222	16·70
K 55	4·040	—	5·620	$5\cdot33 \times 10^{-3}$	2·656	15·30
K 57	3·427	—	6·717	$2\cdot91 \times 10^{-3}$	1·626	9·25*
K 58	2·721	—	8·009	$2\cdot92 \times 10^{-3}$	1·154	15·60
K 59	2·022	—	9·289	$2\cdot90 \times 10^{-3}$	0·675	7·00
K 60	1·320	—	10·574	$2\cdot80 \times 10^{-3}$	0·365	2·50

Polymerizations at 60°.
* $\bar{M}_w$ of the soluble fraction. The sample contained a small amount of gel fraction.

The low reaction order with respect to the initiator (MADIB) in an aqueous solution indicates the participation of primary radical termination.(11) It is interesting, however, that this phenomenon has not been observed for the polymerization of other hydrophilic monomers.(1,2,4) This result can therefore be regarded as specific for the system N-HPMA–H_2O–MADIB. An explanation may be based on the fact that the monomer involved here is strongly hydrophilic and was polymerized in a 60 per cent aqueous solution. Assuming that the concentration of the hydrophobic initiator will be higher in the proximity of the hydrophobic part of the growing polymer chain, it is reasonable to assume a higher concentration of the primary radicals in the proximity of the growing polymer chain. To corroborate this explanation, it can be said that the reaction order with respect to the initiator in the case of ammonium persulphate in water is close to 0·5.(10) Similarly, we observed a concentration fluctuation of the copolymerizing components during the cross-linking copolymerization of diglycol monomethacrylate and glycol dimethacrylate.(3)

The different polymerization rates in water and in dimethyl formamide under otherwise comparable conditions (cf. Fig. 1, Table 1) may be due to two factors, viz. a different initiation activity and an effect of the polarity of the medium on the rate of decomposition of the initiator. In this connection, we determined at 60° the rate of decomposition of 2,2′-azobis (methyl isobutyrate) in a 60 per cent solution of N-(2-hydroxypropyl) isobutyramide (model for the monomer but without the double bond) in water ($k_D = 9\cdot6 \times 10^{-6}$ sec^{-1}) and also in a 60 per cent solution of N-(2-hydroxypropyl) isobutyramide in dimethylformamide ($k_D = 5\cdot6 \times 10^{-6}$ sec^{-1}). It follows from this difference that the hydrophilic character of the medium affects the rate of

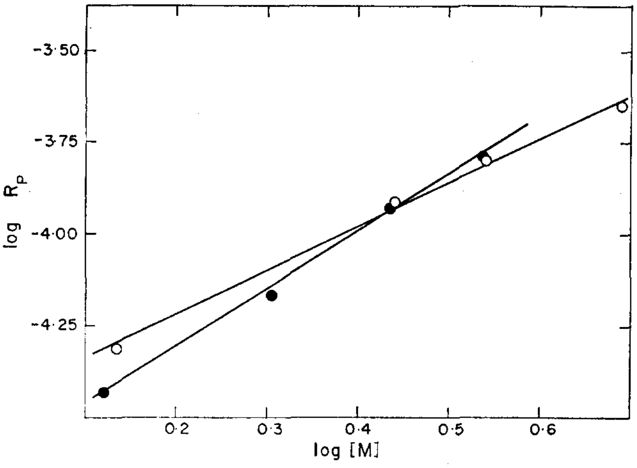
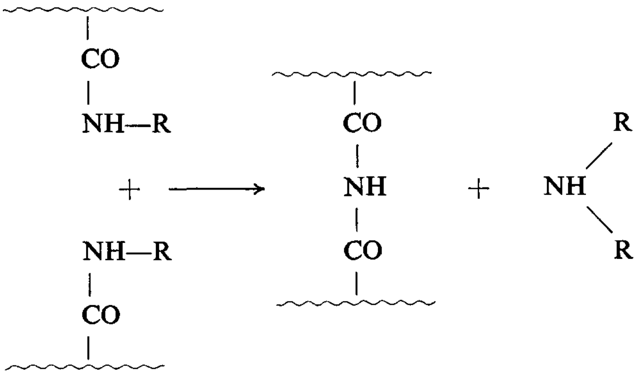


FIG. 2. Dependence of the polymerization rate of N-(2-hydroxypropyl)methacrylamide on the concentration of the monomer: ○ polymerization in H_2O; ● polymerization in DMF.

decomposition of the initiator. The observed differences in the polymerization rates correspond to the differences in k_D.

From a comparison of the reaction orders with respect to the monomer (cf. Fig. 2) in water (1·25) and in dimethyl formamide (1·5) it can be deduced that transfer reactions participate only slightly in the second case,(11,14) and this is confirmed by the molecular weights (cf. Table 1).

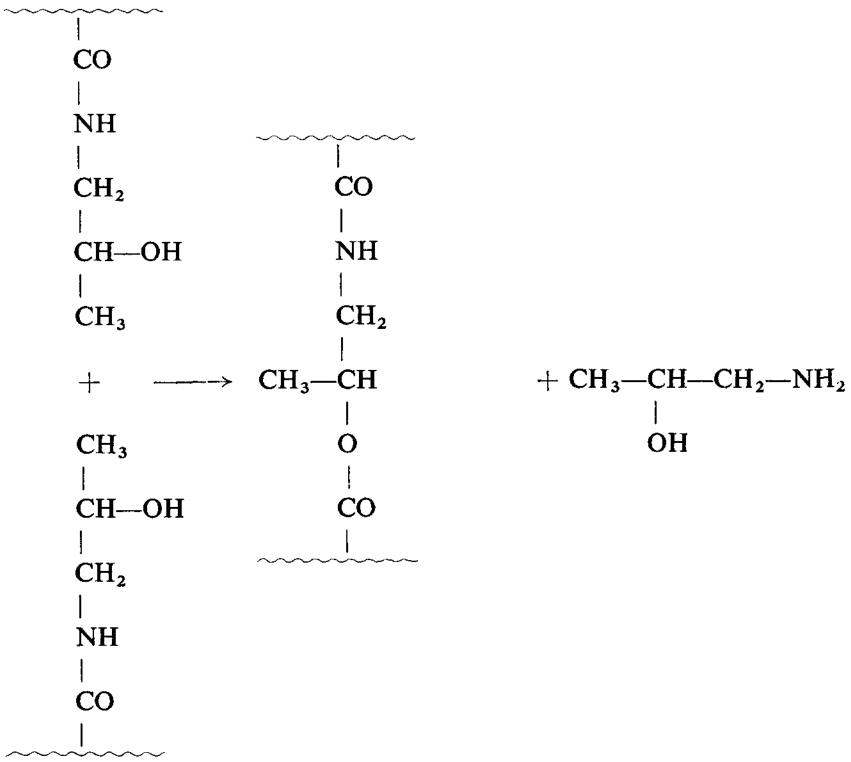
Molecular weights of the polymers obtained are unusually high with respect to the initiator concentrations and the structure of monomers, in spite of the possibility of primary radical termination (Table 1). Although it is possible to visualize the formation of crosslinks according to the scheme



a comparison with the polymerization of N-ethyl methacrylamide under comparable conditions(12) shows that in the latter case the molecular weight is much lower. It seems, therefore, that the formation of imide crosslinks will have no decisive effect on the observed increase in $\bar{M}_w$ for N-HPMA.

The explanation may be found in the presence of the —OH group in the alkyl group bonded to the nitrogen. This group can lead to two further reactions during polymerization:

(a) *trans*-esteramidation of the polymer chains



$$\sim\mathrm{CO{-}NH{-}CH_2{-}CH(OH){-}CH_3} + \mathrm{CH_3{-}CH(OH){-}CH_2{-}NH{-}CO}\sim \longrightarrow \sim\mathrm{CO{-}NH{-}CH_2{-}CH(CH_3){-}O{-}CO}\sim + \mathrm{CH_3{-}CH(OH){-}CH_2{-}NH_2}$$

(b) transfer to monomer and to polymer, because of the enhanced lability of the hydrogen atom bonded to the carbon atom to which the —OH group is bonded. It will cause a broadening of the distribution of molecular weights, especially in the direction of higher molecular weights.(13) This effect can be increased by the possibility of recombination of branches of two independent chains. A detailed study of the effect of reactions (a) and (b) on the observed increase in $\bar{M}_w$ will be the subject of a forthcoming paper.

To check on the possibility of modification of the hydrophilic backbone of poly [N-(2-hydroxypropyl)methacrylamide] by copolymerization with hydrophobic comonomers, we determined the copolymerization parameters of N-(2-hydroxypropyl)-methacrylamide with methyl methacrylate and styrene. Owing to the effect of the solvent on the reactivity of components during the radical copolymerization of methacrylamide,(9) both systems were polymerized in dioxan so that the results were comparable. The results of copolymerizations are listed in Table 2; the corresponding copolymerization diagrams are shown in Figs. 3 and 4. F_1 is the molar fraction of N-HPMA units in the copolymer. The monomer reactivity ratios (r_1, r_2) were calculated by the Fineman and Ross procedure and are as follows: (N-HPMA = monomer-1) with methyl methacrylate $r_1 = 0{\cdot}84 \pm 0{\cdot}05$, $r_2 = 0{\cdot}66 \pm 0{\cdot}07$; with styrene $r_1 = 0{\cdot}53 \pm 0{\cdot}08$, $r_2 = 1{\cdot}72 \pm 0{\cdot}19$.

TABLE 2. COPOLYMERIZATIONS OF N-(2-HYDROXYPROPYL) METHACRYLAMIDE (M_1) WITH METHYL METHACRYLATE AND STYRENE

Molar composition of the monomer mixture (f_1)	% N in the copolymer	Molar composition of the copolymer (F_1)
0·150 (M)	2·46	0·190
0·318 (M)	4·60	0·383
0·417 (M)	5·05	0·427
0·512 (M)	6·11	0·537
0·620 (M)	7·03	0·641
0·734 (M)	7·74	0·725
0·078 (S)	0·61	0·046
0·154 (S)	1·36	0·105
0·301 (S)	2·00	0·157
0·241 (S)	2·20	0·174
0·329 (S)	2·36	0·188
0·437 (S)	4·20	0·353
0·537 (S)	4·96	0·427
0·637 (S)	5·67	0·500
0·765 (S)	6·93	0·638

Copolymerizations were carried out at 60° in 50 per cent by vol. of dioxan. [MADIB] = 3×10^{-3} mol/l. (M) = methyl methacrylate as comonomer. (S) = styrene as comonomer.

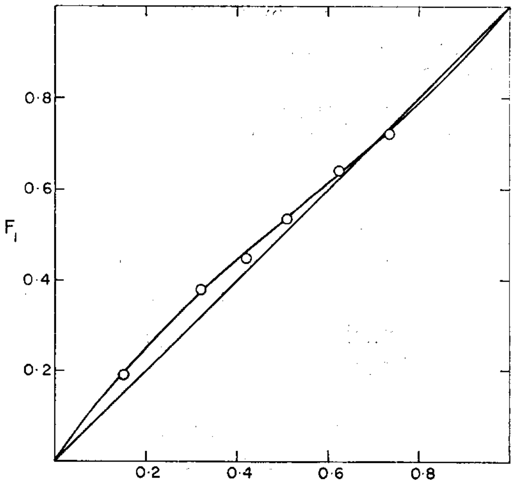


FIG. 3. Copolymerization of (N-HPMA)/MMA in 50 per cent by vol. of dioxan. Composition of the initial mixture, f_1, and composition of the copolymer, F_1, are expressed in molar fractions (N-HPMA). Cf. Table 2.

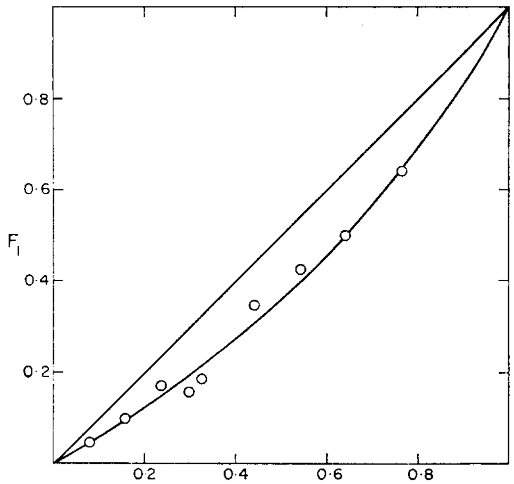


FIG. 4. Copolymerization of (N-HPMA)/ST in 50 per cent by vol. of dioxan. Composition of the initial mixture, f_1, and composition of the copolymer, F_1, are expressed in molar fractions (N-HPMA). Cf. Table 2.

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Résumé—On a étudié la cinétique de polymérisation radicalaire du N-(hydroxy 2 propyl)méthacrylamide. On a trouvé que le caractère hydrophile du mélange réactionnel influençait la vitesse de décomposition de l'amorceur [azobis 2,2′ (méthylisobutyrate)] et la réaction de terminaison des radicaux primaires. La présence des groupes OH dans le groupe alkyle attaché à l'azote conduit à une augmentation du poids moléculaire par rapport au cas des N-alkylméthacrylamide. On interprète ce phénomène par le fait qu'il y ait une possibilité de *trans*esteramidation d'un polymère analogue et une possibilité accrue d'un transfert au monomère et au polymère. On a déterminé les paramètres de copolymérisation du N-(hydroxy-2-propyl)méthacrylamide (M_1) avec le méthacrylate de méthyle et le styrène dans le premier cas $r_1 = 0,84 \pm 0,05$, $r_2 = 0,66 \pm 0,07$; dans le second cas $r_1 = 0,53 \pm 0,08$, $r = 1,72 \pm 0,19$.

Sommario—Si sono fatte delle indagini dal punto di vista cinetico sulla polimerizzazione radicalica del N-(2-idrossipropil metacrilamide. Si è trovato che la idrofilia del mezzo di polimerizzazione influenza la velocità di decomposizione dell'iniziatore [2,2′-azobis(metil isobuttirrato)] e l'andamento della terminazione radicalica primaria. La presenza del gruppo —OH nel gruppo alchilico attaccato all' atomo di azoto, conduce ad un aumento del peso molecolare del polimero, a raffronto dei polimeri di N-alchil metacrilamide. Tale fenomeno è stato interpretato facendo l'ipotesi della possibilità di una trasesteremidazione analoga alla polimerica e di una eventualità ancor maggiore del trasferimento a monomero e polimero. Si sono determinati i parametri di copolimerizzazione del N-(2-idrossipropil) metacrilamide (M_1) con metil metacrilato e stirene; nel primo caso: $r_1 = 0{,}84 \pm 0{,}05$ e $r_2 = 0{,}66 \pm 0{,}07$; nel secondo caso: $r_1 = 0{,}53 \pm 0{,}08$ e $r_2 = 1{,}72 \pm 0{,}19$.

Zusammenfassung—Die radikalische Polymerisation von N-(2-Hydroxipropyl)methacrylamid wurde kinetisch untersucht. Es wurde festgestellt, daß der hydrophile Charakter des Polymerisationsmediums die Zerfallsgeschwindigkeit des Initiators 2,2′-Azobis(methylisobutyrat) und den Verlauf des Abbruchs des primären Radikals beeinflußt. Die Anwesenheit von OH-Gruppen in der am Stickstoffatom gebundenen Alkylgruppe führt, im Vergleich mit Polymeren aus N-Alkylmethacrylamiden, zu einer Zunahme im Molekulargewicht des Polymeren. Diese Erscheinung wird gedeutet als mögliche polymeranalogue *Trans*esteramidierung und einer zunehmenden Wahrscheinlichkeit der Übertragung auf Monomer und Polymer. Die Copolymerisationsparameter von N-(2-Hydroxypropyl)methacrylamid (M_1) mit Methylmethacrylat und Styrol wurden bestimmt; im ersten Fall, $r_1 = 0{,}84 \pm 0{,}05$, $r_2 = 0{,}66 \pm 0{,}07$; im zweiten Fall, $r_1 = 0{,}53 \pm 0{,}08$, $r_2 = 1{,}72 \pm 0{,}19$.