Copolymers of Acrylic Acid with 2-Acryloyloxyethyl 2,4-Dichlorophenoxyacetate: Synthesis and Herbicide Release

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ABSTRACT: Free-radical copolymerization of acrylic acid with 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate using 1.0 mol/L 1,4-dioxane solution and 1.5×10^{-2} mol/L of 2,2′ azobisisobutyronitrile as initiator has been carried out at 50°C. In addition to low conversion solution experiments performed to estimate the monomer reactivity ratios, three different copolymerizations over the whole range of conversions have been made. Theoretical values of cumulative copolymer composition, determined by the Mayo-Lewis terminal model, have been correlated with those experimentally obtained. Finally, the herbicide release in three different aqueous pH buffer solutions has been evaluated in heterogeneous phase. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 102: 4238–4244, 2006

Key words: free radical copolymerization; 2,4-dichlorophenoxyacetic acid; acrylic acid; 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate; reactivity ratios; copolymer composition; herbicide release

INTRODUCTION

Controlled-release technology has emerged as one promising approach to solve the problems that accompany the use of biologically active agents, whether pharmaceutical or agrochemical. These systems find good application in agriculture because of environmental concerns that impose severe restrictions on uses of mobile herbicides with high activity.[1–6]

In most controlled-release formulations, the biologically active agent is dispersed in, or combined with, polymeric matrices,[1,7] i.e., (a) physical mixing of an active agent with a polymer to yield a rate controlling device; or (b) chemical binding of the active agent to the polymer matrix to act as carrier and consequent release of the active ingredient is controlled by the chemical cleavage of polymer-active agent bond or by environmentally induced depolymerization. The macromolecular nature of these formulations allows to control mobility and effectiveness period of the active agent. The selection of either method for achieving controlled-release in a particular application depends on the release rate required, properties of the active agent, and the cost.

In addition, controlled-release administration of agrochemicals has certain advantages over conventional methods of agrochemicals use.[1] The latter provides an initial concentration far in excess of that required for immediate results to ensure the presence of sufficient chemical for a practical period of time; such overdosing wastes much of the chemical potential, and all too often causes toxicity problems for nontarget organisms and produces undesirable side effect in the environmental. To overcome this problem, the principle of dual application of polymer-supported herbicides based on combinations of either herbicide-fertilizer[8,9] or herbicide-water conservation (hydrogels) has also been introduced in an attempt to eliminate the disadvantages of using excessive amount of inert polymers as carriers for herbicides.[10,11]

The herbicide 2,4-dichlorophenoxyacetic acid (2,4-D), a growth regulator herbicide, has been used widely in agriculture, forestry, home and garden applications and to control weeds in parks and rights-of-way for over 50 years. Because of its wide employ and recent concerns over its safety, it is also one of the most studied herbicides in use today. It has been attached to monomers, synthetic and natural polymers,[7–9,12–16] which allow to prevent toxic and harmful effects.

On the other hand, the copolymerization of herbicide-containing monomers let the possibility of changes in the polymer structure using another comonomer and therefore, the ability to control the molecular design of the herbicide/polymer ratio. Therefore, in this work, the free-radical copolymerization of acrylic acid (AA) with a vinyl ester derived of 2,4-D is presented. The herbicide contain-

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ing monomer, 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate, has been previously copolymerized with triethylamine methacrylimide, AA, and methacrylic acid.[17] However, to our knowledge, no studies have been performed to analyze the monomer reactivity ratios and the copolymer composition behavior with respect to the conversion. Therefore, an examination of the changes on the copolymer structure through the reactions has been performed. In addition, the herbicide release in different aqueous pH buffer solutions has been analyzed in heterogeneous phase.

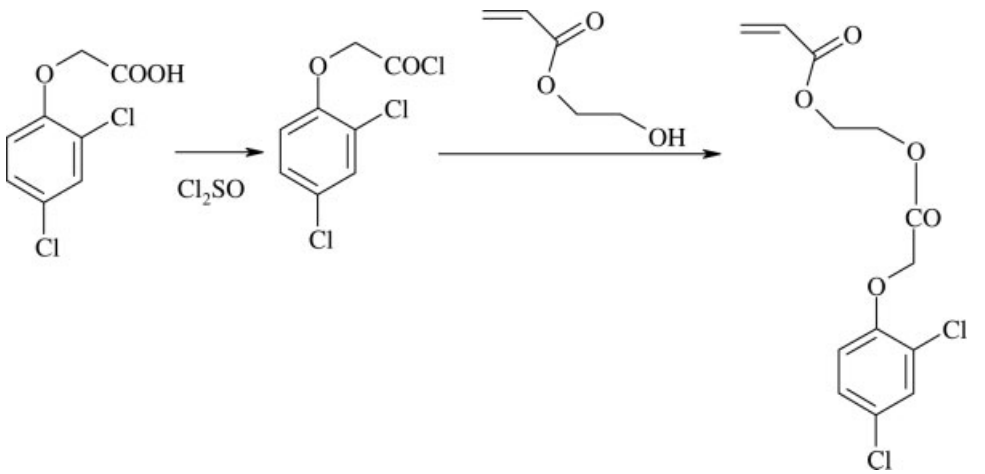
EXPERIMENTAL

Materials

Acrylic acid (AA) and 2-hydroxyethyl acrylate (both Fluka ≥ 99%) were distilled under reduced pressure. Thionyl chloride (Scharlau, Barcelona, Spain) and *N*,*N*-dimethylaniline (Fluka, Buchs, Switzerland) were distilled before use. 2,4-Dichlorophenoxyacetic acid (2,4-D) (Aldrich, Steinheim, Germany) and 1,4-dioxane (Scharlau) were used as received. 2,2′-Azobisisobutyronitrile (AIBN) (Fluka) was purified by crystallization from methanol and dried in vacuum. All other reagents were used as received without further purification.

Monomer synthesis

The monomer synthesis was accomplished according to the following scheme:



cide-containing monomer was recrystallized from ethyl ether with cold hexane yielding a white solid. (^{1}H NMR ($CDCl_3$): δ 7.4–7.3 days, H-1 aromatic, ^4J = 2.64 Hz; δ 7.2–7.0 dd, H-2 aromatic, ^4J = 2.64 Hz, ^3J = 8.67 Hz; δ 6.9–6.7 days, H-3 aromatic, ^3J = 8.67 Hz; δ 6.5–6.3 dd,=CH_2—, ^2J = 1.70 Hz, $^3J_{trans}$ = 17.33 Hz; δ 6.2–6.0 dd, =CH—, ^3J = 17.33 Hz, ^3J = 17.33 Hz; δ 5.9–5.75 dd, =CH_2—, ^2J = 1.51 Hz, $^3J_{cis}$ = 10.36 Hz; δ 4.7 s, —CH_2—; δ 4.5–4.3 m, —CH_2—CH_2—; mp = 41°C). The yield was ∼ 85%.

Acid chloride of 2,4-D synthesis

The synthesis was performed as elsewhere.[8] Accordingly, 2,4-D (75.0 g, 0.34 mol) was added to thionyl chloride (101.2 g, 0.85 mol). The mixture was refluxed at 100°C under dry conditions for 6 h. The excess of thionyl chloride was removed by distillation. The product was dried *in vacuo* for a few days at room temperature in the presence of phosphorus pentoxide until constant weight. The yield was ∼ 95%.

Reaction of 2,4-D acid chloride with 2-hydroxyethyl acrylate

The synthesis of 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate, H, was performed according to the procedure described previously.[18] To a 2-hydroxyethyl acrylate solution (25.5 g, 0.220 mol) and *N*,*N*′-dimethylaniline (30.9 g, 0.255 mol) in 225 mL of anhydrous ethyl ether heated at reflux was slowly added the acid chloride of 2,4-D (52.6 g, 0.220 mol). After the addition was complete, the solution was heated at reflux for 3 h and then, allowed to cool. The *N*,*N*′-dimethylaniline hydrochloride that precipitated was dissolved by the addition of water. The ethereal solution was separated, washed three times with a 10% sulfuric acid solution, and once with a saturated sodium bicarbonate solution. The solution was then dried, first for 2 h over sodium sulfate and then overnight with calcium chloride. The ether was removed under reduced pressure. Thus, the herbi-

Copolymerization reactions

Copolymerization reactions of AA with 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate (AA-H) were carried out in solutions of 1,4-dioxane in glass vessels

sealed with rubber septa. Total monomer and initiator concentrations were 1.0 mol/L and 1.5 10^{-2} mol/L, respectively. The comonomer mixtures in ratios ranging from 0.1 to 0.9 were prepared. Dissolved oxygen was removed from the reaction solution by nitrogen purging for 30 min prior to immersion in a water bath kept at a temperature of (50 ± 0.1)°C. The copolymerization system was homogeneous in all cases investigated. After a specified period of time, each reactor vessel was removed from the water bath. The solutions were poured into a large excess of diethyl ether/heptane mixtures (1 : 1 v/v) to precipitate the copolymers. Then, the polymers were filtered and dried under reduced pressure in the presence of phosphorus pentoxide until constant weight was attained. The polymer conversions were determined by gravimetry.

Copolymer characterization

The ^{1}H NMR spectra were recorded at 300 MHz on a Bruker 300 spectrometer with deuterated acetone, (Scharlau) as the solvent and locking agent at 27°C. The proton solvent signal was used as chemical shift marker. The spectra were obtained by using a sample concentration of 10% w/v solutions. The relative signal intensities of the spectra were measured from the integrated peak area, calculated by means of an electronic integrator.

Herbicide release

For this study, a high degree of conversion copolymer, which was insoluble in water but did swell on standing in the medium, was used. Polymer samples of 50–60 mg in powder form were compressed to produce discs. Each resulting disc was introduced into a small wire basket, which was entirely permeable to water. These devices were placed in Pyrex stoppered test tubes, each containing 25 mL of the aqueous buffer solution. The tubes were then placed in a constant bath at 35°C. A periodic assay of samples was obtained by removing the wire basket, stirring the solution and pipetting a 1 mL sample. The wire basket was quickly reinserted, making sure that the disc remains completely immersed throughout the hydrolysis study. The volume pipetted for each sample was replaced by an equivalent volume of fresh aqueous buffer solution; therefore, the volume corrections were applied in the calculations. The released bioactive compound was measured using a Perkin–Elmer Lambda 16 UV spectrometer at λ_{max} = 283 nm. Calibration curves were obtained from the UV absorbance at 283 nm of suitable herbicide solution in pH 7.0, 8.0, and 9.9 buffers. Concentrations ranging from 2.5×10^{-5} to $2.5 \times 10^{-4} M$ were used.

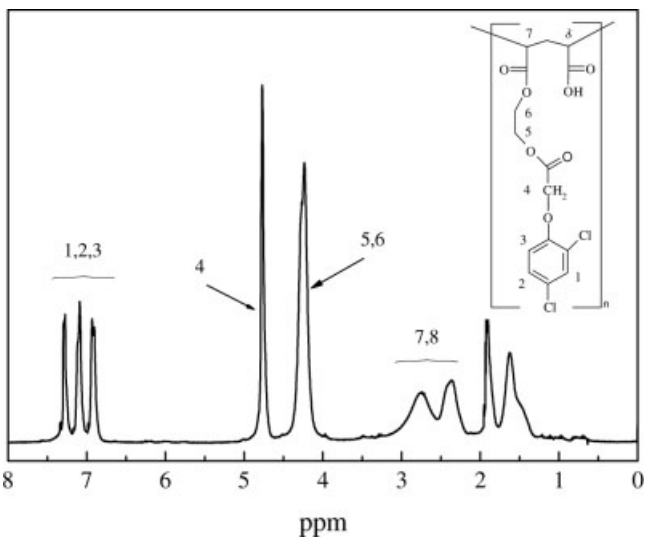


Figure 1 ^{1}H NMR spectra of an acrylic acid-2-acryloyloxyethyl 2,4-dichlorophenoxyacetate copolymer, f_{AA} = 0.2, obtained in 1.4-dioxane solution at 50°C.

TABLE I
The Acrylic Acid Monomer Molar Fraction in the Feed (f_{AA}), the Average Molar Fraction Compositions of Copolymers (F_{AA}), and the Final Conversion

f_{AA}	Conv (%)	F_{AA}
0.1	2.4	0.48_5
0.2	2.9	0.55_9
0.5	3.1	0.68_7
0.6	2.4	0.74_8
0.7	3.0	0.82_0
0.8	3.3	0.86_0
0.9	3.9	0.92_7

RESULTS AND DISCUSSION

Copolymerization reactions

Initially, free-radical copolymerizations of AA with 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate in 1.0 mol/L of 1.4-dioxane solutions using 1.5 × 10^{-2} mol/L of AIBN as initiator have been carried out at 50°C. The copolymers have been obtained at low degree of conversion < 5% to satisfy the differential copolymerization equation.[19] The average molar fraction composition of copolymers has been quantitatively determined from the corresponding NMR spectra of copolymer samples prepared with different monomer feeds. The analysis has been performed from the relative areas of the signals that appeared between 6.5–7.5 ppm (corresponding to the three aromatic protons of the H unit) with the peaks between 2.0–3.5 ppm assigned to the H methine and the AA methine protons (Fig. 1). The AA monomer molar fraction in the feed, f_{AA}, the average molar fraction composition of copolymers, F_{AA}, and the final conversion are collected in Table I. The mono-

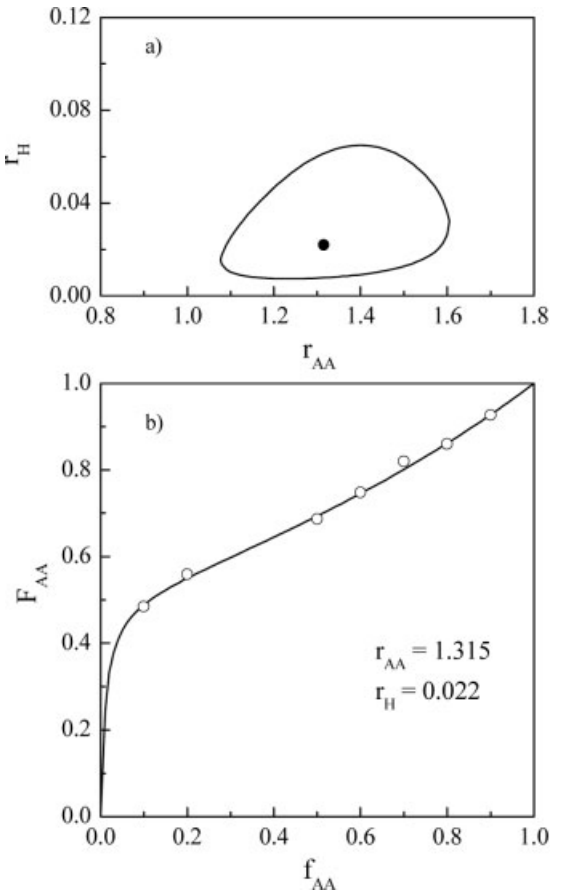


Figure 2 Copolymerization of AA with 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate in 1.4-dioxane solution at 50°C. (a) The 95% joint confidence interval of reactivity ratios. (b) The experimental composition data and the theoretical curves calculated with the reactivity ratios.

mer reactivity ratios have been determined from the average composition of copolymers listed in Table I, through the nonlinear least-squares analysis suggested by Tidwell and Mortimer.[20] The obtained values for AA-H system are $r_{AA} = 1.315$ and $r_H = 0.022$. Figure 2(a) shows the accuracy of the estimated data where the 95% joint confidence interval is drawn. For this system, a fundamental random copolymer rich in AA units can be expected at relatively low conversions but at high conversions most of the 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate monomer molecules will polymerize, giving rise to copolymer chains with relatively long blocks of 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate units. In Figure 2(b) are represented the experimental composition data and the theoretical curves calculated with the obtained reactivity ratios using the Mayo-Lewis copolymerization equation. It can be seen that the agreement is quite satisfactory.

It is well established that the copolymerization of the monomers capable of ionization or hydrogen-bond formation is strongly influence by the reaction medium.[21,22] In previous investigations, it has been found that the aggregation of α-ethyl acrylic acid (AA) in 1,4-dioxane and their interaction with maleimide exerted a great effect on the copolymerization.[23,24] Therefore, it is important to have in mind

TABLE II
Time, Conversion, and Acrylic Acid Monomer Molar Fraction in the Copolymer (F_{AA}) for Three Molar Fractions in the Feed

f_{AA}	Time (min)	Conv (%)	F_{AA}
0.2	2	2.9	0.55_9
	6	9.1	0.55_5
	8	12.0	0.55_9
	10	14.6	0.54_2
	12	17.5	0.51_0
	15	20.7	0.49_7
	20	29.3	0.49_5
	25	36.9	0.47_6
	30	42.8	0.49_9
	35	47.3	0.44_4
	45	54.7	0.37_8
	60	62.8	0.34_5
	75	69.2	0.29_8
	90	74.8	0.28_0
	120	80.9	0.25_2
	120	82.6	0.25_0
	150	87.5	0.23_8
	180	89.1	0.24_2
	210	92.0	0.20_5
0.5	3	3.1	0.68_7
	6	5.8	0.67_4
	8	7.8	0.68_7
	10	9.5	0.70_0
	12	12.7	0.67_3
	20	18.6	0.69_0
	30	27.9	0.66_1
	35	33.2	0.66_1
	45	38.7	0.67_7
	60	47.6	0.67_5
	75	55.5	0.65_1
	90	61.7	0.61_6
	105	67.8	0.62_7
	120	71.2	0.63_0
	140	76.7	0.63_6
	160	79.6	0.62_3
	180	83.6	0.58_8
	210	87.2	0.58_3
	300	93.6	0.52_1
0.8	5	3.3	0.86_0
	7	4.5	0.86_2
	8	5.4	0.85_7
	10	7.1	0.84_7
	12	7.6	0.83_7
	16	11.5	0.85_1
	20	12.3	0.86_3
	30	19.1	0.85_8
	60	36.4	0.84_5
	90	48.0	0.83_4
	120	57.4	0.84_7
	150	66.6	0.82_5
	180	72.8	0.83_6
	210	75.6	0.84_9
	240	84.0	0.81_4
	300	85.6	0.81_2

that the 1,4-dioxane as a solvent could exerted a marked effect on composition of copolymers by the formation of hydrogen bonding between 1,4-dioxane and AA. As a consequence of this fact, the monomer reactivity ratios could be only apparent and distinct from those obtained in bulk conditions.

Subsequently, copolymerizations at three different molar feed compositions in the whole range of conversions have been performed. The time, conversion, and AA monomer molar fraction in the copolymer, F_{AA}, for each composition are collected in Table II. Figure 3 represents the time-conversion plot for AA-H copolymerization at three different molar feed compositions. It is clearly evidenced that the rate of copolymerization increases as AA in the feed molar fraction decreases.

At this time, it is well recognized that terminal model[19] is only a fairly accurate model, which can be used for descriptive purposes[25] being the true physical understanding of the complexity of copolymerization gained by the precise chemistry and physics of the factors governing radical reactivity.[26,27] Therefore, to evaluate the quoted monomer reactivity ratios, the copolymer composition as a function of conversion for the different molar fractions in the feed are compared with the theoretically calculated values.

The cumulative copolymer composition as a function of conversion is shown in Figure 4. The solid lines are drawn according to the integrated copolymer composition equation with the monomer reactivity ratios previously calculated. The instantaneous copolymer composition, which is the chain copolymer composition at a determined conversion, is also displayed in this figure to clarify the characteristics of the copolymer system (dotted lines). A reasonable agreement between experimental and calculated copolymer composition is attained. However, although a gradient of the copolymer composition with conversion should be expected because of the monomer reactivity ratios, two patent regions are well defined with a very abrupt transition between them, in particular when the AA copolymer composition is lower than 0.5. One corresponds to systems rich in AA units and the second one to systems rich in 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate units with a comprehensible origination of long chain or blocks of the 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate monomer.

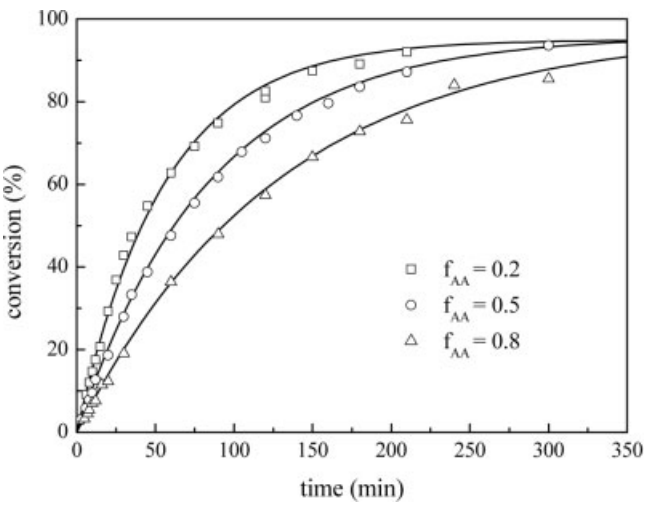


Figure 3 Copolymerization of AA with 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate at three different compositions in the whole range of conversions.

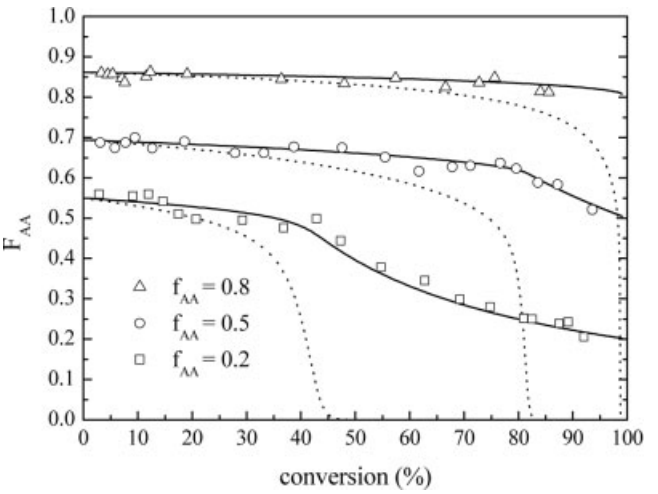


Figure 4 Dependence on the cumulative (solid line) and instantaneous (dotted line) copolymer composition with conversion for the copolymerization of AA with 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate at three different AA molar fractions in the feed. The solid and dotted lines were calculated according to the terminal model with estimated monomer reactivity ratios.

The situation developed when the monomer reactivity ratios differ greatly from one another has been extensively described for different systems such as copolymerization of vinyl acetate[28–33] and vinylpyrrolidone[34–44] with meth(acrylic) monomers.

Herbicide release

The release of bioactive agents from polymer-bioactive agent formulations by a hydrolysis process in the heterogeneous phase is often dependent on a number of factors, including the sample form, the hydrophilic character of the system as well as the pH value of the medium.

The copolymers obtained with high degree of conversion have been immersed in aqueous buffer solutions at pH 7.0, 8.0, and 9.9. The copolymers with AA compositions of 0.5 and 0.8 due to their solubility characteristics have not been evaluated. Therefore, the analysis of herbicide release has been made

in samples with AA copolymer composition of 0.20_5. It is noticeable that this copolymer presents an important heterogeneity in composition. Besides, it has been described that the H homopolymer failed to get hydrolyzed.[1,7] Therefore, the study of herbicide release has been performed in the range of compositions where the sample is mainly formed by statistical copolymer (see Fig. 4). For higher compositions, an expected plateau will be reached since the copolymer residue that is not hydrolyzed will be herbicide-container homopolymer. The analysis has been carried out twice to ensure the obtained results.

Figure 5 depicts typical profiles of the heterogeneous hydrolysis at 35°C in different aqueous buffer solutions. Two general trends are apparent from the inspection of the figure. First, all the kinetic curves show autocatalytic effects. Second, the release of the active agent is reached faster with increasing pH values.

According to the literature, only a few data exist concerning autocatalytic effects and no conclusive explanation has been given.[45,46] Nevertheless, the autocatalytic effects have been tentatively assumed to be related to an increase of hydrophilicity, particularly when the product of the hydrolysis reaction is the bioactive molecule, and a hydrophilic group is created at the backbone that causes the remaining polymer-bioactive agent to swell, thereby facilitating the approach of nucleophilic species to the active sites. This appears to be the cause of the increase in the release rate with time, as shown in Figure 5 for the copolymer with AA copolymer composition of 0.20_5.

In conclusion, the copolymerization of AA with 2-acryloyloxyethyl 2,4-dichlorophenoxyacetate in 1,4-dioxane has been extensively analyzed in terms of monomer reactivity ratios and copolymer composition. Preliminary results of herbicide release have been shown. This former work allows to have the understanding to further design a herbicide-hydrogel with most advantageous characteristics.

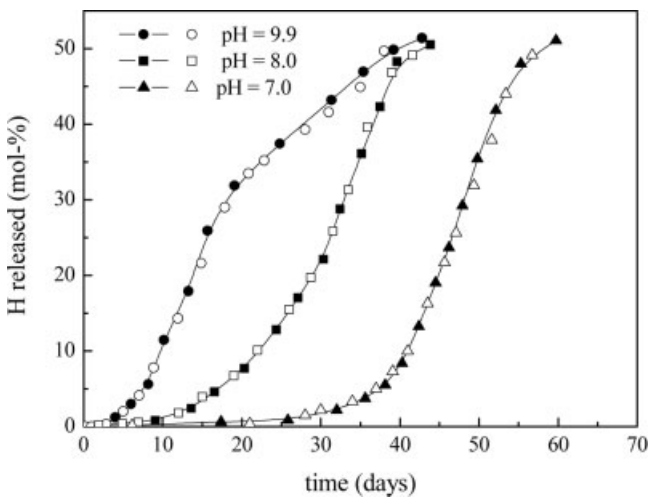


Figure 5 Heterogeneous hydrolysis at 35°C of an acrylic acid-2-acryloyloxyethyl 2,4-dichlorophenoxyacetate copolymer with $F_{AA} = 0.205$ at various pH values (first and second set of measurements are represented by open and close symbols, respectively).

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