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Synthesis and Evaluation of *N*-Phenylalkoxyamines for Nitroxide-Mediated Polymerization

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Introduction. Control over macromolecular structure has become increasingly desirable in polymer science and is now more accessible due to the development of controlled radical polymerization (CRP) techniques. These methods, which include nitroxide-mediated polymerization (NMP),[1] atom transfer radical polymerization[2] (ATRP), and reversible addition−fragmentation chain transfer[3] (RAFT) polymerization, have facilitated the preparation of well-defined materials. CRP methods allow the synthesis of materials with predetermined molecular weights, narrow molecular weight distributions, interesting architectures, and living chain ends for the construction of block copolymers.[1,4]

NMP is an attractive CRP technique because it is simple and straightforward: typically only monomer and an appropriate initiator are needed to effect polymerization. NMP operates on a reversible equilibrium between propagating and dormant states by which nitroxide radicals trap the propagating radical to form the dormant species and is governed by the persistent radical effect which allows growing radicals to predominantly cross-couple with the nitroxide instead of terminating with themselves.[5]

Though NMP holds great promise, it suffers from drawbacks which include difficult initiator syntheses and several classes of unpolymerizable monomers, especially methacrylic esters such as methyl methacrylate (MMA).[1,6] Cross-disproportionation and a large activation−deactivation equilibrium constant, K, are at least two major factors that lead to difficulties with the NMP of MMA.[7] Polymerization of MMA with the widely available nitroxide 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) is uncontrolled due to the cross-disproportionation side reaction which occurs when TEMPO abstracts an H atom from the propagating radical chain to result in an unsaturated chain end and a hydroxylamine.[8−11] While it has been suggested that cross-disproportionation is negligible in MMA polymerizations with newer nitroxides such as 1-(diethoxyphosphinyl)-2,2-dimethylpropyl-1,1-dimethylethylnitroxide (SG1), the large activation−deactivation equilibrium constant still results in an uncontrolled polymerization.[12] Others dismiss cross-disproportionation as a significant termination pathway due to the lack of diagnostic olefinic proton signals in the PMMA ^{1}H NMR spectrum.[13,14] However, the occurrence of cross-disproportionation during MMA polymerization has been demonstrated with an excess of SG1,[9] and Charleux and co-workers have observed the occurrence of both cross-disproportionation and bimolecular combination.[15] Thus, there are at least two possible factors that contribute to the failure of MMA polymerization which in turn makes design of an appropriate initiator difficult.

To address the issue of difficult initiator syntheses, our lab and others have been investigating alkoxyamines that result from the addition of carbon-centered radicals to nitrosoalkanes and nitrosoarenes. A system consisting of CuBr, Cu(0), and PMDETA, similar to those used in ATRP, generates free radicals which add across the double bond of the nitroso compound.[2,4] Previously, we reported the one-step synthesis of an alkoxyamine via the addition of two equivalents of 1-phenylethyl radical to 2-methyl-2-nitrosopropane.[16] This alkoxyamine was able to control the polymerization of styrene, isoprene, and *n*-butyl acrylate with a preheating step.[17] Studer et al. and Zink et al. reported a similar strategy whereby carbon-centered radicals were added across the nitroso group of nitroso-*tert*-octane.[18,19] Here, we report the synthesis of new initiators bearing an *N*-phenyl moiety which result from the addition of 1-phenylethyl or 2-methylpropionic acid phenyl ester radicals[20] to nitrosobenzene. The use of arylnitroxides in NMP has not been investigated in depth and only a few instances have been reported in the literature.[21,22] As has been observed with the previously reported arylnitroxide initiators,[21,22] the alkoxyamines reported here are effective for the controlled bulk homopolymerization of MMA from low to moderate conversions (32−41%).

Results and Discussion. Alkoxyamines **1** and **2** (Scheme 1) were synthesized by a previously reported method.[16] Specifically, carbon-centered radicals derived from (1-bromoethyl) benzene or 2-bromo-2-methylpropionic acid phenyl ester using a CuBr, Cu(0), and PMDETA system were added to the nitroso group of nitrosobenzene to form alkoxyamines **1** and **2** respectively. Initiator **1** was isolated as a viscous, yellow oil in 55% yield after flash chromatography, while **2** was obtained as a white powder in 69% yield after recrystallization.

*Polymerization with Initiator **1**.* Alkoxyamine **1** is structurally similar to the previously reported initiator, 2,2-dimethyl-3-(1-phenylethoxy)-4-phenyl-3-azapentane **3** (Scheme 1), with the main difference being an *N*-phenyl moiety in alkoxyamine **1** versus an *N*-*tert*-butyl moiety in alkoxyamine **3**.[16] We sought to understand the difference this *N*-phenyl group might have on polymerization kinetics since the *N*-*tert*-butyl group is a common feature of most alkoxyamines that are efficient initiators in NMP.

The polymerization of styrene with alkoxyamine **1** was uncontrolled. The molecular weight distributions remained broad throughout a range of conversions (conversion = 6−76%; $M_w/M_n = 1.43-1.77$), and large discrepancies between the theoretical and calculated molecular weights were observed from low to high conversion. The calculated molecular weights were much higher than the theoretical molecular weights which indicates a low initiating efficiency ($I_{eff} = M_{n,th}/M_{n,SEC}$).[23] As the conversion increased, the initiating efficiency increased from $I_{eff} = 0.08$ at 1.5 h (6% conversion) up to $I_{eff} = 0.82$ at 18 h (72% conversion), and the discrepancy between theoretical and calculated molecular weights narrowed. This suggests that homolysis of initiator **1** at 125 °C is not fast relative to propagation. This leads to initiation of polymer chains throughout the course of the polymerization and results in broad molecular weight distributions.[1,5]

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Scheme 1. Addition of Radicals to Nitrosobenzene To Form Alkoxyamines 1 and 2

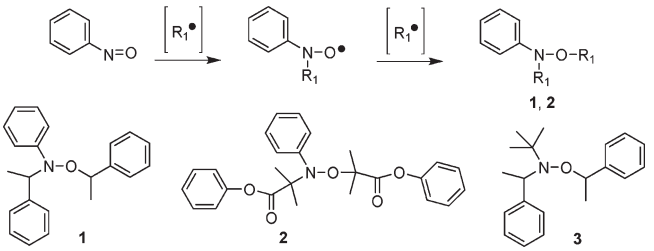

Table 1. Polymerization of MMA with Alkoxyamine 1[a]

entry	time/h	convn[b]/%	M_n(theor)[c]/ kg mol^{-1}	M_n(SEC)[d]/ kg mol^{-1}	M_w/M_n[d]
1	6	2	1.00	3.20	1.25
2	22	32	6.70	8.70	1.40

[a] Polymerizations run at 125 °C under N_2 atmosphere. [MMA]/[**1**] = 200:1. [b] Conversion determined by ^{1}H NMR. [c] Calculated based on conversion. [d] Determined by SEC against polystyrene standards.

Alkoxyamine **2** was also employed in the polymerization of styrene. As was observed with alkoxyamine **1**, initiation with alkoxyamine **2** was not fast relative to propagation which led to discrepancies between the theoretical and calculated molecular weights early in the polymerization and resulted in broad molecular weight distributions. Initiating efficiencies were ~0.64 for the first 6 h before rising to ~1 by 16 h, and the polydispersity indices rose over the range of conversions (conversion = 20−66%; M_w/M_n = 1.36−1.50) which suggests poor control over the polymerization. Even though the homopolymerization of styrene is uncontrolled with **2**, addition of a small amount of styrene to MMA polymerization is an effective way to control the polymerization to high conversion (*vide infra*).

The poor initiating efficiencies for alkoxyamines **1** and **2** may only partially explain the lack of control for styrene. It has recently been shown that certain alkoxyamines containing the arylnitroxide 2,2-diphenyl-3-phenylimino-2,3-dihydroindol-1-yloxyl (DPAIO) have a labile N−O bond that is cleaved due to the resonance stabilization of the resultant aminyl radical.[24] Also, it has long been known that delocalization of the unpaired electron onto the aryl ring of the arylnitroxides can lead to radical coupling with the aryl ring[22] and can also result in nitroxide instability.[25−28] Some alkylarylnitroxides are stable, such as those which contain tertiary alkyl centers with no α-H atoms or those with *para*-blocking groups, but the stabilities of the nitroxides released from alkoxyamines **1** or **2** are unknown at this time. Both of these decomposition pathways may affect the control of polymerizations with alkoxyamines **1** and **2**.

*Polymerization of Methyl Methacrylate with **1***. Recently, Guillaneuf et al. reported the use of alkoxyamines based on an arylnitroxide, DPAIO, for MMA polymerization.[21] They were able to control MMA polymerization to approximately 60% conversion and suggested that this was achieved through radical delocalization on the phenyl ring of the nitroxide which may prevent cross-disproportionation with the chain end. Since the nitroxide radical can be delocalized through the *N*-phenyl moiety of alkoxyamines **1** and **2**, we examined these initiators for MMA polymerization.

Moderate control was achieved for the polymerization of MMA with **1** (Table 1, entries 1 and 2). The molecular weight increased with conversion, and the polydispersity indices remained fairly narrow for NMP of MMA (M_w/M_n = 1.25−1.40). However, increasing the reaction time did not result in higher conversion which suggests that the polymerization effectively shut down by 32% conversion due to irreversible termination reactions. Vinylic resonances attributed to an alkene terminated chain end (δ 6.2 and δ 5.5) were observed in the ^{1}H NMR spectrum, indicating that cross-disproportionation occurred to some extent. This would lead to dead chains and to the build up of free nitroxide, which would both contribute to the polymerization stopping at low conversion.

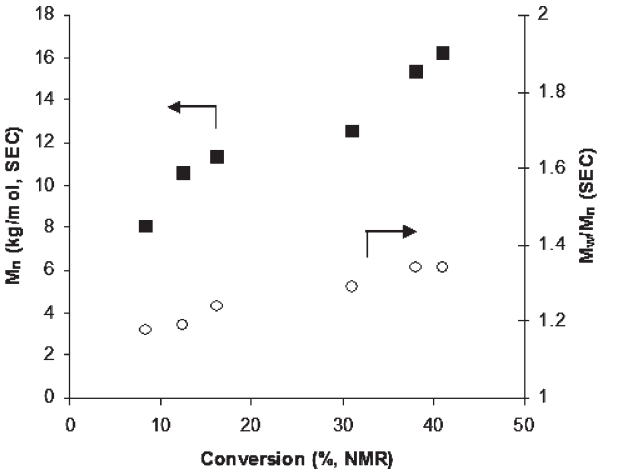

Figure 1. Relationship between M_n, M_w/M_n, and conversion at 125 °C for [MMA]/[**2**] = 300/1.

Since initiator **1** failed to carry MMA polymerization to high conversion, alkoxyamine **2** was examined as an initiator for MMA. This structure was selected because Haddleton and co-workers demonstrated that the 2-methylpropionic acid phenyl ester radical was effective for the ATRP of MMA,[20] and Guillaneuf et al. also successfully employed this initiating radical for the NMP of MMA.[21] Additionally, the absence of α-H atoms in the nitroxide generated from alkoxyamine **2** should provide greater stability for this nitroxide when compared to the nitroxide derived from alkoxyamine **1**. In the polymerization of 300 equivalents of MMA from alkoxyamine **2**, M_n was observed to increase with conversion up to 41%, and the molecular weight distributions remained narrow (M_w/M_n from 1.18 to 1.36) throughout the polymerization (Figure 1). Attempts to obtain higher conversion did not result in higher molecular weight material which indicates the occurrence of termination reactions that shut the polymerization down by 41% conversion.

The livingness of the chain ends was ascertained by growth of a second block of polymer. Attempts at preparing block copolymers of PMMA-*b*-PS showed evidence of chain extension, though the molecular weight distributions after extension were broad.

Addition of a small percent (4−10 mol %) of a comonomer with a low association−dissociation equilibrium constant, *K*, can reduce the overall *K* of a quickly propagating monomer such as MMA.[6,7,29−34] Styrene is a popular choice since it is readily available and polymerizes well under most nitroxide-mediated conditions. Studies of the copolymerization of MMA and styrene found that the majority of polymer chains are capped by an MMA−styrene−nitroxide sequence, which illustrates how even a low concentration of a monomer with a low *K* can effect control over these polymerizations.[30]

Copolymerization of a 10:1 mixture of MMA and styrene was analyzed with alkoxyamine **2**. The plot of molecular weight versus conversion was linear, and the polydispersity

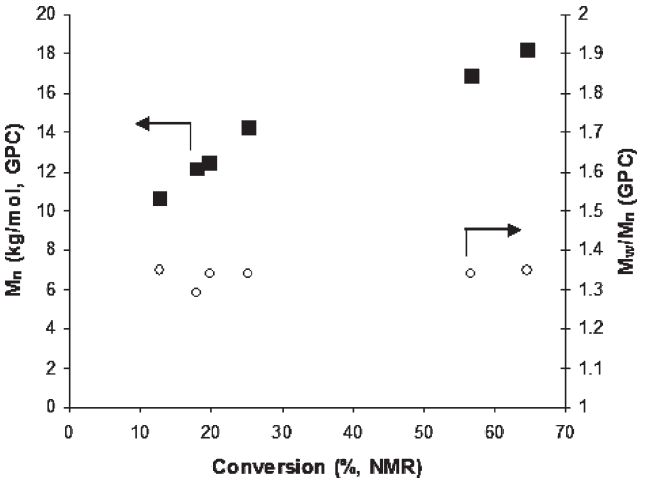

Figure 2. Relationship between M_n, M_w/M_n, and conversion at 125 °C for [MMA]/[styrene]/[**2**] = 300/30/1.

indices remained ~1.35 throughout the polymerization which demonstrates controlled behavior (Figure 2). However, high conversion of MMA (65%) was possible, making this a viable method for the synthesis of PMMA with a small amount of styrene incorporation. Charleux and co-workers copolymerized MMA with styrene in a controlled manner to high conversion (60%) using the SG1 nitroxide, though they observed polydispersity indices as low as 1.18.[30] It should be noted, however, that no additional nitroxide for control was included in this work in contrast to the study by Charleux and co-workers.

Conclusion. Alkoxyamines bearing an *N*-phenyl moiety were synthesized by the addition of carbon-centered radicals across the double bond of nitrosobenzene and were subsequently tested for polymerization efficacy. Initiators **1** and **2** were not able to control the polymerization of styrene, but were able to effect a controlled MMA polymerization at low to moderate conversions (32−41%). Additionally, initiator **2** was utilized in the copolymerization of MMA with a small percent of styrene (10 mol %) to obtain high conversions and narrow polydispersity indices. This work concludes that alkoxyamines containing an *N*-phenyl moiety are not likely to be useful initiators for NMP with a broad range of monomers, but this class of initiator does show potential for the homopolymerization of MMA, as well as copolymerization with styrene.

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Supporting Information Available: Text giving full experimental protocols and tables of data for the polymerization of styrene with **1** and **2**, as well as a table of data for the copolymerization of MMA/styrene. This material is available free of charge via the Internet at http://pubs.acs.org.

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