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Imidazolidinone Nitroxide-Mediated Polymerization

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ABSTRACT: Derivatives of 2,2,5,5-tetraalkylimidazolidin-4-one-1-oxyl have been found to offer significant advantages over many of the nitroxides previously employed in nitroxide-mediated polymerization: homopolymers [e.g., polystyrene and poly(alkyl acrylate)], statistical copolymers [e.g., poly(styrene-*co*-acrylonitrile)], and block copolymers [e.g., poly(4-methylstyrene)-*block*-polystyrene and poly(*n*-butyl acrylate)-*block*-polystyrene] can be synthesized with controlled molecular weight, narrow molecular weight distribution, and defined end group functionality. The effect of substituents α to the nitroxide nitrogen and at the transannular nitrogen on the outcome of polymerization is explored. Appropriate selection of these substituents provides polymers of lower polydispersities than, for example, 2,2,6,6-tetramethylpiperidin-2-oxyl and derivatives. The nitroxides are synthesized from readily available precursors by a simple experimental route. Moreover, they are subject to fewer side reactions. In particular, disproportionation between the propagating radical with nitroxide appears to be of lesser significance.

Introduction

Alkoxyamine-initiated or nitroxide-mediated polymerization was developed in these laboratories more than 10 years ago¹ but has only recently achieved popularity with the demonstration by Georges, Hawker and others² of the utility of the method in the synthesis of narrow polydispersity polystyrene and related materials. The key step in the mechanism of nitroxide-mediated polymerization is the reversible coupling of the propagating radicals (active chains) with nitroxides to produce the corresponding alkoxyamines (dormant chains) as shown in Scheme 1. This provides a mechanism for equilibration of the active chains and accounts for the living characteristics associated with the process (narrow polydispersity, ability of chain extension, etc.).

A variety of nitroxides have been used in conjunction with this process. Some of those found most effective include 1,1,3,3-tetraethyl-2,3-dihydro-1*H*-isoindolin-2yloxyl (1), 2,2,6,6-tetramethylpiperidin-2-oxyl (2) (TEMPO), and di-*tert*-butyl nitroxide (3).^{1,2} There are some disadvantages associated with the use of these compounds in nitroxide-mediated polymerization. These include the availability of the nitroxide (i.e., expense or

Scheme 1



difficulty of synthesis: only TEMPO and some derivatives are currently readily available) and their propensity to undergo side reactions (e.g., disproportionation between propagating species and nitroxide; see Scheme 2).



In this paper, we report that the use of derivatives of 2,2,5,5-tetraalkylimidazolidin-4-one-1-oxyl (**4** and **5**) offers significant advantages in nitroxide-mediated polymerization.^{3,4} The utility of imidazolidinone nitroxides in nitroxide-mediated polymerization of styrene and (meth)acrylate esters is demonstrated. The nitroxides are synthesized from readily available precursors by a simple experimental route. In styrene polymerization and copolymerization, their use provides faster polymerization rates and narrower polydispersities with respect to many other nitroxides. The effectiveness of the nitroxides is shown to be dependent on substituents α to nitrogen or on the transannular nitrogen.

Experimental Section

General. Monomers were purified by passage through alumina and distillation (to remove inhibitors) and flash distilled immediately prior to use. Gel permeation chromatography (GPC) was used to establish the molecular weight and molecular weight distribution (polydispersity) of the polymers. A Waters Associates liquid chromatograph equipped with differential refractometer and a set of Ultrastyragel columns (10^6 , 10^5 , 10^4 , 10^3 , 500, and 100 Å) was used. Tetrahydrofuran (1.0 mL min^{-1}) was used as eluent. The molecular weights are reported as polystyrene equivalents. Samples for GPC analysis were isolated by evaporation of monomer. No precipitation or fractionation was performed.

Imidazolidinone Nitroxides. The syntheses of imidazolidinone nitroxides **4a** and **5a** are described in detail elsewhere.⁴ **N-Alkylimidazolidinone Nitroxides.** These compounds were prepared according to the following general procedure. A suspension of imidazolidinone nitroxide (5.5 mmol **4a** or 1.69 mmol **5a**) and sodium hydride (1.33 mol equiv, 80% dispersion in oil) was allowed to stir under an atmosphere of nitrogen in acetonitrile solvent (20 mL for **4a** or 10 mL for **5a**) at room temperature for 15 min when the required amount of an alkyl halide (1.20 mol equiv) was added. Workup and purification by column chromatography gave the *N*-substituted nitroxide in good-to-excellent yield (45–93%; see below).

2,5-Diethyl-2,3,5-trimethylimidazolidin-4-one-1-oxyl (**4b**). The title compound was isolated (45.6% yield) by column chromatography (Kieselgel-60, 70–230 mesh, ethyl acetate/*n*-hexane 1:3 as eluent) as a yellow liquid. MS (CI): 200 (M + 1, 43.0%), 199 (M⁺, 16.0), 186 (23.5), 185 (40.0), 171 (58.0), 170 (34.0), 155 (23.0), 149 (20.2), 141 (11.6), 140 (15.6), 128 (10.0), 126 (16.1), 116 (13.7), 112 (14.4), 111 (12.7), 100 (12.2), 73 (52.0).

2,5-Diethyl-2,5-dimethyl-3-n-butylimidazolidin-4-one-1-oxyl (**4c**). The title compound was isolated (87.0% yield) by column chromatography (Kieselgel-60, 70–230 mesh, ethyl acetate/n-hexane 1:9 as eluent) as a yellow liquid. MS (CI): 242 (M + 1, 74.0%), 241 (M⁺, 38.3), 227 (100.0), 213 (86.7), 211 (45.0), 198 (12.0), 197 (88.0), 184 (M – ⁿBu, 7.6), 170 (27.0), 156 (16.3), 128 (27.0), 126 (30.0), 116 (4.3), 98 (8.0), 72 (7.6).

2,5-Diethyl-2,5-dimethyl-3-benzylimidazolidin-4-one-1-oxyl (**4d**). The title compound was isolated (93.0% yield) by column chromatography (Kieselgel-60, 70–230 mesh, ethyl acetate/ *n*-hexane 1:5 as eluent) as a yellow solid. Mp: 64–65 °C. MS (CI): 276 (M + 1, 56.7%), 275 (M⁺, 22.0), 262 (22.0), 261 (100.0), 247 (62.6), 245 (M – NO, 26.0), 231 (86.0), 218 (5.3), 190 (12.3), 170 (15.0), 162 (24.6), 126 (20.1), 102 (4.0), 91 (21.5), 72 (4.0).

2,5-Bis(spirocyclohexyl)-3-methylimidazolidin-4-one-1-oxyl (**5b**). The title compound was isolated (89.7% yield) as a yellow solid by column chromatography (Kieselgel-60, 70–230 mesh, ethyl acetate/*n*-hexane 1:4 as eluent). Mp: 103-105 °C. MS (CI): 252 (M + 1, 100%), 251 (M⁺, 30.7), 237 (87.6), 236 (12.3), 235 (29.3), 222 (24.5), 221 (40.6), 196 (18.7), 193 (10.5), 142 (24.7), 140 (53.9), 112 (16.0), 99 (23.5).

Alkoxyamine Synthesis. 1-(2-tert-Butoxy-1-phenylethoxy)-2,5-diethyl-2,5-dimethylimidazolidin-4-one (10). A degassed solution of styrene (5 mL), di-*tert*-butyl peroxalate (0.21 g, 0.9 mmol) and nitroxide **4a** (0.389 g, 2.1 mmol) was heated for 2 h at 50 °C. The styrene was evaporated under reduced pressure, and the residue was chromatographed on silica gel with ethyl acetate/petroleum spirit 40–60 °C 3:7 as eluent to give the title compound as a mixture of four isomers (0.28 g, 43% yield). ¹H NMR: δ (CDCl₃) 0.30–2.40 (m, 16H), 1.15 (s, 9H, (CH₃)₃C), 3.30 (m, 1H, (CH₃)₃COCH), 3.60 (m, 1H, (CH₃)₃-COCH), 4.65 (m, 1H, CH(Ph)ON), 5.90, 6.10, 6.20, 6.35 (br s, total of 1H, NH) and 7.30 (br s, 5H, phenyl-H).

1-(2-tert-Butoxy-1-phenylethoxy)-2, $\hat{5}$ -*bis(spirocyclohexyl)imi-dazolidin-4-one* (**11a**). A degassed solution of styrene (10 mL), di-*tert*-butyl peroxalate (0.468 g, 2.0 mmol), and nitroxide **5a** (1.05 g, 4.43 mmol) was heated for 2 h at 50 °C. The compound **11a**, which crystallized from the reaction mixture as a mixture of two isomers, was collected by filtration (1.31 g, 79% yield). Mp: 244–247 °C. ¹H NMR: (CDCl₃) δ 0.40–2.60 (m, 20H, cyclohexyl-CH₂), 1.25 (s, 9H, (CH₃)₃C), 3.35 (m, 1H, (CH₃)₃-COCH), 3.67 (dd, 1H, (CH₃)₃COCH), 4.72 (m, 1H, CH(Ph)ON), 6.25, 6.45 (br s, total 1H, NH), 7.32 (br s, 5H, phenyl-H).

1-(2-tert-Butoxy-1-phenylethoxy)-2,5-bis(spirocyclohexyl)-3methylimidazolidin-4-one (**11b**). A procedure similar to that described for the synthesis on the *N*-alkylated nitroxides was used. Thus, 1-(2-tert-butoxy-1-phenylethoxy)-2,5-bis(spirocyclohexyl)imidazolidin-4-one (**11a**) was treated with excess methyl iodide in the presence of sodium hydride in dimethyl sulfoxide. The product was isolated as a white solid in 93% yield. Mp: 129–131 °C (aq. MeOH). ¹H-NMR (CDCl₃) δ 0.40– 2.60 (m, 20H, cyclohexyl CH₂), 1.10 (s, 9H, tert-butyl CH₃), 2.90, 3.0 (s, total 3H, N–CH₃), 3.30 (dd, 1H, (CH₃)₃COC**H**), 3.66 (dd, 1H, (CH₃)₃COC**H**), 4.69 (dd, 1H, C**H**(Ph)ON), 7.25 (br s, 5H, phenyl-**H**).

Styrene Polymerizations. The reaction components were combined to form a stock solution (5 or 10 mL) containing

Table 1. Molecular Weight and Conversion Data for Benzoyl Peroxide-Initiated Polymerization of Styrene Carried out in the Presence of Various Nitroxides at $130 \ ^{\circ}C^{a}$

nitroxide	time/hr	$ar{M}_{\mathrm{n}}{}^{b}$	$ar{M}_{ m w}/ar{M}_{ m n}$	% conv.
$\mathbf{5a}^d$	2	510	1.31	1.5
$\mathbf{5a}^d$	4	1 600	1.27	5
$\mathbf{5a}^d$	8	4 900	1.26	34
$\mathbf{5a}^d$	23	7 100	1.21	67
$\mathbf{5a}^d$	72	12 300	1.20	90
$\mathbf{5a}^d$	23	16 000	1.23	99
5b	2	800	1.18	6
5b	4	3 100	1.13	21
5b	8	8 800	1.09	56
5b	18	16 300	1.09	96
5b	23	16 300	1.09	99
4 a	23	16 000	1.49	99
4b	2	500	1.36	5
4b	4	1 400	1.29	10
4b	8	2 500	1.34	22
4b	18	4 700	1.29	49
4b	23	8 100	1.24	60
4d	4	1 400	1.23	9
4d	18	5 100	1.28	47
4 c	4	1 400	1.22	9
4 c	18	6 000	1.25	53
2	4	1 700	1.11	10
2	18	12 800	1.13 ^c	76
1	4	800	1.09	4
1	18	17 500	1.08	87

^{*a*} [BPO] = 0.029 M and [nitroxide] = 0.061 M. ^{*b*} Molecular weights >500 have been rounded to the nearest 100. ^{*c*} Bimodal molecular weight distribution. ^{*d*} Some variability in conversions and molecular weights was observed for experiments carried out under nominally the same reaction conditions (compare two entries for reaction time 23 h). This may in part be related to difficulties associated with the poor solubility of nitroxide **5a** in styrene and consequent difficulties in making up the reaction solutions.¹⁸

Table 2. Molecular Weight and Conversion Data for Styrene–Acrylonitrile Copolymers Prepared with Thermal Initiation at 130 °C in the Presence of Various Nitroxides

nitroxide ^a	$ar{M}_{ m n}{}^b$	$\bar{M}_{ m w}/\bar{M}_{ m n}$	% conv.
5b	23 100	1.16	>95.0
4b	17 000	1.34	84.0
4d	17 600	1.35	89.0
2	14 300	1.34	83.0

 a [nitroxide] = 0.0055 M b Molecular weights have been rounded to the nearest 100.

nitroxide (0.061 M) and benzoyl peroxide (0.029 M) in styrene. Aliquots of these solutions (2 mL) were transferred to ampules. Degassing was accomplished by three freeze–evacuate–thaw cycles. The ampules were flame-sealed under vacuum and completely submerged in an oil bath at 130 °C for the specified times. Conversions were determined gravimetrically and are reported in Table 1, together with the GPC analyses.

Styrene–Acrylonitrile Copolymerizations. A stock solution of styrene (7.27 g) and acrylonitrile (2.27 g) was prepared. Aliquots of this stock solution (2 g) were transferred to ampules containing the nitroxide (12.3 mmol). The ampules were degassed by three freeze evacuate–thaw–cycles, sealed under vacuum, and heated at 130 °C for 18 h when it was opened, and the polymer was isolated by evaporation of the monomer. Further details are shown in Table 2.

tert-**Butyl Acrylate Polymerizations.** Stock solutions were prepared as follows: (A) alkoxyamine (71.3 mg) and *tert*-butyl acrylate (1.0 mL) in benzene (4.0 mL) and (B) alkoxyamine (71.3 mg) and *tert*-butyl acrylate (5.0 mL). Aliquots of these solutions (2 mL) were transferred to ampules, which were

Table 3. *tert*-Butyl Acrylate Polymerizations (benzene, 120 °C) in the Presence of Alkoxyamine (11b; 0.033 M)

time (hr)	[BA]	$ar{M}_{\!\mathrm{n}}{}^a$	$ar{M}_{ m w}/ar{M}_{ m n}$	% conv.
24	20% v/v	1550	1.39	28.0
49	20% v/v	1850	1.32	34.4
24	bulk	8250	1.51	28.6
49	bulk	9000	1.41	39.8

^a Molecular weights have been rounded to the nearest 50.

Table 4. Molecular Weight/Conversion Data for Polymerizations (90 °C, bulk) of Methyl Methacrylate in the Presence of Various Nitroxides^a

nitroxide	\overline{M}_{n}^{b}	$\overline{M}_{_{\scriptscriptstyle W}}$ / $\overline{M}_{_{\scriptscriptstyle N}}$	Conv. %	[nitroxide] M	calcd $M_n^{b, c}$
4a	35 700	1.57	38	0.0077	36 800
	33 800	1.65	36	0.0069	34 500
	20 400 ^d	1.70	19	0.0077	18 500
4 b	31 021	1.63	17	0.0077	18 200
$5a^e$	6 500	1.44	6	0.0077	6 100
$5 b^e$	28 800	1.89	21	0.0077	22 500
1	18 300	1.71	18	0.0079	17 400
	5 600	1.68	7	0.0115	5 900
N-0.	10 500	2.24	11	0.0076	10 800
	17 000	3.30	18	0.0077	16 900
$\sqrt{\frac{N}{N}}$	22 100	3.11	14	0.0076	13 800
$ \begin{array}{c} $	19 200	4.10	18	0.0076	17 200

^{*a*} [Azobis(2,4-dimethyl-2-pentanenitrile)] = 0.0054 M. ^{*b*} Molecular weights have been rounded to nearest hundred. ^{*c*} Calculated molecular weight = 2f[monomer consumed]/[initiator] where the initiator efficiency (*f*) is 90%. Values rounded to nearest hundred. ^{*d*} Reaction temperature = 100 °C. ^{*e*} [Azobis(2,4-dimethyl-2-pentanenitrile)] = 0.0049 M.

degassed by three freeze-evacuate-thaw cycles, flame-sealed under vacuum, and heated at 120 °C in a thermostated oil bath for the specified times. Conversions were determined gravimetrically. Further details are reported in Table 3.

Methyl Methacrylate Polymerizations. The reaction components were combined to form a stock solution containing nitroxide (0.0077 M) (unless indicated otherwise) and azobis-(2,4-dimethyl-2-pentanenitrile) (0.0054 M) in methyl methacrylate. Aliquots of these solutions (2 mL) were transferred to ampules. Degassing was accomplished by three freeze–evacuate–thaw cycles. The ampules were flame-sealed under vacuum and completely submerged in an oil bath at 90 °C (unless indicated otherwise) for the specified times. Conversions were determined gravimetrically and are reported in Table 4, together with the GPC analyses.

Block Copolymer Syntheses. A solution of polystyrene (250 mg, $\bar{M}_n = 8800$, $\bar{M}_w/\bar{M}_n = 1.09$, prepared with nitroxide **5b** according to the procedure given above) was dissolved in the appropriate monomer (1 mL) and transferred to an ampule. The ampule was degassed by three freeze–evacuate–thaw cycles, sealed under vacuum, and heated at 130 °C for 18 h.



The polymer was isolated by evaporation of the monomer to give a block copolymer as follows: *Poly(4-methylstyrene)-block-polystyrene.* **850** mg, 95% conversion, $\overline{M}_w/\overline{M}_n = 36$ 900, and $\overline{M}_{w/}\overline{M}_n = 1.14$. *Poly(n-butyl acrylate)-block-polystyrene.* **608** mg, **68%** conversion $\overline{M}_w/\overline{M}_n = 21$ 500, $\overline{M}_w/\overline{M}_n = 1.29$.

Molecular Orbital Calculations. Semiempirical molecular orbital calculations (AM1, PM3) were performed using MNDO93 as implemented as part of the Unichem package (Oxford Molecular, version 4.0) on a Cray J90. Discussion on the methodology employed is provided in our previous publication.⁵ Free-radical heats of formation were calculated using the AM1 method with minimal configuration interaction (CI). Use of other methods (e.g., PM3, AM1–UHF), although giving somewhat different heats of formation, gave data exhibiting the same general trends.

Results and Discussion

Nitroxide/Alkoxyamine Synthesis. The parent nitroxides **4a** and **5a** have been previously described in a series of papers by Murayama et al.^{6–9} However, their use in nitroxide-mediated polymerization has not previously been described.

For the present work, the synthesis of the nitroxides **4a** and **5a** was accomplished by the sequence of reactions shown in Scheme $3.^4$ Thus, condensing an aminonitrile (**6**) with a ketone in the presence of ammonium sulfide produced the corresponding 2,2,5,5-tetraalkylimidazolidin-4-thione (**7**). The cyclic thione was oxidized to the nitroxide (**9**) presumably via cyclic amide (**8**). Overall yields based on ketone were high, >80%.

The nitroxides **4a** and **5a** and the derived alkoxyamines show relatively low solubility in many solvents and monomers, and this limits their application in nitroxide-mediated polymerization. The *N*-alkylated analogues (**4b**-**d** and **5b**) show markedly improved solubility, permitting their application in a wide range of systems. The *N*-alkylated nitroxides (**4b**-**d** and **5b**) are readily prepared in good-to-excellent yield simply by treating the parent compound with sodium hydride and the appropriate alkyl halide (see Scheme 4).

The imidazolidinone nitroxides **4a** and **5a** were converted to the corresponding alkoxyamines (**10** and **11a**, respectively) by heating a solution of the nitroxide and di-*tert*-butyl peroxalate¹⁰ in excess styrene at 60 °C according to the procedure described earlier (cf. Scheme 5).¹ Under these conditions, only one unit of styrene is appended.¹¹ Alkoxyamine **11b** was prepared in >90% yield by methylation of **11a**.

Nitroxide-Mediated Polymerization. Styrene Polymerizations and Copolymerizations. The most wide-



spread application of nitroxide-mediated polymerization has been in the synthesis of narrow polydispersity polystyrene and related polymers.¹² Most of this work has used TEMPO (2) or a derivative thereof. The results of a series of styrene polymerizations performed with various nitroxides and with benzoyl peroxide as initiator are summarized in Table 1. The evolution of molecular weight distribution with conversion is illustrated in Figure 1. The reaction conditions are similar to those reported by Georges et al.^{13–15} except that a larger excess of nitroxide over benzoyl peroxide has been used. The half-life of benzoyl peroxide at 130 °C (1.2 min¹⁶) is such that it should largely be consumed in less than 10 min (even if nitroxide-induced decomposition¹⁷ is not allowed for). After that time, alkoxyamine dissociation and the thermal generation of radicals from the monomer should be the only processes leading to radical generation. This initial stage of the polymerization accomplishes formation of a low-molecular-weight alkoxyamine.

Under the conditions employed, all nitroxides used (see Table 1) were found to give low polydispersities $(\bar{M}_w/\bar{M}_n < 1.5)$ with reference to conventional polymerization and all, except **4a**, gave $\bar{M}_w/\bar{M}_n < 1.3$. Use of the *N*-alkylated imidazolidinone nitroxide **5b** provides narrower polydispersities than did other nitroxides tested during this investigation, including **2**.¹⁸

The utility of the nitroxides **4b**, **4d**, **5b**, and **2** were also explored in thermally initiated styrene–acrylonitrile copolymerization at 130 °C (see Table 2). Styrene– acrylonitrile copolymerization with **2** has previously been reported by Fukuda et al.¹⁹ The nitroxide **5b** provided a higher polymerization rate and a lower polydispersity than those observed with nitroxides **4b** or **4d** or TEMPO.

Acrylate Polymerization. There are only a few reports of nitroxide-mediated polymerization of acrylates in the literature. Early work carried out in these laboratories has demonstrated that it is possible to synthesize acrylic homo- and block copolymers.^{1,20–22} Since that time, there



Figure 1. Evolution of molecular weight distribution with reaction time for benzoyl peroxide-initiated polymerization of styrene carried out in the presence of nitroxide **5b** at 130 °C. For further details see Experimental Section and Table 1.

have been several literature reports of the synthesis of such polymers by nitroxide-mediated polymerization indicating some difficulties with the process.^{23–28} It is noteworthy that, in these experiments, nitroxide (2) or derivatives thereof were employed and many of the problems experienced may directly be related to this choice of nitroxide and reaction conditions. The problems led some workers to develop relatively complex strategies for the synthesis of acrylic block copolymers to overcome these apparent problems.^{25,27} We^{1,21} have found that use of 3 or 1 gives superior results to 2; a result recently confirmed by Goto and Fukuda.²⁸ Listigovers et al.²⁴ have reported some success with the use of 4-oxo-2,2,6,6-tetramethylpiperidin-1-yloxyl. However, reaction temperatures used were high (>145 °C), and the polydispersities obtained were still comparatively broad (1.3-1.5). A recent report by Benoit et al.²⁹ describes the synthesis of low polydispersity poly(nbutyl acrylate)s using nitroxide (12) and AIBN as initiator. Very narrow polydispersities (<1.2) and relatively high conversions were obtained.

Polymerizations of *tert*-butyl acrylate were initiated by the alkoxyamine, 1-(2-tert-butoxy-1-phenylethoxy)-2,5-bis(spirocyclohexyl)-3-methylimidazolidin-4-one (11b), either in bulk or in 20% (w/w) tert-butyl acrylate in benzene at 120 °C (Table 3). Molecular weights were found to increase in line with conversion and monomer concentration. However, it was found that the rate of polymerization slowed significantly with reaction time such that the maximum conversion under these conditions was <40% even after an extended (49 h) reaction time. It is notable that conversions obtained for a given reaction time appear to show no significant dependence on the monomer concentration. The retardation is attributed to side reactions (in particular, radicalradical termination), which leads to a build-up in the concentration of free nitroxide.^{22,26-28} We have shown by kinetic simulation that in these circumstances only a very small nitroxide concentration (ca. 10^{-4} M) is required to give substantial retardation.²² A further potential complication is chain transfer to polymer.³⁰

Methyl Methacrylate Polymerization. We have reported a comparison of a series of nitroxides, including the imidazolidinone nitroxides **4a** and **5a**, in controlling MMA polymerization as part of a recent conference proceedings.³¹ In that work, MMA polymerizations were carried out at 90 °C with azobis(2,4-dimethyl-2-pentanenitrile) as initiator in the presence of the various

nitroxides. Azobis(2,4-dimethyl-2-pentanenitrile) was chosen as the initiator because it has a very short halflife at 90 °C (<20 s).³² This means that the initiatorderived radicals would rapidly be converted to an alkoxyamine. The results (conversions, polydispersities, and molecular weights) of these experiments, along with the results of additional experiments performed with the *N*-methylated imidazolidinone nitroxides (4b, 5b), are summarized in Table 4. Narrowest polydispersities, in the range 1.4-1.7, are obtained with the fivemembered ring nitroxides (1, 4a, 5a, 4b, 5b). Although these polydispersities are not exceptional, as compared with the very narrow polydispersities obtained in styrene polymerizations, the results compare very favorably with the values in the range 3.1-4.1 obtained with six-membered ring (TEMPO or 4-oxo derivative) or open-chain nitroxides (tert-amyl tert-butyl nitroxide).

In all experiments, polymerization ceased after less than 1 h reaction time. Best conversions (up to 38%) were obtained with the imidazolidinone nitroxide **4a**. All other nitroxides gave conversions <20% under these conditions. The product in all cases appeared to be a methyl methacrylate macromonomer as would be formed by disproportionation of the MMA propagating species with nitroxide. Evidence for this pathway is provided by NMR analysis, in the case of lower molecular weight polymers (the olefinic resonances of the macromonomer at δ 5.5 and 6.2 are characteristic and appear in a region uncomplicated by other signals), and by the formation of hydroxylamine, which can rapidly be oxidized to nitroxide by exposure of the reaction mixture to air.

It is believed that the reaction proceeds until the nitroxide concentration builds so as to retard polymerization. After this time, little propagation occurs, and the propagating radical ultimately disproportionates with nitroxide to give the observed product. The results of kinetic simulations³¹ support this hypothesis. They also suggest that the dependence on nitroxide type can be attributed to the combination-disproportionation ratio for the reaction: the MMA propagating species and nitroxide being less in the case of the five-membered ring nitroxides than it is with six-membered ring or open chain nitroxides. The possibility of improving conversions by adding reagent to consume the excess of nitroxide, as has previously been reported for styrene and acrylate polymerizations (vide infra), should be examined.

Block Copolymer Syntheses. The utility of the imidazolidinone nitroxides in block copolymer synthesis was investigated by heating a polystyrene alkoxyamine with either *n*-butyl acrylate or 4-methylstyrene (130 °C for 18 h; see Scheme 6). Results of these experiments are shown in parts a and b of Figure 2 respectively.

Both experiments were successful in yielding narrow polydispersity block copolymers. The molecular weights obtained correspond within experimental error to that expected based on the measured conversions. A somewhat lower polydispersity was obtained with 4-methylstyrene than with *n*-butyl acrylate.

GPC analysis with diode-array UV detection was also performed on the poly(*n*-butyl acrylate)-*block*-polystyrene. At wavelengths \geq 254 nm, absorption by acrylate units in the chain should be minimal; thus, it is possible to more easily follow the fate of the polystyrene first block. Any significant amount of residual polystyrene first block would be manifest as a low-molecular-weight shoulder on the molecular weight distribution for the

nitroxide	(k	$\Delta H_{\rm f}$ (kJ M ⁻¹)		bond length (Å)		bond angle (degrees)
	nitroxide	alkoxyamine	(C-0	C-N	C-N-C
b	-62.8	-140 3	66.2	1 471	2 394	107.3

Table 5. Properties of Nitroxides and Derived tert-Butyl Alkoxyamines Estimated from Molecular Orbital Calculations^a



^{*a*} Heats of formation (ΔH_{f}) based on use of the AM1 method. Those for free radicals were obtained with minimal CI.⁵ ΔH_{f} for *tert*-butyl is -11.3 kJ mol^{-1.5} ^{*b*} Data taken from Moad and Rizzardo.⁵

block copolymer.³⁵ No such shoulder was observed (see Figure 3 in Supporting Information). We conclude that the initiation efficiency is high and that the greater degree of tailing observed for this copolymer is due to (a) a greater incidence of side reactions during *n*-butyl acrylate polymerization (see above), (b) a faster rate of propagation with respect to deactivation, or (c) a slower rate of activation (alkoxyamine homolysis).^{31,33,34}

The syntheses of polystyrene-n-butyl acrylate block copolymers from polystyrene alkoxyamines based on TEMPO have previously been reported by Yoshida et

al.³⁵ and by Listigovers et al.²⁴ Polydispersities obtained in those experiments were broad, >1.6. However, it is difficult to directly compare these experiments because polymerization conditions differ (Yoshida et al.,³⁵ 120 °C and 6 h; Listigovers et al.,²⁴ 145 °C and 1 h).

Substituent Effects. A variety of factors may be responsible for the narrower polydispersities and higher conversions found with the imidazolidinone nitroxides. These include (a) the kinetics of C–O bond homolysis and (b) the occurrence (or not) of various side reactions.



The rate constants and equilibrium constant associated with C–O bond homolysis and reformation are known to be of critical importance.^{31,33,34} Thus, the nitroxide (or alkoxyamine) used in nitroxide-mediated polymerization should be selected such that the R–O bond of the initial alkoxyamine and the R(M)_n–O bond of any formed alkoxyamine undergo facile homolysis under the selected reaction conditions. In general, it is also desirable that the equilibrium constant $K (= k_N/k_{-N})$ be high^{31,33,34} because rapid exchange between dormant and active chains is essential for narrow polydispersity. However, a too-high value for K will also mean a greater rate of chain death if disproportionation between the propagating radical and nitroxide is significant (this is discussed below).³¹

In a recent study,⁵ we examined the effect of varying the nitroxide/alkoxyamine structure on C-O bond homolysis rates. We presented experimental data and theoretical calculations to show that factors that reduce steric congestion about the C-O bond also lead to a reduction in this rate. Rates of C-O bond homolysis were found to increase in the series as follows: fivemembered ring < six-membered ring (e.g., 2) < open chain (e.g., 3) < seven-membered ring. Rate constants for the reverse coupling reaction^{36,37} have been shown to follow the opposite trend, although differences are small. We also predicted on the basis of calculated bond dissociation energies (D_{C-0}) that the presence of electronwithdrawing substituents should strengthen the C-O bond. On the basis of these findings, the five-membered imidazolidinone nitroxides (4 and 5) should be anticipated to be less effective than a similarly substituted piperidin-N-oxyl (e.g., TEMPO). Semiempirical molecular orbital calculations (see Table 5) carried out for the series of imidazolidinone nitroxides support this expectation. A number of experimental studies also attest to five-membered ring nitroxides being less effective in nitroxide-mediated polymerization than equivalently substituted six-membered ring nitroxides.³⁸⁻⁴⁰

For the compounds 4a and 5a, the above-mentioned effects should, in part, be compensated for by the presence of more bulky substituents α to the nitroxide functionality (ethyl or methyl in 4a or spirocyclohexyl in **5a** vs dimethyl in TEMPO). However, the calculations indicate that values of D_{C-O} for the alkoxyamines based on the imidazolidinone nitroxides 4a and 5a are, in fact, still significantly less favorable than for the corresponding TEMPO-derived alkoxyamine, notwithstanding the above-mentioned substituent effect. This may simply indicate that factors other than differences in D_{C-0} are responsible for superior properties of these compounds (vide infra). However, because of the imprecision inherent in the calculations (which can be large when comparing markedly dissimilar structures), further work using higher order calculations is required to confirm this before definite conclusions are drawn.

The presence of a transannular alkyl substituent in 4b-d and 5b appears to significantly enhance the effectiveness of the imidazolidinone nitroxides (see Table 1). However, the nature of the alkyl group (whether methyl, n-butyl, or benzyl) does not appear to be significant. Molecular orbital calculations carried out for the N-methyl derivatives (see Table 5), in accord with the experimental results, indicate a lower D_{C-O} for these alkoxyamines than that for the corresponding N–H compounds. The transannular substituent is remote from the C–O bond undergoing homolysis, and there is no direct steric interaction with the O-alkyl. Examination of the optimized geometries predicted by the molecular orbital calculations shows that the substituent causes the five-membered ring to adopt a slightly more puckered geometry. It also interacts with the substituents α to nitrogen, forcing them into marginally closer proximity of the breaking C–O bond. These changes are reflected in small changes in the C–N bond length and a trend for D_{C-O} to decrease with an increase in the C-N bond length can be observed for the imidazolidinone nitroxides (see Table 5). In that



Figure 2. (a) Molecular weight distributions for polystyrene $(\bar{M}_n = 8800 \text{ and } \bar{M}_w/\bar{M}_n = 1.09)$ prepared by benzoyl peroxideinitiated polymerization of styrene in the presence of nitroxide **5b** at 130 °C and block copolymer formed with 4-methylstyrene (poly(styrene-*block*-4-methylstyrene) $\bar{M}_n = 36$ 900 and $\bar{M}_w/\bar{M}_n = 1.14$; for further details, see Experimental Section). (b) Molecular weight distributions for polystyrene ($\bar{M}_n = 8800$ and $\bar{M}_w/\bar{M}_n = 1.09$) prepared by benzoyl peroxide-initiated polymerization of styrene in the presence of nitroxide **5b** at 130 °C and block copolymer formed with *n*-butyl acrylate (poly-(styrene-*block-n*-butyl acrylate) $\bar{M}_n = 21500$ and $\bar{M}_w/\bar{M}_n = 1.29$; for further details, see Experimental Section).

the C–O and N–O bond lengths remain the same (within ± 0.001 Å), changes in the C–N bond length are directly related to changes in the C–O–N bond angle. Because steric congestion is relieved on C–O bond cleavage, such steric effects should also show up (possibly to a greater extent) in the entropy of activation.³⁸ There are some previous reports of remote substituents affecting the effectiveness of nitroxides in living radical polymerization.^{39,41,42} Yamada et al.³⁹ have shown that the presence of the transannular substituents in pyrrolidine nitroxides provide an enhanced rate of C–O homolysis and account for a faster rate of polymerization and a faster rate of polydispersity narrowing with conversion.

Polar solvents are known to enhance the rate of alkoxyamine C–O bond homolysis.^{5,38} A pertinent result is that the half-life for the cyanoisopropyl derivative of nitroxide **1** decreases from 38 min in *n*-hexane to 20 min in *N*,*N*-dimethylformamide.⁵ It is also noteworthy that several authors have attributed the mechanisms whereby various reagents (acylating agents⁴³ or acids⁴⁴) accelerate the rate of nitroxide-mediated polymerization to a solvation effect. It is possible that the greater effective-

ness of the imidazolidinone nitroxides is a related phenomenon.

It is also known that faster rates of polymerization may result if there is a mechanism that leads to the destruction of the excess nitroxide formed during the course of polymerization. The mechanism for destruction may involve reaction with an added reagent^{27,43,45–47} or it may be due to the inherent instability of the nitroxide.^{48,49} Available data provide no indication that the imidazolidinone nitroxides are inherently unstable under the conditions used in polymerization.

It is intended that the measurement of rate constants and Arrhenius parameters for the association-dissociation equilibria between the imidazolidinone (and other) nitroxides and the propagating species will form part of our future work, which is aimed at gaining a better understanding of the mechanism.

Another factor that may be responsible for the narrower polydispersities and higher rates of polymerization found with the imidazolidinone nitroxides is a lower incidence of the side reactions which lead to a build-up in the nitroxide concentration. A particular concern is disproportionation between the propagating species and nitroxide.^{31,50,51} Fischer³⁴ has employed kinetic simulation to examine nitroxide-mediated polymerization in some detail. He calls such disproportionation "the most deteriorating side process that we have found so far". Recent work by Gridnev⁵² indicates that the ratio of disproportionation (hydrogen transfer from the propagating radical to the nitroxide; see Scheme 2) to combination during styrene polymerization at 90 °C is approximately 3-fold lower in the case of the tetramethylimidazolidinone nitroxide (**9**; R^1 , R^2 , R^3 , $R^4 = Me$) than it is for TEMPO (2). Analysis by kinetic simulation of MMA polymerizations³¹ indicate that the finding that five-membered ring nitroxides (in particular, 1, 4a, and 5a) provide narrower polydispersities and higher conversions can be explained in terms of a lower disproportionation-combination ratio.

Conclusions

Imidazolidinone nitroxides (e.g., 4 and 5) offer significant advantages over many of the nitroxides previously employed in nitroxide-mediated polymerization: homopolymers, statistical copolymers, and block copolymers can be synthesized with controlled molecular weight, narrow molecular weight distribution, and defined end group functionality. With appropriate selection of the substituents, the use of the imidazolidinone nitroxides offers lower polydispersities and better living character than those of, for example, TEMPO (2). Further advantages are that (a) the nitroxides are synthesized from readily available precursors by a simple experimental route; (b) they are subject to fewer side reactions (e.g., disproportionation of propagating radical with nitroxide or chain transfer to nitroxide); and (c) they are involatile, which provides an advantage over some commonly used nitroxides (i.e., TEMPO and di-tert-butylnitroxide) that are odorous.

Supporting Information Available: GPC traces obtained with (a) refractive index detection and (b) UV (254 nm) detection for polystyrene ($\bar{M}_n = 8800$, $\bar{M}_w/\bar{M}_n = 1.09$) prepared by benzoyl peroxide-initiated polymerization of styrene in the presence of nitroxide **5b** at 130 °C and block copolymer formed with *n*-butyl acrylate (poly(styrene-*block-n*-butyl acrylate) $\bar{M}_n = 21500$, $\bar{M}_w/\bar{M}_n = 1.29$). This material is available free of charge via the Internet at http://pubs.acs.org.

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