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Radical copolymerization studies of an amphiphilic macromonomer derived from Triton X-100. Reactivity ratios determination by in situ quantitative ^{1}H NMR monitoring

Elena Larraz, Carlos Elvira*, Alberto Gallardo, Julio San Román

Macromolecular Chemistry Department, Institute of Polymer Science and Technology, CSIC. c/Juan de la Cierva, 3, 28006 Madrid, Spain

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Abstract

This article deals with the estimation of the reactivity of a novel methacrylic macromonomer with amphiphilic character derived from Triton X-100 (MT) in radical copolymerisation reaction with acrylic acid (AA). Two approaches to estimate the reactivity ratio of the macromonomer are described. The first involves the use of the Jaacks equation valid for systems with a large excess of one of the comonomers and leads to $r_{AA}=0.31$. The second method uses a low molecular weight model monomer (MTm) that reproduces the chemical structure of the macromonomer. A non-linear fitting of the experimental data of the system MTm–AA to an integrated form of the copolymerisation equation which describes the terminal model postulated by Mayo and Lewis, gave reactivity ratio values of $r_{MTm}=2.5$ and $r_{AA}=0.30$. The results obtained from the two estimations suggest that methacrylic double bond reactivity is not affected by poly(oxyethylene oxide) chain length. In situ quantitative ^{1}H NMR analysis was used to monitor monomer consumption and therefore to follow the course of the copolymerisation reaction in both approaches.

Keywords: Amphiphilic macromonomer; Copolymerisation; Reactivity ratios

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1. Introduction

Amphiphiles are molecules which have an affinity for two different types of environments due to the presence in the molecule of at least two parts of different chemical character and solution properties. As a result, amphiphilic molecules self-organize at interfaces and in solution giving rise to a rich variety of phase structures enhancing in this way interfacial compatibility. Types, length and distribution of different parts of amphiphilic molecules determine the morphology and the properties of the assemblies. Therefore, mixing the right components at the right conditions is required in order to achieve self-assembled morphologies of very well-defined structural order and desired dimensions [1].

The interest on the synthesis and characterization of large amphiphiles, such as macromonomers [1–3] or random, star, graft and block copolymers [1,3,4], has considerably increased in the last decades. Large amphiphiles are very flexible in attaining a great variety of micro-assemblies due to the wide range of different copolymer architectures, and show a lower critical micelle concentration and slower exchange kinetics. Thus, these compounds are mainly applied as emulsifiers, surface active agents, compatibilizers and so forth [5], but also for biomedical use [6,7]. In this sense, a great variety of amphiphilic copolymers are being synthesized to be used in pharmaceutical and biomedical applications as drug delivery systems [8,9], hydrogels [10], blood-compatible systems [11,12]. Particularly, amphiphilic graft copolymers involving poly(ethylene oxide) macromonomers have been extensively studied in the mentioned applications [9,13,14].

As indicated above, the control of microstructural characteristics of the amphiphilic graft system allow to design materials with specific properties which can be modulated by the chemical structure and length of the graft

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* Corresponding author. Tel.: +34 915 622900; fax: +34 915 644853.
E-mail address: celvira@ictp.csic.es (C. Elvira).

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segments, as well as the average composition and monomer sequence distribution [15]. Former features are fixed with the selected macromonomer while later characteristics are given by the type of comonomers used and monomer reactivity ratios. Some difficulties arise when working with macromonomers derived from their high molecular weight which make not possible to work with macromonomer concentrations higher than 20–30 mol%. In such cases, macromonomer reactivity can be estimated by different approaches. In a previous paper [2], we described the copolymerisation behaviour of a new amphiphilic macromonomer derived from Triton X-100 with hydrophobic methyl methacrylic MMA monomer. Macromonomer reactivity was estimated by means of an appropriate low molecular weight model monomer. Results suggested that the reactivity of the methacrylic double bond was not affected by the length of PEO side chain and indicated the formation of MT–MMA random copolymers.

In the present work, we describe the radical copolymerisation of the amphiphilic macromonomer derived from Triton X-100, MT, with hydrophilic acrylic acid monomer, AA, by ^{1}H NMR monitoring. These are systems of biomedical interest and are being applied as part of modified glass-ionomer dental cements. Identically, a parallel study of a lower molecular weight monomer, which reproduces the reactive structure of the macromonomer, has been carried out to compare their reactivity towards AA in radical polymerization reactions. Studies of the evolution of the copolymerization reaction with conversion have also been carried out.

2. Experimental

2.1. Reagents

The methacrylic derivative of Triton X-100, macromonomer MT, and the model monomer MTm were synthesized as described before [2] and were used immediately after their synthesis. AA (Fluka) was distilled and freshly used (bp = 141 °C). 2,2′-Azobis-isobutyronitrile, AIBN (Fluka) was purified by fractional crystallization from ethanol (mp = 104 °C). Other reagents were used as received.

2.2. Copolymerization

Copolymerization reactions of the prepared monomers with AA were performed inside a NMR equipment using deuterated dioxane as solvent at 60 °C and 2,2′-azobis-isobutyronitrile, AIBN, as radical initiator in concentration 0.015 M. The total monomer concentration was 1 M in all cases, using 1 ml as the volume size of the polymerization batches. Two monomers solutions were prepared for the MTm–AA system with feed molar composition of MTm–AA 0.7–0.3 and 0.5–0.5, respectively and a conversion range of 0–80% approximately was considered. The feed molar fraction of MT, for the MT–AA system, was 0.05. In this case, a smaller degree of conversion was considered (50%) for the NMR data treatment.

2.3. ^{1}H NMR analysis

The experiments were carried out in a Varian 400 spectrometer. To perform quantitative experiments, the following conditions were used: a pulse sequence of 7 μs equivalent to a 90° tip angle and a 600 s delay time, or 200 s in the case of the MT–AA copolymerization, were applied in order to allow the total relaxation of the protons and to process the individual data. The spinning rate of the samples was 7 Hz, and for each datum only one acquisition (FID), nt = 1, was used to ensure that the measurement corresponds to instantaneous composition/conversion. The sample temperature was maintained at 60 °C using the heater controller of the NMR equipment. A solution of *N*,*N*-dimethylaminopyridine (DMAP, 10 mg) in deuterated dimethylsulfoxide (DMSO-d_6) in a thin wall capillary tube introduced in the NMR tube was used as reference. Spectra were thus obtained and signals were integrated using the electronic integration of the apparatus after Fourier Transform of the FIDs, and the concentrations were determined as follows:

$$[\mathrm{MTm}, \mathrm{MT}] = \frac{M_1}{R} \tag{1}$$

$$[\mathrm{AA}] = \frac{A_1 + A_2 + A_3 + M_2 - M_1}{3R} \tag{2}$$

where M_1 and M_2 correspond to the contribution of protons assigned to MTm or MT in Fig. 1, A_1, A_2 and A_3 are the acrylic protons assigned to AA and R is the reference peak (DMAP).

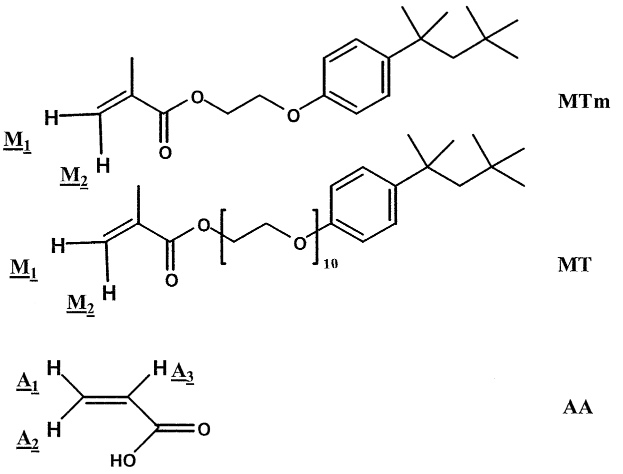

Fig. 1. Chemical structure of the monomers used in the copolymerisation reactions together with the nomenclature of the acrylic and methacrylic protons.

3. Results and discussion

3.1. Copolymerization data acquisition

In order to know the macromonomer behaviour in radical copolymerization processes with AA and due to the difficulties when working with MT high molar fractions, the MT reactivity was estimated by two different approaches. First, by the Jaacks simplified method and, secondly using the model monomer MTm, with one ethylene oxide side unit (Fig. 1). In both cases, copolymerisation reactions have been monitored by ^{1}H NMR. Figs. 2 and 3 show some spectra of the MTm–AA and MT–AA systems at different reaction times together with the assignments of the peaks employed in the determination of the monomer concentrations. DMAP was used as reference for the quantitative analysis of the monomer peaks, and the molar concentrations of the monomers have been determined as detailed in Section 2.

3.2. Jaacks method estimation

A number of copolymerization reactions involving macromonomers have been studied and almost invariably treated according to the terminal model, Mayo–Lewis equation [16], or to the simplified model established by Jaacks [17]. The Mayo–Lewis equation (Eq. (3)), that relates the instantaneous compositions of the monomer mixture to the copolymer composition, can be approximated to a simplified form (Eq. (4)) when working with a great excess of one of the comonomers. This is the case of copolymerisation reactions between a conventional comonomer and a macromonomer of relatively high molecular weight, where using low molar concentrations of macromonomer is mandatory due to its restricted solubility and the extremely viscous media resulted.

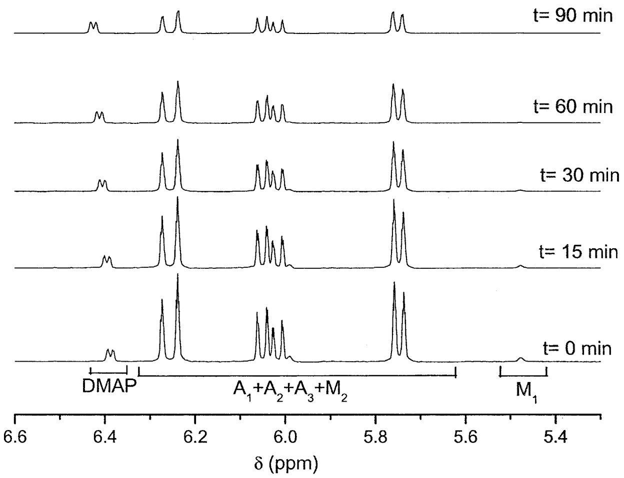

Fig. 2. Some representative ^{1}H NMR spectra of the MT–AA copolymer system, with feed molar composition $F_{\mathrm{MT}}=0.056$, at different times of reaction. Only the acrylic region used for calculations is shown.

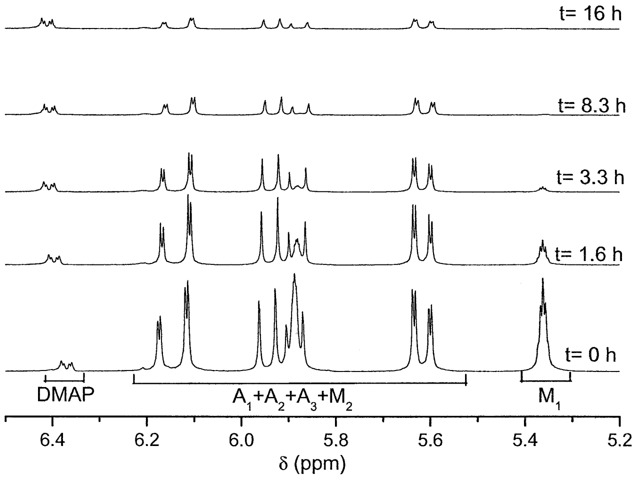

Fig. 3. Some representative ^{1}H NMR spectra of the MTm–AA copolymer system, with feed molar composition $F_{\mathrm{MTm}}=0.7$, at different times of reaction. Only the acrylic region used for calculations is shown.

$$\frac{d[M_1]}{d[M_2]}=\frac{[M_1]}{[M_2]}\frac{r_1[M_1]+[M_2]}{[M_1]+r_2[M_2]} \tag{3}$$

$$\frac{d\left[M_2\right]}{d\left[M_1\right]}=r_2\frac{M_2}{M_1} \tag{4}$$

According to Eq. (4), the copolymer composition or the frequency of branches is essentially determined by the monomer composition and the monomer reactivity ratio of the comonomer r_2 (inversely proportional to the macromonomer reactivity).

In order to obtain reliable values, it is frequently necessary to run the copolymerisation at different conversions or to carry out several copolymerisations with different initial monomer ratios. In such cases, an integrated form of Eq. (4) is used:

$$\ln\frac{[M_2]_t}{[M_2]_0}=r_2\ln\frac{[M_1]_t}{[M_1]_0} \tag{5}$$

where $[M_i]_t/[M_i]_0$ is the ratio among the composition of monomer i at time t and the initial feed composition. A plot of $\ln([M_2]_t/[M_2]_0)$ versus $\ln([M_1]_t/[M_1]_0)$ should result in a straight line with a slope that equals to r_2 (the reactivity ratio of the comonomer). The parameter r_1 is of little practical importance, since, in general, low concentrations of macromonomer are used, and unless r_1 is particularly large, the probability of two macromonomers units being installed in adjacent positions on a polymer chain is very small [18]. Thus, the parameter r_2 is more commonly quoted to express the relative reactivity of the macromonomer.

Feed composition values obtained at different reaction times by means of the ^{1}H NMR monitoring technique (as previously explained), have been fitted to Eq. (5) (Fig. 4) and a linear least-squares optimization would give us the best value of r_2 (r_{AA}). In this case $r_{\mathrm{AA}}=0.31$, indicating a relative higher reactivity of the macromonomer in the

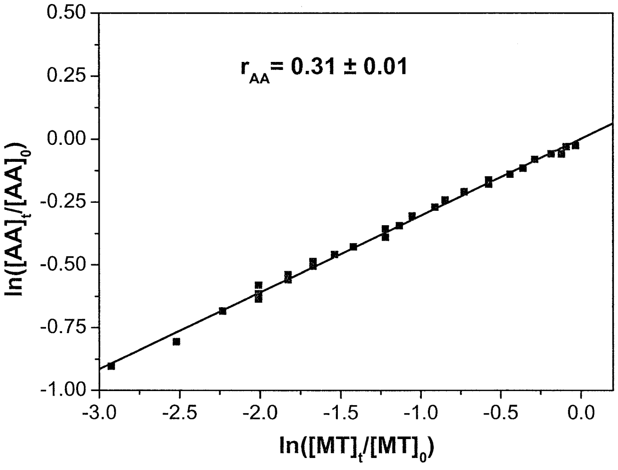

Fig. 4. Linear least-square fitting of experimental data of the system MT–AA to integrated Jaacks equation.

copolymerization reaction. The former result differs, as expected, from that reported in a previous paper in which copolymerisation reaction between MT and MMA was studied [2].

3.3. Model monomer estimation

There is a complex interplay of factors, such as the chemical nature of the polymerizable end group of the macromonomer, its degree of compatibility with the propagating comonomer chain or the molecular weight, that can affect the reactivity of macromonomers in copolymerization reactions [18]. Although there is not yet an agreement in the literature on the relative importance of these factors, it appears from a number of monomer reactivity ratios reported so far [18,19], that the nature of the polymerizing end-groups largely determines the reactivity of macromonomers in copolymerization with a conventional monomer and that other factors are usually of less importance. In fact, model monomers for the end group can provide a useful first approximation to the reactivity of a given macromonomer. We previously reported [2] an estimation of the reactivity of macromonomer MT in copolymerization with hydrophobic monomer MMA by using the model monomer MTm which posses just one ethylene oxide side unit in its chemical structure (Fig. 1). In that paper, MTm was proved as a good model to estimate macromonomer MT reactivity and the obtained results suggested that the length of the side poly(ethylene oxide) chain did not affect the reactivity of the methacrylic double bond in the copolymerization reactions with MMA. In the present paper is reported the behaviour of the macromonomer MT in radical copolymerisation with a hydrophilic monomer, the acrylic acid (AA), by means of the model monomer proposed. For this purpose, a new methodology earlier described by Aguilar et al. [20] was employed determining the reactivity ratios via a quantitative in situ NMR analysis of the course of the copolymerisation reaction. From the variation in monomer concentration determined as described above, the reactivity ratios have been determined by using a well-known integrated form of the copolymerisation equation (terminal model) (Eq. (6):

$$\frac{[M_2]}{[M_{20}]} = \left[\frac{[M_{20}][M_1]}{[M_{10}][M_2]}\right]^{\frac{r_2}{1-r_2}}\left[\frac{(r_1-1)([M_1]/[M_2])-r_2+1}{(r_1-1)([M_{10}]/[M_{20}])-r_2-1}\right]^{\frac{r_1r_2-1}{(1-r_1)(1-r_2)}} \tag{6}$$

if $[M_1]/[M_2]=x$, $[M_{10}]/[M_{20}]=x_0$, $[M_2]=y$ and $[M_{20}]=y_0$

$$y = y_0\left(\frac{x}{x_0}\right)^{\frac{r_2}{1-r_2}}\left(\frac{1-r_2+(r_1-1)x}{1-r_2+(r_1-1)x_0}\right)^{\frac{r_r r_2-1}{(1-r_1)(1-r_2)}} \tag{7}$$

$$y = kx^{\frac{r_2}{1-r_2}}[1-r_2+(r_1-1x]^{\frac{r_1r_2-1}{(1-r_1)(1-r_2)}} \tag{8}$$

where k is a constant that includes the initial conditions. Former authors developed two approaches to estimate the reactivity ratios based on a non-linear least-squares fitting of the experimental data (x, y) to Eqs. (7) (Section 3.3.2) and (8) (Section 3.3.1). By this procedure, the experimental error associated to the NMR technique employed (coming from the 2% intrinsic error and some other factors such as the sample preparation, integration, etc.) can be minimized.

3.3.1. Method 1

The experimental error was averaged by using k as the third parameter in the non-linear fitting (Eq. (8)), instead of using a given x_0, y_0. Fig. 5 shows the experimental data obtained by NMR analysis of the two particular feed compositions together with the optimised r_{MTm} and r_{AA} values resulted from the fitting to Eq. (8). These values, with

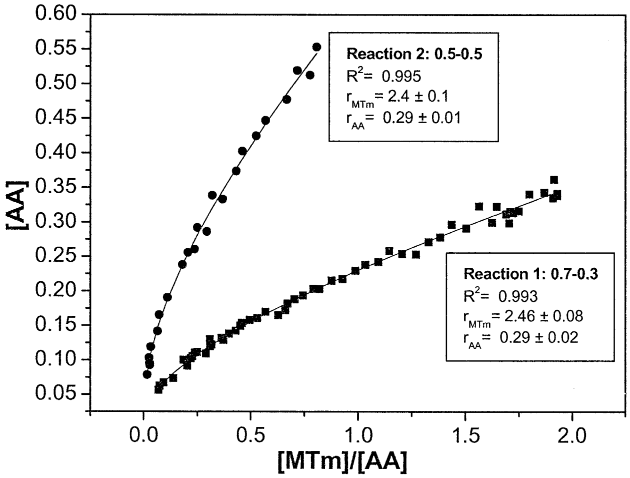

Fig. 5. AA molar concentration versus the [MTm]/[AA] ratio, obtained from the in situ ^{1}H NMR analysis of the MTm–AA copolymeric reaction with a molar feed composition of MTm: F(MTm)=0.7 and 0.5 (reaction 1 and 2, respectively).

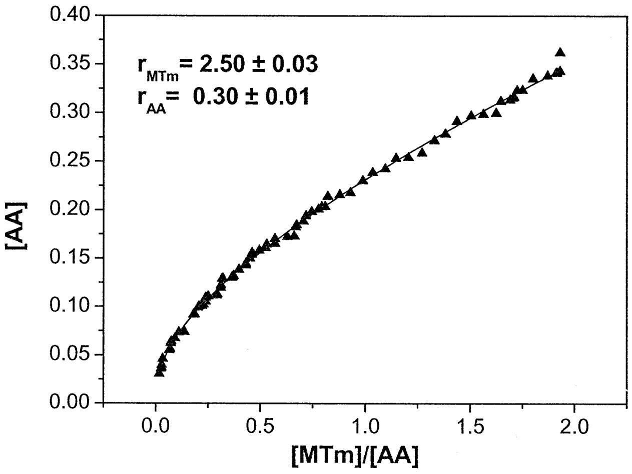

Fig. 6. Corrected global molar concentrations of AA versus the [MTm]/[AA] ratio using the shift factor treatment proposed in the text (Section 3.3.1).

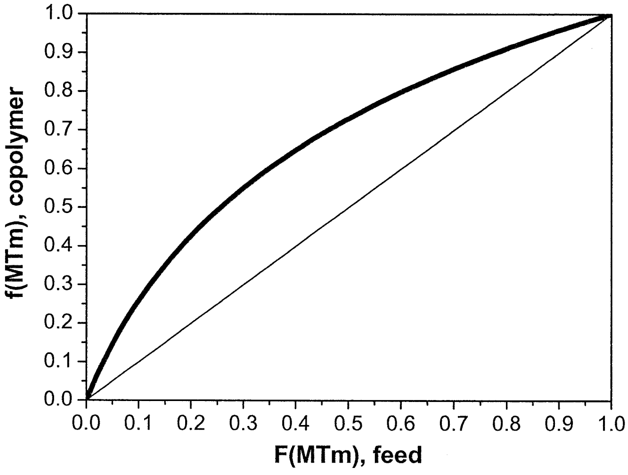

Fig. 7. Composition diagram obtained with the reactivity ratios determined by the first approach using the corrected global data.

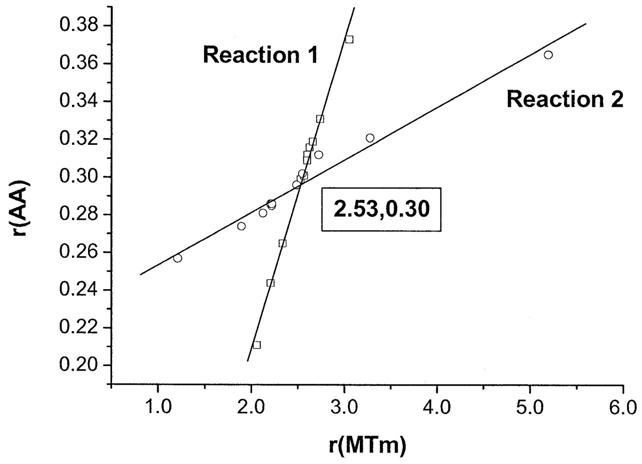

Fig. 8. Diagram of reactivity ratios r_{AA} versus r_{MTm} obtained as described in the text (Section 3.3.2).

$r_{MTm} > 1$ and $r_{AA} < 1$, indicate that MTm is consumed faster than AA. As a consequence of that, and as it can be observed in Fig. 5, it is possible to obtain reliable reactivity ratios from one unique reaction when properly selecting the initial feed composition. Apparently, there is a good agreement between the reactivity ratios obtained for the two selected reactions. In order to achieve more reliable data, the data of reactions 1 and 2 have been compatibilized by using the shift factor $p = [AA]_{fit2}/[AA]_{fit1} = 2.59$ at the common [MTm]/[AA] ratio = 0.705, as it has been previously described [20]. Multiplying the data of reaction 2 by $1/p$ the combined data drawn in Fig. 6 were obtained, which have been fitted to Eq. (8), leading to the reactivity ratios $r_{MTm} = 2.50$ and $r_{AA} = 0.30$. From these values, the theoretical composition diagram has been calculated (Fig. 7).

3.3.2. Method 2

The second approach [20] to estimate the reactivity ratio is summarized in Fig. 8. This method considers any given experimental point x_t, y_t as starting point for the rest of the reaction. In this sense, the first 5–10 points were used for the two reactions, and the least-squares optimisation to Eq. (7) leads to the r_1–r_2 data depicted in Fig. 8.

The crossing point of the lines is considered to be the real reactivity ratios of the two monomers [20], those independent of the unavoidable error introduced by x_0, y_0 and able to fit the whole copolymer reaction. Thus, the more reliable reactivity ratios seem to be $r_{MTm} = 2.53$ and $r_{AA} = 0.30$, which is in very good agreement with the values obtained by the first approach.

The reactivity ratio value for AA with respect to model monomer MTm, obtained by these two methods (equal to 0.30), is very close to that obtained by the Jaacks' estimation, when it is copolymerised with the macromonomer MT. This result suggests that the length of the side PEO chain (in this chain length range) does not affect the reactivity of the methacrylic double bond in the prepared monomers in their copolymerization with AA. This point is confirmed when analysing the inverse ratio $1/r_2 = k_{21}/k_{22}$, which is sometimes considered as the relative copolymerization reactivity of a macromonomer [15]. This quantity is the ratio between the crosspropagation and homopropagation rate constants of comonomer 2, which is directly proportional to the reactivity of the macromonomer (1) and gives a clear idea of the relative reactivity of a growing radical ending in a 2 unit towards the addition of monomer *1*, in comparison to the tendency for the homopropagation. Table 1 summarizes the values of the relative reactivity of growing radicals ending in AA and MMA (values reported elsewhere [2]) towards the macromonomer MT($1/r_2$) as well as towards its homologous model monomer MTm ($1/r'_2$). As it can be seen, rather similar values are obtained for the addition of AA (or MMA) ending radicals to macromonomer MT or to the model monomer MTm. These results demonstrate that the reactivity of the growing free radicals is practically not affected by the length of the side

Table 1
Relative reactivity of macromonomer MT and model monomer MTm with respect to AA and MMA comonomers in free radical copolymerization

Comonomer 2	$1/r_2$	$1/r'_2$	$k_{2\text{-MT}}/k_{2\text{-MTm}}$
AA	3.22	3.33	0.97
MMA^2	0.97	1.05	0.92

$r_2=k_{22}/k_{2\text{-MT}}$. $r'_2=k_{22}/k_{2\text{-MTm}}$.

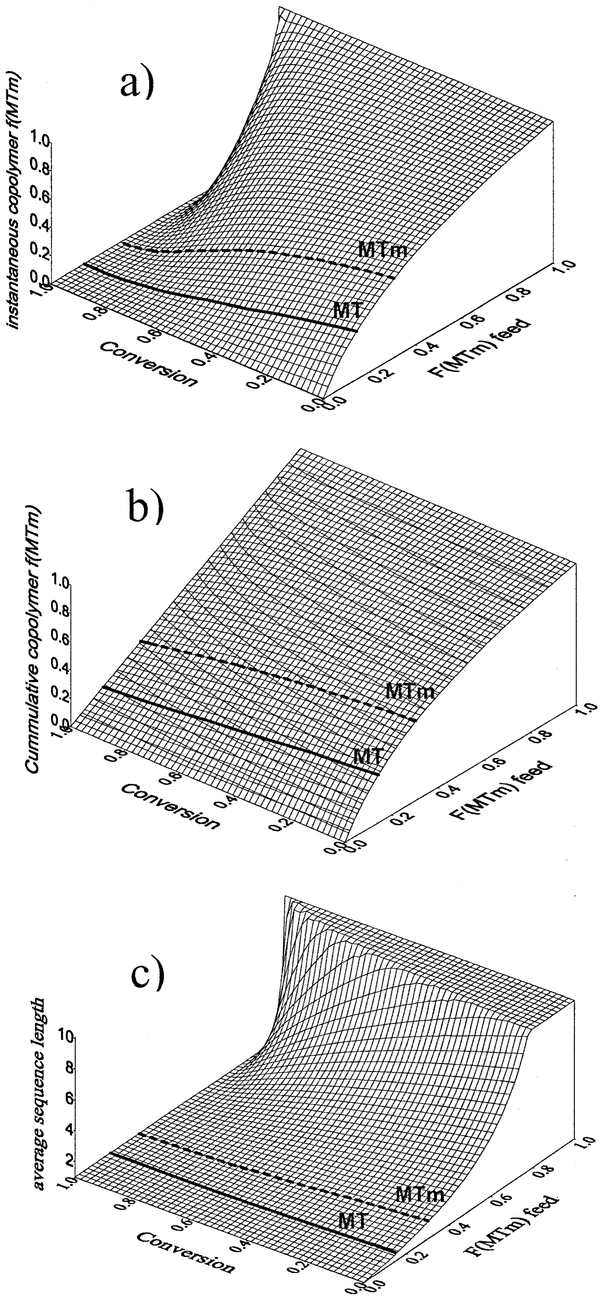

Fig. 9. Instantaneous (a) and cumulative (b) copolymer molar fraction and the average sequence length (c) for the system MTm–AA as a function of the conversion and the feed molar fraction. The thick solid and dashed lines represent the course of a reaction starting at 20% weight of either MT or MTm (corresponding to approximately 0.15 or 0.30 feed molar fraction respectively).

poly(oxyethylene) chains in the case of relatively low polar species as have been observed for macromonomers of poly(L-lactide) in copolymerization with vinyl and acrylic monomers [21], and as was found for compatible systems such as macromonomers of (vinyl acetate)-terminated polystyrene with vinyl acetate [4]. However, in the case of non-compatible systems such as macromonomers of poly(ethylene oxide) with styrene the increase of PEO side chain length reduces the reactivity in the copolymerization reaction [22].

If it is considered that the homopropagation rate constant k_{22} of monomers AA or MMA is not affected by the comonomer used (namely MT or MTm), then, according to the definition of reactivity ratio, the following expression can be estimated a good approximation:

$$[r'_2/r_2] = [k_{2-\mathrm{MT}}/k_{2-\mathrm{MTm}}] \tag{9}$$

Eq. (9) indicates that the ratio of the kinetic parameters of copolymerization directly provides the ratio of the cross-propagation rate constants for the addition of active growing radicals to the macromonomer MT or the homologous model monomer MTm. The data obtained are recorded in the fourth column of Table 1, and confirm that the cross-propagation is not affected by the length of the oxyethylene side chains in the case of the copolymerization with AA or MMA.

It is interesting to stress out that the reactivity of AA ending radicals towards both the macromonomer MT and model monomer MTm is approximately three times that of the reactivity towards its own monomer AA. However, in the case of MMA, no preference is detected in the addition reaction. Similar behaviour has been described for poly(L-lactide) macromonomer in its copolymerisation reaction with methacrylic acid (MA) and MMA [21]. Mentioned behaviour may be related with the reactive structure of comonomers, acrylic in the case of AA, MA or methacrylic in the case of MMA, in regard to the ending methacrylic double bond of macromonomers, besides the hydrophilic character of the comonomer.

3.4. Evolution of the copolymerization reaction with conversion

The variation of instantaneous copolymer composition with the feed molar concentration can be analyzed from the theoretical composition diagram (Fig. 7). However, 3D graphs (Fig. 9) clearer predict the evolution of different parameters that provide information of the copolymer microstructure, such as the molar fractions of any sequence besides the instantaneous and cumulative copolymer molar fractions, with the conversion and the feed molar fraction. As an example, Fig. 9(a)–(c) shows the instantaneous and cumulative copolymer molar fraction and the average sequence length for the system MTm–AA as a function of the conversion and the feed molar fraction. The shown graphs have been obtained by using the algorithm 'Conversion' developed by Gallardo et al. [23]. This algorithm has been proved useful to theoretically predict, from the knowing reactivity ratio values and without any approximation (except those considered by the terminal model), the course of any binary copolymerization reaction with the conversion. From Fig. 9(a) it can be observed that macromolecules rich in the most reactive monomer (i.e. MTm) are initially formed (at low and medium conversion) and after the consumption of a great quantity of this monomer, chains rich in the less reactive monomer (i.e. AA) are formed (at high conversion). Fig. 9(b) shows that the average composition increases gradually until the system reaches the initial feed composition. This trend does not reveal information about the real distribution of the macromolecular chains, which is heterogeneous (r_1 and r_2 are far from unity) and can have a large influence on the material properties. Former information is given by other parameters such as the average sequence length or the sequence molar fraction. Fig. 9(c) shows the average length of the sequences centred in the most reactive monomer (MTm). Large sequences of MTm are initially formed for high feed molar fractions while at high conversions, when MTm has been almost completely consumed, large sequences of AA are predominant. In between, species of intermediate composition are formed. Making use of the consideration of similar reactivity of macromonomer MT and model MTm, the course of a model reaction starting at 20% weight in any of these monomers (corresponding to 0.15 or 0.30 feed molar fractions, respectively) has been depicted in Fig. 9. This illustration allows predicting the structure and properties of high conversion MT–AA copolymers, which are currently being studied in our group for their application in restorative dentistry.

4. Conclusions

In situ quantitative ^{1}H NMR analysis has been used to monitor the radical copolymerization of a new methacrylic macromonomer MT with AA. Macromonomer reactivity has been estimated by Jaacks equation and by using an appropriate model monomer. Both estimations have led to similar results suggesting that the length of the PEO side chain does not affect to the reactivity of the methacrylic double bond. Reactivity ratios were found to be $r_{\mathrm{MTm}} = 2.53$ and $r_{\mathrm{AA}} = 0.30$ indicating that the commercial monomer AA is less reactive than the model monomer MTm and the macromonomer MT. These values are representative of a copolymerisation reaction with heterogeneous character leading to the formation of two main species rich in each one of the monomers at low and high conversions and some intermediate species.

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References

[1] Lindman B, Alexandridis P. In: Alexandridis P, Lindman B, editors. Amphiphilic block copolymers. 1st ed. Amsterdam: Elsevier; 2000. p. 1–12.
[2] Larraz E, Elvira C, San Román J. J Polym Sci, Polym Chem 2003;41: 1641–9.
[3] van Os NM. In: van Os NM, Haak JR, Rupert LAM, editors. Physicochemical properties of selected anionic, cationic and nonionic surfactants. Amsterdam: Elsevier Science; 1993.
[4] Teoderescu M. Eur Polym J 2001;37:1417–22.
[5] Maniruzzaman M, Kawaguchi S, Ito K. Des Monomers Polym 2001; 3(3):255–61.
[6] Bae YH, Huh KM, Kim Y, Park KH. J Controlled Release 2000;64(1-3):3–13.
[7] Businelli L, Deleuze H, Gnanou Y, Maillard B. Macromol Chem Phys 2000;201(14):1833–9.
[8] Cölfen H. Macromol Rapid Commun 2001;22:219–52.
[9] Kim SY, Shin IG, Lee YM. Biomaterials 1999;20:1033–42.
[10] Suggs LS, Krishnam RS, García A, Peter SJ, Anderson JM, Mikos AG. J Biomater Sci, Polym Ed 1998;9:653–60.
[11] Guo S, Shen L, Feng L. Polymer 2001;42(3):1017–22.
[12] Park KD, Kim WG, Jacobs H, Okano T, Kim SW. J Biomed Mater Res 1992;26(6):739–56.
[13] Park JH, Bae YH. Biomaterials 2002;23(8):1797–808.
[14] Perez C, Sanchez A, Putnam D, Ting D, Langer R, Alonso MJ. J Controlled Release 2001;75(1-2):211–24.
[15] Ito K. Progr Polym Sci 1998;23(4):581–620.
[16] Mayo FR, Lewis FM. J Am Chem Soc 1944;66:1594–8.
[17] Jaacks V. Makromol Chem 1972;161:161–72.
[18] Meijs GF, Rizzardo E. J Macromol Sci, Rev Macromol Chem Phys 1990;C30(3 and 4):305–77.
[19] Ito K, Kawaguchi S. Adv Polym Sci 1999;142:129–78.
[20] Aguilar MR, Gallardo A, Fernández M, San Roman J. Macromolecules 2002;35:2036–41.
[21] Eguiburu JL, Fernandez-Berridi MJ, San Roman J. Polymer 1996; 37(16):3615–22.
[22] Ito K, Tsuchida H. Polym Bull 1986;15:425–30.
[23] Gallardo A, Aguilar MR, Abraham GA, San Roman J, J Chem Ed; 2004;81:1210–5.