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SG1 Nitroxide-Mediated Polymerization of Isoprene: Alkoxyamine Structure/Control Relationship and α,ω−Chain-End Functionalization

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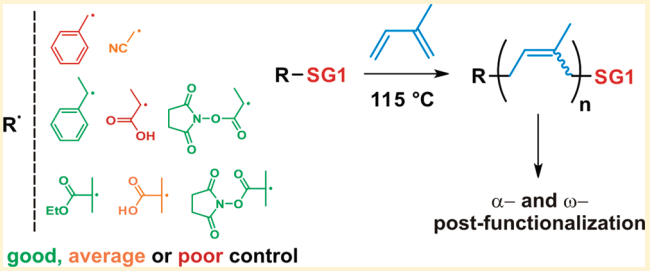
Supporting Information

ABSTRACT: Nitroxide-mediated polymerization of isoprene was carried out at 115 °C using a small library of SG1-based alkoxyamine initiators. Well-defined polymers were obtained, with no need to add free SG1. Efficient postfunctionalization reactions in α- (reaction of ethylene diamine with a succinimidyl-ester-functional initiator) and ω-positions (replacement of SG1 by benzyl trithiocarbonate) were demonstrated. Polymerizations mediated by alkoxyamines with tertiary initiating groups were observed to follow first order kinetics with respect to monomer, with number-average molecular weights (M_n) approximately 77% of theoretical M_n ($M_{n,theo}$). Use of alkoxyamines with primary and secondary initiating groups gave 2/3 order kinetics with respect to monomer and slightly lower molecular weights ($M_{n,exp} \sim 0.61 \times M_{n,theo}$). At higher conversions, the polydispersity of all polyisoprenes approached 1.1. At low conversions, however, significant differences in polydispersity were observed, indicating differences in the rate of consumption of the initiators. Significantly, the alkoxyamines with propionic acid and isobutyric acid initiating groups were consumed substantially more slowly than their ester analogues or even cyanomethyl-SG1. This may be a result of intramolecular hydrogen bonding between the acid and phosphonate groups of the initiators.



INTRODUCTION

Among polymers that are accessible by controlled/living radical polymerization (CLRP), poly(1,3)-dienes such as polyisoprene are unusual for their inclusion of double-bond functionality in the polymer backbone. This imparts interesting properties such as chemical,[1−3] enzymatic[4] and bacterial[5] degradability, and potential for subsequent functionalization.[6−9] The unsaturated hydrocarbon structure of polyisoprene and polybutadiene is strongly hydrophobic, while their low glass transition temperatures (T_g) allow surfactants with long polydiene chains to be directly dissolved in water.[10] Thus, these polymers are a natural choice for use as the lipophilic component of surfactants.[9−13] Additionally, isoprene is the basic structural motif of naturally occurring terpenes such as squalene, retinol or vitamin E, which are biocompatible compounds, therefore suggesting that synthetic polyisoprenes of controlled structure may have interesting biomedical applications analogous to those recently developed for squalene.[14−17]

Despite these enticing properties, the CLRP of 1,3-dienes presents numerous experimental challenges. Although anionic polymerization is unsurpassed in terms of the structural control that can be achieved,[10,13] it is highly sensitive to air and electrophilic or acidic impurities. In contrast, radical polymerization is tolerant of a much greater range of functionalities, but pressurized equipment is needed to handle butadiene and isoprene at the elevated temperatures required for polymerization at a reasonable rate. Perhaps for this reason, reports related to CLRP of isoprene are rather scarce.

Of the common CLRP techniques, atom transfer radical polymerization (ATRP)[18−20] cannot be applied due to chelation of the copper catalyst by the isoprene.[21] There have been several recent reports of RAFT polymerization of isoprene,[12,21−23] but the most commonly used technique remains nitroxide-mediated polymerization (NMP).[3,11,24−30] Early studies on NMP of isoprene produced relatively polydisperse polymers (PDI of 1.36−1.53).[26,27] A major advance was reported by Hawker and co-workers[30] in 2000 with the use of a TIPNO-based initiator, 2,2,5-trimethyl-3-(1′-phenylethoxy)-4-phenyl-3-azahexane (Figure 1, **1**), in place of the TEMPO (Figure 1, **2**) employed by previous researchers.[26−29] This allowed production of polyisoprenes and polybutadienes with number-average molar masses up to 100 000 g mol^{-1} and polydispersities typically as low as 1.1−1.2.

In 2000, a new nitroxide was introduced, *N*-*tert*-butyl-*N*-[1-diethylphosphono-(2,2-dimethylpropyl)] nitroxide, termed SG1 (Figure 1, **3**).[31] Initiators containing the SG1 moiety, such as BlocBuilder MA (Figure 2, **4g**) have high dissociation rate constants[32] allowing excellent control over styrene[33] and acrylate polymerizations.[34] To our knowledge, however, there has been only one report on the use of SG1 as a control agent for the polymerization of isoprene.[35] In that work, only chain-extension of a poly(*tert*-butyl acrylate)-SG1 macroinitiator with isoprene was reported with no kinetic investigation.

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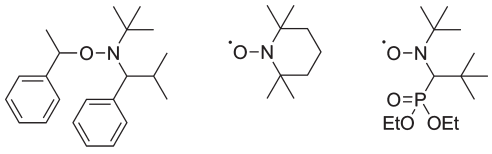

Figure 1. Structure of the 2,2,5-trimethyl-3-(1′-phenylethoxy)-4-phenyl-3-azahexane alkoxyamine (**1**), the TEMPO nitroxide (TEMPO, **2**) and of the *N*-*tert*-butyl-*N*-[1-diethylphosphono-(2,2-dimethylpropyl)] nitroxide (SG1, **3**).

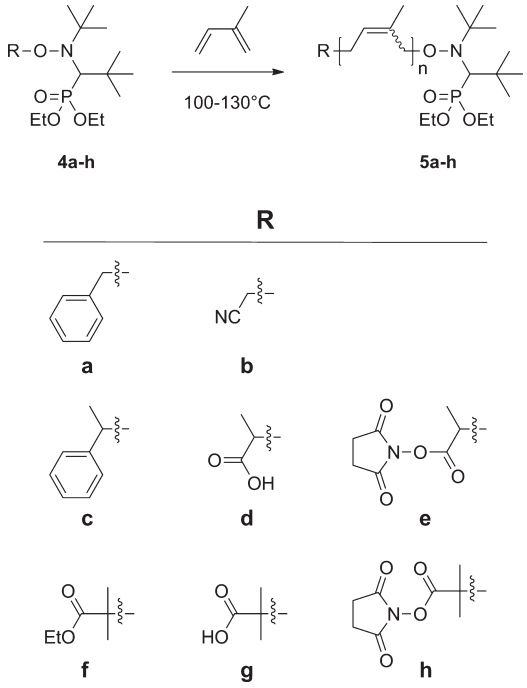

Figure 2. Nitroxide-mediated polymerization of isoprene from SG1-based alkoxyamine initiators.

In the present study, we report on the effects of temperature, initiator concentration, and initiator structure on the preparation of polyisoprenes from a range of SG1-based initiators containing primary, secondary or tertiary initiating groups with various functionalities (Figure 2), in order to extract an alkoxyamine structure/control relationship. In addition, both α- and ω-chain-end functionalization is reported to demonstrate the flexibility of the method. To the best of our knowledge, this is the first comprehensive kinetic investigation of the NMP of isoprene together with the functionalization of the derived polymers.

EXPERIMENTAL SECTION

Materials. Isoprene (99%) was obtained from Aldrich and distilled before use. BlocBuilder MA^{TM} (**4g**, 99%) and dibenzyl trithiocarbonate (99%) were supplied by Arkema and used as received. Alkoxyamines **4a**−**4d** and **4f** were prepared according to a published method.[36] Alkoxyamines **4e** and **4h** were prepared from **4d** and **4g** according to a published method.[34,37]

Nuclear Magnetic Resonance Spectroscopy (NMR). NMR spectroscopy was performed in 5 mm diameter tubes in $CDCl_3$ at 25 °C. ^{1}H and ^{13}C NMR spectroscopy was performed on a Bruker Avance 300 spectrometer at 300 MHz (^{1}H) or 75 MHz (^{13}C). The chemical shift scale was calibrated on the basis of the solvent peak (δ = 7.26 and 77.0 ppm, respectively). ^{31}P NMR spectroscopy was performed on a Bruker 200 spectrometer at 81 MHz. The chemical shift scale was calibrated relative to an external standard (85% H_3PO_4).

Table 1. Polyisoprenes Prepared at Varying Ratios of Isoprene:4g for 16 h at 115 °C

isoprene:**4g**	$[\mathbf{4g}]_0$ (mM)	conversion[a]	k' (h^{-1})[b]	$M_{n,theo}$[c]	M_n[d]	PDI[d]
50:1	2.00	0.55	0.049	2240	2110	1.13
100:1	1.00	0.41	0.037	3170	2780	1.15
200:1	0.50	0.35	0.025	5080	3350	1.13
496:1	0.20	0.28	0.021	9930	6010	1.19
992:1	0.10	0.19	0.013	13 400	8350	1.20

[a] Determined by gravimetry. [b] Apparent rate constant, $k' = -\ln(1-\text{conversion})/t$. [c] $M_{n,theo} = [\text{isoprene}]/[\mathbf{4g}] \times \text{conversion} \times MW_{isoprene} + MW_{\mathbf{4g}}$. [d] Determined by SEC, calibrated with PS standards and converted to PI using MHS constants from ref 38.

Size Exclusion Chromatography (SEC). SEC was performed at 30 °C with two columns from Polymer Laboratories (PL-gel MIXED-D; 300 × 7.5 mm; bead diameter 5 mm; linear part 400 to 4 × 10^5 g mol^{-1}) and a differential refractive index detector (SpectraSystem RI-150 from Thermo Electron Corp.). The eluent was chloroform at a flow rate of 1 mL min^{-1} and toluene was used as a flow-rate marker. The calibration curve was based on polystyrene (PS) standards (peak molar masses, M_p = 162−523 000 g mol^{-1}) from Polymer Laboratories. A polyisoprene (PI) calibration curve was constructed by converting the PS standard peak molecular weights, M_{PS}, to PI molecular weights, M_{PI}, using Mark−Houwink−Sakurada (MHS) constants determined for both polymers in CCl_4 at 25 °C (eq 1).[38] For PI, the MHS constants used were K_{PI} = 2.44 × 10^{-4} and α_{PI} = 0.712. For PS, K_{PS} = 7.1 × 10^{-4} and α_{PS} = 0.54 (MW < 16 700 g mol^{-1}) or K_{PS} = 1.44 × 10^{-4} and α_{PS} = 0.713 (MW ≥ 16 700 g mol^{-1}).

$$K_{PI}M_{PI}^{\alpha PI} = K_{PS}M_{PS}^{\alpha PS} \quad (1)$$

This technique allowed M_n (the number-average molar mass), M_w (the weight-average molar mass), and M_w/M_n (the polydispersity index, PDI) to be determined. Further details of molecular weight determination, and polystyrene-equivalent weights and polydispersities are provided in the Supporting Information.

Polymerization of Isoprenes 5a−h. In a typical procedure, **4a** (100 mg, 0.26 mmol) was placed in a 15 mL capacity pressure tube (Ace Glass 8648−164) fitted with a plunger valve and thermowell. Isoprene (2.6 mL, 1.77 g, 26 mmol) was added and the tube was subjected to three cycles of freeze−thaw degassing, then backfilled with argon. The tube was placed in an oil bath at 115 °C for 2 h and then cooled to room temperature by placing in a bath of cold water. The contents of the tube were transferred to a preweighed flask and weighed. Unreacted isoprene was removed *in vacuo* at 30 °C and the residual polyisoprene and any unreacted alkoxyamine, which has negligible volatility at this temperature, were weighed. The conversion of isoprene was calculated from the following formula: conversion = $(m_{residue}/m_{total} - X_{4a})/(1 - X_{4a})$, in which $m_{residue}$ is the mass of polyisoprene after drying, m_{total} is the mass of the contents of the tube, and X_{4a} is the mass fraction of **4a** in the original reaction mixture (X_{4a} = 0.1/(1.77 + 0.1) = 0.053). Samples of polyisoprene were analyzed by NMR and SEC.

Identical pressure tubes were prepared, degassed and allowed to react for 4, 8, and 16 h in order to trace the evolution of M_n and isoprene conversion with time.

A similar procedure was followed for all bulk isoprene polymerizations, with appropriate changes in the volume of isoprene added to preserve an isoprene:**4** molar ratio of 100:1.

The relative proportions of 1,2, 3,4, and 1,4 addition were determined by comparing the intensities of peaks corresponding to the vinylic

Table 2. Polyisoprenes Produced by Nitroxide-Mediated Polymerization at 115 °C for 16 h

alkoxyamine[a]	k_d (120 °C, s^{-1})[b]	conversion[c]	$M_{n,theo}$ (g mol^{-1})	M_n (g mol^{-1})[d]	PDI (g mol^{-1})[d]	$M_{n,NMR}$ (g mol^{-1})[e]
4a	3.3×10^{-4}	0.37	2940	2070	1.16	2570
4b	2.0×10^{-4}	0.42	3240	2220	1.11	*f*
4c	5.5×10^{-3}[g]	0.39	3080	2130	1.10	2580
4d	5.3×10^{-4}, 1.0×10^{-3}[h]	0.36	2780	2330	1.17	*f*
4e	*i*	0.40	3000	2110	1.10	2590
4f	*i*	0.35	2770	2410	1.10	*f*
4g	0.28	0.41	3400	2780	1.15	*f*
4h	5	0.44	3260	2390	1.13	2910

[a] Ratio of isoprene:**4** = 100:1. [b] Dissociation rate constant: data from ref 32 (**4a**−**g**) and ref 34 (**4h**). [c] Measured by gravimetry. [d] Determined by SEC, calibrated with PS standards and converted to PI using MHS constants from reference.[38] [e] Calculated from integration of ^{1}H NMR spectrum of isolated polymer. [f] ^{1}H NMR spectrum unsuitable for determination of M_n. [g] Both diastereomers show the same rate constant. [h] Diastereomers have different rate constants. [i] No data available.

protons of the polymer in the region 4.5−6.0 ppm, viz. −C*H*═CH_2 (1,2-addition) at 5.6−5.9 ppm, −C*H*═$C(CH_3)$− (1,4-addition) at 5.0−5.5 ppm, and the mixture of −$C(CH_3)$═CH_2 (3,4-addition) and −CH═CH_2 (1,2-addition) at 4.4−5.0 ppm.[23] Analysis of eight polyisoprene samples prepared using initiators **4a**−**4h** gave the following proportions: 1,2-addition, 6.0% ± 0.9%; 1,4-addition, 81.2% ± 1.0%; 3,4-addition, 12.8% ± 1.8%. These values are similar to those obtained by previous researchers in RAFT[23] and NMP[3,11,39] of isoprene. The resonance at 5.0−5.5 ppm was also used to determine the M_n of polymers **5a** and **5c** (aromatic end groups) and **5e** and **5h** (succinimidyl end groups) (Table 2). The area of this resonance ($A_{1,4}$, 0.81 H/isoprene unit) was compared to the area of the resonance due to the aromatic protons (**5a** and **5c**, A_{Ar}, δ 7.0−7.5 ppm, 5H) or the succinimidyl ring protons (**5e** and **5h**, A_{Su}, δ 2.8 ppm, 4H). It was not possible to perform a similar analysis on **5b**, **5d**, **5f**, and **5g** due to the absence of suitably isolated end group peaks.

Reaction of 5h with Ethylene Diamine. Amine-functionalized polymers were prepared by dissolving 50 mg of polyisoprene **5h** (M_n = 900 g mol^{-1}, PDI = 1.13, 0.056 mmol) in 1 mL of CH_2Cl_2 then adding 0.1 mL of ethylene diamine (90 mg, 1.5 mmol, 27-fold excess). A white precipitate of *N*-hydroxysuccinimide formed. The mixture was stirred at room temperature for 1 h and then was diluted with CH_2Cl_2, washed twice with water and once with brine, and dried over $MgSO_4$. Solvent was removed *in vacuo*. The product (39 mg, 78%) was not characterized by SEC due to interactions of the NH_2 group with the column packing. Analysis by ^{1}H NMR showed the disappearance of the resonance at 2.83 ppm corresponding to the protons of the succinimidyl group of **5h**, and appearance of new peaks at 2.23 (*s*, 2H), 2.81 (*t*, *J* = 5.7 Hz, 2H), 3.27 (*t*, *J* = 5.6 Hz, 2H) and 6.17 (br *s*, 1H) ppm, assigned to the NH_2, CH_2NHCO, CH_2NH_2, and CH_2NHCO protons of the (2-aminoethyl)amide group, respectively.

Reaction of 5g with Benzyl Trithiocarbonate. Polyisoprene **5g** (M_n = 1890 g mol^{-1}, PDI = 1.13, 500 mg, 0.26 mmol) and benzyl trithiocarbonate (0.581 g, 2.0 mmol) were dissolved in toluene (1 g), degassed by bubbling with N_2 for 10 min, and heated to 90 °C for 16 h. The polymer was purified by precipitation in methanol and dried under vacuum. ^{1}H NMR analysis showed the disappearance of resonances at 3.2 and 3.8−4.2 ppm corresponding to the SG1 moiety, and the appearance of new resonances at 4.0 and 7.2−7.4 ppm corresponding to protons α to sulfur in the terminal isoprene unit and the aromatic protons of the benzyl trithiocarbonate group, respectively. Analysis by SEC: M_n = 2110 g mol^{-1}; PDI = 1.13.

RESULTS AND DISCUSSION

Determination of Appropriate Polymerization Temperatures. The first series of isoprene nitroxide-mediated polymerizations was undertaken using the commercially available initiator, BlocBuilder MA (**4g**), which has proven to be one of the most potent alkoxyamines developed so far.[40−45] The polymerizations were carried out at temperatures of 100, 115, and 130 °C. Isoprene and **4g** (**4g**:isoprene molar ratio = 1:100) were placed in a glass pressure tube equipped with a plunger valve and freeze−thaw degassed, then backfilled with argon. The tube was then placed in an oil bath at the required temperature for 2, 4, 8, or 16 h. Conversion was measured by gravimetry and the molar mass distribution of the polyisoprene produced was determined by SEC. Polymerization kinetics are typically governed by the persistent radical effect (PRE),[46] which results in the following power-law equation (eq 2) when the initial concentration of nitroxide $[Y]_0 = 0$.[33,47−49]

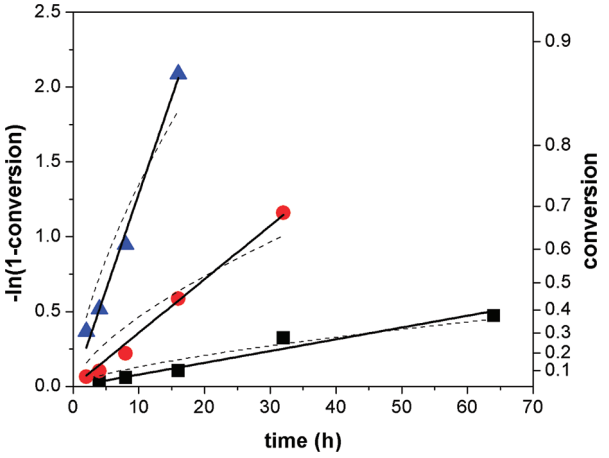

Figure 3. ln[1/(1 − conversion)] vs time plot of **4g**-mediated isoprene polymerizations at 100 (■), 115 (●), and 130 °C (▲). Solid lines show best linear fit (−ln(1-conversion) = *at*) to each data set; dashed lines show best fit to Fischer's PRE model (−ln(1-conversion) = $at^{2/3}$).[46]

$$-\ln(1-\text{conversion}) = 3/2k_p(k_d[I]_0/3k_ck_t)^{1/3}t^{2/3} \qquad (2)$$

with k_p, the propagation rate constant, k_d, the dissociation rate constant, $[I]_0$, the initial alkoxyamine concentration, k_c, the combination rate constant, k_t, the termination rate constant, and *t*, the time. In these polymerizations, however, the relationship between −ln(1-conversion) and *t* was linear at all temperatures (Figure 3) and poorly fitted by a 2/3-order relationship with respect to time (dashed lines in Figure 3). First order kinetics with respect to monomer have previously been observed in

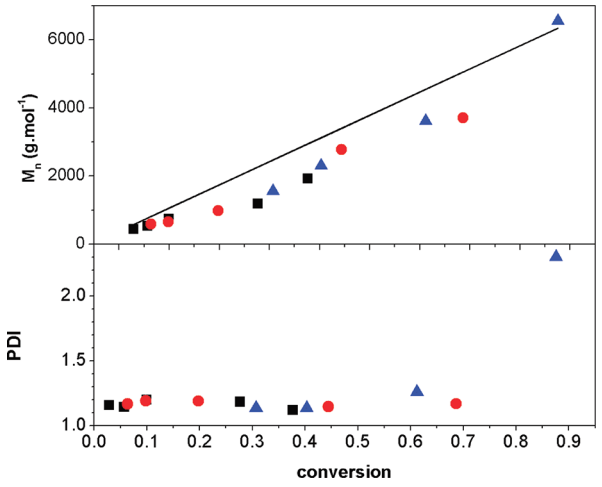

Figure 4. Evolution of the number-average molar mass, M_n and polydispersity index, M_w/M_n (PDI) with isoprene conversion for **4g**-mediated isoprene polymerizations at 100 (■), 115 (●), and 130 °C (▲). The line in the upper plot represents the theoretical molar mass, $M_{n,theo}$ = [isoprene]/[**4g**] × conversion × $MW_{isoprene}$ + MW_{4g}.

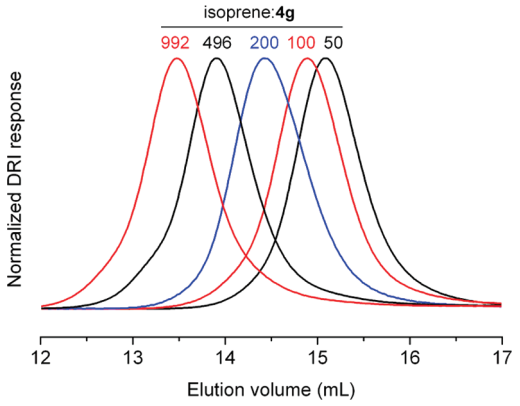

Figure 5. Final size exclusion chromatograms for the synthesis of polyisoprenes from **4g** prepared using different ratios of isoprene:**4g**. Polymerization conditions: 16 h at 115 °C.

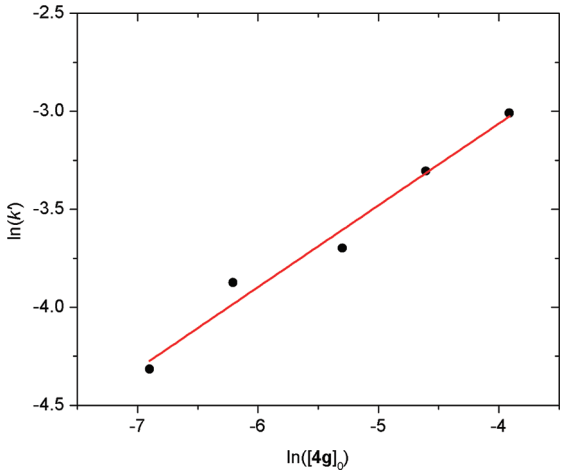

Figure 6. log−log plot of pseudofirst order rate constant of isoprene (k') vs initiator concentration ([**4g**]$_0$), showing line of best fit: ln(k') = 0.42 ln([**4g**]$_0$) − 1.4, R^2 = 0.970.

polymerizations of acrylic and styrenic monomers mediated by tertiary alkoxyamines, such as **4g**[50,51] and **4h**,[34] and are a result of the rapid dissociation of these alkoxyamines at polymerization temperatures. This results in a high initial radical flux, termination of nonpersistent radicals, and generation of a significant concentration of free SG1 in the early stages of polymerization. The resulting kinetics are similar to those of a polymerization performed in the presence of an initial excess of persistent radicals which is large enough that the persistent radical concentration remains essentially unchanged throughout the polymerization. The kinetics of polymerization under these conditions are given by eq 3,[46,49] in which K is the activation−deactivation equilibrium constant. This equation is linear with respect to time, in accordance with observation.

$$-\ln(1 - \text{conversion}) = k_p K([I]_0/[Y]_0)t \quad (3)$$

Polymerization at 130 °C was relatively rapid, with 88% conversion achieved after 16 h. The number-average molar mass, M_n, increased with conversion, but control over the polymerization was lost after approximately 60% conversion; polydispersity ranged from 1.13 in the early stages of the reaction to 2.30 after 16 h (Figure 4). Good control over molar mass and polydispersity was achieved throughout the reaction at temperatures of 115 and 100 °C. A linear relationship between molar mass and conversion was observed, while polydispersities remained below 1.2. The rate of polymerization was very low at 100 °C however, requiring 64 h to reach 38% conversion. At 115 °C, the same conversion was reached after only 16 h and 69% conversion was achieved after 32 h reaction. Thus, a reaction temperature of 115 °C provides a controlled polymerization at an acceptable rate of reaction.

Effect of Alkoxyamine Concentration. Subsequently, polyisoprenes with molar masses ranging from 2 000 to 8 500 g mol^{-1} and polydispersities of 1.13−1.20 (Table 1, Figure 5) were prepared by heating isoprene for 16 h at 115 °C in the presence of varying amounts of **4g**. Number-average molar masses were 62−94% of the theoretical M_n. The discrepancy between theoretical and experimental molecular weight increased with the molecular weight of the polymer. A slight increase in polydispersity was also observed, which may indicate limited occurrence of irreversible termination reactions and/or some chain transfer to monomer or polymer.

The rate of polymerization increased in a nonlinear manner with the concentration of **4g** (Table 1). The conversion after 16 h was used to derive the apparent rate constant, k' at each initiator concentration (from the equation $-\ln(1\text{-conversion}) = k't$). A plot of ln($k'$) against ln([**4g**]) (Figure 6) gave a straight line with gradient 0.42, indicating that the rate of polymerization is proportional to [**4g**]$^{0.42}$. This unusual dependence of the rate on the initiator concentration may be due to the changing rate constants of alkoxyamine dissociation, radical-SG1 recombination and bimolecular termination, all of which depend on the polymer chain length and change by orders of magnitude as the 2-methyl-2-propionic acid radicals generated by dissociation of **4g** are converted into polyisoprenyl radicals. To our knowledge, this is the first study of the rate dependence on initiator concentration for rapidly dissociating alkoxyamines such as **4g**. Further studies will be required to determine whether the order observed here is specific to polymerizations of isoprene or a general feature of these polymerizations.

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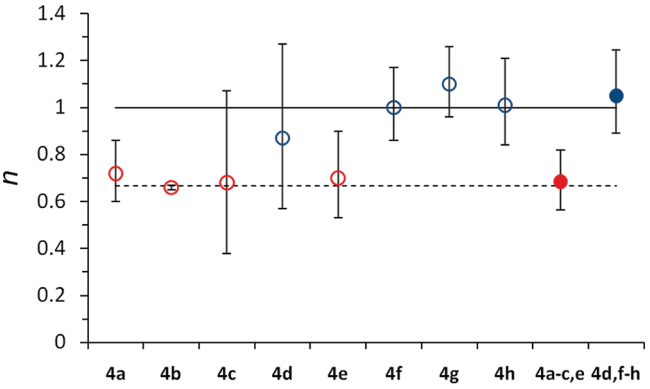

Figure 7. Point estimates and 95% confidence intervals for the value of the exponent, n, when conversion vs time, t, data of polymerizations mediated by **4a**−**h** were fitted to equations of the form $-\ln(1\text{-conversion}) = at^n$. Filled circles represent combined data sets for primary and secondary alkoxyamines **4a**−**c** and **4e** and the acid-functionalized secondary alkoxyamine and tertiary alkoxyamines **4d** and **4f**−**h**. Solid and dashed lines represent $n = 1$ and $n = 2/3$, respectively.

Influence of the Initiating Moiety. The effectiveness of a range of SG1-based alkoxyamines carrying different initiating moieties was evaluated by carrying out the polymerization of isoprene at 115 °C in the presence of alkoxyamines **4a**−**h**. After 16 h, all polymerizations had reached approximately 40% conversion and polyisoprenes with M_n of 2−3 × 10^3 g mol^{-1} and polydispersities of 1.10−1.17 were produced (Table 2).

Additional polymerizations were carried out with each initiator and stopped after 2, 4, and 8 h. The conversion vs t data was then fitted to curves of the form $-\ln(1\text{-conversion}) = at^n$. The best fit values (with 95% confidence intervals) of the exponent n for each initiator are shown in Figure 7. The primary and secondary alkoxyamines **4a**−**c** and **4e** gave values of n close to 2/3, consistent with the PRE model (eq 2). Tertiary alkoxyamines **4f**−**4h** and the secondary acid-functional amine **4d** gave values of n close to 1, indicating a nearly constant persistent radical concentration throughout the polymerization (eq 3). This is consistent with results obtained in previous work on polymerization of styrenic and acrylic monomers mediated by secondary[33] or tertiary[34,50,51] SG1 alkoxyamines.

Combining the data for **4a**−**c**/**4e** and **4d**/**4f**−**h** allowed the values of n to be estimated with greater precision, yielding 95% confidence intervals of 0.57−0.82 (point estimate 0.69) for **4a**−**c**/**4e** and 0.89−1.25 for **4d**/**4f**−**h** (point estimate 1.05).

The number-average degree of polymerization, DP_n, increased with conversion for all initiators (Figure 8a). As for the kinetics, however, polymerizations controlled by the tertiary alkoxyamines **4f**−**h** and the acid-functionalized secondary alkoxyamine **4d** behaved differently to the remaining primary and secondary initiators **4a**−**c** and **4e**. In polymerizations initiated by the first group of alkoxyamines, the measured M_n was approximately 25% lower than the theoretical M_n. The polymerizations of the second group gave measured M_n approximately 40% lower than the theoretical M_n. The higher molecular weights obtained with the first group of alkoxyamines may be due to a high level of termination in the early stages of the reaction, resulting in a buildup of free SG1 and establishment of a linear $\ln[1/(1\text{-conversion})]$ vs t relationship as discussed above. The remaining discrepancy between theoretical and experimental M_n in all samples may be due to a number of factors, including error in the SEC calibration,

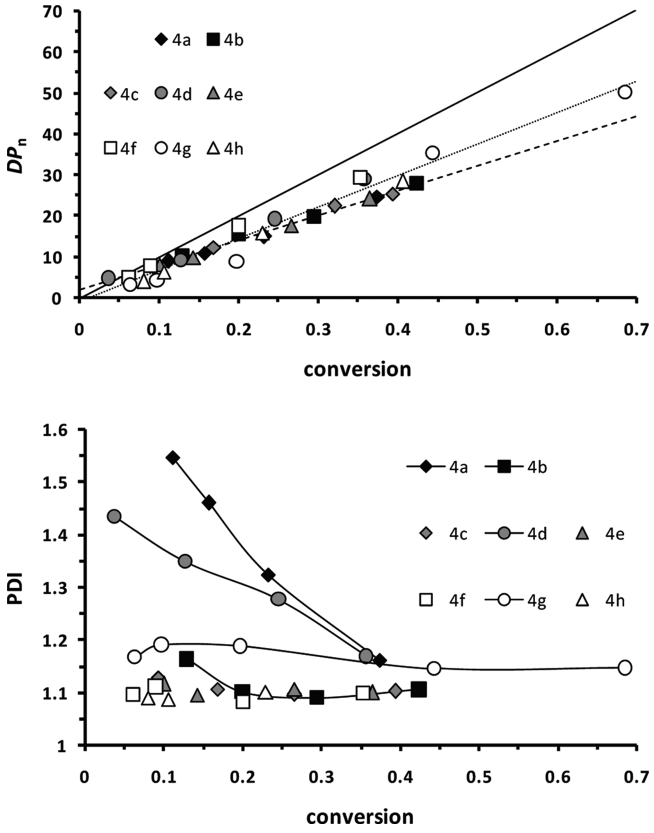

Figure 8. Evolution of the number-average degree of polymerization, DP_n (a) and the polydispersity index, M_w/M_n (b), with isoprene conversion for the polymerization of isoprene initiated by alkoxyamines **4a**−**h**. The solid line in part a represents the theoretical degree of polymerization, given by $DP_{n,theo}$ = [isoprene]/[**4**] × conversion. The dashed line represents the best fit to alkoxyamines **4a**−**c** and **4e** (1° and 2° nonacid initiating groups) and is given by $DP_n = 60.8 \times DP_{n,theo} + 1.9$. The dotted line represents the best fit to the remaining alkoxyamines **4d** and **4f**−**h** (acid and 3° alkoxyamines) and is given by $DP_n = 76.6 \times DP_{n,theo} - 0.8$.

band broadening during SEC[52] and chain transfer to monomer or polymer.

For alkoxyamines with aromatic or succinimidyl substituents (**4a**, **4c**, **4e**, and **4h**), ^{1}H NMR provided an alternative method for the determination of M_n. Comparison of the area of the resonances of the α-end group with the area of the vinylic proton resonance of the polyisoprene repeat unit allowed determination of the DP_n and hence the M_n. These values, shown in Table 2, are intermediate between the theoretical molecular weight and the SEC results. This method could not be used for alkoxyamines **4b**, **4d**, **4f**, and **4g** due to the lack of suitable end group resonances in the ^{1}H NMR spectrum.

Significant differences in the polydispersity of polyisoprenes produced by the different alkoxyamines were observed at lower conversions. Alkoxyamines **4a** and **4b**, which contain primary initiating groups (Bn and CH_2CN, respectively) are slow to dissociate relative to the corresponding polyisoprenes **5a** and **5b**, and produce polymers with relatively high polydispersity in the early stages of polymerization (Figure 8b). In polymerizations initiated by **4a**, a shoulder corresponding to unreacted alkoxyamine is still evident in the SEC trace after 16 h of polymerization. This may be contrasted with the more labile 2° and 3°

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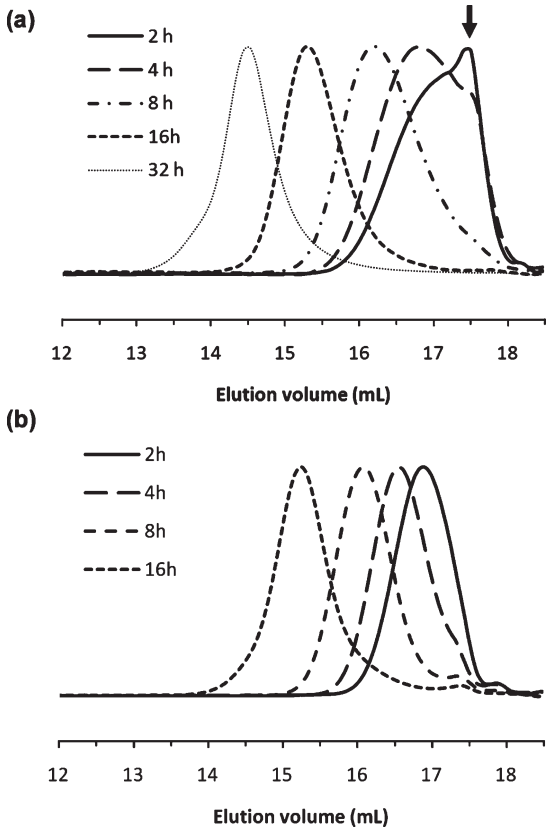


Figure 9. Normalized SEC traces of polyisoprene initiated by **4g** (a) and **4h** (b) in bulk at 115 °C. The arrow indicates the peak/shoulder corresponding to unreacted **4g**.

alkoxyamines **4c**, **4e**, **4f**, and **4h**. Polymerizations mediated by these alkoxyamines show PDI of about 1.1 throughout the polymerization, suggesting that dissociation of these alkoxyamines is rapid relative to dissociation of the dormant polyisoprenes **5c**, **5e**, **5f**, and **5h**. It is interesting to note that while the dissociation rate constant of **4a** is 1.7 times higher than that of **4b** (Table 1), **4b** provides substantially better control over the polymerization. This indicates that the electrophilic cyanomethyl radical reacts more rapidly with isoprene than the neutral or slightly nucleophilic benzyl radical. While rate constants for the addition of these radicals to isoprene have not been measured, the rate constant of addition of the cyanomethyl radical to styrene, a similarly electron-rich olefin, is 600 times greater than the analogous addition of the benzyl radical (6.6×10^5 L mol^{-1} s^{-1} vs 1.1×10^3 L mol^{-1} s^{-1} at 300 K).[46]

Acid-Functional Alkoxyamines. Polymers produced using the acid functional initiators **4d** and **4g** show higher than expected polydispersities given their 2° or 3° structure and known dissociation constants. This is particularly evident in the case of **4g**, whose dissociation constant has been measured to be 0.28 s^{-1} at 120 °C.[32] This corresponds to a half-life of 2.5 s at that temperature. Despite this short half-life, a low molar mass shoulder corresponding to unreacted alkoxyamine remains visible in the SEC trace of polyisoprene initiated by **4g** after 4 h at 115 °C (Figure 9a and Figure S2). The 2° alkoxyamine **4d** shows a similar evolution of molar mass, suggesting slow initiation of polyisoprene by the 2-propionic acid radical. These acid-functional initiators present a marked contrast with regard to their corresponding succinimidyl esters, **4e** and **4h** (Figure 9b), or the ethyl

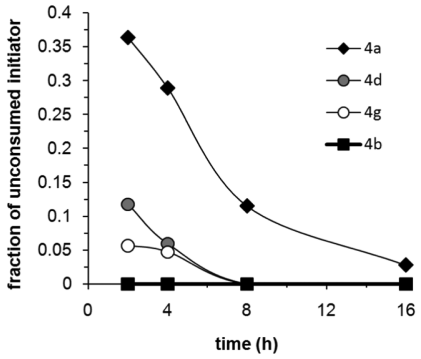
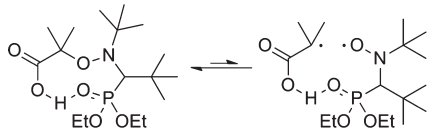


Figure 10. Fraction of unconsumed initiator (determined by integration of ^{31}P NMR spectra) as a function of time at 115 °C for polymerizations of isoprene initiated by **4a**, **4b**, **4d** and **4g**.

Scheme 1. Hypothesized Recombination of 4g Enhanced by Intramolecular Hydrogen Bonding



ester **4f**, which are rapidly consumed and provide polyisoprene with PDI about 1.1 throughout the reaction.

Phosphorus-31 NMR spectra of the isolated polymers (after evaporation of unreacted isoprene) revealed resonances corresponding to unreacted initiator which were clearly distinguished from those of polyisoprene-SG1. Integration of the NMR spectra revealed that, as indicated by the evolution of PDI, the rate of consumption of initiator increased in the order **4a** < **4d** < **4g** < **4b** (Figure 10). Initiators **4b, 4c, 4e, 4f** and **4h** were completely converted to polyisoprene after 2 h at 115 °C.

This result is unexpected, as there is no obvious reason why the acid-functionalized initiators should be consumed so much more slowly than their ester analogues. The measured rates of dissociation of **4d** and **4g** are respectively 2.5−5× and 1000× greater than that of **4b** (Table 2). These measurements were carried out in *t*-butyl benzene,[32] a solvent of similar polarity to isoprene, and solvent effects on the dissociation of **4g** are known to be small.[53,54] The other reactions that can affect the rate of consumption of **4** are the rate of addition of the radical to isoprene, k_i, and the rate of recombination of the radical and SG1 to reform **4**. While the former reaction is unlikely to be greatly affected by the presence of a carboxylic acid in place of an ester, the latter reaction may be accelerated as a result of intramolecular hydrogen bonding between the carboxylic acid and the phosphonate (Scheme 1). This would effectively convert the recombination reaction to a unimolecular reaction, leading to an increased rate of recombination relative to ester initiators of similar structure.

Evidence of an interaction between the acid and phosphonate groups is obtained from ^{31}P NMR. The ^{31}P chemical shifts of **4d** ((*R*,*R*) and (*R*,*S*) diastereomer) and **4g** are shifted downfield by 2−3 ppm relative to the other initiators in this study, which otherwise show little variation (Figure 11a). A slight concentration dependence of the chemical shift is observed (Figure 11b), with the peak moving even further downfield as the concentration decreases. This suggests an *intra*molecular interaction,

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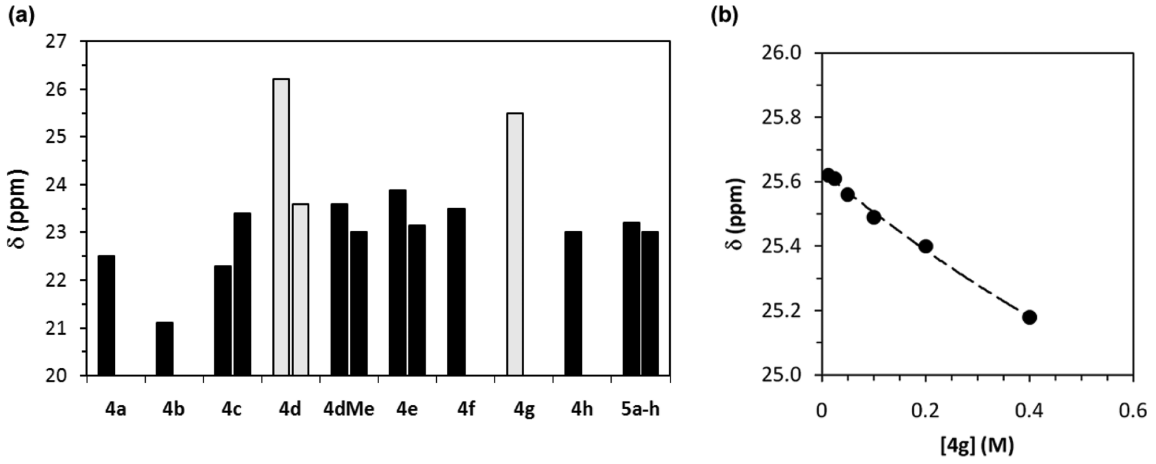
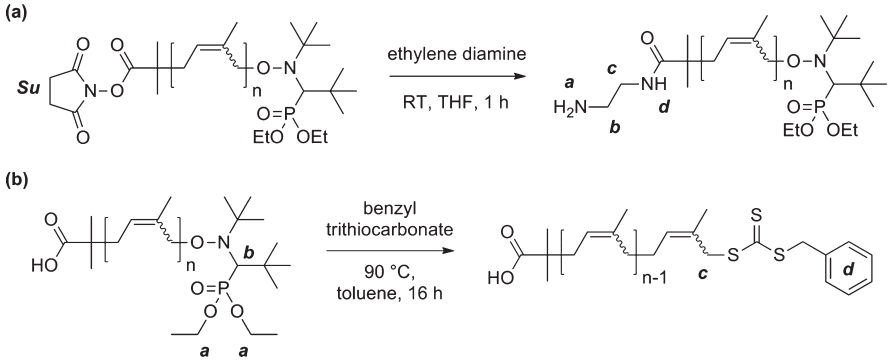


Figure 11. ^{31}P NMR chemical shifts of SG1-based alkoxyamines **4a**−**h** (**4dMe** represents the methyl ester of **4d**—data from ref 55) and polyisoprenes **5a**−**h** (a). The acid-functionalized initiators **4d** and **4g** are highlighted. Dual values shown for **4c**−**4e** represent (*R*,*R*) and (*S*,*S*) diastereomers (left) and (*R*,*S*) and (*S*,*R*) diastereomers (right) (assignments from ref 55 (**4c**, **4d**, **4dMe**) and ref 37 (**4e**)). The ^{31}P NMR spectrum of polyisoprene **5a**−**h** consists of two broad overlapping peaks centered on 23.2 and 23.0 ppm. Concentration dependence of ^{31}P NMR spectrum of **4g** (b).

Scheme 2. Functionalization of Polyisoprenes in α (a) and ω (b) Positions (Letters in Italics Correspond to Labeled Peaks in NMR Spectra, Figures 12 and 13)



as an *inter*molecular interaction would become weaker as the concentration decreases, producing an upfield shift in the peak position. The observed concentration dependence may be due to the formation of carboxylic acid dimers at higher concentrations, reducing the availability of the acidic proton to form a hydrogen bond with the phosphonate. Further evidence of an intramolecular interaction is found in the large difference in chemical shift between the diastereomers of **4d**, suggesting that it is favored ((*R*,*R*) and (*S*,*S*) diastereomer) or disfavored ((*R*,*S*) and (*S*,*R*) diastereomer) by the steric effect of the methyl substituent. Hydrogen bonds are weak compared to covalent bonds, and thus the intramolecular hydrogen bonding observed at room temperature in $CDCl_3$ would be less favored at the polymerization temperature of 115 °C. However, this may be counterbalanced by the low polarity of isoprene which favors intramolecular hydrogen bonding, and the high pressure at which the polymerization is carried out, which would favor more compact cyclic structures over linear structures. Further studies will be required to determine the true extent of hydrogen bonding under polymerization conditions.

Functionalization of Polyisoprene in α and ω Positions. From a practical point of view, the good control provided by the

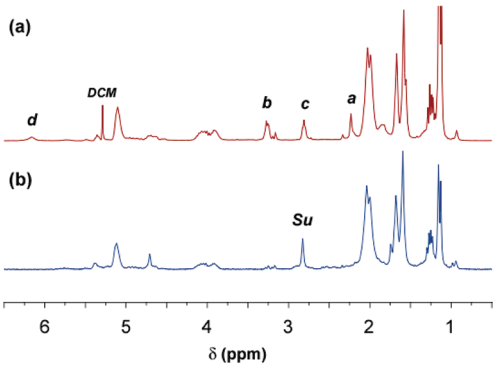


Figure 12. ^{1}H NMR spectra of polyisoprene initiated by **4h** after reaction with ethylene diamine (a), and prior to reaction (b) showing replacement of the resonance due to the succinimidyl ring protons (*Su*) by resonances due to protons from the (2-aminoethyl)amide group (*a*−*d*, see Scheme 2a for peak assignment).

succinimidyl esters **4e** and **4h** suggests their use as alternatives to the acid-functional initiators **4d** and **4g**. If an acid-functionalized polyisoprene is required, succinimidyl esters are readily

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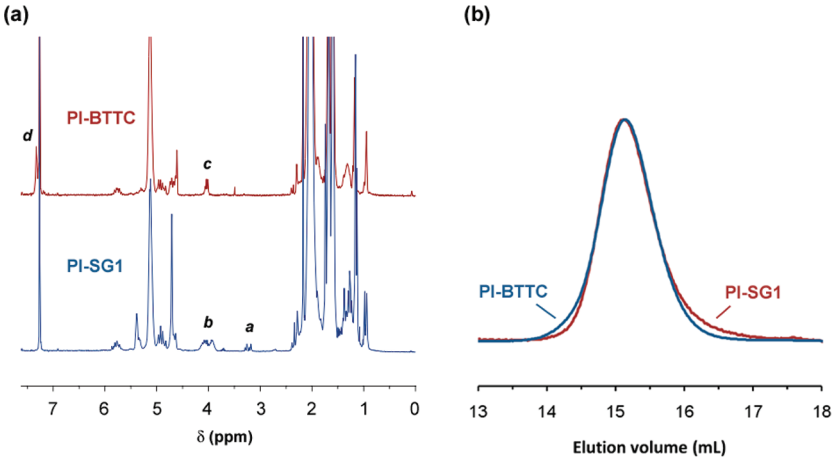

Figure 13. ^{1}H NMR spectra (a) and SEC traces (b) for polyisoprene **5g** (M_n = 1890 g mol^{-1}, PDI = 1.13) before (PI-SG1) and after (PI-BTTC) reaction with benzyl trithiocarbonate (M_n = 2112 g mol^{-1}, PDI = 1.13). Refer to Scheme 2b for assignment of peaks labeled *a*−*d*.

hydrolyzed to acids. On the other hand, acid-functional polymers are frequently employed in further conjugation reactions. Succinimidyl esters react readily with amines to form peptide linkages, and this reaction has previously been demonstrated on a range of substrates using acrylic and styrenic polymers deriving from CLRP.[34,37,56−58] When polyisoprenes synthesized from **4h** were allowed to react with ethylene diamine (Scheme 2), a change was observed in the ^{1}H NMR spectrum of the polymer, with disappearance of the resonance due to the succinimidyl ring protons at 2.8 ppm and appearance of new peaks corresponding to the protons from the (2-aminoethyl)amide group (Figure 12). These changes indicate the clean conversion of the succinimidyl ester to an aminoethyl amide and the introduction of amine functionality to the polymer.

Functionalization in the ω position was demonstrated by replacing the SG1 end group of a polyisoprene derived from **4g** (PI-SG1) with a benzyl trithiocarbonate group (PI-BTTC, Scheme 2). This was achieved by heating the polymer with a 10-fold excess of dibenzyl trithiocarbonate in toluene at 90 °C for 16 h.[59] The polymer was recovered by precipitation from methanol. Analysis by ^{1}H NMR revealed complete disappearance of peaks assigned to the SG1 moiety and the appearance of new resonances corresponding to the benzyl trithiocarbonate group. Size exclusion chromatography showed almost no change in the molecular weight distribution of the polymer (Figure 13b). A slight increase in M_n was observed, however, possibly due to a small amount of bimolecular termination leading to a slight high MW shoulder in the PI-BTTC sample, and loss of low-MW polyisoprene during precipitation from methanol.

Thus, we have demonstrated three methods for the introduction of functionality into SG1-mediated polyisoprenes: (i) either directly through use of a functional initiator such as **4d** or **4g**, (ii) by use of the succinimidyl ester functionalized initiators **4e** and **4h**, (iii) or by replacement of the SG1 moiety by a trithiocarbonate group. The introduction of ω-trithiocarbonate functionality opens the way to a wide range of functional polyisoprenes, as numerous techniques have been developed for the further transformation of polymers carrying this group.[60−62]

CONCLUSIONS

In this study, the nitroxide-mediated polymerization of isoprene was successfully controlled by alkoxyamine initiators based on the nitroxide SG1. An optimal balance between control over molar mass and rate of polymerization was achieved at 115 °C, which allowed conversions of ∼40% to be achieved in 16 h (isoprene:alkoxyamine = 100:1). Well-controlled polyisoprene was obtained without addition of extra SG1.

Alkoxyamines carrying primary, secondary and tertiary homolytic leaving groups were found to control the polymerization, providing polyisoprenes with very narrow polydispersities of approximately 1.1 throughout the reaction. It is interesting to note that polymerizations mediated by the alkoxyamine **4b** (R = CH_2CN), with the lowest dissociation rate constant of all alkoxyamines tested, were well-controlled, while those mediated by **4a** (R = $CH_2C_6H_5$) were poorly controlled, despite this alkoxyamine having a dissociation rate constant nearly twice that of **4a**. This demonstrates that a simple analysis of dissociation rate constants is not sufficient to determine the suitability of an alkoxyamine to control a particular polymerization; its rate of addition to the monomer in question must also be considered. Overall, best control over the polymerization was obtained from the secondary and tertiary nonacid alkoxyamines **4c**, **4e**, **4f**, and **4h**.

Control over polymerizations mediated by alkoxyamines **4d** and **4g** (R = $CH(CH_3)COOH$ and $C(CH_3)_2COOH$) was poor compared to the corresponding succinimidyl esters **4e** and **4h**, and even compared to **4b** (R = CH_2CN). These acid-functional initiators are consumed much more slowly than their ester analogues, with measurable quantities remaining after 4 h at 115 °C. We propose that the recombination of these compounds may be favored in nonpolar solvents such as isoprene due to the formation of an intramolecular hydrogen bond between the SG1 phosphonate and the carboxylic acid of the leaving group. Further experiments to test this hypothesis are in progress. As succinimidyl esters are readily hydrolyzed to acids and are reactive toward amines and alcohols, these compounds should be acceptable substitutes for acid-functional initiators in applications where good control over the polymerization is desired across the whole range of conversion.

ASSOCIATED CONTENT

Supporting Information. Details of the procedure used to convert PS-equivalent molecular weights to PI molecular weights, PS-equivalent molecular weights, and polydispersities

for polymers shown in Table 1 and Table 2. This material is available free of charge via the Internet at http://pubs.acs.org.

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