RAFT/MADIX Copolymerization of Vinyl Acetate and 5,6-Benzo-2-methylene-1,3-dioxepane

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ABSTRACT: The synthesis of well-defined degradable poly(vinyl acetate) analogues is achieved by RAFT copolymerization of 5,6-benzo-2-methylene-1,3-dioxepane (BMDO) and vinyl acetate (VAc) using methyl (ethoxycarbonothioyl)sulfanyl acetate (MEA) as controlling agent. Several monomer mixtures with low BMDO contents ($<$30 mol %) are employed to prepare different copolymers. In all the cases, the evolution of molar masses and the dispersity values ($<$1.26) confirm the controlled feature of the polymerization. The livingness of the obtained chains is demonstrated by successful chain extension experiments with VAc, although the presence of dead chains is also shown. The introduction of ester groups into the main chain of these P(VAc-*co*-BMDO) copolymers allows their degradation when treated with a mixture of KOH/MeOH in reflux during 2.5 h. © 2013 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2014**, *52*, 104–111

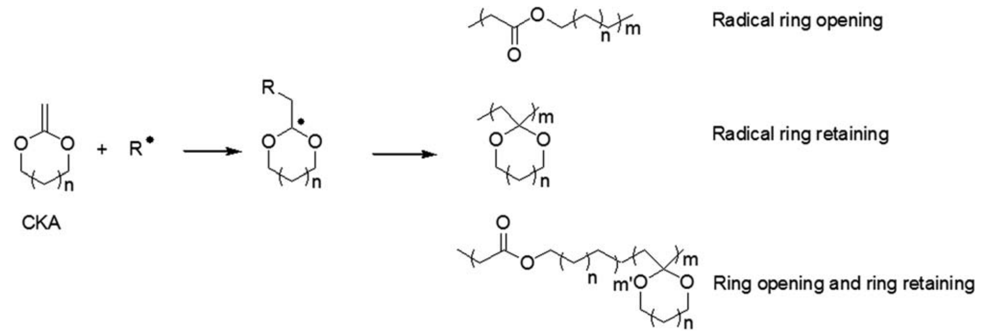
KEYWORDS: copolymerization; cyclic ketene acetal; degradable polymer; reversible addition fragmentation chain transfer; vinyl acetate

INTRODUCTION The free radical polymerization of vinylic monomers leads to the formation of polymers with carbon–carbon link between the monomer units. In 1982, Bailey et al.[1] showed that ester links could also be incorporated into the polymer backbone by free radical ring opening polymerization of specific monomers such as cyclic ketene acetals (CKAs). These monomers can indeed undergo radical addition on their C=C double bond that subsequently leads to propagation either by ring opening or ring retaining or by a combination of both depending especially on their structure (Scheme 1).

When the propagation step occurs only by successive radical ring opening reactions, the produced polymer is a polyester that can thus be obtained under much less demanding conditions than those required by the techniques usually employed to synthesize this type of polymers such as polycondensation, ionic, and coordination ring opening polymerizations.[2] Free radical copolymerization of cyclic ketene acetals with vinylic monomers has thus rapidly been foreseen as a powerful tool to produce degradable polymers by taking advantage of the presence of ester groups along the backbone. A recent article by Agarwal[3] reviews the concepts and the progress in the field of free radical polymerization of cyclic ketene acetals for the synthesis of polyesters based materials. Among the different cyclic ketene acetal monomers, 5,6-benzo-2-methylene-1,3-dioxepane (BMDO, Scheme 2) has been shown to polymerize via free radical polymerization by successive ring opening reactions only. First homopolymerized by Bailey et al.,[1] BMDO has then been copolymerized with methyl methacrylate (MMA),[4,5] styrene (S),[6] *N*-isopropylacrylamide (NIPAM),[7,8] methacrylic acid (MAA),[9] *n*-butyl acrylate (BA),[10] poly(ethylene glycol) methacrylate (PEGMA)[11,12] to produce the corresponding degradable vinylic polymers.

Since the advent of controlled/living free-radical polymerization (CRP) based on reversible deactivation of the propagating radicals,[13] the design of complex macromolecules is much simpler and a myriad of macromolecular architectures has been made accessible under very simple synthetic conditions. Combining the best attributes of CRP with those of free radical ring opening polymerization should thus lead to degradable polymers with controlled and narrowly

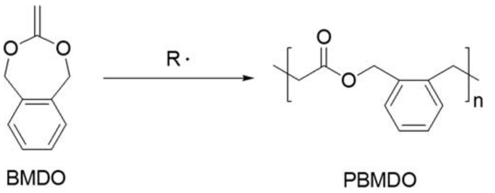
Additional Supporting Information may be found in the online version of this article.



SCHEME 1 Free radical polymerization of cyclic ketene acetals: possible propagation routes.

distributed molar masses, along with potentially original and switchable properties. In this regard, most of the works dedicated to CRP involving BMDO[6–8,10–12,14–16] was essentially focused on atom transfer radical polymerization (ATRP)[4,6,7,10–12,15–17] and performed at rather high temperature (around or above 100 °C), although very recent reports on NMP seem to be promising.[14b,c] For example, block copolymers composed of a PBMDO segment and a polystyrene (PS), poly(methyl methacrylate) (PMMA), or poly(methyl acrylate) segment could be formed.[16] Only two papers report on the reversible addition–fragmentation chain transfer (RAFT)[18] radical polymerization of BMDO either homopolymerized[16] or copolymerized with NIPAM.[8] The RAFT homopolymerization of BMDO was depicted to be successful (molar mass dispersity [*Đ*] values around 1.3) when conducted in THF in sealed vials at 120 °C in the presence of 1-ethoxy(carbonyl)prop-1-yl dithiobenzoate (EPDTB) as a chain transfer agent. Conversions ranged between 16 and 66 % after polymerization times up to 52 h. The use of NIPAM as a comonomer in RAFT copolymerization allowed to circumvent the poor reactivity of BMDO and to perform the polymerization at 60 °C. *S*−1-Dodecyl-*S*′-(α,α′-dimethyl-α″-acetic acid) trithiocarbonate was also used as a chain transfer agent and the polymerization was performed during 10 h to produce well-controlled copolymers (*Đ* < 1.3) incorporating less than 14 mol % of BMDO units.

With a special interest in producing well-defined biodegradable poly(vinyl acetate) (PVAc) or potentially poly(vinyl alcohol), the copolymerization of cyclic ketene acetals with vinyl acetate is of particular interest.[19,20] To the best of our knowledge, there is no example of controlled radical copolymerization of cyclic ketene monomer with VAc. In such context, this article depicts our first investigations into the copolymerization of BMDO with VAc by RAFT.



SCHEME 2 Radical ring-opening polymerization of 5,6-benzo-2-methylene-1,3-dioxepane (BMDO).

EXPERIMENTAL

Materials

Vinyl acetate (VAc, Aldrich, 99 %), was distilled over CaH_2 under vacuum. 2,2′-Azobisisobutyronitrile (AIBN, Merck, 98 %), used as initiator, was purified by recrystallization in ethanol. Toluene was degassed by argon passage and purified with an SPS800 MBraun solvent purification system. 5,6-Benzo-2-methylene-1,3-dioxepane (BMDO) has been synthesized according to a slightly modified procedure originally proposed by Agarwal and coworkers.[6] Dimethyl orthophthalate (Acros, 99 %), $LiAlH_4$ (Aldrich, 95 %), chloroacetaldehyde dimethylacetal (Acros, 97 %), *p*-toluenesulfonic acid (Acros, 99%), potassium *tert*-butylate (*t*-BuOK, Aldrich, 95 %), methyl bromoacetate (Sigma, 97 %), and *O*-ethyl xanthic acid potassium salt (Sigma, 96 %) were used as received.

Analytical Techniques

^{1}H- and ^{13}C-NMR spectra of sections B.3–B.5 were obtained, respectively, on a Bruker Advance DRX 300 MHz spectrometer at 300 MHz (^{1}H) and on a Bruker DRX-600 spectrometer at 150.9 MHz (^{13}C). The chemical shifts were referenced to the solvent peak for $CDCl_3$ (^{1}H-NMR: $\delta = 7.26$ ppm and ^{13}C-NMR: $\delta = 77.16$ ppm).

The individual conversions of VAc and BMDO were evaluated by ^{1}H-NMR spectroscopy analyses performed in toluene-d_8 at room temperature (Bruker DRX 300). 1,3,5-Trioxane was used as an internal reference (isolated resonance at 4.7 ppm in toluene-d_8; Supporting Information). At regular time intervals during the copolymerization reaction, the individual

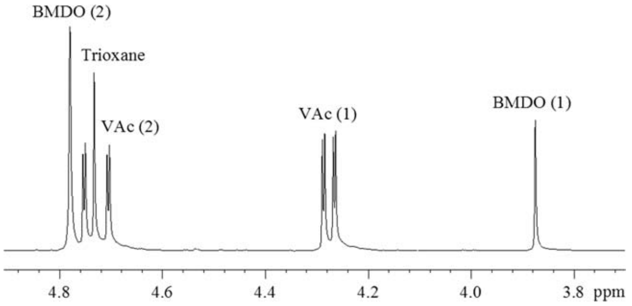


FIGURE 1 ^{1}H-NMR (toluene-d_8, 300 MHz) spectrum of reaction mixture at time zero. Enlargement between 3.7 and 4.9 ppm.

molar conversions of the monomers (x_{VAc} for VAc and x_{BMDO} for BMDO) were determined by relative integration of the vinyl and vinylidene protons of VAc and BMDO, respectively (Fig. 1: peak VAc (1) at 4.25 ppm and peak BMDO (2) at 3.85 ppm) and the protons of 1,3,5-trioxane. The resonance of the trioxane protons overlapping those of VAc, their integral was therefore calculated as the difference between the total integral in the range 4.65–4.75 ppm (trioxane + VAc (2)) and the integral of VAc (1) at 4.25 ppm (Fig. 1).

The individual conversion of the monomers was calculated as follows:

$$x_{\mathrm{VAc}} = \frac{(H_{\mathrm{VAc}(1)}/H_{\mathrm{trioxane}})_{t_0} - (H_{\mathrm{VAc}(1)}/H_{\mathrm{trioxane}})_t}{(H_{\mathrm{VAc}(1)}/H_{\mathrm{trioxane}})_{t_0}} \times 100 \qquad (1)$$

$$x_{\mathrm{BMDO}} = \frac{(H_{\mathrm{BMDO}}/H_{\mathrm{trioxane}})_{t_0} - (H_{\mathrm{BMDO}}/H_{\mathrm{trioxane}})_t}{(H_{\mathrm{BMDO}}/H_{\mathrm{trioxane}})_{t_0}} \times 100 \qquad (2)$$

The total weight conversion $\%\mathrm{wt}_{\mathrm{conv.}}$ of the monomers was calculated as follows:

$$\%\mathrm{wt}_{\mathrm{conv.}} = x_{VAc} \times \%\mathrm{wt}_{\mathrm{VAc}} + x_{\mathrm{BMDO}} \times \%\mathrm{wt}_{\mathrm{BMDO}} \qquad (3)$$

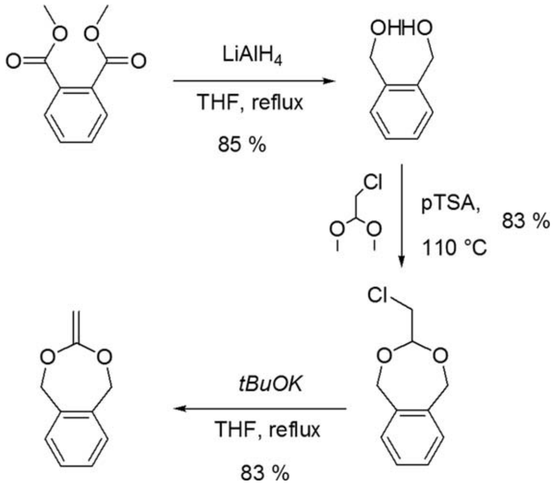
where $\%\mathrm{wt}_{\mathrm{VAc}}$ and $\%\mathrm{wt}_{\mathrm{BMDO}}$ are the initial mass fraction of VAc and BMDO, respectively.

The molar mass of the polymers was determined by size exclusion chromatography (SEC) measurements, using either THF or DMF as eluent (SEC-THF and SEC-DMF, respectively). For SEC-THF, samples were analyzed at 40 °C at a flow rate of 1 mL min^{-1} using toluene as a flow rate marker. The samples were analyzed at a concentration of 5 mg mL^{-1} after filtration through a 0.45 μm pore-size membrane. The separation was carried out on three Polymer Laboratories columns (3× PLgel 5 μm Mixed C [300 × 7.5 mm] and a guard column [PL gel 5 μm]). The setup was equipped with a refractive index (RI) detector (Waters 410 Differential Refractometer). The average molar masses (number-average molar mass (M_n) and weight-average molar mass (M_w)) and the dispersity ($Đ = M_w/M_n$) were derived from the RI signal by a calibration curve based on polystyrene (PS) standards (from Polymer Laboratories).

For SEC-DMF, the analyses were performed using an EcoSEC semi-micro SEC system from Tosoh equipped with a dual flow refractive index detector and a UV detector. The samples were analyzed in DMF (with LiBr at 0.01 mol L^{-1}) at 50 °C using a flow rate of 1 mL min^{-1}. Toluene was used as a flow rate marker. All polymers were injected at a concentration of 2 mg mL^{-1}, after filtration through a 0.45 μm pore-size membrane. Separation was performed with a guard column and two PSS GRAM columns (7 μm, 300 × 7.5 mm). M_n, M_w, and $Đ = M_w/M_n$ were derived from the RI signal by a calibration curve based on PS standards.

Synthesis of BMDO

The overall route is depicted in Scheme 3 and the synthetic steps are detailed below.



SCHEME 3 Synthetic routes for the preparation of BMDO.

Synthesis of 1,2-Benzenedimethanol

In a pre-dried three-neck flask fitted with a cooler and a dropping funnel, 400 mL of dry THF and 20 g (0.53 mol) of LiAlH$_4$ were placed under argon. A solution of 95.2 g (0.49 mol) of dimethyl orthophthalate in 120 mL of dry THF was then added dropwise under stirring. The mixture was then refluxed at 75–80 °C during 5 h. After returning to room temperature, the reaction content was gently put in a 1 L flask filled with 120 mL of water; the gray mixture went deep orange. Then, 30 mL of 30 % HCl solution was added to obtain a clear and limpid solution with a white precipitate. The product was then extracted three times with 400 mL of diethyl ether. The organic phase was washed with water and dried over Na$_2$SO$_4$. Finally, the product was concentrated and recrystallized in pentane, giving 56 g (yield 85 %) of white crystals. ^{1}H-NMR (300 MHz, CDCl$_3$, δ): 7.32 (s, 4H, Ar), 4.68 (s, 4H, —CH_2OH), 3.37 (br. s., 2H, —CH$_2$OH); ^{13}C-NMR (300 MHz, CDCl$_3$, δ): 139.4, 129.7, 128.5 (6C, Ar), 63.8 (2C, —CH$_2$OH).

Synthesis of 5,6-Benzo-2(chloromethyl)−1,3-dioxepane

In a 200 mL large diameter neck round bottom flask, 50 g (0.37 mol) of 1,2-benzenedimethanol, 48 g (0.37 mol) of chloroacetaldehyde dimethylacetal and 80 mg of *p*-toluenesulfonic acid were heated at 110 °C for 3 h until the mixture came dark orange. After cooling at room temperature, the solidified product was dissolved in 400 mL of chloroform to be washed with 100 mL of NaHCO$_3$ solution and 100 mL of water. The crude product was then dried over MgSO$_4$, concentrated and recrystallized in a mixture of pentane with chloroform to give 61.5 g (yield 83 %) of white crystals.^{1}H-NMR (300 MHz, CDCl$_3$, δ): 7.24–7.20 (m, 4H, Ar), 5.10 (t, 1H, (—CH$_2$O)$_2$CH–CH$_2$Cl), 4.94 (s, 4H, C$_6$$H_4$—(CH$_2$O)$_2$—), 3.61 (d, 2H, (–CH$_2$O)$_2CH$–CH$_2$Cl); ^{13}C NMR (75.5 MHz, CDCl$_3$, δ): 138.62, 127.92, 127.66 (6C, Ar), 106.35 (1C, (—CH$_2$O)$_2$CH— CH_2Cl), 72.15 (2C, C$_6$H$_4$–(CH$_2$O)$_2$–), 44.11 (1C (—CH$_2$O)$_2$CH— CH$_2$Cl).

Synthesis of BMDO

A 20 g (0.1 mol) of 5,6-benzo-2(chloromethyl)−1,3-dioxepane, 13 g (0.11 mol) of t-BuOK, and 200 mL of dry THF were refluxed at 90 °C for 4 h under argon to give a light brown turbid mixture. THF was then evaporated and replaced by 400 mL of diethyl ether before filtration. The resulting organic layer was concentrated and distillated under reduce pressure to give 13.2 g (81%) of white needle shaped crystals.

^{1}H-NMR (400 MHz, $CDCl_3$, δ) 3.72 (s, 2H, $(\text{—}CH_2O)_2C\text{=}CH_2$), 5.07 (s, 4H, $C_6H_4CH_2O\text{—}$), 7.08–7.11 (m, 2H, Ar), 7.23–7.26 (m, 2H, Ar). ^{13}C (75.5 MHz, $CDCl_3$, δ) 69.67 (1C, $(\text{—}CH_2O)_2C\text{=}CH_2$), 72.23 (2C, $C_6H_4CH_2O\text{—}$), 126.35, 127.59, 135.99 (6C, Ar), 164.41 (1C, $(\text{—}CH_2O)_2C\text{=}CH_2$)

Synthesis of MEA

For the synthesis of methyl (ethoxycarbonothioyl)sulfanyl acetate (MEA), methyl bromoacetate (7.6 g) dissolved in ethanol (30 mL) was added dropwise to a dispersion of *O*-ethyl xanthic acid potassium salt (9.2 g) in ethanol (40 mL) over an ice bath. The mixture was stirred for 24 h at room temperature. The solvent was evaporated and dichloromethane was added. The resulting white precipitate of KBr was washed twice with water. The organic phase was dried over $MgSO_4$ and concentrated by evaporation under reduced pressure. The obtained yellow product (yield 95 %) was analyzed by NMR spectroscopy in $CDCl_3$. ^{1}H-NMR (300 MHz, $CDCl_3$, δ): 1.41 (t, 3H, $\text{—}OCH_2CH_3$), 3.76 (s, 3H, $CH_3OCO\text{—}$), 3.92 (s, 2H, $\text{—}OCOCH_2S$), 4.64 (q, 2H, $\text{—}OCH_2CH_3$).

Copolymerization of VAc and BMDO

The homopolymerization of VAc and all the copolymerization reactions were performed under argon in Schlenk tubes under RAFT reaction conditions. In a typical copolymerization reaction, 1.86 g (21.6 mmol) of VAc, 0.39 mg (0.22 mmol) of BMDO, 39 mg of MEA, 108 mg (1.2 mmol) of trioxane, 12 mg (0.073 mmol) of AIBN, and 6.0 mL of toluene were placed in a Schlenk tube under argon and stirred for 10 min. The mixture was divided into several tubes and bubbled with argon for 5 min. The flasks were then placed in a preheated oil bath at 80 °C for 24 h. Each tube was taken and placed into the ice at different times during the polymerization in order to evaluate the conversion of the monomers and the molar mass of the formed polymer. The reaction mixture was dissolved in THF and precipitated twice and washed with hexane. The copolymers were dried under vacuum at room temperature until constant weight. Different copolymers were prepared by changing the molar ratio of the two monomers in the feed.

The theoretical number-average molar mass of copolymers based on VAc and BMDO is calculated as follows:

$$M_{\text{ntheo}}=\frac{\left([\text{VAc}]_0\times M_{\text{VAc}}+[\text{BMDO}]_0\times M_{\text{BMDO}}\right)}{[\text{MEA}]_0}\times\frac{\%\ \text{wt}_{\text{conv.}}}{100}+M_{\text{MEA}} \tag{4}$$

where M_{MEA} is the molar mass of the RAFT agent, $[\text{VAc}]_0$, $[\text{BMDO}]_0$, and $[\text{MEA}]_0$ are the initial concentrations of the two monomers and MEA, respectively, and $\%\text{wt}_{\text{conv.}}$ is the weight conversion of monomers (eq (3)).

Chain Extension Test

In order to investigate the living character of the synthesized polymers, a chain extension experiment was performed. A sample of the VB10 copolymer (260 mg, $M_n = 3080$ g mol^{-1}, $Đ = 1.27$) was employed as a RAFT agent (macrocontrolling agent) in the polymerization of vinyl acetate. In particular, 260 mg of VB10 were dissolved in 2 mL of toluene in presence of AIBN ([VB10]/[AIBN] = 3), trioxane and vinyl acetate (3 mol L^{-1}). The polymerization reaction was performed at 80 °C. After 24 h, the reaction was stopped and the monomer conversion was evaluated by ^{1}H-NMR analysis. The reaction mixture was dissolved in THF and precipitated in hexane. The products were dried under vacuum at room temperature and the molar mass of the obtained polymer was determined by SEC-THF.

Hydrolysis of P(VAc-*co*-BMDO)

About 50 mg of copolymer (VB10) were dissolved in a mixture of 5 mL of KOH in methanol (0.1 *M*) in a round-bottomed flask. The resulting mixture was stirred at 60 °C under reflux. After 2.5 h, the solvent was evaporated under vacuum and the remaining solid was dissolved in DMF and analyzed by SEC-DMF and ^{1}H-NMR in DMSO-d_6.

RESULTS AND DISCUSSION

Preliminary Comments

As mentioned in the "Introduction" section, due to its low reactivity, high polymerization temperatures are often required to (co)polymerize BMDO. In addition, performing reactions in bulk is most of the time preferred provided that the mixture of monomers is homogeneous. In our case, due to the insolubility of BMDO into vinyl acetate, it was not possible to perform the reaction in bulk. Several experiments were then first performed in solution using different solvents such as toluene and DMF, in order to identify optimal conditions for future RAFT copolymerizations of BMDO and VAc. In addition, several parameters such as the temperature and the concentration of radical initiator were also adjusted in absence of MEA in order to observe a sufficient consumption of the two monomers before investigating the RAFT copolymerization.

Although not always mentioned in the literature, the use of dried solvent is necessary when working with BMDO which turned to be a quite sensitive monomer. For example, dissolution of BMDO in DMF, used as received, led to a quantitative degradation of BMDO. In Figure 2(a), a complete disappearance of vinylidene protons of BMDO in the ^{1}H-NMR spectrum was observed together with the appearance of resonances consistent with a structure shown in Figure 2(a). This showed the presence of acidic impurities in DMF that can add onto the double bond of BMDO.[9]

The use of dried toluene was indeed shown to be appropriate [Fig. 2(b)] and further copolymerizations were thus conducted in this solvent. In addition, setting the copolymerization temperature at 80 °C, the minimum concentration of AIBN necessary to observe a sufficient monomer conversion

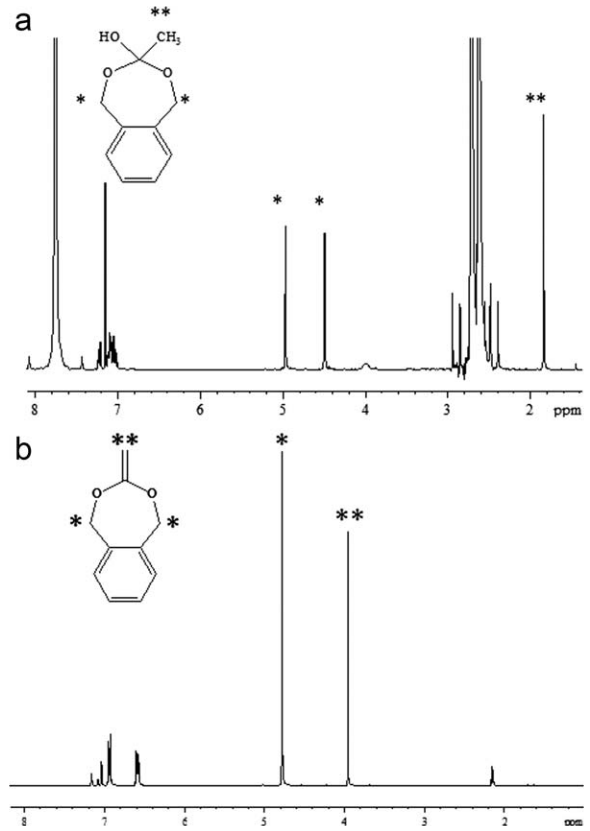


FIGURE 2 Comparison between ^{1}H-NMR spectra of BMDO in (a) DMF and (b) dried toluene.

TABLE 1 Monomer Conversions, Calculated by ^{1}H-NMR Analyses, After 24 h of RAFT Copolymerization of VAc and BMDO in Toluene at 80 °C

Experiment Number	BMDO Initial Molar %	x_{VAc}	x_{BMDO}	%wt$_{\mathrm{conv.}}$[a]
V100	0	53	–	53
VB5	5	45	44	45
VB10	10	41	28	39
VB20	20	27	24	26
VB30	30	21	15	18

[a] Total weight monomer conversion, calculated as described in the "Experimental" section.

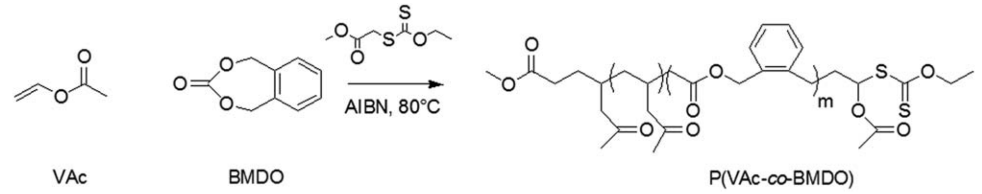
within a reasonable time frame (>50 % in less than 24 h) was around 1 mol % of the total monomer concentration. Temperatures higher than 80 °C did not really improve the final conversion obtained.

RAFT Copolymerization of BMDO and VAc

In order to design a well-defined degradable copolymer based on BMDO, a low fraction of incorporated BMDO units is enough. In this particular case, the control of the polymerization can be dictated by the choice of a controlling agent suitable for the polymerization of the main comonomer. As we targeted degradable PVAc, the copolymerization of VAc and BMDO was performed with a low proportion of BMDO using the RAFT/MADIX (macromolecular design by interchange of xanthate) process, well adapted to the homopolymerization of VAC. The latter is now well documented and a very good control over molar mass and molar mass distribution was obtained; however only when dithiocarbonates (i.e., xanthates) such as MEA were used as controlling agents.[21] Considering the data gained from the preliminary experiments discussed above, the copolymerization reactions were carried out with AIBN as a radical initiator in the presence of MEA as a controlling agent in dried toluene at 80 °C (Scheme 4). First, a pure PVAc was synthesized under these conditions as a blank experiment (V100 in Tables 1 and 2). The relatively high value of dispersity ($Đ = 1.38$) compared to the already published results,[21,22] may be due to the transferring ability of toluene used as a solvent and generally not employed for the polymerization of VAc. Nevertheless, the control of the polymerization of VAc achieved under these conditions allowed to further evaluate the copolymerization with BMDO.

Four different copolymers were prepared by varying the initial molar composition in VAc and BMDO (5, 10, 20, and 30 % of BMDO: see experiments noted VB5, VB10, VB20, and VB30 in Table 1). The monomer conversion and the molar mass characteristics of the obtained (co)polymers are summarized in Tables 1 and 2, respectively.

Whatever the reaction performed, the total molar monomer conversion versus time profiles obtained is similar [Fig. 3(a)]. A plateau was reached after 8 h of reaction after which the conversion did not increase anymore (similar values obtained after 24 h of reactions). As this trend also holds for the homopolymerization of VAc, this may be related to depletion of radicals generated by AIBN at 80 °C ($t_{1/2}$ around 1 h at 80 °C, calculated with $t_{1/2} = \ln 2/k_{\mathrm{d}}$ and k_{d} (80 °C) = 1.69×10^{-4} s^{-1}).[23] An increase of BMDO content in the starting monomer mixture led to a decrease of the



SCHEME 4 P(VAc-*co*-BMDO) synthesis via RAFT/MADIX.

TABLE 2 Experimental Conditions and Molar Mass Characteristics of the Copolymers Obtained by RAFT Copolymerization of BMDO and VAc Performed in Toluene at 80 °C with AIBN as an Initiator.

				Copolymer Composition (molar ratio)	
Experiment Number	$M_{\mathrm{n\ theo}}$ (g mol^{-1})	M_{n}[a] (g mol^{-1})	$Đ$	VAc	BMDO
V100	4290	3370	1.38	100	–
VB5	4650	3020	1.26	95	5
VB10	4220	2590	1.20	90	10
VB20	3140	1900	1.21	82	18
VB30	2380	1300	1.25	76	24

[a] Determined by SEC-THF based on a polystyrene calibration for samples isolated after 24 h of polymerization and after precipitation in *n*-hexane.

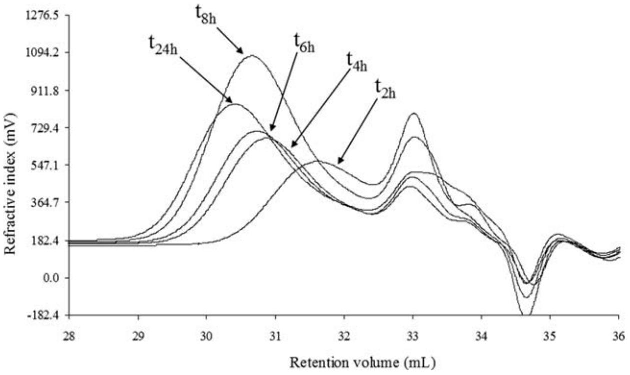


FIGURE 4 SEC-THF chromatograms of samples withdrawn from the reaction medium during the MEA-mediated RAFT copolymerization of VAc and BMDO (VB5: VAc/BMDO 95/5: mol/mol) performed at 80 °C in toluene.

polymerization rate, the plateau value reached being decreased accordingly with the lack of radicals observed after 8 h (down to *ca.* 20 % for VB30).

Samples were withdrawn at different times and analyzed by SEC-THF. Figure 4 shows the evolution of the corresponding chromatograms in the case of VB5. The shift of the chromatograms towards higher molar mass values suggests a controlled nature of the copolymerization. Nevertheless, polymer peaks partially overlapping those related to the residual monomers, particularly when conversion was low, the molar mass and dispersity values were difficult to estimate (Supporting Information Fig. S1). Therefore, for each sample, the polymer was isolated by precipitation in *n*-hexane, filtered, dried, and then analyzed by SEC-THF (Fig. 5).

The molar mass distribution of the precipitated copolymers shows a slight tailing toward the low molar mass values, which could be due to the formation of low molar mass species resulting from chain transfer reactions to toluene during the RAFT polymerization. The molar mass values obtained (Table 2) were difficult to compare to the theoretical ones considering the use of a calibration based on PS standards. Nevertheless, M_{n} increased with conversion and the $Đ$ values remained lower than 1.30 (Fig. 6). This was also confirmed for the other copolymerization reactions (Table 2).

Radical depletion suspected above was confirmed in the case of VB10 for which AIBN was further added once the conversion reached the plateau value of 36 % after 24 h of reaction [Fig. 3(a)]. The copolymerization did resume and the conversion determined after additional 24 h increased to 48 %. In addition, the SEC-THF chromatogram of the copolymer obtained after this AIBN addition was compared to the chromatogram of the starting copolymer (Fig. 7). The shift of the distribution toward higher molar mass values was a good indication (but not an evidence, see below) that a majority of chains were living.

The final copolymers were additionally analyzed by ^{1}H-NMR spectroscopy. An example of such analyses is shown in Figure 8 in the case of VB10. The characteristic resonances of BMDO units (methylene at 2.6 ppm) and VAc units (4.9 ppm,

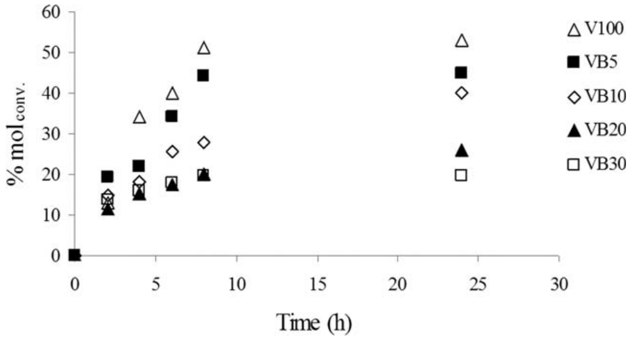


FIGURE 3 Evolution of total molar monomer conversions versus time for the MEA-mediated RAFT copolymerizations of VAc and BMDO performed at 80 °C in toluene using AIBN as an initiator. Molar ratio VAc/BMDO = 95/5 (VB5); 90/10 (VB10); 80/20 (VB20); 70/30 (VB30).

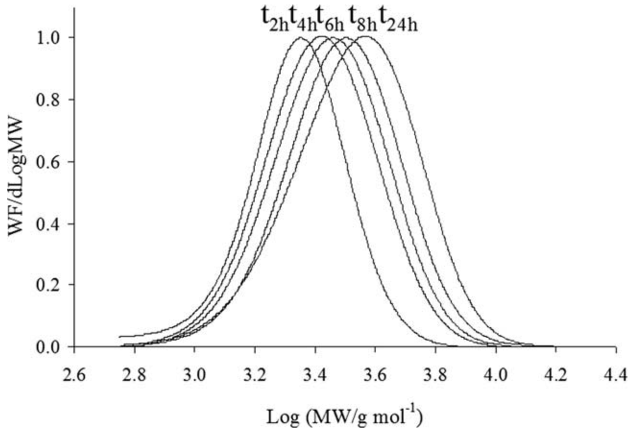


FIGURE 5 SEC-THF chromatograms of the precipitated copolymers for VB5 experiment.

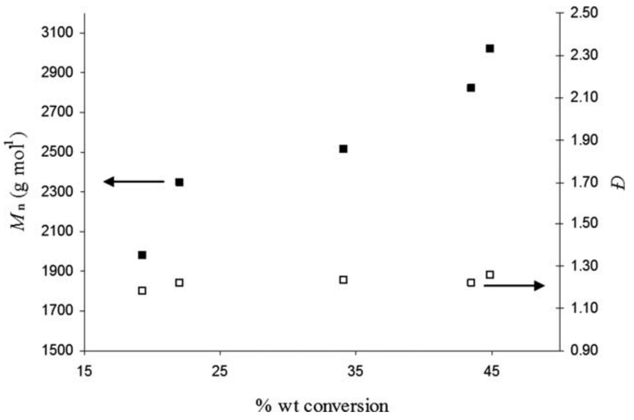


FIGURE 6 Molar mass and Đ evolution versus weight conversion obtained by SEC-THF during the MEA mediated RAFT copolymerization of VAc and BMDO (VB5: 95/5, mol/mol) performed at 80 °C in toluene.

–CH–main chain) were observed. The presence of the resonance at 5.1 ppm can be assigned to the –CH– protons of VAc units connected to BMDO unit in the copolymer and confirms that copolymerization indeed took place. Furthermore, the typical resonances of end groups originating from MEA at 4.1 ppm (f, CH_3CH_2O–), 1.4 ppm (g, CH_3CH_2O–), and 3.6 ppm (a, $CH_3OC(=O)$–) confirm that the control of the copolymerization was induced by MEA.

Further characterization of the copolymer by ^{13}C-NMR showed the absence of resonances between 100 and 120 ppm characteristic of acetal carbons and confirmed that BMDO was only introduced in the main chain by radical ring opening reactions (Supporting Information Fig. S2).

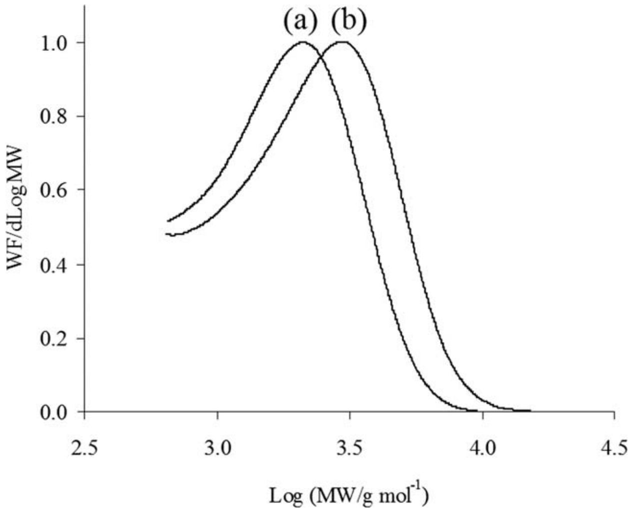


FIGURE 7 SEC-THF chromatograms of the reaction medium (without precipitation step) during the MEA-mediated RAFT copolymerization of VAc and BMDO (VAc/BMDO: 90/10 mol/mol) performed at 80 °C in toluene: (a) after first 24 h of reaction (VB10), (b) after the addition of AIBN to VB10 reaction medium and 24 h of additional polymerization.

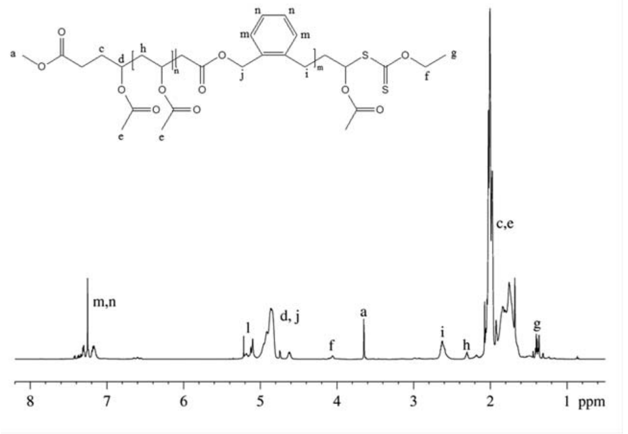


FIGURE 8 ^{1}H-NMR analysis of P(VAc-*co*-BMDO) (VB10) in $CDCl_3$.

Chain Extension Test

The experiment involving a further addition of AIBN in VB10 discussed above seemed to show the livingness of the copolymer chains. However, as the increase in conversion did not represent a sufficient increase in molar mass to unambiguously conclude on the livingness of the polymerization, a proper chain extension experiment was carried out. In that respect, the copolymer VB10 was used as a macroRAFT agent for the homopolymerization of VAc (VB10-ext). The extension reaction was carried out at 80 °C and the employed [VAc]/[VB10] ratio was such that the expected extension should double the molar mass of the starting copolymer ($M_{n\ VB10} = 2590$ g mol^{-1}; $M_{n\ theo\ targeted} = 6000$ g mol^{-1}). After 24 h of reaction, 55% of VAc was converted. The copolymer was recovered by precipitation in *n*-hexane and analyzed by SEC-THF (Fig. 9).

Figure 9 shows that the molar mass distribution has been shifted toward higher molar mass values. However, a

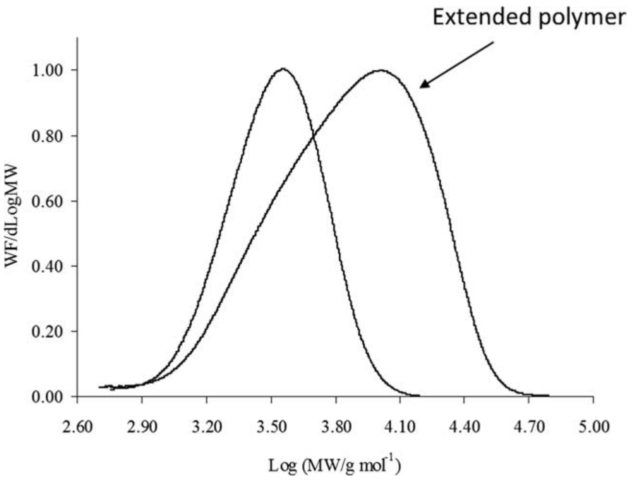


FIGURE 9 SEC-THF chromatograms showing the evolution of molar mass for the chain extension experiment using P(VAc-*co*-BMDO) (VB10) as a macroRAFT agent for the polymerization of VAc (VB10-ext).

shoulder was clearly visible on the low molar mass side corresponding to the presence of a certain proportion of dead chains in the starting VB10. Chain extension of P(VAc-*co*-BMDO) was nevertheless possible.

Hydrolysis of P(VAc-*co*-BMDO) Copolymer

A preliminary study on the hydrolytic degradation of P(VAc-*co*-BMDO) (VB10) copolymer was performed under alkali conditions at 60 °C during 2.5 h. Under these conditions, both the VAc units and the ester links between BMDO and VAc units should be hydrolyzed. This should result in the formation of species including short segments of poly(vinyl alcohol).

After hydrolysis reaction, the solubility properties of VB10 changed completely, the hydrolysis product being not soluble in THF, unlike the starting copolymer. As the residue was, however, soluble in DMF, SEC-DMF analysis was possible. The complete disappearance of the main molar mass distribution originally observed for VB10 showed that the copolymer was hydrolytically degraded as expected. The ^{1}H-NMR analysis of the final residue was additionally performed in DMSO-d_6 (Supporting Information Fig. S3). It clearly confirmed the degradation of the backbone by the modification of the overall spectrum compared to the spectrum of VB10, notably the absence of the main chain methylene proton resonances. The spectrum still showed the presence of compounds containing aromatic protons and the observed broadness of the resonances is also consistent with structures incorporating acid or alcohol moieties [poly(vinyl alcohol) segments].

CONCLUSIONS

With the view of targeting degradable poly(vinyl acetate) based macromolecules, the RAFT copolymerization of BMDO and VAc was successfully carried out using MEA as a controlling agent. The copolymerization reactions were performed in toluene at 80 °C in the presence of AIBN as an initiator. Monomer mixtures with low BMDO contents (lower than 30 mol %) were used. In all the cases, well-defined P(VAc-*co*-BMDO) exhibiting molar masses from 1300 to 3000 g mol^{-1} were obtained with molar mass dispersities lower than 1.26. The livingness of the obtained chains was shown by successful chain extension experiments with VAc, although the presence of dead chains was also evidenced. The final P(VAc-*co*-BMDO) was shown to degrade when treated by a mixture of KOH/MeOH in reflux during 2.5 h, confirming that ester groups were successfully introduced in the main chain. This is the first study on RAFT copolymerization of VAc and BMDO additionally demonstrated that the manipulation of BMDO and the design of macromolecular architectures obtained by radical ring opening copolymerization of BMDO is not trivial and requires fine tuning of the reaction conditions, particularly to reach higher molar masses.

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