Verdazyl-Mediated Polymerization of Styrene

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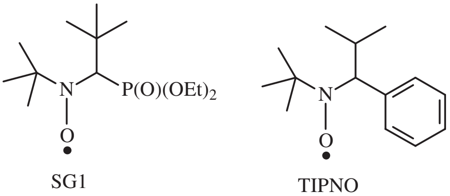
Summary: Attempted controlled polymerizations of styrene, conducted in the presence of either 1,3,5-triphenyl-6-oxoverdazyl or 1,5-dimethyl-3-phenyl-6-oxoverdazyl radicals initiated with benzoyl peroxide or 1,1′-azobis(cyclohexanecarbonitrile) were universally unsuccessful regardless of the reaction temperature and the initiator/verdazyl molar ratio. No improvement was observed using a verdazyl-terminated styrene initiator adduct prepared by an exchange reaction between a styrene-TEMPO alkoxyamine and a 1,3,5-triphenyl-6-oxoverdazyl radical. However, controlled polymerizations of styrene were achieved at 125 °C using a styrene-verdazyl adduct containing the 1,5-dimethyl-3-phenyl-6-oxoverdazyl radical. Polydispersity indexes remained low throughout the polymerizations and plots of number average molecular weight ($\overline{M}_n$) versus time were linear. However, the actual $\overline{M}_n$ values were considerably lower than theoretical, an unexpected result that is under investigation.

Keywords: living-radical polymerization; verdazyl radcials

Introduction

The use of nitroxides in the stable free radical polymerization (SFRP) process to reversibly terminate the propagating polymer chain enables the controlled polymerization of monomers with activated double bonds. However, while the polymerization of styrene with TEMPO is rather straightforward, the polymerization of acrylates and methacrylates has proven to be more difficult. Two reasons have been advanced for these difficulties. Firstly, the equilibrium constant K for *n*-butyl acrylate polymerization mediated by TEMPO has been reported to be unfavorably small because of a low dissociation rate constant k_d and a high recombination rate constant k_c.[1] This prevents a linear increase in molecular weight with increasing monomer conversion and a narrow final molecular weight distribution ($\overline{M}_w/\overline{M}_n$). To address this problem a series of novel nitroxides have been synthesized[2] and applied with good success to the polymerization of acrylates, two of the more successful of these nitroxides being SG1[2f] and TIPNO.[2e] The *K* value for SG1 has been shown to be significantly lower than that for TEMPO.[1]



Although the ability of TEMPO to mediate the polymerization of acrylates may be adversely affected by an unfavorable equilibrium constant as compared to other nitroxides, a second, and arguably more serious problem may be the persistence of TEMPO radicals in the polymerization. Unavoidable termination reactions by chain-chain coupling causes accumulation of free nitroxide in the reaction solution.[3] Since acrylates do not exhibit an autopolymerization mechanism that can

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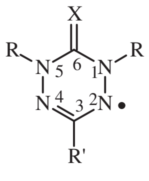
generate new propagating radicals to consume the excess nitroxide,[4] the accumulation of free nitroxide inhibits further polymerization.[2h–j] To circumvent this problem ene-diol additives have been effectively used to destroy the excess nitroxide and allow the polymerization of acrylates to proceed in a controlled manner in the presence of TEMPO.[5]

Obviously, the use of nitroxides as agents to control polymerizations remains interesting, however, their limitations makes one wonder whether there are other stable radicals which may be superior. Unfortunately, there are a limited number of stable radicals available, and those that have been studied have not been particularly successful. Earlier studies with galvinoxyl radicals[6] have been followed recently with the use of triazolinyl radicals[7] and verdazyl radicals **1**.[8] However, in the only reported use of verdazyl radicals to mediate styrene polymerizations no control was observed with **2**, an adduct of the 1,3,5-triphenylverdazyl radical and the 2-(2-cyano-2-propyl) radical derived from 2,2′-azobisisobutyronitrile (AIBN), at reaction temperatures between 80 °C and 120 °C.[8] In the case of the triazolinyl radicals, a spirotriazolinyl radical controlled the polymerization of styrene reasonably well, but was only moderately effective for methyl methacrylate[7].



X= H_2, O, S
R = alkyl, aryl
R' = alkyl, aryl, H

1a- X = O, R = R' = Ph
1b- X = O, R= CH_3, R' = Ph

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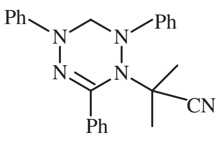

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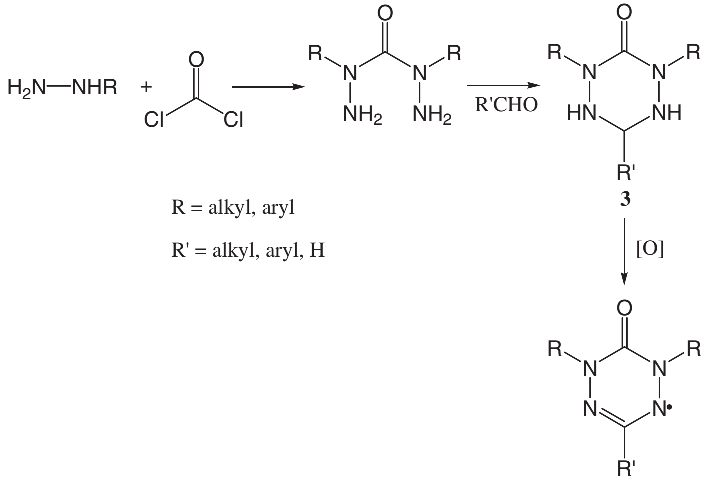
Despite these results the verdazyl radicals piqued our interest, primarily because they could be synthesized with a variety of substituents, each with the potential to affect the stability of the radical and its steric interactions with a propagating polymer chain. First reported in 1963, many verdazyl radicals are stable enough to be isolated and stored, such as 1,3,5-triphenyl-6-oxoverdazyl, or are stable as a complex, such as 1,5-dimethyl-3-(4-pyridyl)-6-oxoverdazyl with dihydroquinone. Other verdazyl radicals, such as 1,3-diphenyl-5-methyl-6-oxoverdazyl are reported to be too unstable to allow for isolation in a pure state.[9] Interest in verdazyl radicals has led to the study of other similar structured stable radicals, including acyclic and 5-membered analogues, a very comprehensive overview of which is provided by Neugebauer.[10]

Structurally, the verdazyls are allylic radicals, possessing a ring structure with a conformation determined in large part by the substituents at C6. Thus, in the case of **1**, where X is oxygen, the verdazyl ring is nearly planar, whereas when X is sulfur, the ring is in a flat boat conformation. The C6 substituent can also effect the conformation at C1, C3, and C5. In the 1,3,5- triphenyl-6-oxoverdazyl radical, for example, the phenyl groups at C1 and C5 are slightly twisted (about 5 °) out of the plane of the verdazyl ring while the phenyl group at C3 is similarly twisted out of the plane, but to a lesser degree. Alternatively, when X is sulfur the twists of the phenyl groups are much more pronounced.[11b]

Various synthetic approaches to the verdazyl radicals have been reported. All the syntheses lead to a tetrazine intermediate **3** (Scheme 1) which can be oxidized to the verdazyl radical by a variety of oxidants, including benzoquinone,[12] lead oxide in acetic acid[9] and potassium ferrocyanate.[11a] Other oxidants include silver carbonate, hydrogen peroxide, thallium oxide

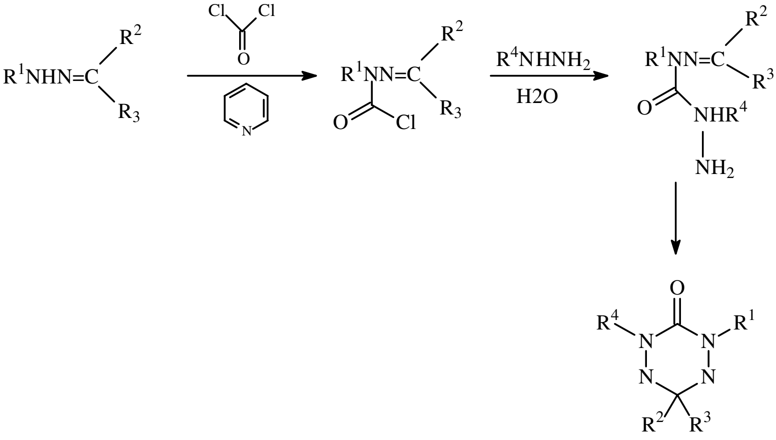


Scheme 1.
General synthesis of 6-oxoverdazyl radicals beginning with a monosubstituted hydrazine.

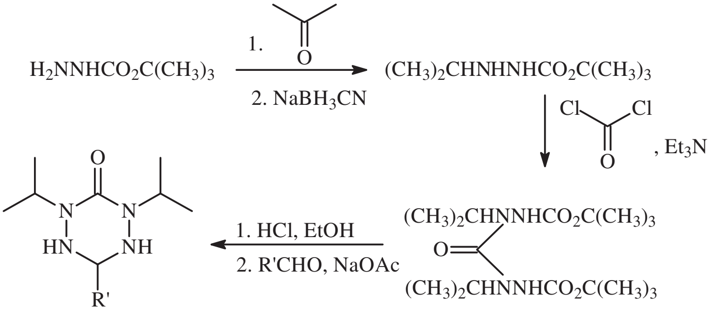
and manganese oxide.[9] The 6-oxoverdazyl radicals, of particular interest to the work presented herein, are synthesized by condensation of a substituted alkyl or aryl hydrazine with phosgene, followed by condensation of the resulting bis-hydrazide with an aldehyde to afford the tetrazine intermediate (Scheme 1).[13] While the use of phosgene is problematic, the reactions proceed in high yield and are relatively simple to execute.

Two other general approaches to the tetrazine **3** have been reported. In one approach a hydrazone is reacted with phosgene to give a 2-chloroformylhydrazone, which is subsequently reacted with hydrazine followed by condensation with an aldehyde to afford **3** in good yield (Scheme 2).[9]

In the second approach the commercially available *tert*-butyl carbazate is condensed with a ketone of choice and the



Scheme 2.
General synthetic scheme for 6-oxotetrazines beginning with a substituted hydrazone.



Scheme 3.
General synthetic scheme for 6-oxotetrazines beginning with *tert*-butyl carbazate.

resulting hydrazone is reduced to afford the BOC protected alkyl hydrazide. Reaction of the hydrazide with phosgene affords the bis-hydrazide which cyclizes in the presence of acid to yield **3** (Scheme 3).[12b]

The described syntheses offer easy access to a variety of structurally different verdazyl radicals providing the opportunity to extend the initial work of Yamada and coworkers[8] to determine if these stable radicals have the potential to solve some of the problems associated with nitroxides as mediating reagents for living-radical polymerizations.

Experimental Part

Styrene Polymerization Using 1a Initiated with Benzoyl Peroxide (BPO)

In a typical experiment, styrene (10 mL, 87 mmol), BPO (28 mg, 0.12 mmol) and 1,3,5-triphenyl-6-oxoverdazyl radical **1a** (86 mg, 0.26 mmol), prepared according to the procedure of Neugebauer[13c], were placed in a 50 mL 3-necked round bottom flask equipped with a thermometer, a condenser equipped with a gas outlet adapter, and a septum, through which argon was introduced and samples were removed via syringe. The reaction solution was purged with argon for 10 min and heated to 110 °C. Samples were withdrawn occasionally beginning after the first 30 min, but typically after every hour beginning with the first. A stream of air was used to remove excess monomer from the samples and the conversion was measured gravimetrically once constant weight was reached. The molecular weights and molecular weight distributions of the remaining polymer were estimated by gel permeation chromatography (GPC) using a Waters 2690 Separations Module equipped with Styragel HR4 (7.8×300 mm), Styragel HR2 (4.6×300 mm) and Styragel HR1 (4.6×300 mm) columns calibrated with polystyrene standards in the range of $\overline{M}_n = 400–188{,}000$ g/mol^{-1} and a Waters model 410 differential refractometer (RI) detector. THF was used as eluent at 40 °C and a flow rate of 0.35 mL min^{-1}.

Styrene Polymerization Using 1a Initiated with 1,1′-Azobis(cyclohexanecarbonitrile), (Vazo® 88)

The procedure described in the previous paragraph was repeated with Vazo® 88 (130 mg, 0.53 mmol), 1,3,5-triphenyl-6-oxoverdazyl radical **1a** (203 mg, 1 mmol) in 10 mL styrene at 135 °C.

BSV Synthesis

In a typical reaction, 2-phenyl-2-(2,2,6,6-tetramethylpiperidin-1-oxy)ethyl benzoate (BST)[14]**4**, (1 molar eq.) and 1,3,5-triphenyl-6-oxoverdazyl radical **1a** (2 molar eq.) were heated in toluene under argon at 110 °C for 3 h. The solvent was evaporated and the resulting oil was passed though a silica gel column with CH_2Cl_2 as the eluent to give the 2-phenyl-2-(1,3,5-triphenyl-6-

Table 1.
Polymerizations of styrene initiated with BPO in the presence of 1,3,5-triphenyl-6-oxoverdazyl radical **1a** at 110 °C. Polymerizations were performed in 10 mL styrene.

Entry	BPO ($\times 10^{-2}$ M)	**1a**($\times 10^{-2}$ M)	**1a**/BPO	Time (h)	$\overline{M}_n$ g/mol^{-1}	$\overline{M}_w/\overline{M}_n$	Conv'n (%)
1	1.16	2.63	2.25	0.5	27700	1.6	23
				1	28700	1.65	25
				2	29200	1.65	26
2	1.16	3.12	2.7	1	24500	1.7	23
				2	24000	1.7	21

oxoverdazyl)ethyl benzoate unimer **5a** in 30–35% yield unimer (BSV **5a**).[15] The 2-phenyl-2-(1,5-dimethyl-3-phenyl-6-oxoverdazyl)ethyl benzoate unimer (BSV **5b**)[15] was prepared in a similar manner.

Styrene Polymerization Initiated with BSV Polymerizations were performed in 10 mL (87.3 mmol) of styrene with 100 mg of BSV **5a** or **5b**, (0.18 to 0.19 mmol, respectively) in a similar manner described for styrene polymerization initiated with BPO.

Results and Discussion

We began our investigation with a styrene polymerization in the presence of 1,3,5-triphenyl-6-oxoverdazyl radical **1a** initiated with BPO at a reaction temperature of 110 °C, using a verdazyl to BPO molar ratio of 2.25:1. The results of a typical experiment are summarized in Table 1, entry 1. The monomer conversion after 30 min was 23% and did not change in the subsequent 2 h. Only a minimal increase in $\overline{M}_n$ was observed over that time period. The fast initial reaction and high $\overline{M}_w/\overline{M}_n$ values suggested a deficiency of verdazyl radical at the beginning of the polymerization. However, an increase of the verdazyl to BPO ratio to 2.7:1 gave virtually no change in the polymerization results (Table 1, entry 2).

The polymerization of styrene initiated with Vazo® 88 in the presence of 1,5-dimethyl-3-phenyl-6-oxoverdazyl radical **1b** was similarly unsuccessful (Table 2). An initial polymerization attempt with a verdazyl/Vazo® 88 ratio of 2.6 at a reaction temperature of 115 °C gave an 18% monomer conversion after 30 min. However, shortly after 30 min the reaction temperature rose to 119 °C and then slowly decreased to 115 °C.

The reaction mixture quickly became viscous and the conversion after 50 min was 65%. The correlation between the actual and theoretical $\overline{M}_n$ was poor and the higher actual $\overline{M}_n$ suggested the occurrence of some chain termination reactions or a low initiator efficiency. A series of reactions were performed with lower concentrations

Table 2.
Polymerizations of styrene initiated with Vazo® 88 (1,1′-azobis(cyclohexanecarbonitrile) in the presence of 1,5-dimethyl-3-phenyl-6-oxoverdazyl radical **1b**. Polymerizations were performed in 10 mL of styrene.

Entry	Vazo®88 ($\times 10^{-2}$ M)	**1b** ($\times 10^{-2}$ M)	**1b**/ Vazo®88	Time (h)	$\overline{M}_n$ g/mol^{-1}	$\overline{M}_{nthe}$[a] g/mol^{-1}	$\overline{M}_w/\overline{M}_n$	Conv'n (%)
1[b]	3.9	10.3	2.6	0.5	2000	–	2.1	18
				0.9	9600	7500	1.5	65
2[c]	1.6	5.2	3.2	3	1280	1700	1.5	6
				5	15900	17900	1.5	63
				6	18800	19600	1.4	69

[a] Reaction temperature 115 °C.

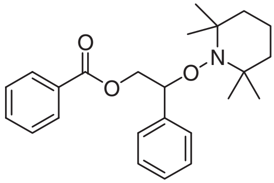
[b] Reaction temperature 105 °C for the first 3h and 110 °C for the last 3h.

[c] Calculation for the theoretical molecular weight: $\overline{M}_{nthe} = [(\text{moles monomer} \div 2\times \text{ moles of initiator}) \times \text{MW monomer}] \times \%$ conversion.

Table 3.
Characterization results for the polymerization of styrene (10 mL, 8.7×10^{-2} mol) at 130 °C initiated with BSV **5a** (0.1 g, 1.8×10^{-4} mol).

Rxn. Time (h)	$\overline{M}_n$ g/mol^{-1}	$\overline{M}_{nthe}$ g/mol^{-1}	$\overline{M}_w/\overline{M}_n$	Conv'n (%)
0.5	17400	1000	1.7	2
1.5	25100	4500	1.8	9
4	30500	11100	1.7	22
6	32700	20000	1.6	39

of Vazo® 88 and verdazyl, higher verdazyl/Vazo® 88 ratios, and at lower temperatures to avoid this exotherm, but no improvement was observed. A typical result for these reactions is summarized in Table 2, entry 2. After 3 hours at 105 °C the monomer conversion was 6%. A 5 °C increase in temperature caused a sharp increase in the rate of polymerization resulting in a 63% monomer conversion after 5h. While the $\overline{M}_w/\overline{M}_n$ values of the resulting polystyrene samples are not particularly low, it is interesting to note that the actual and theoretical $\overline{M}_n$ values are in good agreement. However, a high verdazyl/Vazo® 88 molar ratio was required to achieve this result suggesting that the verdazyl radical is not particularly efficient at capping the propagating chain or is not very stable at 110 °C.



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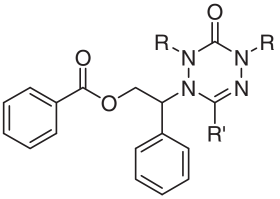

5a R, R' = Ph
5b R = Me; R' = Ph

With these poor results in hand we turned our attention to using the BSV unimers **5** as the initiating species, prepared by an exchange reaction with BST.[14] The results of a styrene polymerization at 130 °C initiated with unimer **5a** were similar to previous reactions initiated with BPO and mediated with the 1,3,5-triphenyl-6-oxoverdazyl radical (Table 3). High molecular weight was obtained early in the reaction mixture with some increase over time, however, there was no correlation between actual and theoretical molecular weights. While the polydispersity values remained low an overlay of the GPC curves showed that there was no livingness associated with these polymerizations (Figure 1). At 0.5 h a significant amount of unimer remained in the reaction mixture, as observed in the GPC analysis, and not until 4 h was most of the unimer consumed. This result clearly shows the dissociation of the triphenylverdazyl-styrene bond in the BSV unimer is quite slow even at 130 °C, accounting for the poor livingness of this polymerization.

Significantly better results were obtained with the BSV unimer **5b**. At 125 °C the polymerization of styrene proceeded with an incremental increase in $\overline{M}_n$ over time, while the *PDI* remained low (Table 4 and Figure 2). However, while a plot of $\overline{M}_n$ vs conversion is linear (Figure 3), the correlation between the actual and theoretical $\overline{M}_n$ is poor, with the actual $\overline{M}_n$ values considerably lower than expected. There is also a slight upward trend in the $\overline{M}_w/\overline{M}_n$ numbers and observable tailing in the GPC plots at higher conversions. These results would suggest some chain transfer is

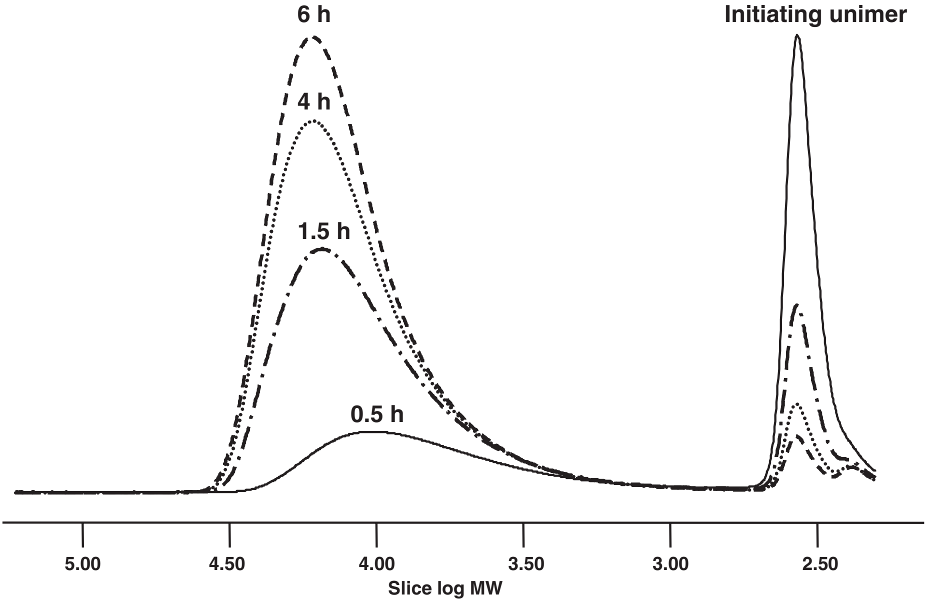

Figure 1.
GPC distribution overlap for the polymerization of styrene (10 mL, 8.7×10^{-2} mol) at 130 °C initiated with BSV **5a** (0.1 g, 1.8×10^{-4} mol). The $\overline{M}_n$ and $\overline{M}_w/\overline{M}_n$ values are listed in Table 3.

occurring and we are presently investigating this possibility.

Conclusions

While we are not sure at this moment what is causing the discrepancy in the actual and theoretical molecular weights for the 1,5-dimethyl-3-pheny-6-oxoverdazyl radical mediated styrene polymerizations, we are quite encouraged by the fact that there is some degree of livingness associated with the system. As such, we are continuing to synthesize and investigate a series of verdazyl radicals by changing the substituent at C-3. Preliminary results of this investigation have shown that there is clearly a difference in the ability of these various verdazyl radicals to control the radical polymerization of styrene and acrylates, and we are attempting to correlate the stability of the verdazyl radicals to their ability to control radical polymerizations. In addition, we recently reported the use of ^{1}H NMR to determine the bond dissociation constants of model alkoxyamines,[16] and we are in the process of extending this methodology to the verdazyl unimers to provide bond dissociation constants for the verdazyl systems.

Table 4.
Characterization results for the polymerization of styrene (10 mL, 8.7×10^{-2} mol) at 125 °C initiated with BSV **5b** (0.1 g, 1.9×10^{-4} mol).

Rxn. Time (h)	$\overline{M}_n$ g/mol^{-1}	$\overline{M}_{nthe}$ g/mol^{-1}	$\overline{M}_w/\overline{M}_n$	Conv'n (%)
1	4200	4600	1.13	12
2	7700	8900	1.14	23
3	9800	11600	1.19	30
4	11200	13500	1.22	35
5	12100	15500	1.22	40

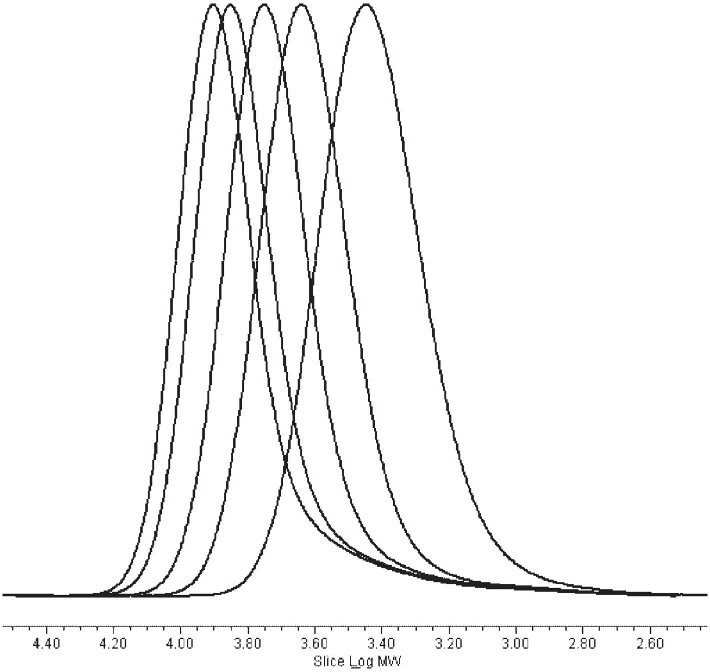

Figure 2.
GPC plot for the polymerization of styrene (10 mL, 8.7×10^{-2} mol) at 125 °C initiated with BSV **5b** (0.1 g, 1.9×10^{-4} mol). Samples were taken from the reaction mixture after each hour for 5 hours. The $\overline{M}_n$ and $\overline{M}_w/\overline{M}_n$ values are listed in Table 4.

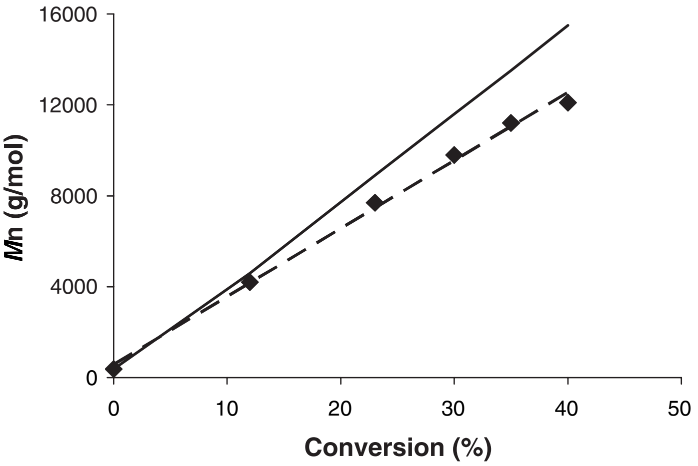

Figure 3.
Demonstration of the linear dependence of $\overline{M}_n$ on monomer conversion for styrene at 125 °C initiated by BSV **5b**. The solid line indicates $\overline{M}_{nthe}$, the values listed in Table 4. [styrene]/[BSV **5b**]: $8.7 \times 10^{-2}/1.9 \times 10^{-4}$.

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