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Synthesis of Reactive Poly(vinyl oxazolones) via Nitroxide-Mediated "Living" Free Radical Polymerization

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ABSTRACT: Low-polydispersity poly(vinyl oxazolone) has been prepared using nitroxide-mediated living free radical polymerization. Bulk homopolymerization of 2-vinyl-4,4-dimethyl-5-oxazolone (VDMO) in the presence of the α-hydrido alkoxyamine initiator **2** and the corresponding nitroxide **1** proceeds to high conversion with polydispersities of less than 1.10. Accurate molecular weight control and low polydispersities (∼1.04−1.10) were obtained on statistical copolymerization with styrene. Well-defined reactive statistical copolymers with polydispersities ranging from 1.05 to 1.30 were also prepared by copolymerization of oxazolone-functional monomers with acrylates, acrylamides, and *N*-vinylamides. Reactive block copolymers were prepared by polymerization of VDMO from poly(*n*-butyl acrylate) starting blocks as well as by polymerization of styrene from poly(VDMO) starting blocks. New polymers were prepared from VDMO-containing polymers and copolymers by nucleophilic ring-opening of the pendant oxazolone rings with amines.

Introduction

Vinyl-functionalized oxazolones, or azlactones, represent a unique class of bifunctional monomers that have been be used to prepare reactive soluble polymers and insoluble polymer supports.[1] Perhaps the most widely studied monomer in this category is 2-vinyl-4,4-dimethyl-5-oxazolone (VDMO) (Figure 1).[2,3] VDMO, also commonly referred to as vinyl azlactone, has been used extensively as the reactive constituent for a number of acrylamide- and acrylate-based insoluble polymer supports for enzyme immobilization and affinity chromatography.[1,4,5] Poly(VDMO) has also been grafted onto molded macroporous polymer monoliths,[6,7] and these materials have been demonstrated to perform as highly effective amine scavengers for solution-phase organic synthesis.[8,9]

Homopolymers can be prepared by classical free radical polymerization of VDMO and similar vinyl-functionalized oxazolone monomers.[10−14] Poly(oxazolones) react readily with amines at room temperature to produce the corresponding amide functionalized poly(acrylamides) (Scheme 1).[1,14] Alternatively, they can be reacted with alcohols in the presence of base to afford ester-functionalized poly(acrylamides).[1,14] This ring-opening addition reaction is particularly attractive for polymer modification, since it proceeds without any external reagents and no condensation byproducts are produced, thereby greatly simplifying purification.

Polymer modification is a versatile and attractive method of introducing a wide variety of functionalities that does not necessitate the preparation of individual functional monomers and their corresponding statistical copolymers. Often the functionalities one may wish to introduce into the final polymer are not compatible with the polymerization conditions. It is not uncommon for one or more comonomers to be immiscible in the polymerization medium or for the growing polymer chain to become insoluble in its monomer. The preparation of soluble polymer conjugates of biological molecules such as peptides and proteins, for example, may be more conveniently accomplished through the functionalization of a reactive polymer such as a poly(oxazolone), rather than by the copolymerization of peptide or protein functionalized macromonomers.

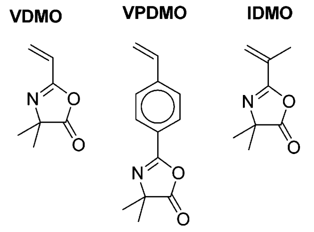
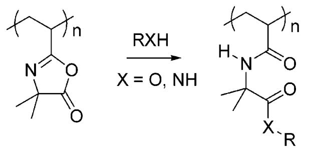


Figure 1. Vinyl-functionalized oxazolone monomers.

Scheme 1. Addition of Nucleophiles to Poly(vinyl oxazolones)



There have been several reports regarding the traditional free radical copolymerization of VDMO using azo-initiators,[1−3] and several experimentally determined reactivity ratios for the copolymerization parameters of VDMO have been reported.[12,14] Upon examination of the published reactivity ratios, the data suggest that the copolymerization behavior of VDMO correlates to many structurally and electronically similar acrylates. In many of these examples, it has been observed that VDMO has a tendency to homopolymerize relative to the comonomer, resulting in depletion of VDMO at low

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conversions. Consequently, the resulting product is a complex mixture of copolymer chains with a compositional variation among the chains and a broad distribution of molecular weights. Attaining a higher degree of control over copolymer microstructure requires the utilization of controlled or "living" radical polymerization methods.[15-17]

Living free radical polymerization (LFRP) is clearly a far more attractive and convenient method for statistical copolymer synthesis, especially for preservation of homogeneity on the microscopic level of individual polymer chains. Since all chains initiate at approximately the same time and propagate at approximately the same rate, all chains experience the same monomer feed. The resulting copolymer is homogeneous with respect both to molecular weight and to monomer composition among individual polymer chains.

In this study we report on a novel polymerization of VDMO with accurate molecular weight contol and low polydispersities (PDI < 1.10) utilizing nitroxide-mediated LFRP. In this study, we have explored the homopolymerization of VDMO as well as statistical and block copolymerization with a variety of comonomers. Additionally, examination of the reactivity of these poly(oxazolones) toward nucleophiles for the preparation of novel functional copolymers is discussed.

Experimental Section

General Materials and Methods. Nitroxide **1**,[18] alkoxyamine **2**,[18] VPDMO,[13] and IDMO[10,11] were synthesized according to published procedures. VDMO (99%) was purchased from TCI-America (Portland, OR) and distilled immediately prior to use. Styrene (99%), 4-acetoxystyrene (96%), methyl acrylate (99%), ethylene glycol methyl ether acrylate (98%), *n*-butyl acrylate (99+%), *tert*-butyl acrylate (98%), methyl methacrylate (99%), methacryloyl chloride (98+%), *N*,*N*-dimethylacrylamide (99%), 1-vinyl-2-pyrrolidinone (99+%), and acrylonitrile (99+%) were purchased from Sigma-Aldrich (Milwaukee, WI) and were all distilled immediately prior to use. 4-Vinylbenzoic acid (97%) and α-aminoisobutyric acid (99%) were purchased from Fluka Chemical Corp. (Milwaukee, WI) and used without further purification. 2-Pentadecyl-4,4-dimethyl-2-oxazolin-5-one (99%) was purchased from Lancaster Synthesis (Windham, NH) and used without further purification. Anhydrous grade solvents were purchased from Sigma-Aldrich (Milwaukee, WI) and used without further purification. A 0.1 M solution of nitroxide **1** in cyclohexane was prepared and used for a more accurate volumetric addition to polymerizations.

Nuclear magnetic resonance spectroscopy was performed on a Bruker Avance DPX-400 in $CDCl_3$. Size exclusion chromatography (SEC) was carried out at ambient temperature with THF as eluent at a flow rate of 1.0 mL/min on a system consisting of a K-501 pump (Knauer), a K-3800 Basic autosampler (Marathon), a set of two PLgel 5 μm mixed-D columns (300 × 7.5 mm, rated for linear separations for polymer molecular weights from 200 to 400 000 Da, Polymer Laboratories), and a PL-ELS 1000 evaporative light scattering detector (Polymer Laboratories). Data were acquired through a PL Datastream unit (Polymer Laboratories) and analyzed with Cirrus GPC software (Polymer Laboratories) based upon a calibration curve built upon polystyrene standards with peak molecular weights ranging from 580 to 400 000 g/mol (EasiCal PS-2, Polymer Laboratories). New calibration curves were constructed for each set of samples run. Thermal analysis was carried out on a Q100 differential scanning calorimeter (TA Instruments) under nitrogen. Samples were analyzed with a heat/cool/heat cycle between 40 and 180 °C at a heating/cooling rate of 10 °C/min. Glass-transition temperatures (half-ΔC_p) were recorded during the second heating cycle. Infrared spectra were collected using a Nicolet Avatar 360FT-IR E.S.P. equipped with Nicolet Smart Dura Sample IR.

General Procedure for Bulk Polymerization of VDMO ($DP_n = 250$). A solution of VDMO (4.00 g, 29.0 mmol), alkoxyamine **2** (36.7 mg, 0.116 mmol), and nitroxide **1** (1.3 mg, 5.8 μmol) was degassed by three freeze/pump/thaw cycles and sealed under nitrogen. The solution was stirred at 123 °C for 4 h. The clear, solid plug was then dissolved in chloroform and precipitated into hexanes (2 L). The fine, white precipitate was filtered, washed with additional hexanes, and dried under vacuum to give the desired poly(VDMO) as a very fine white powder (3.28 g, 81%). $M_n = 31.5$ kDa, PDI = 1.04. $T_g = 91$ °C (reported $T_g = 92$ °C).[2]

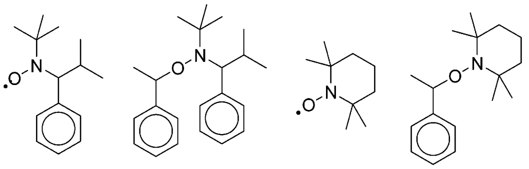
General Procedure for Statistical Copolymerization of VDMO ($DP_n = 250$). A solution of VDMO (1.00 g, 7.25 mmol), the desired comonomer (21.75 mmol), alkoxyamine **2** (36.7 mg, 0.116 mmol,) and nitroxide **1** (1.3 mg, 5.8 μmol) was degassed by three freeze/pump/thaw cycles and sealed under nitrogen. The solution was stirred at 123 °C until the reaction reached approximately 95% conversion (~8 h for styrenes and ~16 h for acrylates). The solid reaction mixture was then dissolved in chloroform and precipitated into hexanes or ether (2 L). The precipitate was filtered, washed with additional hexanes, and dried under vacuum.

General Procedure for Polymerization of VPDMO ($DP_n = 200$). A mixture of VPDMO (2.00 g, 9.30 mmol), acetic anhydride (8.8 μL, 0.093 mmol), and alkoxyamine **2** (11.8 mg, 0.047 mmol) in a vial was purged with nitrogen for 5 min and sealed. The mixture was stirred at 123 °C for 16 h. The solid plug was dissolved in chloroform, precipitated into hexanes, filtered, and dried under vacuum, affording poly(VPDMO) as a fine white powder (1.68 g, 84%) $M_n = 43.6$ kDa, PDI = 1.24.

General Procedure for Statistical Copolymerization of IDMO with Styrene ($DP_n = 250$). A solution of IDMO (1.00 g, 6.53 mmol), styrene (1.59 g, 15.2 mmol), and alkoxyamine 2 (28.3 mg, 0.087 mmol) was degassed by three freeze/pump/thaw cycles and sealed under nitrogen. The mixture was stirred at 123 °C for 8 h. The solid plug was then dissolved in chloroform, precipitated into hexanes, filtered, and dried under vacuum, affording the copolymer as a fine white powder (2.11 g, 81%). $M_n = 46.1$ kDa; PDI = 1.31; $T_g = 128$ °C.

General Procedure for Block Copolymer Formation: Preparation of Poly(VDMO)-*b*-poly(styrene), 6. A solution of VDMO (2.00 g, 14.4 mmol), alkoxyamine **2** (16.1 mg, 0.049 mmol), and nitroxide **1** (2.45 μmol) was degassed by three freeze/pump/thaw cycles and sealed under nitrogen. The stirring solution was heated at 123 °C for 4 h. The clear, solid plug was then dissolved in dichloromethane and precipitated into hexanes (2 L). The fine, white precipitate was filtered, washed with additional hexanes, and dried under vacuum to give the desired poly(VDMO) **5** as a very fine white powder (1.71 g, 85%); $M_n = 25.0$ kDa, PDI = 1.04. The poly(VDMO) starting block **5** (0.80 g, 32 μmol) was dissolved in styrene (2.40 g, 2.3 mmol) and acetic anhydride (15 μL, 0.15 mmol), degassed by three freeze/pump/thaw cycles, and sealed under nitrogen and heated to 123 °C for 8 h. The solid plug was then dissolved in chloroform and precipitated into hexanes, filtered, washed with hexanes, and dried under vacuum to afford poly(VDMO)-*b*-poly(styrene) as a white powder (2.67 g, 83%). $M_n = 90.8$ kDa, PDI = 1.18, composition VDMO/styrene = 30/70.

General Procedure for Block Copolymer Formation: Preparation of Poly(*n*-butyl acrylate)-*b*-poly(VDMO), 12. A mixture of alkoxyamine **2** (50.8 mg, 0.156 mmol), nitroxide **1** (7.8 μmol), and *n*-butyl acrylate (2.00 g, 15.6 mmol) was degassed by three freeze/pump/thaw cycles, sealed under nitrogen, and heated to 123 °C for 16 h. Upon cooling to room temperature, the crude polymer **11** ($M_n = 13.6$ kDa, PDI = 1.06) was dissolved in VDMO (2.00 g, 14.4 mmol), degassed by three freeze/pump/thaw cycles, sealed under nitrogen, and heated to 123 °C for 4 h. The solid plug was then dissolved in dichloromethane and precipitated into hexanes, filtered, washed with hexanes, and dried under vacuum to afford poly(*n*-butyl acrylate)-*b*-poly(VDMO) **(12)** as a tacky white powder (3.16 g, 79%). $M_n = 34.9$ kDa, PDI = 1.11, composition *n*-BA/VDMO = 45/55.



1 **2** **TEMPO** **3**

Figure 2. Alkoxyamine unimolecular initiators.

Table 1. Bulk Homopolymerization of VDMO[a]

initiator	temp (°C)	time (h)	M_n (kDa)[b]	PDI[b]
2 only	123	0.5	9.7	1.22
		1	13.4	1.14
		2	24.3	1.13
		4	27.7	1.15
		8	29.6	1.16
		16	33.2	1.13
1 and **2** (5%)	123	0.5	4.2	1.08
		1	5.3	1.09
		2	10.3	1.09
		3	28.5	1.02
		4	31.5	1.04
		5	34.3	1.04
		8	33.9	1.14
		16	32.5	1.19
1 and **2** (5%)	115	8	35.5	1.07
1 and **2** (5%)	110	8	20.6	1.04
		16	29.9	1.07
		48	32.0	1.05
1 and **2** (5%)	105	8	20.9	1.03
		24	29.8	1.04
		80	33.0	1.09
3 only	123	24	33.2	1.22
3 + **TEMPO** (5%)	123	24	35.8	1.26

[a] VDMO:alkoxyamine:(nitroxide) = 250:1:(0.05). Theoretical molecular weight = 34.5 kDa. [b] Determined by SEC vs PS standards.

General Procedure for Functionalization of Poly(VDMO). Poly(VDMO) **5** (500 mg, 3.68 mmol equiv, 17.0 kDa, PDI = 1.03) was dissolved in dichloromethane (5.0 mL). Benzylamine (0.50 mL, 4.58 mmol) was added, and the reaction mixture was stirred at room temperature for 24 h, precipitated into methanol (400 mL), filtered, and dried under vacuum to afford **13** as a fine white powder (728 mg, 81%, 17.4 kDa, PDI = 1.04). FTIR (cm^{-1}): 1648 (CONH).

General Procedure for Functionalization of Block Copolymer. Poly(VDMO)-*b*-poly(styrene), **6** (500 mg, 44.7 kDa, PDI = 1.17), was dissolved in dichloromethane (5.0 mL). Morpholine (0.50 mL) was added, and the reaction mixture was stirred at room temperature for 24 h, precipitated into methanol (400 mL), filtered, and dried under vacuum to afford **14** as a fine white powder (514 mg, 45.4 kDa, PDI = 1.19). FTIR (cm^{-1}): 1621 (amide C=O).

Results and Discussion

The α-hydrido family of alkoxyamines is a highly versatile class of unimolecular initiators for the controlled polymerization of a wide range of monomers.[17−23] We chose nitroxide **1** and alkoxyamine **2** (Figure 2) to explore the polymerization of vinyl-functionalized oxazolones for both their exceptional versatility and relative ease of synthesis. We initially examined the bulk homopolymerization of VDMO and its dependence on both time and temperature. Using alkoxyamine **2** alone as unimolecular initiator, an appreciable degree of control is preserved throughout the course of the polymerzation to high conversions upward of 90%, with polydispersities around 1.15 (Table 1). Hawker and coworkers have previously shown that the addition of a slight excess of free nitroxide—ca. 5% relative to alkoxyamine—has a significant effect on the polymerization of acrylates, providing a much higher degree of control with polydispersities below 1.10.[18] A similar effect has been observed in this work with VDMO, as polydispersities of 1.02−1.09 were routinely achieved at very high conversions (ca. 90−95%) with the addition of 5% free nitroxide **1** relative to alkoxyamine **2**.

At long reaction times (≥8 h) where conversions approach 100%, a slight high molecular weight shoulder with a molecular weight exactly double that of the primary peak begins to appear in the SEC trace. This presumably is due to termination via chain−chain coupling, which is not surprising given the low glass transition temperature of poly(VDMO) (T_g = 92 °C)[2] relative to the temperature of the bulk polymerization (123 °C). A similar tendency was previously observed for the bulk nitroxide-mediated LFRP of isoprene ($T_g \approx -60$ °C).[19] The undesired chain−chain coupling of poly(VDMO) is easily avoided either by stopping the polymerization of VDMO after approximately 4 h when conversions of approximately 90−95% have been attained[24] or by decreasing the temperature of the bulk polymerization. Several lower temperatures were examined down to 105 °C, and a high degree of control was still preserved with polydispersities below 1.10 in each case (Table 1). Although the time required to reach full conversion was increased considerably, no high molecular weight shoulder was observed in the GPC traces for bulk polymerizations of VDMO conducted at 115 °C or below.

To examine the effect of initiator structure on VDMO polymerization, bulk homopolymerization of VDMO at 123 °C in the presence of the TEMPO-derived unimolecular initiator **3** both with and without excess TEMPO (5% relative to **3**) was also conducted. At high conversions, there is a noticeably lesser degree of control compared to the polymerization with alkoxyamine **2**, with polydispersities typically in the range 1.20−1.30 (Table 1). As the polymerization of VDMO in the presence of **3** approaches full conversion (both with and without excess TEMPO), no high molecular weight shoulder is observed in the SEC trace. However, it is possible that a high molecular weight shoulder may simply be obscured beneath the relatively broad main peak of the polymer.

The living character of nitroxide-mediated polymerization provides the capability for easy tuning of the desired molecular weight by merely varying the monomer-to-initiator ratio. To demonstrate this, a series of polymerizations were carried out at 123 °C with VDMO: initiator ratios ranging from 50:1 to 1000:1. In each case, the polymerization was stopped after 4 h at approximately 90% conversion. As shown in Figure 3, excellent control over molecular weight is obtained to ca. 100 kDa, as illustrated by both a linear relationship between theoretical and experimental molecular weights and polydispersities consistently under 1.10. At higher target molecular weights, polydispersities are slightly increased, ranging from 1.1 to 1.20.

The capability of synthesizing homopolymers of VDMO using nitroxide-mediated LFRP suggested that the preparation of statistical copolymers should be as straightfoward. Bulk copolymerization of VDMO with styrene at 123 °C was initially examined (Table 2). Monomer feed ratios were varied from 10% styrene to 90% styrene, and excellent control was preserved in each case with polydispersities consistently at or below 1.10. Previous studies have shown that additives such

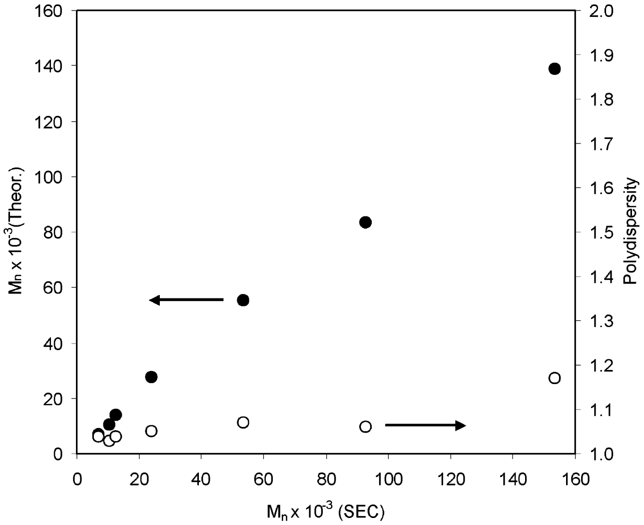


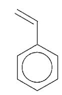
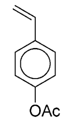
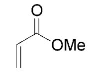
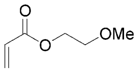
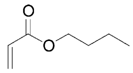
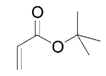
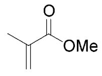
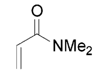
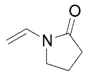
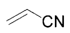
Figure 3. Relationship between theoretical molecular weight and experimental molecular weight (M_n) as a function of polydispersity for the bulk polymerization of VDMO in the presence of **1** and **2** at 123 °C for 4 h.

as acetic anhydride and other acylating agents increase the rate of nitroxide-mediated polymerization of styrenes.[23] We wanted to determine whether the oxazolone ring, itself a reactive acylating agent, had any effect on polymerizations involving oxazolone-containing monomers. To demonstrate this, the bulk homopolymerization of styrene with alkoxyamine **1** was performed alone and in the presence of 2-pentadecyl-4,4-dimethyl-2-oxazolin-5-one (**15**, 2.0 equiv relative to alkoxyamine). Several polymerization times were examined, but there was no observable difference in conversion or molecular weight between the polystyrene prepared in the presence or absence of 2-alkyl oxazolone (Table 3).

Copolymerization of VDMO with several nonstyrenic functional monomers was also examined (Table 2). In most cases, copolymerization of VMDO with nonstyrenic monomers was generally tolerated and afforded statistical copolymers with low polydispersities (PDI < 1.30) throughout a wide range of comonomer feed ratios. Well-defined statistical copolymers of VDMO and methyl methacrylate (MMA) could be prepared with high concentrations of MMA in the feed, with polydispersities below 1.25 even at MMA feed as high as 75%. Furthermore, copolymerization with acrylates and methacrylates did not result in termination via disproportionation or hydroxylamine elimination, as was determined by lack of alkene resonances (5.50−6.50 ppm) in the proton NMR. In general, the preparation of well-defined reactive statistical copolymers with a wide variety of properties is readily feasible using α-hydrido nitroxide-mediated methodology.

We have also investigated the nitroxide-mediated LFRP of other oxazolone-functionalized monomers, such as 2-(4′-vinyl)phenyl-4,4-dimethyl-5-oxazolone[13] (VPDMO) and 2-isopropenyl-4,4-dimethyl-5-oxazolone[2,10,11] (IDMO) (Figure 1). The bulk homopolymerization of VPDMO at 123 °C in the presence of either alkoxyamine **2** or **3** gives similar results (Table 4). Both polymerizations proceed to high conversions (>95%) after 16 h, with a similar degree of control being achieved regardless of initiator used. Namely, polydispersities for poly(VPDMO) consistently ranged from 1.2 to 1.30 regardless of the initiator used, target molecular weight, or additives.

Table 2. Statistical Bulk Copolymerization of VDMO in the Presence of Alkoxyamine 2

	10/90	30.0	1.04	A
	20/80	28.7	1.07	
	30/70	27.3	1.04	
	40/60	31.2	1.09	
	50/50	31.4	1.05	
	60/40	32.5	1.07	
	70/30	32.4	1.08	
	80/20	33.7	1.07	
	90/10	33.9	1.09	
	25/75	38.1	1.04	A
	75/25	36.1	1.05	
	25/75	10.7	1.21	B
	50/50	17.1	1.17	
	75/25	34.6	1.22	
	25/75	12.0	1.11	B
	50/50	15.1	1.12	
	75/25	26.4	1.11	
	25/75	23.1	1.09	B
	50/50	37.1	1.27	
	75/25	31.1	1.28	
	50/50	33.8	1.25	B
	10/90	22.2	1.39	B
	15/85	18.5	1.26	
	25/75	18.1	1.24	
	50/50	24.3	1.13	
	75/25	25.2	1.15	
	25/75	20.6	1.22	B
	50/50	33.2	1.18	
	75/25	27.7	1.22	
	50/50	22.0	1.20	B
	75/25	34.4	1.25	
	25/75	13.0	1.05	B
	50/50	18.8	1.08	
	75/25	25.8	1.09	

[a] Conditions A: alkoxyamine **2**:Ac_2O:total monomer = 1:2:250; 123 °C, 8 h. Conditions B: ratio of nitroxide **1**:alkoxyamine **2**:total monomer = 0.05:1:250, 123 °C, 16 h.

Table 3. Effect of Oxazolone Additive 15 (2 equiv) on Bulk Polymerization of Styrene (250 equiv) in the Presence of Alkoxyamine 1 at 123 °C

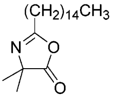
additive	time (h)	conv (%)	M_n (kDa)	PDI
15: 	4	65	16.9	1.04
none	4	68	17.0	1.03
15	6	85	21.9	1.04
none	6	82	20.3	1.03
15	8	98	27.6	1.05
none	8	97	25.5	1.03

Table 4. Bulk Homopolymerization of VPDMO (200 equiv) in the Presence of an Alkoxyamine Initiator and Additive at 123 °C for 16 h

initiator	additive	M_n (kDa)	PDI
2	Ac_2O (2.0 equiv)	32.8	1.30
2	1 (0.05 equiv)	25.3	1.27
3	Ac_2O (2.0 equiv)	35.6	1.29

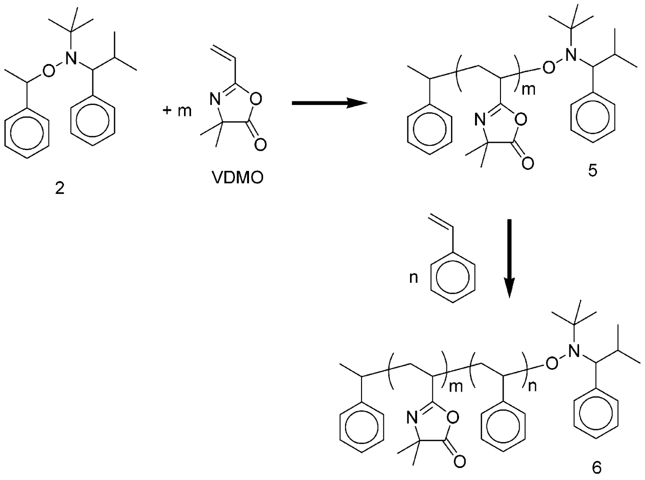
Conversely, no appreciable degree of molecular weight control was obtained for the bulk homopolymerization of IDMO in the presence of alkoxyamine initiator **2**. The

Table 5. Bulk Polymerization of IDMO Alone and with Styrene[a]

% IDMO	% styrene	M_n (kDa)	PDI
100	0	6.1	1.54
100	0	6.6	1.62
70	30	38.0	1.69
50	50	31.5	1.36
30	70	46.1	1.31

[a] Nitroxide **1**:alkoxyamine **2**:total monomer = 0.05:1:250, 123 °C, 8 h.

Scheme 2. Synthesis of Block Copolymer Poly(VDMO)-*b*-poly(styrene)



resulting low molecular weight poly(IDMO) product was polydisperse, with values for M_w/M_n typically well above 1.50 (Table 5). This was not altogether unexpected considering its structural and electronic similarity to methyl methacrylate. An enhanced degree of molecular weight control was achieved when IDMO was copolymerized with 30% styrene in the initial monomer feed (Table 5, entry 3), although the copolymer product possessed a broad molecular weight distribution. At 50% or greater initial concentration of polystyrene, the polydispersities lessen considerably, as the resulting copolymers obtained approached target molecular weights with polydispersities below 1.40. The polymerization behavior of IDMO bears a notable similarity to that of methyl methacrylate. The bulk homopolymerization of either IDMO or MMA in the presence of an alkoxyamine initiator is uncontrolled, leading to low molecular weight homopolymer products with high polydispersities. However, the addition of styrene into a polymerization of either IDMO or MMA leads to reasonable control and results in the formation of statistical copolymers with polydispersities below 1.40.

In addition to having a narrow molecular weight distribution, poly(VDMO) chains prepared using nitroxide-mediated LFRP methodology also bear a latent nitroxide-capped initiation center at the chain end (Scheme 2). This reactive chain end can thus be employed to prepare block copolymers by the introduction of a second monomer. Living free radical methodologies offer a unique advantage over anionic procedures in terms of a more extensive functional group compatibility.[17] To date, oxazolone-containing monomers such as VDMO have not been polymerized successfully using anionic procedures;[1] hence, LFRP provides access to novel well-defined block copolymers containing poly(VDMO) segments.

Table 6. Molecular Weight and Polydispersity for Poly(VDMO)-*block*-poly(styrene) Block Copolymers Prepared Using 1 and 2 under Bulk Conditions at 123 °C

poly(VDMO) starting block (**5**)		poly(VDMO)-*b*-PSt block copolymer (**6**)		
M_n (kDa)	PDI	composition[a] (VDMO/Sty)	M_n (kDa)[b]	PDI[b]
7.1	1.04	20/80	42.6	1.15
10.3	1.03	25/75	34.3	1.16
10.3	1.03	35/65	44.7	1.17
25.0	1.04	50/50	37.3	1.26
25.0	1.04	30/70	90.8	1.18

[a] Determined by ^{1}H NMR spectroscopy and C, H, and N elemental analysis. [b] Polystyrene equivalent molecular weights.

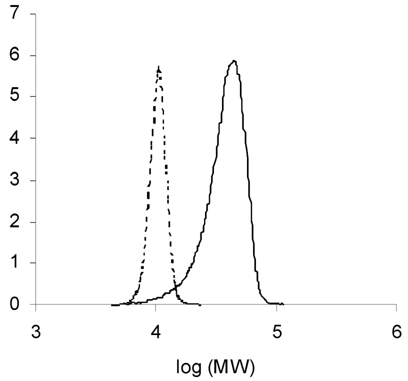
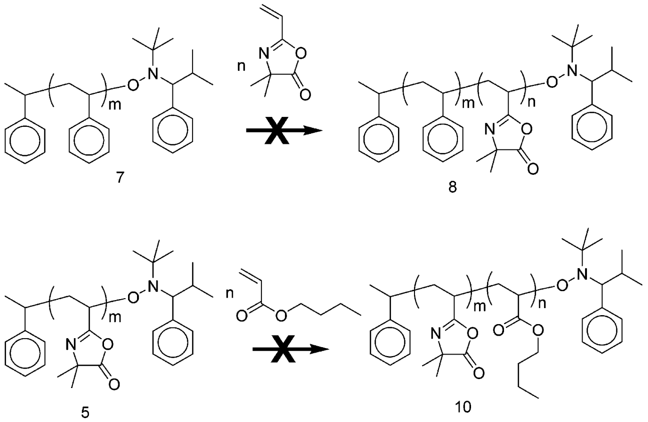


Figure 4. Comparison of molecular weight distributions for (a) poly(VDMO) macroinitiator **5**, M_n = 10.3 kDa, PDI = 1.03 (dashed line), and (b) poly(VDMO)-*block*-poly(styrene) block copolymer **6** (solid line) after chain extension with styrene. M_n = 34.3 kDa, PDI = 1.16, composition VDMO/styrene = 25/75.

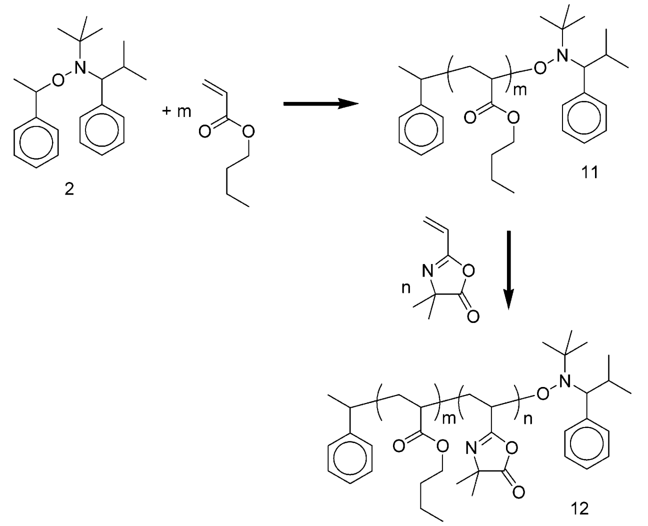
We initially investigated the preparation of VDMO/styrene block copolymers. Poly(VDMO) macroinitiators of several molecular weights were prepared by polymerization of VDMO in the presence of varying ratios of alkoxyamine initiator **2** and 5% nitroxide **1**. In an illustrative example, poly(VDMO) macroinitiator **5** (M_n = 10.3 kDa, PDI = 1.03) was dissolved in styrene (300 equiv), degassed, and heated to 123 °C for 8 h. The resulting block copolymer poly(VDMO)-*b*-poly(styrene) (**6**) was obtained with high conversion for the styrene monomer and possessed the expected increase in molecular weight (M_n = 34.3 kDa, PDI = 1.16) (Table 6). Comparison of SEC traces for macroinitiator **5** and diblock copolymer **6** shows no evidence of contamination of the diblock copolymer with unreacted VDMO macroinitiator (Figure 4). This sequential polymerization strategy works well using VDMO macroinitiators with a range of molecular weights to allow preparation of well-defined block copolymers with molecular weights approaching 100 kDa (Table 6).

We have also made a number of attempts to prepare styrene/VDMO block copolymers by employing the reverse strategy, namely, by growing a VDMO block from a poly(styrene) macroinitiator **7** (Scheme 3). This strategy works well only when a relatively low molecular weight (M_n < 10 kDa) poly(styrene) macroinitiator is used. Most attempts at preparing such block copolymers failed when using poly(styrene) macroinitiators with M_n > 10 kDa (Scheme 3), as evidenced by broad polydispersities and a persistent low molecular weight shoulder in the SEC traces. This is not surprising considering that Hawker and co-workers demonstrated that the polymerization of acrylates from low molecular weight poly(styrene) macroinitiators (M_n = 4.5 kDa) resulted in well-defined block copolymers, but when

Scheme 3



Scheme 4. Synthesis of Block Copolymer Poly(*n*-butyl acrylate)-*b*-poly(VDMO)



higher molecular weight poly(styrene) macroinitiators were used, the resulting block copolymers also possessed a low molecular weight shoulder.[18]

Next, we investigated the preparation of VDMO/acrylate block copolymers—in this case, successful polymerization also depends on the nature of the initiating block. Specifically, in the case of poly(*n*-butyl acrylate)-*b*-poly(VDMO), **12** (Scheme 4), the use of a poly(*n*-butyl acrylate) starting block **11** to initiate the polymerization of a second poly(VDMO) block results in well-defined block copolymers with no detectable quantities of unreacted poly(*n*-butyl acrylate) macroinitiator (Figure 5). In fact, block copolymer formation proceeds smoothly and efficiently regardless of whether the second VDMO block is polymerized in a second step from an isolated poly(*n*-butyl acrylate) macroinitiator or whether the entire synthetic scheme is performed in a single pot (Table 7).

First, an alkoxyamine-functionalized poly(*n*-butyl acrylate) macroinitiator **11** is prepared according to the previously reported procedures.[18] The resulting poly(*n*-butyl acrylate) macroinitiator then can be either isolated by precipitation or simply dissolved in VDMO and heated to give a diblock copolymer poly(*n*-butyl acrylate)-*b*-poly(VDMO) (**12**). Block copolymer **12** is well-defined and possesses the expected increase in molecular weight. Comparison of the molecular weight distributions of the macroinitiator **11** and that of the resulting block copolymer **12** clearly demonstrates that the block copolymer product **12** is free from any unreacted poly(*n*-butyl acrylate) macroinitiator (Figure 5).

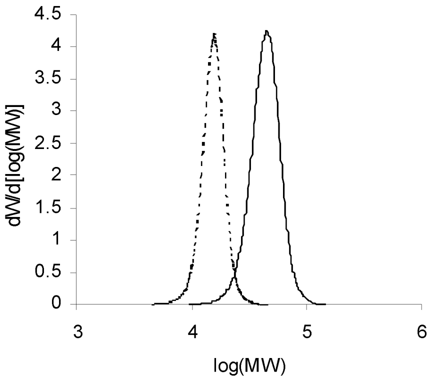


Figure 5. Comparison of molecular weight distributions for (a) poly(*n*-butyl acrylate) macroinitiator **11,** $M_n = 14.8$ kDa, PDI = 1.06 (dashed line), and (b) poly(*n*-butyl acrylate)-*block*-poly(VDMO) block copolymer **12** (solid line) after chain extension with VDMO. $M_n = 41.6$ kDa, PDI = 1.09, composition *n*-BA/VDMO = 55/45.

Table 7. Molecular Weight and Polydispersity for Poly(*n*-BA)-*block*-poly(VDMO) Block Copolymers Prepared Using 1 and 2 under Bulk Conditions at 123 °C

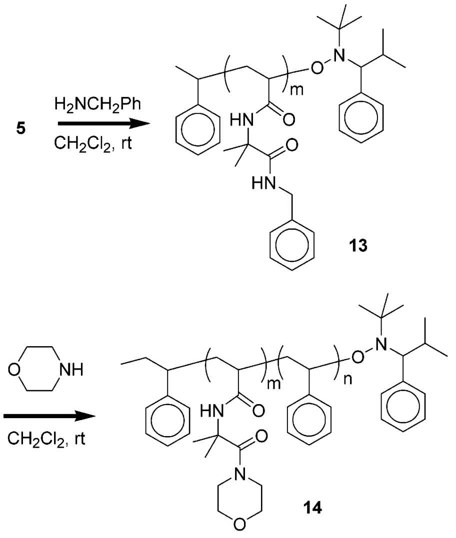
poly(*n*-BA) starting block (**11**)		poly(*n*-BA)-*b*-poly(VDMO) block copolymer (**12**)		
M_n (kDa)	PDI	composition[a] (*n*-BA/VDMO)	M_n (kDa)[b]	PDI[b]
11.9	1.09	50/50	26.6	1.11
13.6	1.06	45/55	34.9	1.11
14.8	1.06	55/45	41.6	1.09
15.1	1.06	50/50	29.7	1.12
17.9	1.11	60/40	39.7	1.19

[a] Determined by ^{1}H NMR spectroscopy and C, H, and N elemental analysis. [b] Polystyrene equivalent molecular weights.

In contrast, block copolymer formation via acrylate polymerization from an alkoxyamine-functionalized VDMO starting block **5** (Scheme 3) was unsuccessful despite attempts at changing several reaction parameters including molecular weight of the VDMO macroinitiator, nature of acrylate monomer, monomer/macroinitiator ratio, and type and amount of solvent (Scheme 3). In each attempt, incomplete initiation and/or early termination was observed and resulted in a multimodal product mixture containing both unreacted poly(VDMO) starting material and a higher molecular weight fraction, which could likely be either block copolymer or homopoly(*n*-butyl acrylate).

In general, several noteworthy observations can be drawn regarding the polymerization behavior of VDMO during the preparation of block copolymers. For example, when considering the preparation of styrene—VDMO block copolymers, the behavior of VDMO can be compared to that of *n*-butyl acrylate and many other acrylate monomers in general.[18] Specifically, the polymerization of styrene from both poly(VDMO) and poly(*n*-butyl acrylate) macroinitiators is well controlled. However, the reverse process usually fails, as polymerization of either VDMO or butyl acrylate from a poly(styrene) macroinitiator is successful only when a low molecular weight poly(styrene) macroinitiator is used. On the other hand, when considering the preparation of VDMO—acrylate block copolymers by nitroxide-mediated LFRP, VDMO behaves in a manner similar to isoprene.[19] For example, the polymerization of VDMO from a poly(*n*-butyl acrylate) macroinitiator proceeds

Scheme 5. Ring-Opening Modification of Poly(oxazolones) with Amines



smoothly, leading to the formation of well-controlled *n*-BA−VDMO block copolymers. However, attempts to grow a poly(*n*-butyl acrylate) block from a poly(VDMO) macroinitiator did not lead to clean block copolymer formation. These results are analogous to those obtained by Hawker and co-workers[19] whereby isoprene block polymerization from a poly(*tert*-butyl acrylate) macroinitiator was shown to proceed efficiently, but the reverse process, namely polymerization of *tert*-butyl acrylate from a poly(isoprene) macroinitiator, was unsuccessful. This suggests that VDMO behaves like an acrylate in polymerizability but that terminal poly(VDMO) alkoxyamines are not efficient initiators for the synthesis of acrylate block copolymers.

To demonstrate susceptibility of these polymers to modification, we examined the reaction of several representative poly(vinyl oxazolones) with amines. Reaction of poly(VDMO) **5** with benzylamine quantitatively affords the benzyl acrylamide adduct **13** in excellent yield (Scheme 5). Conversion was monitored by FT-IR, which showed the disappearance of the characteristic oxazolone band at 1820 cm^{-1} ($C{=}O$) and the appearance of the corresponding acrylamide band at 1648 cm^{-1} (CONH). Likewise, reaction of poly(VDMO)-*block*-poly(styrene) **6** with morpholine (Scheme 5) results in clean conversion to the copolymer product **14**, with the associated emergence of the amide band at 1621 cm^{-1}. Molecular weights and polydispersities of the poly(amide) products did not vary significantly from those of the starting materials. The facile chemical modification of poly(oxazolones) with amines and other weak nucleophiles clearly demonstrates the potential for LFPR methods toward well-defined polymers containing rich chemical functionality.

Conclusion

Nitroxide-mediated living free radical polymerization provides a highly efficient method for the synthesis of well-defined poly(vinyl oxazolones) with narrow polydispersities. The LFRP of poly(vinyl oxazolones) provides access to highly functionalized well-defined polymers via modification with amines and other nucleophiles. Alkoxyamine **2** has demonstrated versatility in mediating the copolymerization of VDMO with a wide range of monomers. Furthermore, the synthesis of oxazolone-functionalized reactive block copolymers can be readily achieved using nitroxide-mediated LFRP methods. In conclusion, this work demonstrates a novel synthetic approach toward a variety of reactive oxazolone-containing polymers and copolymers. Future work will focus on tapping into the versatility of well-defined poly(oxazolones) prepared using LFRP as precursors to polymers with novel chemical functionality as well as investigating applications of well-defined reactive oxazolone-based materials with compositional and architectural variation.

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