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Experimental and computational studies of bulk polymerization of styrene in the presence of *N*-(*O*-(1-phenylmethyl)oxy) phthalimide or cyclohexanone-*O*-(1-phenylmethyl)oxime

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Summary

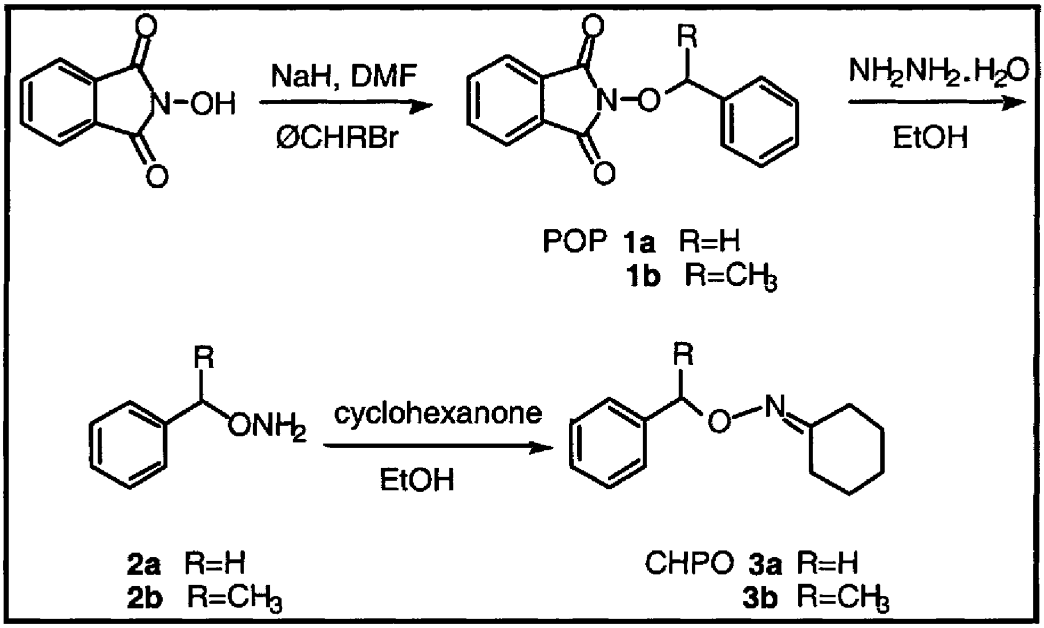
Syntheses of potential initiators *N*-(*O*-(1-phenylethyl)oxy)phthalimide, *N*-(*O*-(1-phenylmethyl)oxy)phthalimide (POP), cyclohexanone-*O*-(1-phenylethyl)oxime, and cyclohexanone-*O*-(1-phenylmethyl)oxime (CHPO) are described. Bulk polymerization of styrene in the presence of POP or CHPO and molecular weight measurement by GPC indicate that the polymerization is not a living process. *Ab initio* calculations show that the C-O or O-N bond cleavage energies of POP and CHPO are close to each other (**3**: C-O: 46.4, O-N: 47.3 kcal/mol; **1**: C-O: 46.9, O-N: 63.0 kcal/mol) and much higher than the similar analogs of 2,2,6,6-tetramethylpiperidinyloxy (TEMPO) (C-O: 20.9, O-N: 34.4 kcal/mol). The similar C-O and O-N bond cleavage energies of the synthesized initiators (POP/CHPO) indicate two possible cleavage pathways and may explain the non-living nature of the polymerization. These results may be helpful in finding future reversible terminator compounds for living polymerization.

Introduction

The ability to control macromolecular architecture is becoming an increasing important theme in polymer science with the interest being driven by the desire to prepare materials with new and/or improved properties [1-2]. A number of investigators have successfully prepared polymers with well-defined molecular weight and low polydispersities via 2,2,4,4-tetramethyl-1-piperidinyloxy nitroxide (TEMPO) living free radical polymerization [3-4]. Compared to other controlled polymerization methods such as anionic, cationic, and group transfer polymerization, living free radical polymerization does not require extraordinary conditions such as low temperature, or carefully purified reagents. TEMPO-based stable free radical polymerization (SFRP) was able to control the molecular weight and polydispersities in the polymerization of styrene and the copolymerization of styrene with acrylates [5]. Recently, Li et al. examined the TEMPO-based SFRP polymerization of *N*,*N*-dimethylacrylamide and found the polymerization was not a living process as evidenced by an unsuccessful incremental monomer-addition experiment [3].

With the limitation of monomer choice, TEMPO-based living free radical polymerization mainly works for the synthesis of well-controlled polymer structure with a polystyrene backbone and at a polymerization temperature normally higher than 90 •C. We have experienced that the TEMPO-based polymerization of disaccharide-containing styrenes leads to browning (decomposition) without the protection of the hydroxyl group [6]. Therefore, the exploration of other living polymerization processes yielding a wider range of monomer choices and polymerization temperatures would be very interesting to polymer science. Druliner reported that another oxygen-centered radical (·ON=NAr) could associate with the growing end of the polymer initiated by a carbon radical (Ar·) in a living process to give block copolymers at relatively low temperatures [7]. However, broad polydispersities (2.0-3.0) and low conversion of monomer were observed. In this regard, Benoit et al reported new alkoxyamine-based acyclic nitroxide initiators which have been successfully applied in the controlled free-radical polymerization of styrene and acrylic esters [8-11]. Hawker also screened a variety of alkoxyamines and found the universal initiator for the polymerization of a wide range of monomers [12]. Moad and Rizzardo studied the C-O bond homolysis rate of a series of alkoxyamine initiators with different polar and steric factors. Their experimental results correlated well with their semiempirical molecular orbital calculations and therefore offered insight into the design of new initiators for living radical polymerization [13].

Recently, Ishii et al [14-16] reported the *N*-hydroxyphthalimide-catalyzed oxidation reaction via an oxygen-centered *N*-oxyphthalimide free radical spieces. Here, we report the syntheses of POP/CHPO (Scheme 1) and their influence on bulk polymerization of styrene. The experimental results coupled with the *ab initio* calculations offer insight into why the polymerization is not living and provide substantial direction in the selection of future reversible terminator compounds.



Scheme 1. Syntheses of POP or CHPO

Experimental

Materials

N-Hydroxyphthalimide, benzyl bromide, (1-bromoethyl)benzene, sodium hydride (60% dispersion in mineral oil), and cyclohexanone were obtained from Aldrich Chemical Co. and were used without further purification. Hydrazine monohydrate was purchased from Fisher Chemical. Styrene (Aldrich) was distilled immediately prior to use. *N,N*-dimethylformamide (DMF) was used after drying over 4Å molecular sieves obtained from EM Science and distillation. All other chemicals and solvents were reagent grade and were used without further purification unless otherwise indicated.

General Procedures

Melting points were determined with a melting point apparatus (9100, Elecrothermal Engineering Ltd., England) and were uncorrected. Elemental analyses were determined by Midwest Microlabs. ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) were recorded on a QE-300 instrument (General Electric, NMR-Instruments, Freemont CA) in $CDC1_3$ using TMS as internal standard. Fourier transform infrared spectroscopy (FTIR) measurements were performed on a Galaxy 3000 FTIR (Mattson, Madison, WI) using KBr disks at a resolution of 2 cm^{-1}. Reactions were monitored by thin-layer chromatography (TLC) on a precoated plate of silica gel $60F_{254}$ (layer thickness, 0.25mm; E. Merck, Darmstadt, Germany).

The weight-averaged molecular weight (M_w), number-averaged molecular weight (M_n), and the molecular weight distribution (M_w/M_n) were determined using gel permeation chromatography (GPC) in THF at 30 •C. Three Polymer Standard Services columns (100 Å, 1000 Å, and linear) were connected in series to a Thermoseparation Products P-1000 isocratic pump, autosampler, column oven, and Knauer refractive index detector. Calibration was performed using polystyrene samples (Polymer Standard Services; M_p=400 to 1,000,000; M_w/M_n M_w/M_n < 1.10).

N-(*O*-(1-phenylethyl)oxy)phthalimide (**1b**)[17]: 16.32 g of *N*-hydroxy phthalimide (0.10 mol) was dissolved in 100 mL of dry DMF and placed in a round-bottom flask equipped with a condenser which was capped by a drying tube. A 4.8 g amount of sodium hydride (60% in mineral oil, 0.12 mol) was added to the above solution at room temperature. The color changed from light yellow to red. The reaction was kept at room temperature and stirred for an additional 1 h. Then, 18.50 g of (1-bromoethyl)benzene (0.10 mol) was added to the above mixture. The flask was placed in an oil bath at 55 •C. After 18 h, the solvent was removed under reduced pressure, and the reside was dissolved in 180 mL of chloroform. The solution was washed with aqueous 0.20N sodium hydroxide solution (150x3 mL), water (150x3 mL), and then concentrated. The white product was crystallized from hexane/ethyl acetate to yield 19.6 g (73%) of white crystal. TLC (EtOAc/hexane 3:7) R_f 0.62; mp 90.4-91.2 •C . ^{1}H NMR (300 MHz, $CDC1_3$): δ(ppm) 1.72 (d, *J* =6.6Hz, 3H), 5.50(dd, *J* =6.6Hz, 1H), 7.33 (m, 3H), 7.50(m, 2H), 7.69(m, 2H), 7.73(m, 2H). ^{13}C NMR(75 MHz, $CDC1_3$): δ(ppm) 20.47, 85.15, 123.34, 127.64, 128.37, 128.96, 134.27, 139.10, 163.79. IR (KBr disk): 3088, 3067, 3037, 2970, 2924, 1792, 1710, 1383, 1193, 1111, 983, 886, 702 cm^{-1}.

N-(*O*-(1-phenylmethyl)oxy)phthalimide (**1a**): Compound **1a** was prepared as described above. Crude product was crystallized from ethyl acetate to give a white crystal in 79% yield. TLC (EtOAc/hexane 5:5) R_f 0.66; mp 142.2-143.2 •C. ^{1}H NMR (300 MHz, $CDC1_3$): δ(ppm) 5.21(s, 2H), 7.38(m, 3H), 7.53 (m, 2H), 7.72(m, 2H), 7.80(m, 2H). ^{13}C NMR (75 MHz, $CDC1_3$): δ(ppm) 79.86, 123.47, 128.54, 128.89, 129.33, 129.88, 133.71, 134.41, 163.46. IR(KBr disk): 3075, 3037, 2955, 2886, 1788, 1733, 1381, 1186, 1132, 877, 763, 701 cm^{-1}.

O-(1-Phenylethyl)oxyamine (**2b**): One equivalent of *N*-(*O*-(1-phenylethyl)oxy) phthalimide (**1b**, 10.68 g, 0.04 mol) was added in 150 mL ethanol in a 250-mL, three-necked, round-bottom flask fitted with a reflux condenser and mechanical stirrer. After refluxing for 0.5 to 1 h, the starting material dissolved. To this mixture was added dropwise a solution of 2.0 equivalent of hydrazine monohydrate (4.01g, 0.08 mol) in 10 mL ethanol. After the addition was complete, a white stiff crystalline mass immediately started to precipitate. Refluxing and vigorous mechanical stirring were continued for 4 h. The precipitate was filtered and the filtrate was concentrated to dryness. The combined solids were treated with an aqueous potassium hydroxide solution (11.6 g KOH in 100 mL water). The aqueous mixture was extracted with anhydrous ether several times (80 mLx4, 50 mLx4). The combined ether solutions were then washed with four portions of 30 mL 2% potassium carbonate solution and dried over potassium carbonate. The ether was evaporated and the pure resultant was colorless liquid; yield 4.52g (82.4%). TLC (EtOAc/hexane 3:7) R_f 0.49. ^{1}H NMR (300 MHz, $CDC1_3$): δ(ppm) 1.41(d, *J* =6.59Hz, 3H), 4.63 (dd, *J* =6.59Hz, 1H), 5.18(s, 2H), 7.32(m, 5H). ^{13}C NMR (75 MHz, $CDC1_3$): δ(ppm) 21.75, 82.78, 126-34, 127.67, 128.51, 143. 07. IR (neat, NaCl plate): 3315, 3244, 3155, 3082, 3061, 3029, 2976, 2929, 2890, 1585, 1493, 1451, 1366, 1305, 1186, 1073, 1008, 919, 851, 760, 701 cm^{-1}.

O-(1-Phenylmethyl)oxyamine (**2a**): Compound **2a** was prepared as described above. **2a** was obtained as a yellow liquid in 85.0% yield. TLC (EtOAc/hexane 3:7) R_f 0.43. ^{1}H NMR(300 MHz, $CDC1_3$) δ(ppm) 4.66(s, 2H), 5.36 (brd, 2H), 7.34(m, 5H). ^{13}C NMR(75 MHz, $CDC1_3$): δ(ppm) 77.84, 127.76, 128.34, 129.02, 137.34. IR(neat, NaCl plate): 3315, 3241, 3154, 3086, 3062, 3030, 2913, 2856, 1585, 1495, 1454, 1363, 1208, 998, 746, 699 cm^{-1}.

Cyclohexanone-*O*-(1-phenylethyl)oxime (**3b**): One equivalent of cyclohexanone (0.49 g, 5 mmol) was dissolved in 5 mL of ethanol in a 15-mL flask with a magnetic stirrer. To this was added one equivalent of **2b** (0.69 g, 5 mmol) in 1 mL of ethanol. The reaction was continued at room temperature for 1 h. After this time, the ethanol was removed and the product was purified by flash silica chromatography using EtOAc/hexane (2:8) to give a colorless liquid in 95% yield. TLC (EtOAc/hexane 3:7) R_f 0.75. ^{1}H NMR (300 MHz, $CDC1_3$) δ(ppm) 1.53 (d, *J* =6.6Hz, 3H), 1.61 (m, 6H), 2.17 (m, 2H), 2.55 (m, 2H), 5.18 (dd, J =6.6Hz, 1H), 7.23~7.32(m, 5H). ^{13}C NMR (75 MHz, $CDC1_3$): δ(ppm) 22.33, 25.47, 26.96, 32.10, 79.86, 125.94, 126.97, 128.08, 143.95, 160.35. IR (neat, NaCl plate): 3084, 3062, 3029, 2975, 2931, 2857, 1641, 1493, 1449, 1365, 1320, 1082, 941, 873, 758, 699 cm^{-1}. Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 78.07; H, 9.05; N, 6.47.

Cyclohexanone-*O*-(1-phenylmethyl)oxime (**3a**): Compound **3a** was prepared using the same procedure as above and separated by flash silica chromatography using EtOAc/hexane (12:88) to give a yellow liquid in 94% yield. TLC (EtOAc/hexane 2:8) R_f 0.55. ^{1}H NMR (300 MHz, $CDC1_3$) δ(ppm) 1.59~1.66 (m, 6H), 2.20 (t, 2H), 2.50 (t, 2H), 5.03 (s, 2H), 7.35 (m, 5H). ^{13}C NMR (75 MHz, $CDC1_3$): δ(ppm) 25.49, 25.83, 27.04, 32.20, 75.11, 127.52, 127.85, 128.26, 138.32, 160.82. IR (neat, NaCl plate): 3085, 3063, 3030, 2931, 2857, 1640, 1496, 1450, 1365, 1318, 1045, 933, 887, 748, 698 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 77.02; H, 8.53; N, 6.86.

Bulk Polymerization of Styrene in the Presence of POP or CHPO.

A mixture of the POP (0.18 mmol: R=CH_3, 39.1 mg; R=H, 37.6 mg) or CHPO (0.18 mmol: R=CH_3, 48.1 mg or R=H, 45.6 mg) and styrene (1.87 g, 18 mmol) was heated at 125•C under N_2 for 70 h to ensure polymerization completion. During the first few hours the polymerization mixture became more viscous and eventually solidified. The solidified materials were then dissolved in dichloromethane and precipitated into methanol (600 mL). The obtained white polymer was filtered, washed with methanol, and vacuum dried at 60 •C for 24 h. ^{1}H NMR (300 MHz, $CDC1_3$) δ(ppm) 1.40 (brd, 2H), 1.80 (brd, 1H), 6.53 (brd, 2H), 7.10 (brd, 3H). IR (KBr disk): 3078, 3047, 3027, 2904, 2847, 1608, 1490, 1460, 1034, 901, 743, 697 cm^{-1}.

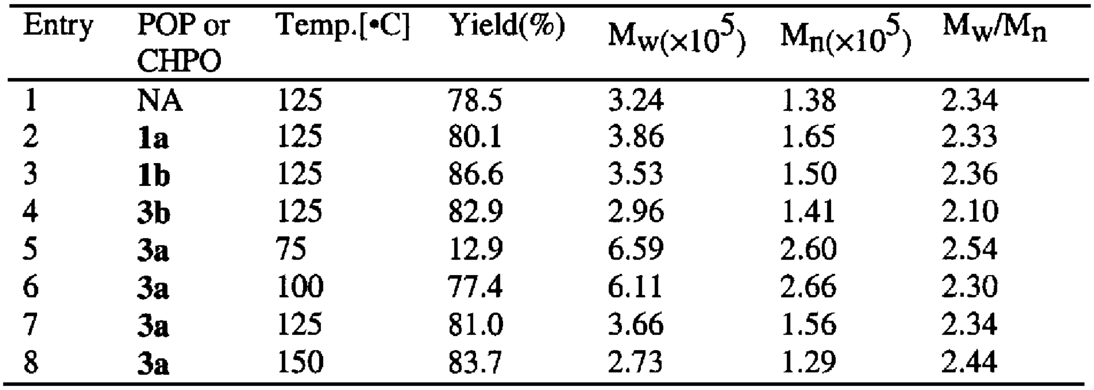
Computational Methods

Starting geometries for the *ab initio* calculations were obtained by geometry optimization with the PM3 semiempirical method using the Spartan 3.1 program [18] and graphical interface on a Silicon Graphics Indigo workstation. *Ab initio* geometry optimization were performed with the Gaussian 98 program [19] at the unrestricted Hartree-Fock and B3LYP levels of theory, using the 3-21G and 6-31+G* basis sets, on Digital Alpha workstations or a Silicon Graphics Origin 2000. The SEF=QC Gaussian keyword was used for molecules that experienced difficulty in energy convergence using the default algorithms.

Results and Discussion

Compound **2a** and **2b** were synthesized by deprotonation of *N*-hydroxyphthalimide with sodium hydride in DMF at room temperature, followed by alkylation with benzyl bromide or (1-bromoethyl)benzene for 18 h. Hydrazination of the previous product (**1a** and **1b** were recrystallization in EtOAc/hexane and ethyl acetate, respectively) in refluxing ethanol as described in our previous work [17] led to compound **2a** as a yellow liquid, and **2b** as a colorless liquid in good yields. Oxime formation of **2** with cyclohexanone in ethanol at room temperature led to **3** in 95% yields after flash silica chromatography. Compound **3** are characterized by NMR, IR, and elementary analysis.

Bulk polymerization of styrene in the presence of POP or CHPO with a styrene: POP(CHPO) ratio of 100:1 and varied temperatures led to polymers with the number-average molecular weight in the range of $1.29\text{x}10^{5}$ to $2.66\text{x}10^{5}$ and the polydispersities 2.10 to 2.54 (Table 1). Clearly, the highest polymerization temperature of 150 •C led to lowest MW polystyrene (entry 8) while the lower polymerization temperature of 75 •C and 100 •C led to highest MW polymer (entry 5 & 6). The polydispersities are all higher than 1.5 suggesting the polymerization is not a living process. Furthermore, bulk polymerization of styrene without POP/CHPO (entry 1) affords the resulting polymer with a polydispersity of 2.34 which is within the range of polydispersities obtained with POP or CHPO, indicating that they have no effect on the polydispersity control.



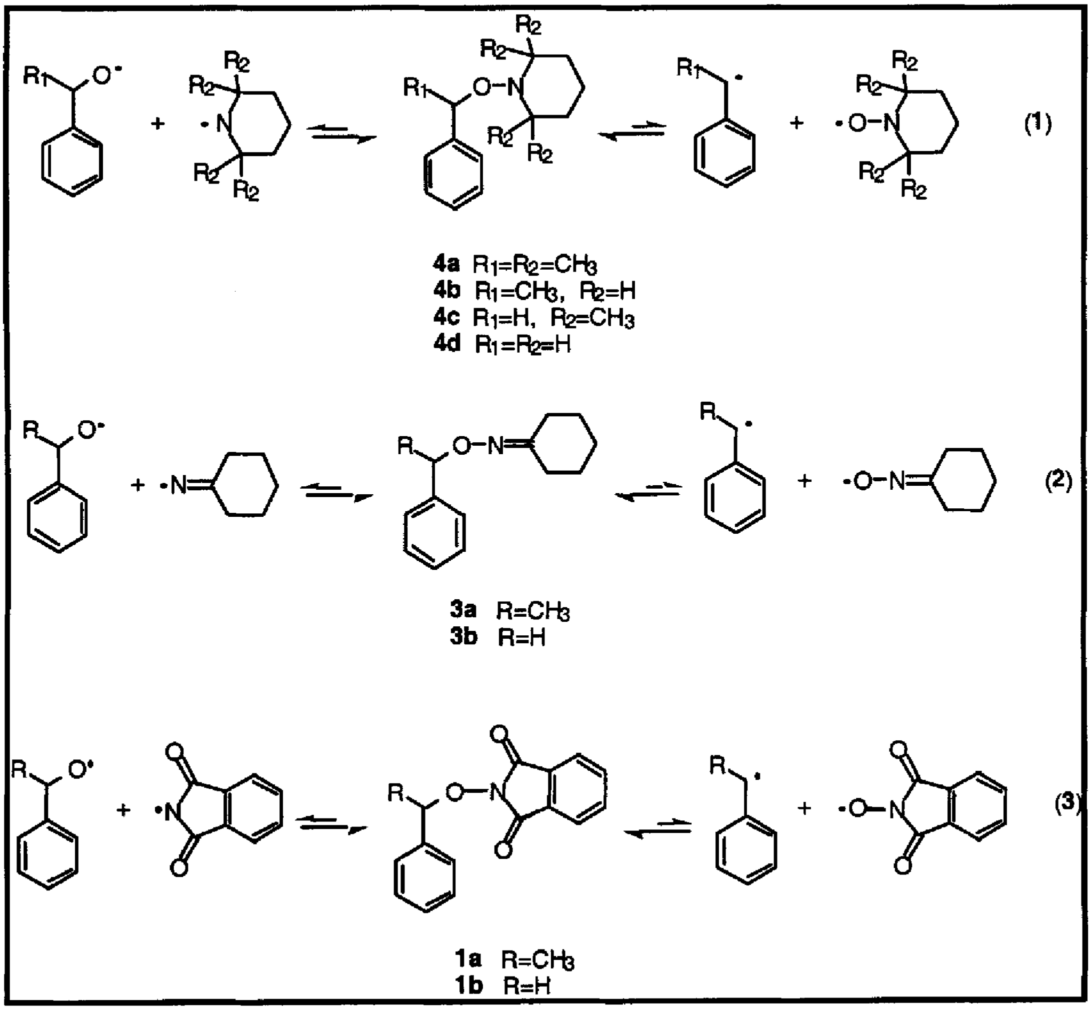
Entry	POP or CHPO	Temp.[•C]	Yield(%)	$M_w(\times10^5)$	$M_n(\times10^5)$	M_w/M_n
1	NA	125	78.5	3.24	1.38	2.34
2	**1a**	125	80.1	3.86	1.65	2.33
3	**1b**	125	86.6	3.53	1.50	2.36
4	**3b**	125	82.9	2.96	1.41	2.10
5	**3a**	75	12.9	6.59	2.60	2.54
6	**3a**	100	77.4	6.11	2.66	2.30
7	**3a**	125	81.0	3.66	1.56	2.34
8	**3a**	150	83.7	2.73	1.29	2.44

Table 1. Bulk Polymerization of Styrene in the Presence of POP or CHPO.

The fragmentation energies of the N-O and C-O bonds were calculated for several different initiators (Scheme 2). Comparison of the Hartree-Fock and B3LYP energies indicates the importance of electron correlation in this system, as would be expected for open shell systems. The calculations showed that with the TEMPO based initiators (**4**), the N-O bond energies were much higher than the C-O bond energies, which led to a more facile and reversible C-O bond cleavage. The data in Table 2 show that the dissociation of the TEMPO based chain end, and thus the living character of the polymerization, is due in part to the steric effects of the methyl groups in the TEMPO radical. In contrast to the TEMPO system, dissociation of **3** can take place by either a C-O or N-O bond cleavage. Furthermore, the bond dissociation energy is much higher than that of the TEMPO system, which requires polymerization temperatures that are sufficiently high to initiate a non-living thermal polymerization of styrene. The molecular weight distribution is consistent with such a non-living process. Although the preferred dissociation of POP (**1**) is via C-O bond cleavage, the bond dissociation energy is much higher than that of the TEMPO based system. Thus, the polymerization of styrene in presence of POP (**1**) is also a non-living thermal process. Our computational results combined with the experimental results are consistent with the results reported by Kazmaier [20], in that the reversible terminator of the growing polymer radical must have a calculated bond dissociation enthalpy of less than 35 kcal/mol in order to achieve reasonable rates of chain propagation.

Entry	C-O cleavage (kcal/mol)			N-O cleavage (kcal/mol)		
	UHF/ 3-21G	UHF/ 6-21+G	B3LYP/ 6-31+G*	UHF/ 3-21G	UHF/ 6-21+G	B3LYP/ 6-31+G*
4a	11.6	-2.22	20.9	7.1	-3.28	34.4
4b	25.1	13.0	33.7	18.0	11.3	46.1
4c	12.3	0.98	24.6	11.2	1.76	38.2
4d	21.3	11.2	33.8	17.6	11.3	46.1
3a	34.5	26.8	46.4	7.1	6.4	47.3
3b	30.7	24.5	46.3	6.7	6.0	47.1
1a	27.9	23.2	46.9	22.3	23.1	63.0
1b	23.5	20.5	46.0	21.3	22.3	62.1

Table 2. Calculated Bond Cleavage Energies for the Polymerization Initiators.



Scheme 2

In conclusion, a new series of potential initiators were synthesized and used for controlled living free radical polymerization of styrene. Different levels of calculations were carried out on the bond cleavage energies of C-O and N-O, and correlated with experimental data. This is the first time that the two possible cleavage of the polymerization initiators were reported. This study is important in designing new living free radical initiators especially for low polymerization temperatures.

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