Kinetic Behavior of Methacrylic Monomers with Large Polar Side Substituents in Free Radical Polymerization†

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ABSTRACT: The kinetic behavior of the free radical polymerization of *N*-[4-(methacryloyloxy)phenyl]-2-(4-methoxyphenyl)acetamide, OM, and *N*-[4-[[(4-methoxyphenyl)acetyl]oxy]phenyl]methacrylamide, MA, in solution of DMF is described. The methacrylic monomers OM and MA have the same functional groups and empirical formulas, but differ in the position of the corresponding organic groups in the molecule. Semiempirical calculations with treatments AM1 and PM3 based on the interactions of frontier orbitals and the polarity of the π-double bond, measured by the magnetic shielding of the β-carbon of the methacrylic double bond, indicate that OM should polymerize at a higher rate than MA, which was experimentally demonstrated by the gravimetric study of the free radical polymerization at several temperatures in the interval 50–150 °C. The kinetic results obtained and the molecular weight of polymers prepared at different temperatures indicated that these monomers have a relatively low ceiling temperature, with average values of $T_c \simeq 162$ °C for OM and $T_c \simeq 172$ °C for MA under standard conditions; [M] = 1.0 mol·L^{-1}.

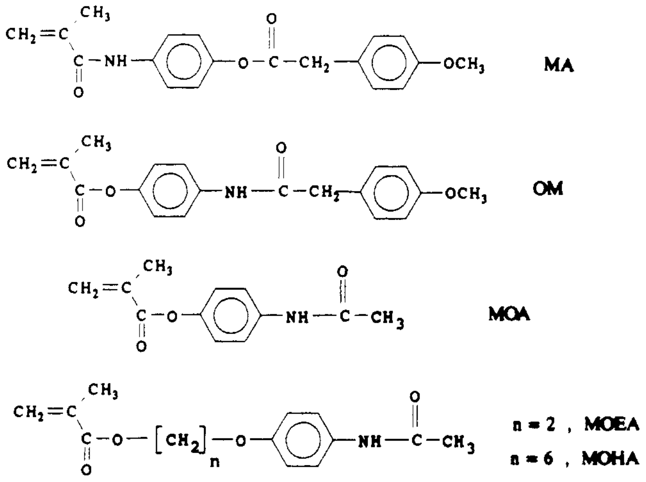
Introduction

The behavior of vinyl and acrylic monomers with the chemical structure $CH_2{=}CR_1R_2$ in polymerization is affected by the polar character of the olefinic double bond and resonance effects associated with the electronegativity of the substituents R_1 and R_2, as well as by the steric hindrance of these groups in the polymerization steps.[1–4] In this sense, several α-substituted acrylates bearing bulky substituents exhibit kinetics in free radical polymerization which deviate from the classical dependence on the concentration and the reaction temperature, with a decrease of the polymerization rate, a limiting conversion to polymer, or even a decrease of the molecular weight of polymers isolated, when the reaction temperature increases beyond values that depend on the chemical structure of the substituents in the α-position.[5–9] The results have been accounted for by the relatively low ceiling temperature of polymerization, T_c. In the same way, Yamada and Otsu et al.[10] have found a correlation between the T_c and the size of phenyl methacrylates with bulky substituents in the ortho position of the aromatic ring.

Recently, we have studied the free radical polymerization of methacrylic monomers bearing bulky and polar phenyl-substituted side groups, linked to the acrylic residue through the ester group, 4-(methacryloyloxy)acetanilide, MOA,[11] or by means of an oxyalkyl spacer group of different length, 4-[[(methacryloyloxy)ethyl]oxy]acetanilide, MOEA,[12], and 4-[[(methacryloyloxy)hexyl]oxy]acetanilide, MOHA[13] (see Chart I). In all cases we obtained kinetic results reflecting the relatively low T_c of these monomers, T_c = 137 °C for MOA, T_c = 175 °C for MOEA, and T_c = 186 °C for MOHA, under standard conditions.

In this work we undertake the kinetic study of the free radical polymerization of a methacrylic ester and a methacrylamide derivative with the same functional groups but different orientation with respect to the methacrylic residue. These monomers were selected because of their properties as compounds or residues with potential pharmacological activity. The details of the synthesis, preparation, and characterization of polymers are reported elsewhere.[14,15]

Chart I



Experimental Section

Synthesis of Monomers. The methacrylic ester *N*-[4-(methacryloyloxy)phenyl]-2-(4-methoxyphenyl)acetamide, OM, was synthesized by a two-step route involving well-known organic reactions described elsewhere.[14] The methacrylamide derivative *N*-[4-[[(4-methoxyphenyl)acetyl]oxy]phenyl]methacrylamide, MA, was also prepared by a two-step route described elsewhere.[15] In both cases 4-methoxyphenylacetic acid and 4-aminophenol were used as starting products.

Reagents. *N,N*-Dimethylformamide, DMF, was dried over anhydrous magnesium for 2 days and later with phosphoric anhydride overnight. After drying, DMF was distilled under reduced pressure of nitrogen.

2,2′-Azobis[isobutyronitrile], AIBN, was purified by fractional crystallization from methanol; mp = 104 °C. Other reagents like methanol or diethyl ether were used without purification.

Polymerization. The monomers OM and MA were polymerized at different temperatures from 50 to 150 °C, in a thermostatic bath (precision of ±0.1 °C), using AIBN as the free radical initiator, [I] = 4.0 × 10^{-2} mol·L^{-1}, and purified DMF as the solvent, [M] = 1.0 mol·L^{-1}. All experiments were carried out in Pyrex glass ampules sealed off under high vacuum (10^{-4} mmHg). At various times, the reaction mixture was quenched in liquid nitrogen and precipitated in a large excess of methanol, washed twice with methanol, and dried to constant weight under reduced pressure.

Characterization. The compounds OM and MA as well as the corresponding polymers prepared at different temperatures were characterized by ^{1}H and ^{13}C NMR spectroscopy. The spectra

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† Dedicated to the memory of Professor Miguel Valero.

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were recorded in deuterated dimethyl sulfoxide, DMSO-d_6, solution on a Varian XLR-300 spectrometer at 80 °C.

The average molecular weight and molecular weight distribution were determined by GPC using a Waters-510 apparatus equipped with an injector, model 7125, and a UV detector, Pye Unicam, PU-4025. The signal of λ_{max} = 245 nm was used as the reference. Columns of ultrastyragel of 10^3, 10^4, and 10^5 Å (Polymer Laboratories) were coupled in order to cover a range of molecular sizes in the interval 10^3 to 4×10^6. The eluent was THF, the flow rate 1 mL/min, and the injection volume 30 μL at room temperature (20 °C). The calibration was performed with 14 poly(methyl metacrylate) standards supplied by Polymer Laboratories, having molecular weights in the range 2990 to 1.4×10^6 with a polydispersity lower than 1.1.

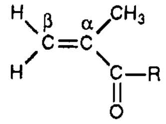
Results and Discussion

In the last few years we have been interested in the preparation of biocompatible polyacrylic formulations with potential pharmacological activity, following the model suggested by Ringsdorf in 1975.[16] The main idea is to attach pharmacological residues to polymeric chain molecules that elicit a characteristic pharmacological action, by bonds that could be degraded easily in the physiologic medium. In this sense we have prepared polymeric drugs with anti-inflammatory activity based on derivatives of phenylacetic and propionic acids, which are known as "nonsteroidic anti-inflammatory agents".[17] We have selected the 4-methoxyphenylacetic acid as the pharmacological residue for both polyacrylic systems, POM and PMA, but using a 4-aminophenyl group as the spacer between the macromolecular chain and the pharmacological residue. This spacer group is also an active metabolite of the popular pharmaco "paracetamol", and therefore, the corresponding polymeric systems could have enhanced analgesic activity, complementary to the anti-inflammatory function. Chart I presents the chemical structure of OM and MA; both monomers have the same elemental composition and functional groups, but the structural difference arises from the position of the ester and amide bonds of the 4-aminophenyl spacer group.

As a consequence of the synthetic route used in the preparation of OM,[14] the 4-aminophenyl group is linked to the methacrylic residue through a carboxylic group and to the phenylacetic residue through an amide function. However, as shown in Chart I, the methacrylamide derivative MA has the 4-aminophenyl spacer oriented in the opposite direction, being linked to the methacrylic residue through the amide group and to the phenylacetic residue through the ester function. The arrangement of functional groups with respect to the methacrylic double bond may have a strong influence on the reactivity of the corresponding double bond, associated with the chemical structure of the functional group (ester or amide) conjugated with the methacrylic double bond, but with a common characteristic for both monomers: The volume of the side substituents will be similar for the monomeric units incorporated to the polymeric growing chains. This is important in analyzing the kinetic behavior of these compounds in free radical polymerization.

The reactivity of monomers and radicals in free radical polymerization can be analyzed in terms of the transition-state theory by the Fukui–Klopman–Salem equation[18-20] which considers the energetic balance of the addition of radicals to carbon–carbon double bonds as a result of the interactions between occupied molecular orbitals, OMO, and unoccupied molecular orbitals, UMO, as well as their corresponding Coulombic interactions. Fleming[21] has reported that radicals should be very soft entities, since most of them do not have a net charge and in most chemical reactions they react with uncharged molecules. Therefore, the Coulombic interactions are usually very small in comparison with the interactions of the corresponding frontier orbitals. The frontier orbital of the propagating radical is the singly occupied one SOMO (single occupied molecular orbital), which could interact with both the HOMO (highest occupied molecular orbital) and the LUMO (lowest unoccupied molecular orbital) of the reacting monomer molecule. Radicals with a high-energy SOMO will react fast with molecules having a low-energy LUMO, and radicals with a low-energy SOMO will react fast with molecules having a high-energy HOMO.[21] The contribution of these interactions to the addition reaction of polymeric growing radicals to the π-double bond can be quantified by the application of semiempirical methods such as AM1[22] and PM3.[23] These methods provide the relative charge of the α- and β-carbons of the double bond, which can be calculated by the use of commercial programs like MOPAC V.6,[24] and are related with the polarity of the π-double bond. The application of this protocol to the free radical polymerization of OM and MA gives the results in Table I. The values calculated by both methods are rather close, giving the charge density at the β-carbon as less negative for the methacrylic monomer OM than for the methacrylamide derivative MA, which indicates a higher reactivity of OM.

Table I
Charge Density of the α- and β-Carbons of OM and MA Monomers, Determined by Semiempirical AM1 and PM3 Treatments, and Polarity of the Methacrylic Double Bond According to the Chemical Shift of the α- and β-Carbons in the ^{13}C NMR Spectra of OM and MA



	OM	MA
charge(C_α) (AM1)	−0.132	−0.126
charge(C_α) (PM3)	−0.153	−0.137
charge(C_β) (AM1)	−0.135	−0.185
charge(C_β) (PM3)	−0.075	−0.128
δ(C_α) (ppm)	135.70	140.45
δ(C_β) (ppm)	126.41	119.90

On the other hand, the ^{13}C NMR chemical shift of the α- and β-carbons of vinyl groups has been reported to be mainly controlled by the π-electron density,[25,26] which is closely related to the reactivity of the vinyl compounds[27,28] so that a lower electron density of the β-carbon of the monomer leads to an easier electron transfer from the polymer radical to the monomer and consequently a higher monomer reactivity.[29] This criterion is fulfilled for the monomers considered in the present work, since the β-carbon of OM is shifted about 6.5 ppm toward lower field relative to the β-carbon of MA, signifying that the electron density of the β-carbon is sensibly lower for the methacrylic ester than for the methacrylamide derivative.

In order to test the validity of these approaches, we analyzed the kinetic behavior of OM and MA in the free radical polymerization in solution of DMF, [M] = 1 mol/L, at several temperatures. Figure 1 shows the conversion–time diagrams obtained for the polymerization of OM at different temperatures in the interval 50–120 °C. The free radical polymerization of OM under our experimental conditions follows first-order kinetics at moderated temperatures. However, at relatively high temperatures, i.e., 90 and 120 °C, the polymerization tends to reach a limiting conversion which decreases drastically with increasing temperature. This behavior has been reported for the free radical polymerization of several α-substituted vinyl

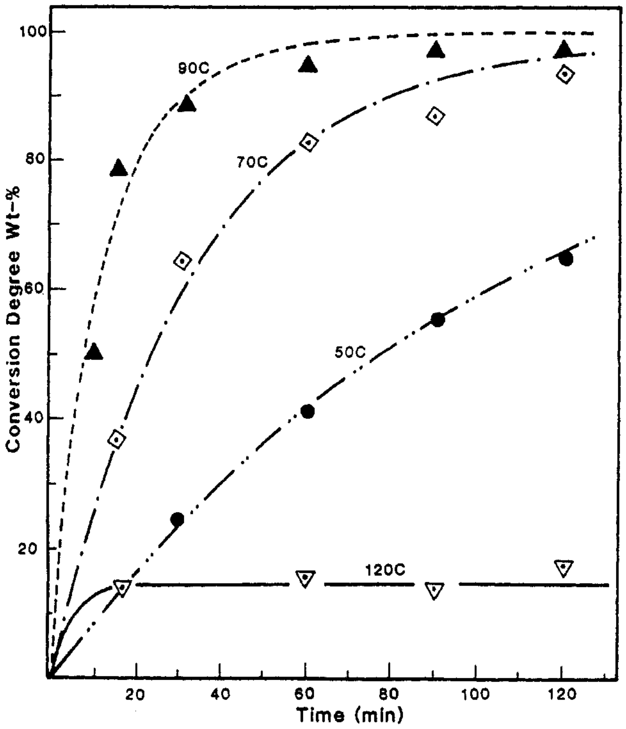


Figure 1. Kinetic diagrams of the free radical polymerization of OM at several temperatures. Points correspond to experimental data obtained gravimetrically. Lines correspond to the application of eq 1, with the set of values quoted in the second and third columns of Table II.

Table II
Kinetic Parameters of the Free Radical Polymerization of OM and MA Initiated by AIBN in DMF Solution ([M] = 1.0 mol/L)

reaction temp (°C)	K_d (s^{-1})	$K_p'/K_t^{1/2}$ OM	$K_p'/K_t^{1/2}$ MA
50	1.81×10^{-6}	0.722	0.216
70	2.90×10^{-5}	0.678	0.247
90	3.42×10^{-4}	0.520	0.165
120	8.53×10^{-3}	0.120	0.104
150	1.37×10^{-1}		0.022

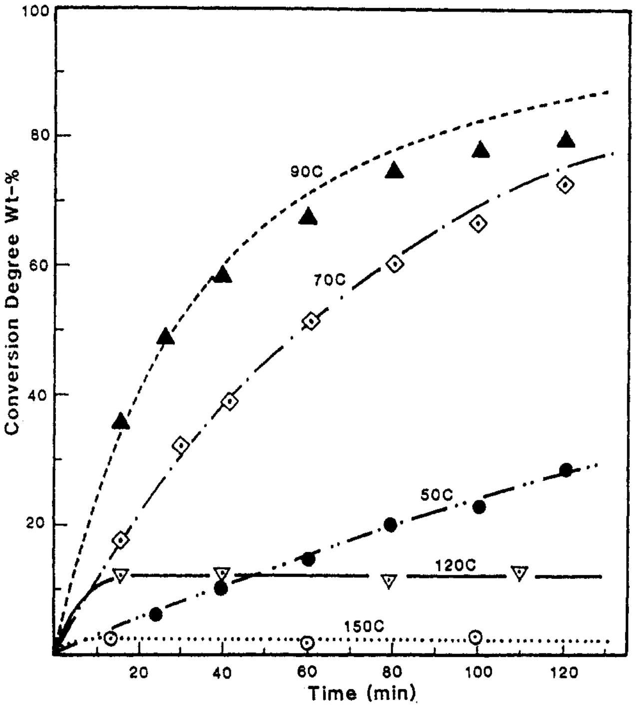


Figure 2. Kinetic diagrams of the free radical polymerization of MA at several temperatures. Points correspond to experimental data obtained gravimetrically. Lines correspond to the application of eq 1, with the set of values quoted in the second and fourth columns of Table II.

and acrylic monomers[6,30] or monomers bearing alkyl or aryl ester groups with steric hindrance.[2]

In a pioneering work Dainton and Ivin[31] reported that the polymerization rate increases as the temperature is raised, but reaches a maximum after which it decreases and becomes zero, at a ceiling temperature T_c at which chain propagation and depropagation are in equilibrium when the monomer concentration is 1 M. As we have indicated above, methacrylic monomers with chemical structures rather close to OM, like MOA, MOEA, and MOHA, have T_c of 137, 175, and 186 °C, respectively.

Considering a kinetic scheme with first-order thermal decomposition of initiator, addition of primary radicals to monomer, and propagation and termination reactions, the variation of conversion X with time can be written accordingly as

$$\ln [1/(1 - X)] = 2k_p/k_t^{1/2}(f[\mathrm{I}]/k_d)^{1/2}[1 - \exp(-k_d t/2)] \tag{1}$$

Using the k_d values for AIBN decomposition reported by Tulig and Tirrell[32] with $f = 0.6$, we obtained the lines in Figure 1, which correspond to the kinetic constants quoted in the second and third columns of Table II. It seems that the free radical polymerization of OM follows a classical kinetic behavior at relatively low temperatures of polymerization, but deviates when the temperature reaches values higher than 90 °C. The concordance between theory and experiments at 120 °C might be explained satisfactorily by taking into account the high decomposition rate of AIBN at this temperature (see second column of Table II). In this sense, the kinetic scheme suggested by Tobolsky[33] as "dead-end radical polymerization" refers to reaction conditions in which free radical initiators decompose so quickly that the half-life of the propagating polymer chains approximates that of the initiator. This treatment is based on eq 1, and the net effect is a limiting conversion of monomer to polymer at infinite reaction time.[2]

Figure 2 shows the kinetic results obtained for the free radical polymerization of MA in the interval of temperatures 50–150 °C, together with the diagrams calculated by the application of eq 1 with the kinetic parameters collected in the second and fourth columns of Table II. The trend is similar to that in the polymerization of OM, but the comparison of the diagrams and the values of $k_p/k_t^{1/2}$ quoted in Table II, for the same reaction temperature, indicate that the rate of polymerization is significantly higher for the methacrylic ester OM than for the methacrylamide derivative MA. This result agrees with the reactivity of the methacrylic double bond deduced semiempirically by the frontier orbital based calculations AM1 and PM3, as well as with the effect of the polarity of the acrylic double bond, determined from the chemical shift of the β-carbon in the ^{13}C NMR spectrum of the corresponding monomers. The ceiling temperature T_c in free radical polymerization is usually determined by the extrapolation to $R_p = 0$ of a plot of the polymerization rate versus the polymerization temperature. However, in order to avoid the effect of the initiation rate on the overall rate of polymerization, Yamada et al.[34,35] have suggested a treatment based on eq 2, where k and R have the usual

$$\frac{\mathrm{d} \ln (k_p' k_t^{-1/2})}{\mathrm{d}T^{-1}} = \frac{k_d E_d/(R[\mathrm{M}]) - k_p E_p/R}{k_p'} + \frac{E_t}{2R} \tag{2}$$

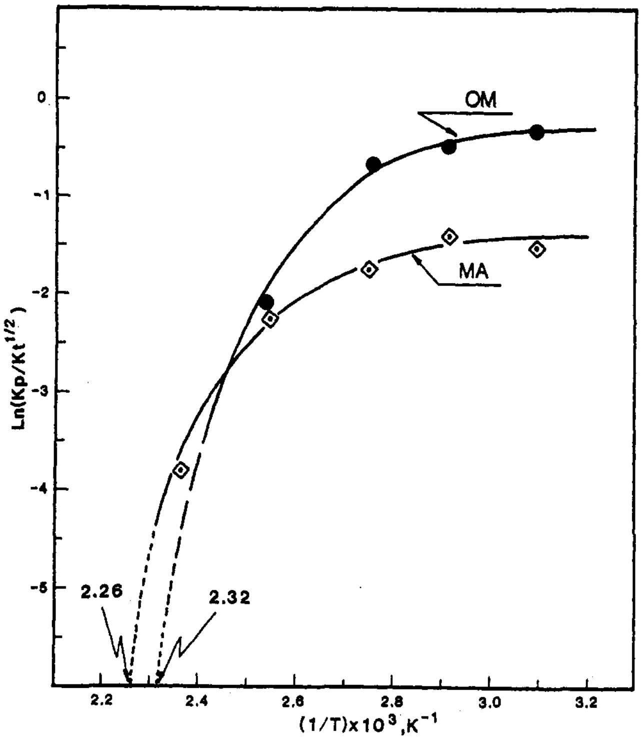


Figure 3. Determination of the ceiling temperature of OM and MA, according to the treatment suggested by Yamada. [M] = 1.0 mol/L.

meaning, E_d is the activation energy for the decomposition of the initiator, E_t is the activation energy for termination, and k_p' is the apparent rate constant for propagation:

$$k_p' = k_p - k_d/[\mathrm{M}]$$

which corresponds to the propagation–depropagation equilibrium

$$\mathrm{M}_n^{\bullet} + \mathrm{M} \underset{k_d}{\overset{k_p}{\rightleftarrows}} \mathrm{M}_{n+1}^{\bullet}$$

When the temperature of polymerization reaches the ceiling temperature, eq 2 leads to ∞:

$$\lim_{T \to T_c} \frac{\mathrm{d} \ln (k_p' k_t^{-1/2})}{\mathrm{d}T^{-1}} = \infty$$

Therefore, a plot ln $(k_p'/k_t^{1/2})$ versus the reciprocal of the polymerization temperature gives a curve with a slope that approaches infinity at the ceiling temperature. This treatment must be considered as an approximation since the apparent ratio $k_p'/k_t^{1/2}$ is calculated considering the classical mechanism of polymerization and the extrapolation of the diagram is not a straight line but a curve with the experimental values usually rather far from the extrapolated onset. Figure 3 shows the diagram obtained by the application of the values of $k_p'/k_t^{1/2}$ in Table II, giving values of T_c = 158 °C for OM and T_c = 169 °C for MA. The methacrylamide derivative has a higher value of T_c than the corresponding methacrylic ester. We have verified the accuracy of this treatment following the change of the molecular weight and molecular weight distribution with the temperature of polymerization.

M_n and M_w average molecular weights of polymers after a polymerization for 40 min in the temperature interval of 50–120 °C are collected in Table III. It is noteworthy that polymers prepared from MA have average molecular weights higher than those of the corresponding methacrylic ester OM, but in both cases, the polydispersity lies in the range 2.1–3.1, independently of the polymerization temperature.

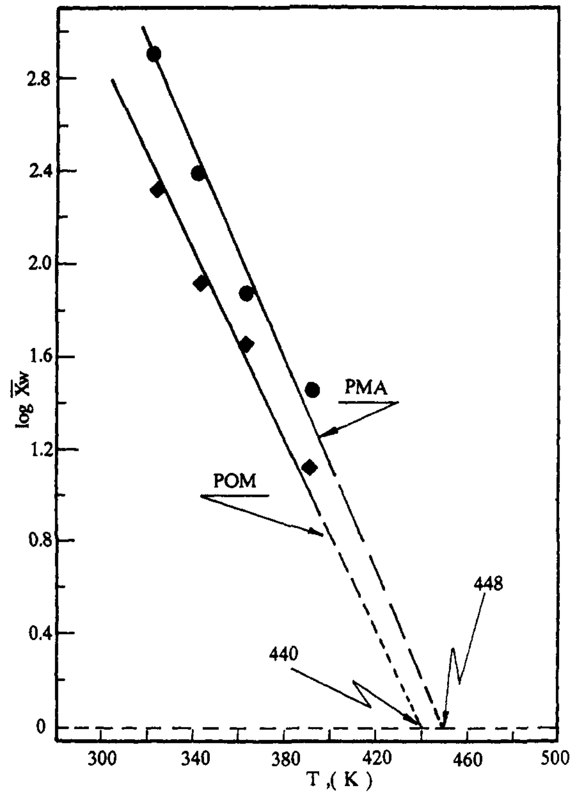


Figure 4. Variation of the average polymerization degree as a function of the reaction temperature: (●) polymers prepared from MA; (◆) polymers prepared from OM.

Table III
Average Molecular Weight and Degree of Polymerization of POM and PMA Prepared in Solution of DMF at Several Temperatures for a Reaction Time of 40 min

polym temp (°C)	POM			PMA		
	M_n	M_w	DP_n	M_n	M_w	DP_n
50	26 000	70 000	80	87 000	270 000	268
70	12 000	27 000	37	26 000	79 000	80
90	7 200	15 000	22	10 000	24 000	31
120	2 200	4 500	7	4 100	9 200	13

The most noticeable phenomenon is the drastic decreasing of the average polymerization degree DP_n with the increase of the reaction temperature when approaching T_c. The rate of the thermal decomposition of AIBN depends only slightly on the nature of the environment,[36,37] and therefore, similar values of R_i can be expected for both polymerization systems, so that the remarkable decrease of DP_n by raising the temperature can be ascribed to the drastic decrease of the propagation near T_c, in agreement with the results of $k_p/k_t^{1/2}$ collected in Table II. In this sense, Figure 4 shows the variation of log X_w with the reaction temperature, obtaining in both cases diagrams that approach straight lines that by extrapolation to X_w = 1 gives values of T_c = 167 °C for OM and T_c = 175 °C for MA, rather close to those determined from kinetic parameters according to the treatment of Yamada.

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References and Notes

(1) Chikanishi, K.; Tsuruta, T. *Makromol. Chem.* **1965**, *81*, 198.
(2) Odian, G. *Principles of Polymerization*, 3rd ed.; Wiley Interscience: New York, 1991.

(3) Cowie, J. M. General Concepts in Chain Polymerization. In *Comprehensive Polymer Science*; Eastmond, G. C., Ledwith, A., Sigwalt, P., Eds.; Pergamon Press: Exeter, U.K., 1989; Vol. 3.
(4) Yamada, B.; Matsumoto, A.; Otsu, T. *Makromol. Chem.* **1991**, *192*, 1921.
(5) Sato, T.; Morino, K.; Tanaka, H.; Ota, T. *Makromol. Chem.* **1987**, *188*, 2951.
(6) Lenz, R. W.; Saunder, K.; Balakrishnan, T.; Hatada, K. *Macromolecules* **1979**, *12*, 392.
(7) Madruga, E. L.; San Román, J.; Lavia, M. A.; Fernández Monreal, M. C. *Macromolecules* **1984**, *17*, 989.
(8) Gisser, H.; Mertwoy, H. E. *Macromolecules* **1974**, *7*, 431.
(9) Yamada, B.; Otsu, T. *Makromol. Chem.* **1991**, *192*, 333.
(10) Yamada, B.; Tanaka, T.; Otsu, T. *Eur. Polym. J.* **1989**, *25*, 117.
(11) San Romań, J.; Madruga, E. L. *Polymer* **1989**, *30*, 949.
(12) Levenfeld, B.; San Román, J.; Madruga, E. L. *Polymer* **1990**, *31*, 160.
(13) Levenfeld, B.; San Román, J.; *Polymer* **1991**, *32*, 3250.
(14) San Román, J.; Gallardo, A. *Polymer* **1992**, *33*, 2840.
(15) Gallardo, A.; San Román, J. *Polymer*, in press.
(16) Ringsdorf, H. *J. Polym. Sci., Polym. Symp.* **1975**, *51*, 135.
(17) Paulus, H. E.; Whitehouse, M. W. *Annu. Rev. Pharmacol. Toxicol.* **1973**, *13*, 107.
(18) Fukui, K.; Fujimoto, H. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 3399.
(19) Klopman, G. *J. Am. Chem. Soc.* **1968**, *90*, 223.
(20) Salem, L. *J. Am. Chem. Soc.* **1968**, *90*, 543.
(21) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: New York, 1976; p 182.
(22) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.
(23) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 207.
(24) MOPAC 6.0: *QCPE* **1983**, 455.
(25) Karplus, M.; Pople, J. A. *J. Chem. Phys.* **1963**, *38*, 2803.
(26) Maciel, G. E. *J. Phys. Chem.* **1965**, *69*, 1947.
(27) Higashimura, T.; Okamura, S.; Morishima, I.; Yonezawa, T. *J. Polym. Sci., Part B* **1969**, *7*, 23.
(28) Herman, J. J.; Teyssié, Ph. *Macromolecules* **1978**, *11*, 839.
(29) Hatada, K.; Nagata, K.; Hasegawa, T.; Yuki, H. *Makromol. Chem.* **1977**, *178*, 2413.
(30) Kang, B. K.; O'Driscoll, K. F.; Howel, J. A. *J. Polym. Sci., Polym. Chem. Ed.* **1972**, *10*, 2349.
(31) Dainton, F. S.; Ivin, K. J. *Q. Rev. Chem. Soc.* **1958**, *12*, 61.
(32) Tulig, T. J.; Tirrell, M. *Macromolecules* **1982**, *15*, 459.
(33) Tobolsky, A. V. *J. Am. Chem. Soc.* **1958**, *20*, 5927.
(34) Otsu, T.; Yamada, B.; Sugiyama, S.; Mori, S. *J. Polym. Sci., Polym. Chem. Ed.* **1980**, *18*, 2197.
(35) Yamada, B.; Sugiyama, S.; Mori, S.; Otsu, T. *J. Macromol. Sci., Chem.* **1981**, *A15*, 339.
(36) Czerwinski, W. K. *Makromol. Chem.* **1991**, *192*, 1285.
(37) Braun, D.; Czerwinski, W. K. *Makromol. Chem.* **1987**, *188*, 2371.

Registry No. MA, 143121-95-3; MA (homopolymer), 143121-97-5; OM, 143086-06-0; OM (homopolymer), 143086-48-0.