Alkylation and Coupling of Living Poly(methyl methacrylate) Ylides at Ambient Conditions

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ABSTRACT: The reaction was studied of living 1-naphthyltriphenylphosphonium poly(methyl methacrylate) ylides (NTPP,PMMA) with methyl iodide and benzyl bromide in tetrahydrofuran at ambient temperatures. NMR characterization shows clean end-functionalizations. The coupling with equimolar bis-1,4-(bromomethyl)benzene was also carried out and was found to be quantitative. The reactions appear to proceed through a rapid and reversible ionization into a highly reactive NTPP,PMMA enolate. The kinetics of methylation and benzylation in the presence of a large excess of electrophile is given by a pseudo-first-order process. The kinetics of these reactions is compared with that of protonation by water and anhydrous acetic acid. The reaction of the latter system is extremely rapid compared to that with water and the alkylating reagents. This indicates that the rate-determining step in the electrophilic reactions is determined by both the ionization and the ion pair collapse to the ylide.

Introduction

The living anionic-type polymerization of methacrylates at ambient temperatures by group transfer polymerization is well documented.[1−7] Recently, we have reported the living polymerization of methacrylates at or above room temperature mediated by phosphor ylides formed by reaction of the PMMA anion and the tetraphenylphosphonium (TPP)[8,9] or 1-naphthyltriphenylphosphonium (NTPP) counterion.[10,11] These studies have indicated that the polymerizations proceed through very small fractions of a much more reactive ionic species, presumably the NTPP,PMMA enolate.

On the other hand, alkylation of living anionic poly(methyl methacrylate) (PMMA) chain ends for instance with alkyl halides is potentially useful in giving end-functionalized intermediates for the synthesis of block, star, and macrocyclic polymers as well as dendrimeric products.[12−16] In order to suppress the Claisen reactions of living PMMA anions and reach acceptable yields, such reactions are typically carried out at low temperatures (−80 to −60 °C) and for extended periods.[14] In the presence of σ- or/and μ-ligands (lithium halides for instance) the alkylation temperatures can be raised to −20 °C. To the best of our knowledge, no alkylation of living PMMA anion at ambient temperatures has been reported.

Here we report the successful alkylation and coupling of living poly(methyl methacrylate) (PMMA) at ambient temperatures. We also report the reaction rates of these reactions as well as the rates of protonation.

Experimental Section

Materials. Tetrahydrofuran (THF) (HPLC grade, >99.99%) was stirred over potassium/sodium alloy until a sky-blue color was observed and distilled in vacuo before use. Methyl methacrylate (MMA) was stirred over CaH_2 for 24 h, distilled in vacuo, and then distilled over triethylaluminum. Benzyl bromide (Alfa Aesar, 99%) and methyl iodide (Aldrich, 99%) were stirred over CaH_2, frozen-degassed under vacuo, and filtered. Bis-1,4-(bromomethyl)-benzene (DBX) (TCI) was recrystallized twice from chloroform and sublimed under high vacuum. 1-Naphthyltriphenylphosphonium bromide (NTPP,Br) and triphenylmethylpotassium (TPMK) were prepared as reported.[10,17]

Polymerizations. These were carried out in THF in vacuo using all glass equipment and break-seals.[10,18,19] In a typical procedure (Table 1, no. 1), NTPP,Br (0.142 g, 0.302 mmol) and TPMK (7.10 mL, 0.0261 mol/L in THF) were mixed in THF and stirred for 1 h at −30 °C before addition of an MMA/THF solution (2.00 mL, 1.29 mol/L) at 25 °C. After polymerization benzyl bromide (1.00 mL, 8.36 mmol) was added via the attached break-seals. The molecular weights of the PMMA solutions obtained in this way were analyzed directly by SEC. The PMMA's were precipitated in hexane for the analysis by NMR.

Characterization. NMR spectra were recorded in $CDCl_3$ on a Varian Mercury-400 (^{1}H: 400 MHz) or a Bruker AMX-500 (^{1}H: 500 MHz; ^{2}H: 77 MHz) instrument. $CHCl_3$ was used as the solvent for the ^{2}H NMR measurements. Size exclusion chromatography (SEC) analyses were carried out at 25 °C on a Waters 510 instrument using three "Polymer Laboratories" (10 μm 10^4 Å (10K−600K), 5 μm 10^3 Å (0.5K−60K), and 5 μm 50 Å (up to 2K) columns and equipped with UV and RI detectors in THF at a flow rate of 1.0 mL/min using PMMA standards for calibration. Molecular weights were also determined by proton NMR. UV−vis spectra were recorded on an HP 8453 UV−vis spectrophotometer.

Reaction Kinetics. Runs were carried out at 25 °C by rapid mixing (<1 s) of the NTPP,PMMA ylide and excess electrophile (alkyl halides and proton donors). The decrease of the band at 360 nm was monitored by UV−vis spectroscopy using a quartz cell with an optical length of path of 0.0482 mm. The concentration of NTPP,PMMA ylide is given by the intensity at 360 nm ($\epsilon = 8240$ L mol^{-1} cm^{-1}) after a correction due to a small residual absorption at 360 nm after completion of the reaction.

Results and Discussion

Here we show that alkylations on these NTPP,PMMA ylides with methyl iodide and benzyl bromide may be carried out at ambient temperatures (25 °C) and in excellent yields. We also demonstrate the successful coupling of a PMMA ylide using bis-1,4-(bromomethyl)benzene (DBX) under these conditions. The progress of the alkylation/protonation is conveniently observed as the tomato red color of NTPP,PMMA ylide turns colorless or slightly yellow.

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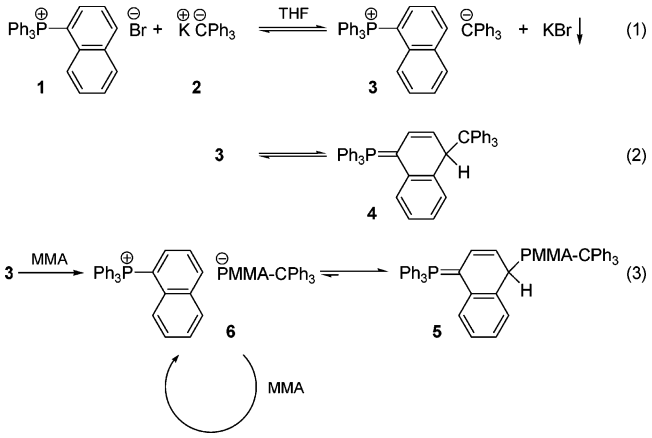
Table 1. End-Capping Reaction of 1-Naphthyltriphenylphosphonium Poly(methyl methacrylate) Ylide[a]

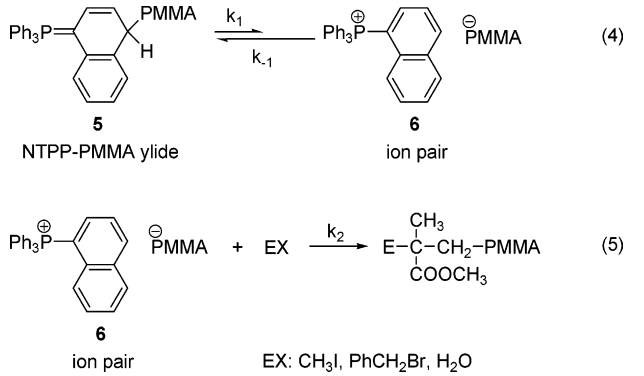
run	end-capper EX	[EX]/[ylide][b]	[ylide] (10^{-3} mol/L)	$M_{n,calc}$[c] (10^3)	$M_{n,NMR}$[d] (10^3)	$M_{n,SEC}$ (10^3)	M_w/M_n	degree of end-capping (%)
1	$PhCH_2Br$	45:1	20.3	1.64	1.93	2.10	1.18	>98
2	MeI	87:1	1.99	2.14	1.85	1.85	1.13	
3	H_2O	1150:1	24.1	3.64	3.34	*e*	*e*	
4	DBX	1:2	18.3	*f*	3.39	3.30	1.22	>98
5	H_2O	140:1	15.7	1.90	2.19	2.25	1.17	
6	DBX	1:2	15.7	*g*	4.20	4.14	1.22	>98

[a] Polymerization conditions: 18 h at 25 °C in tetrahydrofuran, [MMA] is ca. 0.5 mol/L, 1 h for the metathesis reaction of triphenylmethylpotassium and 1-naphthyltriphenylphosphonium bromide at −30 °C. All polymerization gave the yields higher than 95%. The end-capping reaction was carried out at 25 °C by breaking the break-seal of end-capper at the end of polymerization until the red color of ylide/ion pair had completely disappeared. [b] Ratio of the concentrations between end-capper and PMMA ylide. [c] $M_{n,calc}$ = [MMA]/[K,TPM] × yield(%) × $M_{w,MMA}$ + $M_{w,TPM}$. [d] Determined by ^{1}H NMR integration of Ph_3C against the $COOCH_3$ groups. [e] Not detected. [f] The same PMMA precursor as run 2 but without dilution. [g] The same PMMA precursor as run 5.

Scheme 1. Metal-Free Polymerization of Methyl Methacrylate (MMA) Using 1-Naphthyltriphenylphosphonium Triphenylmethanide Initiator



Scheme 2. End-Capping Reaction of 1-Naphthyltriphenylphosphonium Poly(methyl Methacrylate) Ylide/ion Pair with Methyl Iodide, Benzyl Bromide, and Water



The NTPP ylide of low molecular weight (MW) PMMA (**5**) or methylisobutyrate has been reported as a metal-free initiator for the living polymerization of MMA in THF at 25 °C or higher (70 °C), giving narrow MW distribution PMMA with quantitative initiator efficiencies.[10,11] The polymerization is believed to involve a rapid equilibrium between the unreactive ylide and the corresponding highly reactive NTPP,PMMA enolate ion pair formed by dissociation of the ylide (Scheme 1).[9−11]

Because of the very small fractions of active chain ends and the occurrence of the intramolecular side reactions of the NTPP, PMMA enolates, we reasoned that the concentrations of the alkyl halides should be much higher compared to that of the PMMA ylides as the alkylation competes more effectively with the Claisen reaction (Scheme 2). Hence, the alkylating reagents (EX) were used at EX/ylide molar ratios of between roughly 50 and 90. This large excess of alkylating reagent should also ensure pseudo-first-order kinetics. Equivalent amounts of EX also gave quantitative alkylations though obviously the reaction rates were slower (see below).

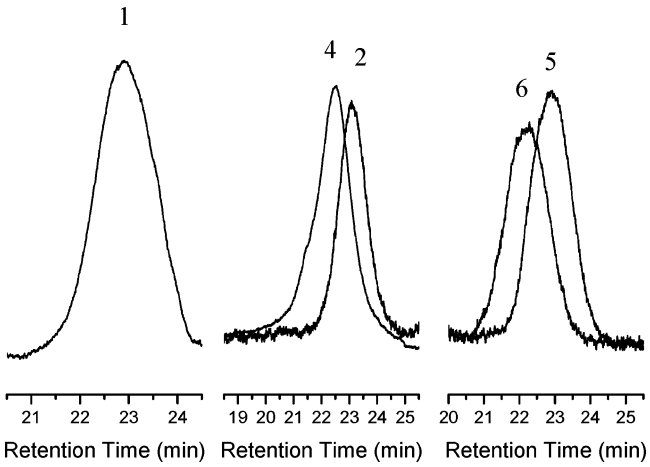


Figure 1. SEC curves of the alkylated poly(methyl methacrylate)s of runs 1, 2, 4, 5, and 6 in Table 1.

The rate constant of protonation of the NTPP,PMMA ylide in THF with proton donors such as water and acetic acid were also measured under comparable conditions. The reaction with equimolar water in THF is very slow (hours) thus requiring experimentally convenient high water/ylide ratios (>1000; see below). Table 1 indicates the results of the alkylation reactions of NTPP,PMMA with benzyl bromide and methyl iodide. The SEC curve of the benzyl bromide end-capped PMMA is shown in Figure 1. The proton NMR spectrum of the benzylated PMMA shows the methylene proton of $PhCH_2$−PMMA at 3.04 ppm. The number-average molecular weights ($M_{n,NMR}$) calculated are in good to excellent agreement with the SEC values. The degree of end-capping by proton NMR calculated from the ratios of the triphenylmethyl and benzyl resonances groups was greater than 98% (Table 1).

Unfortunately, the hydrogen atom of the PMMA terminated with water could not be distinguished by proton NMR because of the large PMMA methylene resonance at 1.80−2.00 ppm. Hence, D_2O was used to terminate the PMMA ylide/ion pair giving a deuterium signal at 2.45 ppm in ^{2}H NMR spectrum, as shown in Figure 2. The resonance at 7.2 is due to the $CDCl_3$ in $CHCl_3$ and is used as internal standard. The resonance at around 7.8 is due to partial deuteration of the 1-naphthyl group of the NTPP,Br deprotonated during initiation.[10] This signal is smaller than it appears. The degree of methylation could not be ascertained as the methyl end group is obscured by the large methyl resonance from the PMMA chain.

Coupling of the living PMMA precursor (Table 1, no. 4 and 6) was carried out using bis-1,4-(bromomethyl)benzene (DBX) at ambient temperatures (Table 1). Runs 2/4 and 5/6 use the

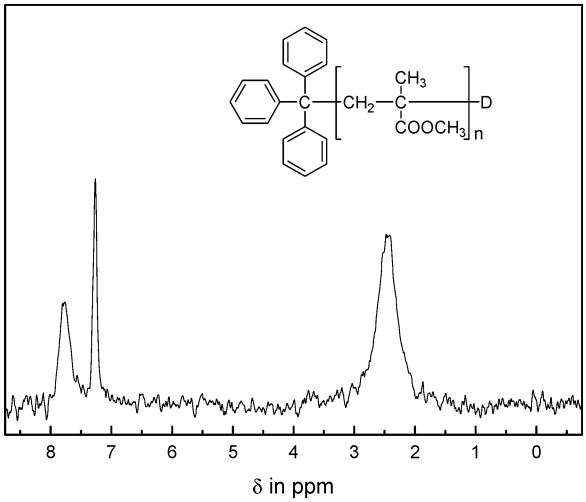


Figure 2. Deuterium NMR of PMMA terminated by D_2O. Precursor is that used in Table 1, no. 1.

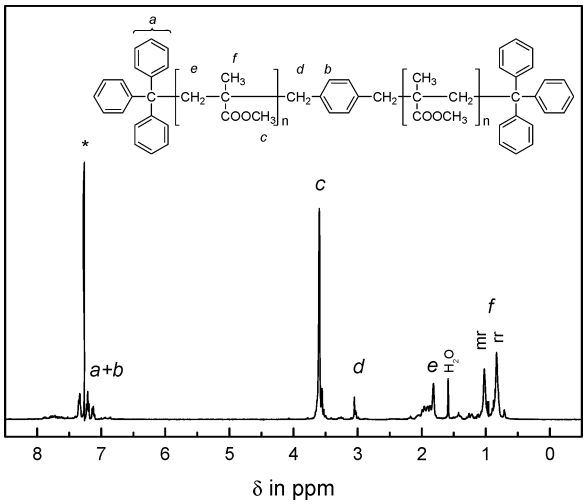


Figure 3. Proton NMR of PMMA coupled by DBX (Table 1, no. 4).

same precursors, and the SEC curves are shown in Figure 1. The molecular weights were nearly exactly doubled, indicating efficient coupling. Figure 3 shows the proton NMR of the coupled PMMA product. The degree of coupling was determined from the (a + b)/(d) ratio and was in very good agreement with the SEC and calculated M_n values (Table 1).

Kinetics. The alkylation rates were monitored by UV−vis analysis as described in the Experimental Section. The NTPP,PMMA ylide has a UV absorption band at 330−460 nm with a broad peak at 360 nm, consistent with the absorption band of 350−450 nm for the NTPP,TPM ylide.[10] Figures 4 and 5 illustrate the relatively rapid disappearance of the NTPP,PMMA ylide after the addition of a large molar excess of benzyl bromide (45-fold) or methyl iodide (87-fold) with the half-life of the NTPP,TPM ylide being less than 1 min.

Because of the large excess of electrophiles, the bimolecular end-capping reaction can be simplified by pseudo-first-order

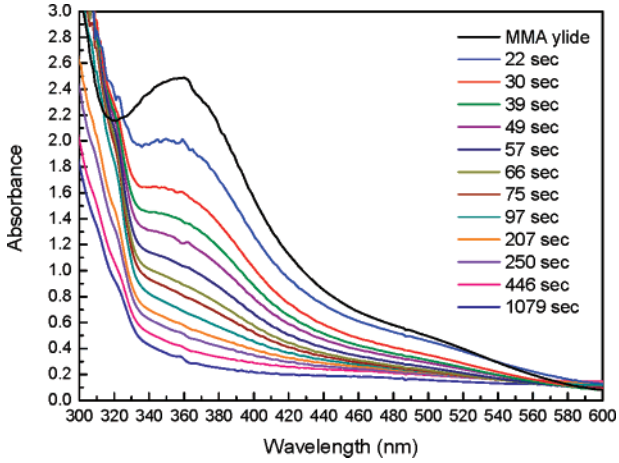


Figure 4. Changes in the UV−vis spectra of PMMA ylide upon addition of benzyl bromide.

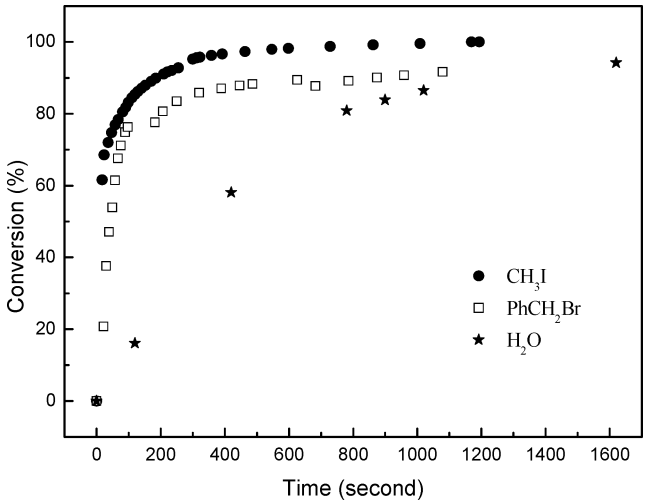


Figure 5. Time-dependent plot of conversions of PMMA ylides by methyl iodide, benzyl bromide, and water.

kinetics shown in eq 6 obtained assuming steady-state conditions with regard to ionic species (**6** in Scheme 2).[10] The apparent rate constant of pseudo-first-order kinetics, k^*_{app} and the corresponding bimolecular rate constant k_{app} are defined in eqs 6−8, where C_0 and C_t are the concentrations of PMMA ylide, **5**, at the start of the reaction and at time t, respectively.

$$\text{reaction rate} = -\frac{\mathrm{d}[\mathbf{5}]}{\mathrm{d}t} = k^*_{app}[\mathbf{5}] \qquad (6)$$

where

$$k^*_{app} = \frac{k_1 k_2[\mathrm{EX}]}{k_{-1} + k_2[\mathrm{EX}]} = k_{app}[\mathrm{EX}] \qquad (7)$$

Table 2. Rate Constants of End-Capping Reactions of 1-Naphthyltriphenylphosphonium Poly(methyl methacrylate) Ylide[a]

run	end-capper EX	[EX]/[ylide]	[ylide] (10^{-3} mol/L)	half-life of ylide	k^*_{app}[b] (s^{-1})	k_{app}[c] (L mol^{-1} s^{-1})
1	MeI	87:1	1.99	14 s	0.052	0.30
2	$PhCH_2Br$	45:1	20.3	44 s	0.016	0.017
3	H_2O	1150:1	24.1	6 min	0.0020	7.3×10^{-5}
4	CH_3COOH	30:1	10.8	≪1 s	≫0.7[d]	≫2[d]

[a] The polymerization conditions are the same as Table 1. [b] k^*_{app} was calculated according to the pseudo first-order reaction in Figure 6. [c] $k_{app} = k^*_{app}/[\mathrm{EX}]$. [d] Estimated assuming first-order kinetics.

$$\ln\left(\frac{C_0}{C_t}\right) = k^*_{app}t \quad (8)$$

The conversion and pseudo-first-order plots of the end-capping reactions by benzyl bromide, methyl iodide, and water are shown in Figures 5 and 6, and the corresponding bimolecular rate constants are summarized in Table 2. The linearity of the first-order plots for the benzylation and protonation is clear, as predicted. That of the methylation is nearly too fast to follow accurately by the techniques we use. However, the data allow an approximate value which is greater (about 17-fold) than that of benzyl bromide, presumably due to its lower steric hindrance and the better leaving group ability of iodide anion. The protonation by water is *much* (1000-fold) slower than that by benzyl bromide and methyl iodide. This correlates with the remarkably low acidity of water in DMSO ($pK_a = 31.4$) and presumably other aprotic media.[20] On the other hand, the rates of protonation with acetic acid (AcOH/methanol 1/3 v/v) are too fast (several orders of magnitude larger than the alkylation rates) to measure accurately.

For the case where $k_2[EX] \gg k_{-1}$, k^*_{app} is given by k_1 so that the reaction rate is independent of the nature or concentration of EX. Evidently this is not the case, indicating that the dissociation of the ylide formation into the ionic species is not the sole rate-determining step. Clearly the rate of collapse to the ylide remains comparable or even rapid compared to the rates of alkylation.

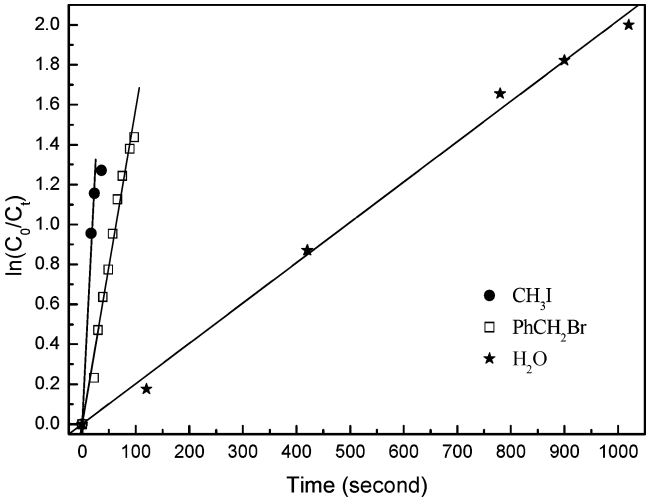


Figure 6. Pseudo-first-order plot of the methylation, benzylation, and protonation of PMMA ylides. The correlation coefficients are larger than 0.99.

In conclusion, the alkylation of NTPP PMMA enolates may be carried out cleanly at ambient temperatures and perhaps at higher temperatures as well as was demonstrated for the polymerizations.[11] These reactions appear to proceed through highly reactive phosphonium enolates. This reaction might find applications in other enolate reactions and this is being investigated.

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