Macromolecules **2001,** *34,* 447−455

Low-Temperature “Living” Radical Polymerization of Styrene in the Presence of Nitroxides with Spiro Structures

Yozo Miura,* Norihiro Nakamura, and Isao Taniguchi

Department of Applied Chemistry, Faculty of Engineering, Osaka City University, Sumiyoshi-ku, Osaka 558-8585, Japan

Received July 20, 2000

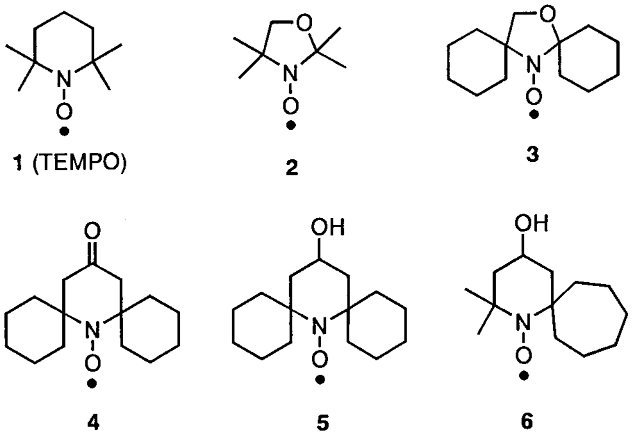
ABSTRACT: Bulk radical polymerizations of styrene (St) in the presence of 7-aza-15-oxodispiro[5.1.5.3]-hexadecane-7-yloxyl (**4**), 7-aza-15-hydroxydispiro[5.1.5.3]hexadecane-7-yloxyl (**5**), and 1-aza-2,2-dimethyl-4-hydroxyspiro[5.6]dodecane-1-yloxyl (**6**) were carried out at 70−110 °C. The $\ln(M_0/M_t)$ vs time plots were linear, and the M_n's of the formed poly(St)'s increased linearly with conversion. Furthermore, the polydispersities (M_w/M_n) were always below 1.3, showing that the polymerization proceeded in a “living” fashion. To increase the polymerization rates, small amounts of camphorsulfonic acid (CSA) or 1,1′-azobis-(cyclohexane-1-carbonitrile) (ACN) were added to the polymerization systems. Addition of 0.50 equiv (vs nitroxide) of CSA increased the polymerization rate by 1.8−2.8 times, and addition of 0.125−1.0 equiv (vs nitroxide) of ACN increased the polymerization rate by 2.3−11.5 times, keeping the “living” nature. The (quasi)equilibrium constants (K) of the C−O bond homolysis and its reformation were determined at 80 °C using the corresponding alkoxyamines from **5**, **6**, and TEMPO; the K constants for **5** and **6** are much larger than that for TEMPO. The bond dissociation energies of the C−O bonds of alkoxyamines calculated by semiempirical and ab initio molecular orbital methods supported the above results.

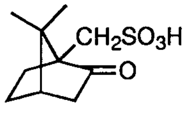
Introduction

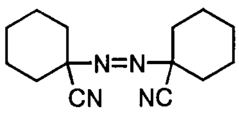
“Living” radical polymerization mediated by stable free radicals (SFR's) such as nitroxides has attracted much attention as a new method for syntheses of well-defined polymers with low polydispersity.[1−3] The SFR-mediated “living” radical polymerization has also been utilized to make a variety of structurally interesting, well-defined polymeric architectures such as block and graft copolymers.[4,5] Since the discovery of the SFR-mediated “living” radical polymerization,[1,2] the ability to control the polymerization of a number of SFR's, including nitroxides, has been widely evaluated.[3] 2,2,6,6-Tetramethylpiperidinyl-*N*-oxyl (TEMPO) (**1**),[1] 2,2,5,5-tetrasubstituted pyrrolidinyl-*N*-oxyls,[6,7] di-*tert*-butyl nitroxide,[8] and their analogues are effective as mediators for the “living” radical polymerization of St (see Chart 1). However, some severe problems to be overcome still remain. For example, applicable monomers are limited to St or St derivatives, and high polymerization temperatures (usually above 110 °C) are required for the polymerization to be “living”. To overcome these problems, many SFR's, including nitroxides, have been studied, and recently, Benoit et al. solved some problems by using sterically hindered noncyclic nitroxides.[9]

We have focused on cyclic nitroxides having spiro structures because we expect that 2,5- and 2,6-dispiro nitroxides yield significant steric congestion around the N−O groups which weakens the N−O bonds of dormant species. Indeed, our previous study showed that, although **2** exhibited no ability to control the radical polymerization of St, dispiro nitroxide **3** controlled the polymerization of St at 110 °C to some extent to give poly(St) with M_w/M_n of ∼1.5.[10] Herein we report the “living” radical polymerization of St mediated by dispiro nitroxides **4**, **5**, and **6** at temperatures of 70−110 °C and the effects of camphorsulfonic acid (CSA) and 1,1′-azobis(cyclohexane-1-carbonitrile) (ACN) on the “living” radical polymerization. We further report the measurements of equilibrium constants and the calculations of the dissociation energies of the C−O bonds.

Chart 1




CSA


ACN

Results and Discussion

Synthesis of Nitroxides 4, 5, and 6. Preparation of **4** and **5** is shown in Scheme 1. According to the reported method,[11] acetonin monohydrate **7**·H_2O was prepared. Reaction of **7**·H_2O with cyclohexanone (excess) in the presence of NH_4Br and H_2O gave **8** in 24% yield.[11] Oxidation of **8** with H_2O_2 in EtOH in the presence of Na_2WO_4 and Triton B gave **4** in 29% yield.[12] Reduction of **8** with $NaBH_4$ in methanol gave **9** in 95% yield, and oxidation of **9** with H_2O_2 in EtOH in the presence of

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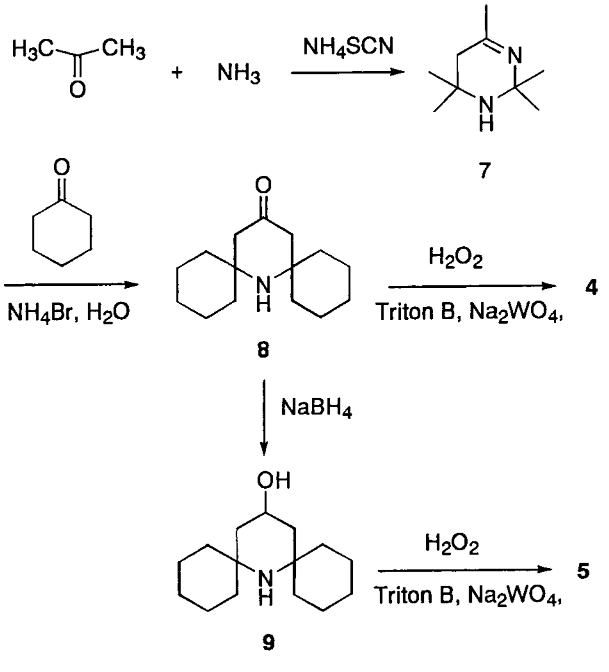
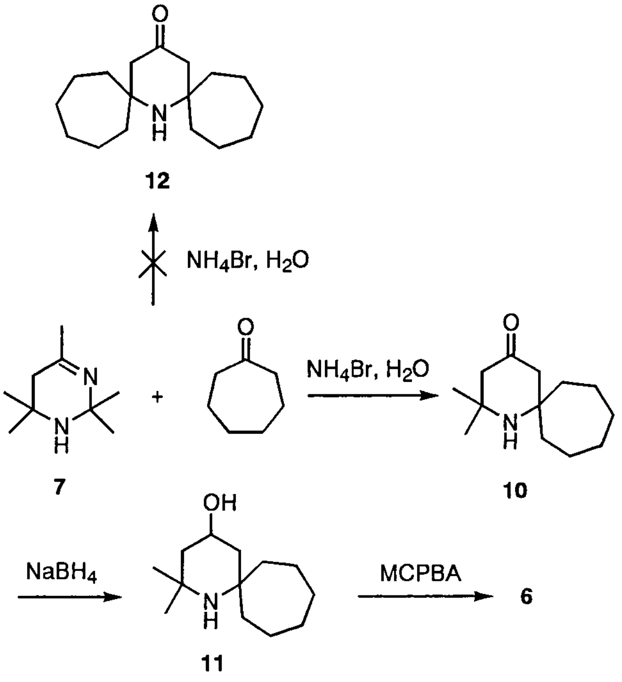
Scheme 1



Scheme 2



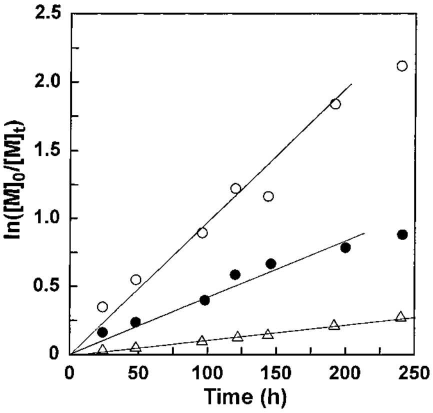


Figure 1. First-order plots for the polymerization of St in the presence of **4** at 70 (△), 80 (●), and 90 °C (○). St 8.7 mmol, BPO 5.0 mM, **4** 6.5 mM.

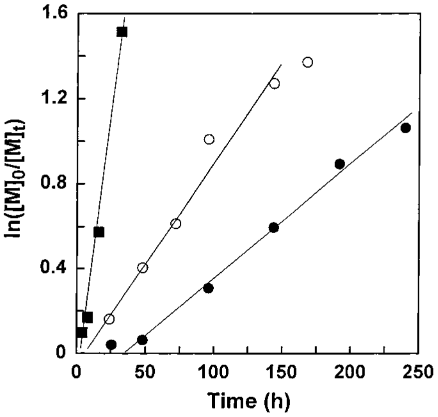


Figure 2. First-order plots for the polymerization of St in the presence of **5** at 80 (●), 90 (○), and 110 °C (■). St 8.7 mmol, BPO 5.0 mM, **5** 6.5 mM.

Na_2WO_4 and Triton B gave **5** in 94% yield. Although the procedures for the oxidation of **8** and **9** were typical for oxidation of secondary amines to nitroxides,[13] there was a large difference in the yields (29% for **4** and 94% for **5**). This is probably due to the difference in solubility of **8** and **9** for EtOH used as the solvent.

Preparation of nitroxide **6** is shown in Scheme 2. Excess cycloheptanone was reacted with **7** under the same reaction conditions as for the reaction of **7** with cyclohexanone. TLC of the reaction mixture showed formation of many compounds. Careful column chromatography gave a monospiro compound **10** in 9.9% yield, together with many unidentified products. However, the dispiro compound **12** was not formed. Reduction of **10** with $NaBH_4$ in methanol gave **11** in 76% yield. Although oxidation of **11** with H_2O_2 in EtOH in the presence of Na_2WO_4 and Triton B was unsuccessful, treatment with *m*-chloroperoxybenzoic acid (MCPBA) in CH_2Cl_2 was successful, giving **6** in 46% yield as red needles.

Polymerization of St Initiated by Benzoyl Peroxide (BPO) in the Presence of 4, 5, and 6. Bulk polymerization of St initiated with BPO in the presence of **4**, **5**, and **6** was carried out in sealed Pyrex tubes using St (8.7 mmol), BPO (5.0 mM), and **4**, **5**, or **6** (6.5 mM). After the contents were once heated at 120 °C for 10 min to completely decompose the added BPO, polymerizations were carried out at 70−110 °C. Conversions were determined by the weights of polymers obtained, and M_n's and M_w/M_n's were measured with SEC using poly(St) standards as the reference.

The $\ln([M]_0/[M]_t)$ vs time plots for the polymerization at 70−110 °C in the presence of **4** or **5** are shown in Figures 1 and 2, respectively. The plots are linear up to high conversion at all temperatures, indicating that the numbers of propagating radical chains are constant during the polymerizations. The M_n vs conversion plots are shown in Figures 3a and 4a. The M_n's increase linearly with conversion up to high conversion, and at 70% conversion the M_n's were beyond 10^5. The experimental values agreed with the calculations within 10% in both figures. For example, the M_n for the poly(St) obtained by the polymerization at 90 °C for 240 h in the presence of **4** is 1.13×10^5, which agrees with the theoretical value of 1.23×10^5 within 10%. As shown by the M_w/M_n vs conversion plots depicted in Figures

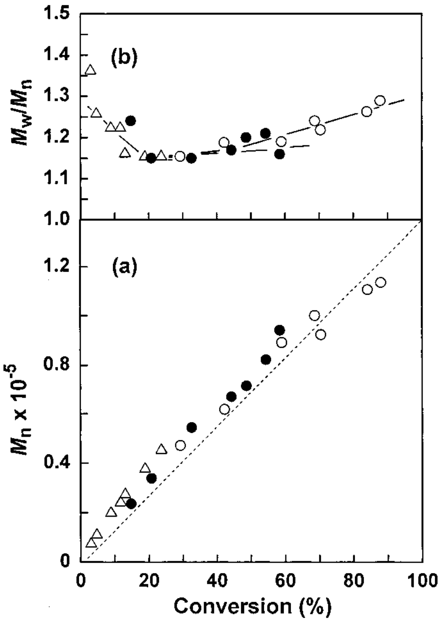


Figure 3. M_n vs conversion (a) and M_w/M_n vs conversion plots (b) for the polymerization of St in the presence of **4** at 70 (△), 80 (●), and 90 °C (○). St 8.7 mmol, BPO 5.0 mM, **4** 6.5 mM. The thoretical values for M_n are indicated by a dotted line

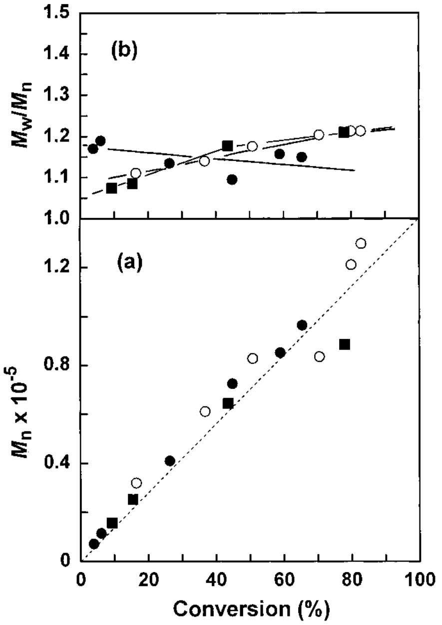


Figure 4. M_n vs conversion (a) and M_w/M_n vs conversion plots (b) for the polymerization of St in the presence of **5** at 80 (●), 90 (○), and 110 °C (■). St 8.7 mmol, BPO 5.0 mM, **5** 6.5 mM. The thoretical values for M_n are indicated by a dotted line

3b and 4b, the M_w/M_n's are kept below 1.3 throughout the polymerizations in the presence of **4** or **5**.

Very similar results were obtained for the polymerizations of St mediated by **6** at 70−110 °C (Figure 6b). Thus, the ln([M]$_0$/[M]$_t$) vs time plots were linear up to high conversion at all temperatures (Figure 5), and the M_n's increased linearly with conversion up to high conversion and agreed with the theoretical values within 10% (Figure 6a). The M_w/M_n's were below 1.2 throughout the polymerization at 100 and 110 °C and below 1.3 in the polymerizations at 70−90 °C.

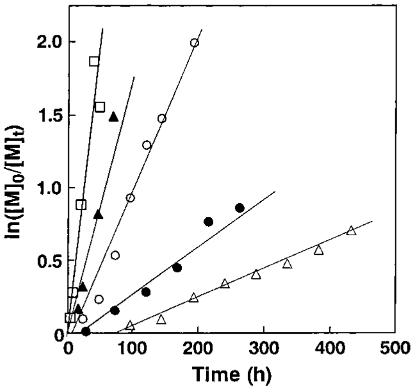


Figure 5. First-order plots for the polymerization of St in the presence of **6** at 70 (△), 80 (●), 90 (○), 100 (▲), and 110 °C (□). St 8.7 mmol, BPO 5.0 mM, **6** 6.5 mM.

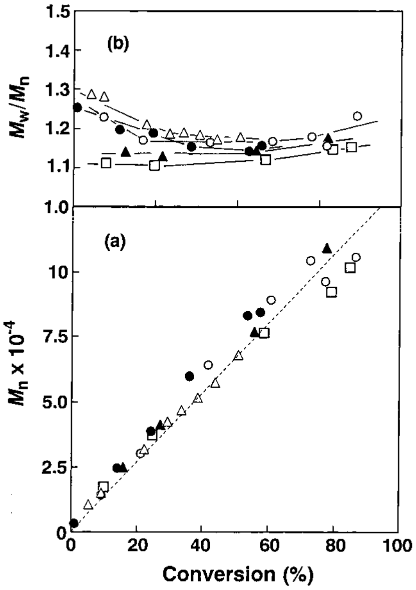


Figure 6. M_n vs conversion (a) and M_w/M_n vs conversion plots (b) for the polymerization of St in the presence of **6** at 70 (△), 80 (●), 90 (○), 100 (▲), and 110 °C (□). St 8.7 mmol, BPO 5.0 mM, **6** 6.5 mM. The thoretical values for M_n are indicated by a dotted line.

Although the ln([M]$_0$/[M]$_t$) vs time plots passed through the origin in the polymerization at high temperatures (90 and 80 °C in Figure 1, 110 °C in Figure 2, and 90−110 °C in Figure 5), the low-temperature polymerizations had induction periods, which increased decreasing temperature.[14] For instance, the induction periods were 20−38 h at 80 °C and 13−75 h at 70 °C. As described below, there were no induction periods in the polymerization initiated by alkoxyamines **13** and **14**. We followed the nitroxide concentrations by ESR as a function of time for the polymerization systems initiated by **6**/BPO (**6**, 6.5 mM; BPO, 5.0 mM). As shown in Figure 7, the concentration of **6** was 3.0 mM at the beginning of polymerization and gradually decreased with polymerization time. After 18 h, the concentration of **6** became constant (1.3×10^{-5} M), which corresponds to the induction period (20 h) for the polymerization at 80 °C initiated by the **6**/BPO system (see Figure 5). In contrast, in the polymerization with **14** (10 mM) the concentration of **6** was constant (7.6×10^{-6} M) throughout the polymerization; this concentration is similar to the constant concentration of **6** after 18 h for the **6**/BPO system. Accordingly, there is an excess of **6** in the **6**/BPO system for the first 18 h, which completely inhibits the polymerization of St. Although the excess amount of **6** is consumed by coupling reactions with the radicals

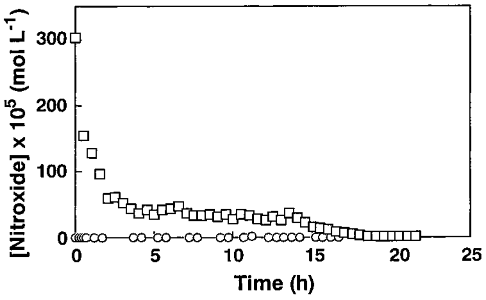
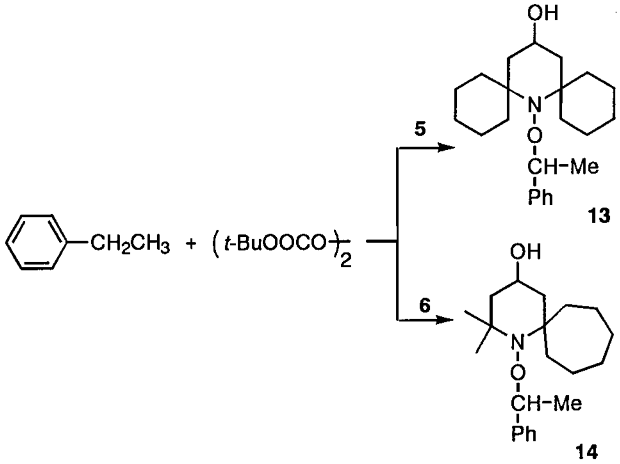


Figure 7. Plots of the concentration of **6** (determined by ESR) vs time at 80 °C. St 4.4 mmol, BPO 5.0 mM, **6** 6.5 mM (□); St 4.4 mmol, **14** 10.0 mM (○).

Scheme 3



derived from the thermal reaction of St, the consumption is very slow at 80 °C. If the ratio of BPO to nitroxide is increased (additional BPO is added), the induction periods will disappear or shorten. However, this would increase the polydispersities of the resultant polymers.[14]

Polymerization of St Initiated by Alkoxyamines. Use of alkoxyamines as the initiator is an alternative method for the "living" radical polymerization, which is superior to the nitroxide/BPO systems because it suppresses side reactions that increase polydispersity. We studied the polymerizations of St initiated by **13** and **14** at 70−90 °C.

Alkoxyamines **13** and **14** were prepared by the reaction of ethylbenzene with di-*tert*-butyl diperoxyoxalate in the presence of **5** or **6** (Scheme 3), according to our previously reported method.[5]

Polymerizations were carried out using 8.7 mmol of St and 4.0 mM of **13** or **14**. Figure 8 shows the $\ln([M]_0/[M]_t)$ vs time plots for the polymerization initiated by **13**. The first-order plots are linear and pass through the origin, with no induction periods. The M_n's increased linearly with conversion, and the M_w/M_n's were 1.22 or below throughout the polymerization (Figure 9). Almost similar results were obtained for the polymerization initiated by **14**. Since there are no induction periods and the M_w/M_n's are lower, the St polymerizations initiated by **13** or **14** are more "living" than the polymerization initiated by **5**/BPO or **6**/BPO at low temperatures.

Polymerization of St with TEMPO at Low Temperatures. Radical polymerization of St mediated by TEMPO proceeds in a "living" fashion above 110 °C.[3,7,15] To evaluate whether the polymerization of St mediated by TEMPO at such low temperatures proceeds in a "living" fashion or not, polymerizations were carried out at 80 and 90 °C using BPO (5.0 mM) and TEMPO (6.5 mM). The concentrations of BPO and TEMPO are the same as above. Although the $\ln([M]_0/[M]_t)$ vs time plots are linear (Figure 10), the M_n's vs conversion plots do not pass through the origin (Figure 11a), and the M_n's deviate from the theoretical values. At 90 °C the M_w/M_n was initially 1.6 and gradually decreased with conversion; at 65% conversion, the M_w/M_n was below 1.3 (Figure 11b). However, the M_w/M_n's were never below 1.5 throughout the 80 °C polymerization. On the basis of the above results, we conclude that TEMPO-mediated radical polymerization no longer proceeds in a "living" fashion below 80 °C.

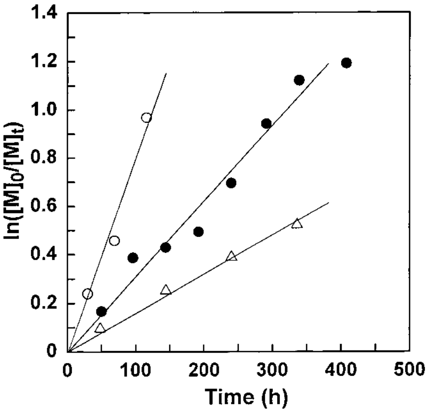


Figure 8. First-order plots for the polymerization of St in the presence of **13** at 70 (△), 80 (●), and 90 °C (○). St 8.7 mmol, **13** 4.0 mM.

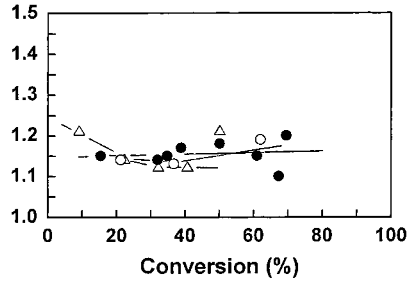


Figure 9. M_w/M_n vs conversion plots for the polymerization of St in the presence of **13** at 70 (△), 80 (●), and 90 °C (○). St 8.7 mmol, **13** 4.0 mM.

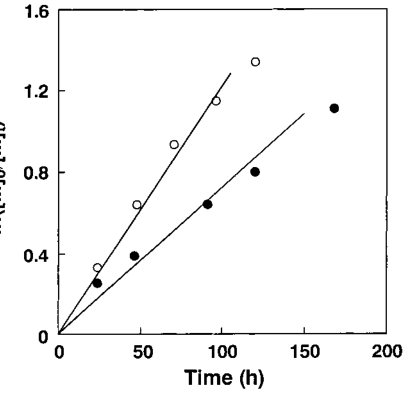


Figure 10. First-order plots for the polymerization of St in the presence of TEMPO at 80 (●), and 90 °C (○). St 8.7 mmol, St 8.7 mmol, BPO 5.0 mM, TEMPO 6.5 mM.

Effects of Camphorsulfonic Acid on the Polymerization Rates. Nitroxide-mediated "living" radical polymerizations are slow even at high temperatures because most propagating radicals are deactivated by

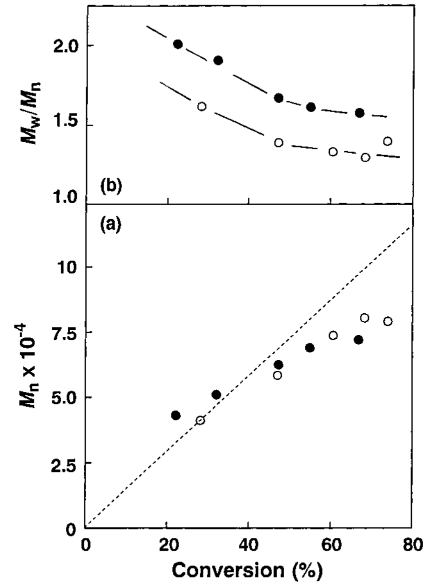


Figure 11. M_n vs conversion (a) and M_w/M_n vs conversion plots (b) for the polymerization of St in the presence of TEMPO at 80 (●) and 90 °C (○). St 8.7 mmol, BPO 5.0 mM, TEMPO 6.5 mM. The theoretical values for M_n are indicated by a dotted line.

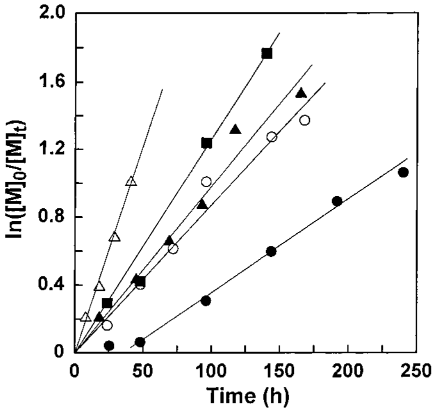


Figure 12. Effects of CSA on the polymerization rates of St in the presence of **5** at 80 and 90 °C. St 8.7 mmol, BPO 5.0 mM, **5** 6.5 mM, CSA 0 (●), 3.25 (▲), and 6.5 mM (■) at 80 °C and CSA 0 (○) and 3.25 mM (△) at 90 °C.

nitroxides, and as described above, the low-temperature polymerizations were extremely slow. For example, the conversions of St in the polymerization mediated by **4** at 70, 80, and 90 °C for 240 h were 24, 59, and 88%, respectively.

Addition of appropriate amounts of organic acids such as CSA or acid anhydrides such as acetic anhydride to polymerization systems increases the polymerization rate, keeping the "living" nature.[16,17] On the basis of these references, we added 0.25, 0.50, and 1.0 equiv (vs nitroxide) of CSA to the polymerization systems.

Figure 12 shows the $\ln([M]_0/[M]_t)$ vs time plots for the polymerizations at 80 and 90 °C in the presence of 3.25 (0.50) and 6.5 mM (1.0 equiv for **5**) of CSA. Upon addition of 0.5 equiv of CSA, the polymerization rates were 1.8 (80 °C) and 2.8 times (90 °C) higher than in the absence of CSA, the M_w/M_n's were below 1.42 (Figure 13), and the induction periods disappeared completely. On the other hand, an addition of 1.0 equiv of CSA increased the polymerization rate by 2.3 times at 80 °C, but the M_w/M_n's increased gradually with conversion up to ~2.0 at 80% conversion.

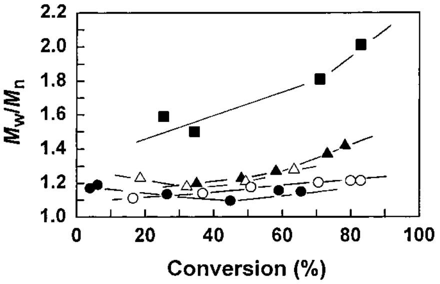


Figure 13. Effects of CSA on the M_w/M_n's for the polymerization of St mediated by **5** at 80 and 90 °C. St 8.7 mmol, BPO 5.0 mM, **5** 6.5 mM, CSA 0 (●), 3.25 (▲), and 6.5 mM (■) at 80 °C and CAS 0 (○) and 3.25 mM (△) at 90 °C.

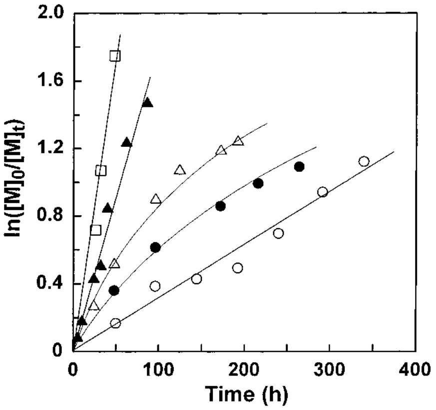


Figure 14. Effects of ACN on the polymerization rates of St mediated by **13** at 80 °C. St 8.7 mmol, **13** 4.0 mM, ACN 0 (○), 0.50 (●), 1.0 (△), 2.0 (▲), and 4.0 mM (□).

Similar effects were observed in the polymerization of St mediated by **6**. When 3.25 mM (0.5 equiv for **6**) of CSA was added to the polymerization system at 80 °C, the polymerization rate was 2.8 times increased, and the M_w/M_n's increased only slightly (~1.35 at 40–70% conversions). On the other hand, an addition of 1.63 mM (0.25 equiv for **6**) showed no significant effects other than an increase in M_w/M_n's.

Effects of 1,1′-Azobis(cyclohexane-1-carbonitrile) on the Polymerization Rates. As described above, addition of appropriate amounts of CSA increased the polymerization rates by 1.8–2.8 times, while keeping the "living" nature. An alternative method for increasing of the polymerization rates is addition of radical initiators.[18] In this case, the half-life time of the initiator is important. In the present study, ACN was chosen as the radical initiator (half-life time $\tau_{1/2} = 31.7$ h at 80 °C in toluene). Polymerizations of St initiated by **13** and **14** in the presence of ACN (0.50–4.0 mM) were carried out at 80 °C.

The $\ln([M]_0/[M]_t)$ vs time plots for the polymerization of St initiated with **13** are shown in Figure 14. Addition of 0.50 (0.125 equiv vs **13**), 1.0 (0.25), and 2.0 mM (0.50) of ACN increased the polymerization rate by 2.3, 3.4, and 6.0 times, and addition of 4.0 mM (1.0 equiv) of ACN increased the polymerization rate by 11.5 times. In the cases of the 0.50 and 1.0 mM addition of ACN, the polymerization rates decreased with time and eventually approached the rate in the absence of ACN. This is due to consumption of the added ACN.

Despite the drastic increases in the polymerization rate, the M_n vs conversion plots were always on the same straight line (Figure 15a), regardless of the amounts of ACN added, indicating that the addition of

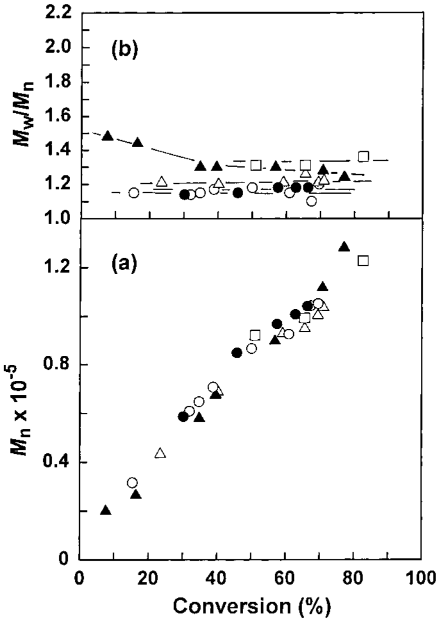
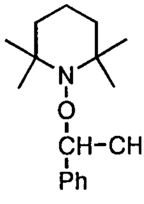


Figure 15. Effects of ACN on the molecular weights and the polydispersities for the polymerization of St mediated by **13** at 80 °C. St 8.7 mmol, **13** 4.0 mM, ACN 0 (○), 0.50 (●), 1.0 (△), 2.0 (▲), and 4.0 mM (□).

ACN gave no significant affect on the M_n's. When the amounts of the added ACN were 0.50−2.0 mM, the M_w/M_n's were below 1.3 (above 40% conversion), as found in Figure 15b, and when 4.0 mM of ACN was added, the M_w/M_n's were slightly larger than 1.3 at 80% conversion. Accordingly, the slow "living" radical polymerization of St at low temperatures could be drastically improved by addition of ACN.



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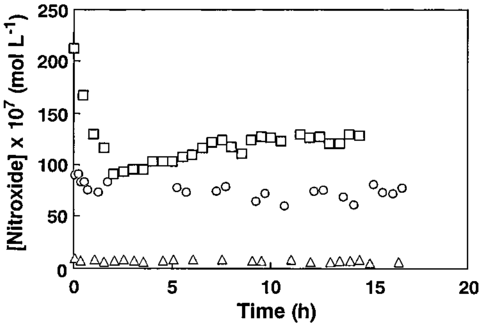


Figure 16. Plots of the nitroxide concentrations (determined by ESR) as a function of time for the polymerization of St initiated by alkoxyamines **13**−**15** at 80 °C. St 4.4 mmol, alkoxyamine 10 mM; **13** (□), **14** (○), and **15** (△).

Table 1. Average Concentrations of Nitroxides and Propagating Radicals and Average Equilibrium Constants for Dormant Species in the Polymerization of St at 80 °C Initiated by 13−15[a]

nitroxide	[nitroxide] × 10^7 (M)	[propagating radical] × 10^9 (M)	[alkoxyamine][b] × 10^3 (M)	$K \times 10^{12}$ (M)
TEMPO	7.4	1.18	10	0.087
5	128	1.60	10	2.05
6	76	1.68	10	1.28

[a] St 4.4 mmol. [b] The initial concentrations of alkoxyamine are shown.

Determination of Equilibrium Constants. The rate constants and equilibrium constants associated with the C−O bond homolysis of dormant species and its reformation are particularly important for estimating the possibility of "living" radical polymerization. Spiro nitroxides **4**−**6** made low-temperature "living" radical polymerization of St possible, as described above. We assume that the N−O bonds of alkoxyamines **13** and **14** and the corresponding dormant species are much weaker than those of alkoxyamine **15** and the corresponding dormant species because of the large steric congestion around the C−O bond in **13** and **14**. To confirm this assumption, we measured the (quasi)-equilibrium constants (K) (eq 1) for the C−O bond homolysis and its reformation using 10 mM of alkoxyamine and 4.35 mM of St at 80 °C according to a reported method.[19] The concentrations of the dormant species are presumably equal to the initial alkoxyamine concentrations. The nitroxide concentrations were determined directly by ESR. The concentrations of the propagating radicals ($P^•$) were determined using eq 2. Constants k were obtained from the slopes of the $\ln([M]_0/[M]_t)$ vs time plots and are equal to $k_p[P^•]$. The propagation rate constant k_p (658 L mol^{-1} s^{-1}) at 80 °C was derived using eq 3.[20]

$$K = [\text{nitroxide}][\text{propagating radical}]/[\text{alkoxyamine}] \quad (1)$$

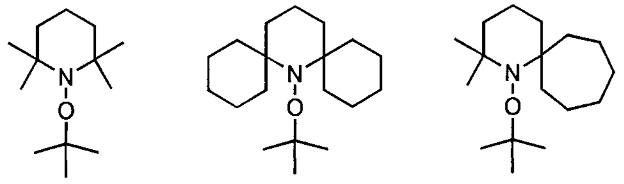
$$\ln([M]_0/[M]_t) = kt = k_p[P^•]t \quad (2)$$

$$k_p = 10^{7.630}\ \text{L mol}^{-1}\ \text{s}^{-1} \exp(-32.51\ \text{kJ mol}^{-1}/RT) \quad (3)$$

Figure 16 plots the concentrations of nitroxides as a function of time. Although the concentrations were not constant for the first 5 h, they were approximately constant after 5 h. The K values were obtained using the concentrations of nitroxides and propagating radicals obtained. The results are summarized in Table 1. K_5 is 1.6 times larger than K_6, and K_6 is 15 times larger than K_{TEMPO}, indicating that the N−O bonds of alkoxyamines **13** and **14** and the corresponding dormant species are much weaker than those of alkoxyamine **15** and the corresponding dormant species. This explains why the radical polymerization of St mediated by **4**−**6** proceeded in a "living" fashion even at low temperatures but was unsuccessful in the case of TEMPO.

Calculations of the Bond Dissociation Energies of the C−O Bonds. The magnitudes of the equilibrium constants K depend largely on the dissociation energy of the C−O bond (D_{C-O}). To rationalize the present results, the bond dissociation energies of the C−O in alkoxyamines **16**−**18** (Chart 2) were calculated by the semiempirical (MNDO/AM1) and ab initio methods (Gaussian 98).[21] The ab initio molecular orbital calculations were peformed using the STO 6-31G basis sets and the DFT Becke 3LYP method. Previously, D_{C-O}'s of some alkoxyamines were calculated using semiempirical[6,22−24] and ab initio methods.[25] In the present calculations, 2-methyl-2-propyl radical was adopted instead of α-phenetyl radical to ease the calculations of

Chart 2



16 **17** **18**

the optimized structure of alkoxyamines. The calculation results are shown in Table 2.

The optimized geometries of **16**−**18** were calculated by the MNDO/AM1 method, giving very similar C−O and N−O bond lengths and the C−N−C bond angles for **16**−**18** (Table 2). Previously, the activation energy (E_a) for the bond homolysis of **16** was experimentally determined to be 97 kJ/mol.[26] On the basis of this value, the D_{C-O} value can be estimated to be 89−95 kJ/mol, which is 2−8 kJ/mol lower than the E_a value. Comparison of this value with those in Table 2 demonstrates that the MNDO/AM1 method (57.8 kJ/mol) substantially underestimates the D_{C-O} value, while the DFT Becke 3LYP method (147.5 kJ/mol) substantially overestimates the value. The agreement with experiment should improve with larger basis sets. However, since many of the errors in these calculations are systematic, we believe that the relative order of ΔH_f (heat of formation) (and D_{C-O}) will be reliably predicted. The decreasing order in D_{C-O} predicted by the AM1 method is **16** ≈ **18** > **17**, while that predicted by the DFT Becke 3LYP method is **16** > **18** ≈ **17**. If the entropy of dissociation for the equilibria is constant or relatively small, the decreasing order in D_{C-O} estimated from K is **16** > **18** ≈ **17**, which agrees with that predicted by the DFT Becke 3LYP method. We can therefore estimate the ability of nitroxides to control radical polymerization from the MO calculations at a high level.

Conclusions

Radical polymerizations of St in the presence of **4**, **5**, and **6** were carried out at 70−110 °C. Those nitroxides showed to have an excellent ability to control the polymerization of St at low temperatures of 70−90 °C, as well as at high temperatures of 100−110 °C. Addition of appropriate amounts of CSA increased the polymerization rate by 1.8−2.8 times, and addition of ACN increased the polymerization rates by 2.3−11.5 times, keeping the "living" nature. The K values determined for **5**, **6**, and TEMPO are 2.05×10^{-12}, 1.28×10^{-12}, and 8.7×10^{-14} mol/L, respectively, which explained that the radical polymerization of St mediated by **4**−**6** proceeded in a "living" fashion at the temperatures below 80 °C but was unsuccessful in the case of TEMPO. The D_{C-O} values of alkoxyamines **16**−**18** calculated by the semiempirical (MNDO/AM1) and ab initio molecular orbital methods (DFT Becke 3LYP) demonstrated that although the calculations by the MNDO/AM1 method showed unsatisfactory agreement with experimental results, the DFT Becke 3LYP method provided an agreement with the experimental results.

Experimental Section

IR spectra were run on a JASCO FT/IR 230 spectrophotometer. ^{1}H NMR (400 mHz) and ^{13}C NMR spectra (100 MHz) were recorded with a JEOL α-400 NMR spectrometer using $CDCl_3$ as solvent and TMS as standard. HR mass spectra (FAB) were measured on a JEOL JMS-700 spectrometer using 3-nitrobenzyl alcohol as a matrix. Silica gel and alumina column chromatography was carried out using a BW-127ZH silica gel (Fiji silysia Co., Ltd.) or aluminum oxide 90 (Merck). Size exclusion chromatography (SEC) was performed with a Tosoh 8020 series using TSK-gel G5000H_{HR} (pore size 9 μm), GmultiporeH$_{XL}$-M (5 μm), and GMH$_{HR}$-L columns (5 μm) calibrated with polystyrene standards, eluting with THF at 40 °C (flow rate 1.0 mL/min). Detection was made with a Tosoh refractive index detector RI8020.

ESR Measurements. ESR spectra were measured with a Bruker ESP300 spectrometer. Radical concentrations were determined by double integration of ESR signals. Calibration curves were drawn using TEMPO as the reference and using the same instrument settings, solvent, and ESR cell.

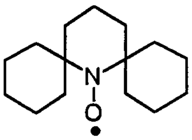
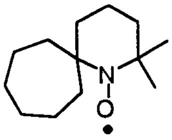
Materials. 2,2,4,4,6-Pentamethyl-2,3,4,5-tetrahydropyrimidine (acetonin) monohydrate (**7**·H_2O) was prepared by the reaction of acetone with ammonia in the presence of NH_4SCN according to a reported method.[11] *N*-(1-Phenylethoxy)-2,2,6,6-tetramethylpiperidine (**15**) was obtained by our previous method.[5] Di-*tert*-butyl diperoxyoxalate was prepared by the reported method.[27] Benzoyl peroxide (BPO) was purified by reprecipitating a solution of BPO in $CHCl_3$ to ether. 3-Chloroperoxybenzoic acid (70% purity) was purchased from Tokyo Chemical Indusctry. Camphorsulfonic acid (98% purity) (CSA) was purchased from Wako Pure Chemical Industry and used without purification. 1,1′-Azobis(cyclohexane-1-carbonitrile) (ACN) was obtained from Wako Pure Chemical Industry and purified by recrystallization from EtOH.

7-Aza-15-oxodispiro[5.1.5.3]hexadecane (8). This compound was prepared according to the reported method, with some modifications.[11] A mixture of **7**·H_2O (10.0 g, 58.1 mmol), cyclohexanone (20.0 g, 204 mmol), NH_4Br (6.5 g), and H_2O (2 mL) was stirred at room temperature for 1 day under a nitrogen atmosphere. After 50% aqueous NaOH (40 mL) was added, the organic layer was extracted with ether. The combined ether extracts were washed with brine, dried over $MgSO_4$, and evaporated. The residue was then distilled at 5 mmHg. A fraction of bp 100−120 °C was collected and chromatographed on silica gel with 1:1 hexane−ethyl acetate to give **8** in 24% yield. On standing at room temperature, this oil solidified to give colorless needles, which were recrystallized from hexane. Mp 101−103 °C (lit.[12] 100.5−101.5 °C). ^{1}H NMR δ: 1.39 (m, $=CCH_2C\mathbf{H}_2CH_2C\mathbf{H}_2CH_2$, 8 H), 1.52 (m, $=CC\mathbf{H}_2CH_2CH_2CH_2C\mathbf{H}_2$, 8 H), 1.64 (m, $=CCH_2CH_2C\mathbf{H}_2CH_2CH_2$, 4H), 2.30 (s, $CH_2C(=O)CH_2$, 4H).

7-Aza-15-oxodispiro[5.1.5.3]hexadecane-7-yloxyl (4). 35% H_2O_2 (4.8 mL, 56 mmol) was added to a stirred solution of **8** (0.30 g, 1.3 mmol), Triton B (1.0 g, 6.0 mmol), and Na_2WO_4·$2H_2O$ (0.10 g, 0.30 mmol) in EtOH (10 mL), and the resulting mixture was stirred at room temperature for 3 days. After water (200 mL) was added, the products were extracted with CH_2Cl_2 (50 mL). The CH_2Cl_2 layer was washed with brine, dried over $MgSO_4$, and evaporated, and the residue was crystallized from EtOH to give **4** as yellow plates with mp 114−116 °C (lit.[12] 114.0−115.0 °C) in 29% yield.

7-Aza-15-hydroxydispiro[5.1.5.3]hexadecane (9). $NaBH_4$ (1.0 g, 26 mmol) was added to a stirred solution of **8** (1.00 g, 4.2 mmol) in EtOH (80 mL), and the mixture was stirred at room temperature for 3 h. After water (300 mL) was added, the products were extracted with CH_2Cl_2 (100 mL), and the CH_2Cl_2 layer was washed with brine and dried over $MgSO_4$. Evaporation of the solvent gave almost pure **9** as colorless microcrystals in 95% yield. This product was used in the following oxidation without further purification. An analytical sample was obtained by recrystallization from hexane. Mp 93−95 °C. IR (KBr): 3280 cm^{-1} (NH and OH). ^{1}H NMR: δ 0.89 (dd, each J = 12.0 Hz, C(O)−C**H**H, 2 H), 1.36−1.67 (m, spirocyclohexyl CH_2, 20 H), 2.16 (dd, J = 12 and 4.2 Hz, C(O)−CH**H**, 2H), 3.98 (tt, J = 12 and 4.2 Hz, C**H**(OH), 1H). Anal. Calcd for $C_{15}H_{27}NO$: C, 75.90; H, 11.46; N, 5.90. Found: C, 75.57; H, 11.39; N, 5.91.

Table 2. Properties of Nitroxides and Alkoxyamines Estimated by Molecular Orbital Calculations[a]

nitroxide	ΔH_f (kJ/mol)[b] nitroxide	alkoxyamine	D_{C-O} (kJ/mol)	bond length (Å) C−O	N−O	N−C distance[c] (Å)	C−N−C bond angle (deg)
TEMPO	−78.2	−148.5	57.8 (MNDO/AM1)[b] 147.5 (DFT Becke 3LYP)[d]	1.469	1.351	2.421	115.1
	−175.1	−223.3[c]	35.7 (MNDO/AM1)[b] 121.2 (DFT Becke 3LYP)[d]	1.471	1.355	2.436	114.1
	−125.4[d]	−194.8[c]	56.9 (MNDO/AM1)[b] 125.7 (DFT Becke 3LYP)[d]	1.472	1.352	2.422	114.4

[a] The optimized molecular structures were calculated by the MNDO/AM1 method. The heat of formation (ΔH_f) of *tert*-butyl radical calculated by the MNDO/AM1 method is 12.5 kJ/mol. [b] ΔH_f and bond dissociation energy (D_{C-O}) calculated by the MNDO/AM1 method. [c] The C−N distance in the C−O−N fragment of alkoxyamines. [d] D_{C-O} calculated by the DFT Becke 3LYP method (basis sets STO 6-31G).

Table 3. Results of Bulk Polymerization of Styrene Initiated with BPO in the Presence of 4[a]

run	temp (°C)	time (h)	conv[b] (%)	M_n[c]	M_w/M_n[c]
1	70	24	3.0	7 400	1.36
2	70	48	4.7	11 100	1.26
3	70	96	8.9	19 900	1.22
4	70	122	12	24 200	1.22
5	70	144	13	27 400	1.16
6	70	192	19	37 700	1.15
7	70	240	24	45 400	1.15
8	80	24	15	23 600	1.24
9	80	48	21	33 900	1.15
10	80	98	33	54 500	1.15
11	80	120	44	66 900	1.17
12	80	146	49	71 400	1.20
13	80	200	54	82 200	1.21
14	80	241	59	94 100	1.16
15	90	24	29	47 200	1.15
16	90	48	42	61 800	1.19
17	90	96	59	89 200	1.19
18	90	120	71	92 300	1.22
19	90	144	69	100 000	1.24
20	90	192	84	110 400	1.26
21	90	240	88	113 400	1.29

[a] St 1.0 mL (8.7 mmol), BPO 1.21 mg (5.0×10^{-3} mmol), **4** 1.63 mg (6.5×10^{-3} mmol). [b] Conversions were calculated from the weights of formed poly(St). [c] Determined by SEC (see Experimental Section).

7-Aza-15-hydroxydispiro[5.1.5.3]hexadecane-7-yloxyl (5). 35% H_2O_2 (5.0 mL, 58 mmol) was added to a stirred solution of **9** (0.50 g, 1.98 mmol), Triton B (1.0 g, 6.0 mmol), and $Na_2WO_4 \cdot 2H_2O$ (0.30 g, 0.91 mmol) in EtOH (10 mL), and the resulting mixture was stirred at room temperature for 3 days. After water (200 mL) was added, the products were extracted with CH_2Cl_2 (50 mL). The CH_2Cl_2 layer was washed with brine, dried over $MgSO_4$, and evaporated to give almost pure **5** in 94% yield. Recrystallization from ethyl acetate gave red prisms with mp 176−178 °C. IR (KBr): 3400 cm^{-1} (OH). Anal. Calcd for $C_{15}H_{26}NO_2$: C, 71.39; H, 10.38; N, 5.55. Found: C, 71.04; H, 10.43; N, 5.59.

1-Aza-2,2-dimethyl-4-oxospiro[5.6]dodecane (10). A mixture of **7**$\cdot H_2O$ (20.0 g, 0.116 mol), cycloheptanone (44 g, 0.39 mol), NH_4Br (13 g, 0.13 mol), and H_2O (4 mL) was stirred for 1 day at room temperature under a nitrogen atmosphere. After 50% aqueous NaOH solution (80 mL) was added, the organic layer was extracted with ether. The combined ether extracts were washed with brine, dried over $MgSO_4$, and evaporated. The residue was then chromatographed on silica gel with 1:2 hexane−ethyl acetate. Crystallization from hexane gave **10** as colorless needles in 9.9% yield. Mp 62−63 °C. IR (KBr): 3300 (NH) 1700 cm^{-1} (C=O). ^{1}H NMR: δ 1.22 (s, Me, 6 H), 1.41−1.66 (m, spirocycloheptyl, 12 H), 2.22 (s, C(=O)−CH_2, 2 H), 2.28 (s, C(=O)−CH_2, 2 H). Anal. Calcd for $C_{13}H_{23}NO$: C, 74.59; H, 11.07; N, 6.69. Found: C, 74.32; H, 11.04; N, 6.62.

1-Aza-2,2-dimethyl-4-hydroxyspiro[5.6]dodecane (11). $NaBH_4$ (0.54 g, 10 mmol) was added to a stirred solution of **10** (0.30 g, 1.4 mmol) in EtOH (30 mL), and the mixture was stirred at room temperature for 3 h. After water (150 mL) was added, the products were extracted with CH_2Cl_2 (50 mL). The CH_2Cl_2 layer was washed with brine, dried over $MgSO_4$, and evaporated to give almost pure **11** as colorless microcrystals in 76% yield. This product was used in the following reaction without further purification. Recrystallization from hexane gave colorless prisms with mp 67−69 °C. IR (KBr): 3280 (OH), 3100 cm^{-1} (NH). ^{1}H NMR: δ 0.86 (dd, each $J = 12$ Hz, −C**H**H−CH(OH)−, 1H), 1.02 (dd, each $J = 12$ Hz, CH**H**−CH(OH), 1 H), 1.14 (s, Me, 3 H), 1.16 (s, Me, 3 H), 1.33−1.78 (m, spirocycloheptyl CH_2, 12 H), 1.92 (ddd, $J = 12$, 3.9, and 1.9 Hz, C**H**H−CH(OH), 1 H), 1.99 (ddd, $J = 12$, 3.9, and 1.9 Hz, CH**H**−CH(OH), 1 H), 4.00 (tt, $J = 12$ and 3.9 Hz, C**H**(OH), 1 H). Anal. Calcd for $C_{13}H_{25}NO$: C, 73.88; H, 11.92; N, 6.63. Found: C, 73.76; H, 11.97; N, 6.48.

1-Aza-2,2-dimethyl-4-hydroxyspiro[5.6]dodecane-1-yloxyl (6). 3-Chloroperoxybenzoic acid (70% purity; 1.6 g, 7.1 mmol) was added to a solution of **11** (1.00 g, 4.7 mmol) in CH_2Cl_2 (30 mL), and the resulting mixture was stirred at room temperature for 2 days. The mixture was then washed with 10% K_2CO_3 and then brine and dried over $MgSO_4$. After evaporation, the residue was chromatographed on alumina with 1:2 hexane−ethyl acetate to give **6** in 46% yield. Recrystallization from hexane gave red needles with mp 71−73 °C. IR (KBr): 3400 cm^{-1} (OH). Calcd for $C_{13}H_{24}NO$: C, 68.99; H, 10.69; N, 6.19. Found: C, 68.99; H, 10.78; N, 6.10.

***N*-(1-Phenylethyloxy)-7-aza-15-hydroxydispiro[5.1.5.3]hexadecane (13).** A solution of **5** (0.30 g, 1.2 mmol) and di-*tert*-butyl diperoxyoxalate (0.42 g, 1.8 mmol) in ethylbenzene (15 mL) was stirred at 38 °C for 3 h under a nitrogen stream. Concentration of the mixture to 2−3 mL under reduced pressure and column chromatography of the concentrate on silica gel with 2:1 hexane−ethyl acetate gave **13** in 70% yield (0.30 g, 0.84 mmol) as a solid. Recrystallization from hexane afforded colorless fine needles with mp 111.5−113.5 °C. ^{1}H NMR (H−H COSY): δ 0.98 and 1.10 (dd, each $J = 12$ Hz, CH(OH)−C**H**H, 2 H), 1.58 (d, $J = 6.8$ Hz, Me, 3 H), 0.61−2.12 (m, spirocyclohexyl CH_2, 20 H), 2.37 and 2.49 (dt, $J = 12$ and 3.7 Hz, CH(OH)−CH**H**, 2 H), 3.81 (m, C**H**(OH), 1 H), 4.73 (q, $J = 6.8$ Hz, PhC**H**(Me), 1 H), 7.20−7.33 (m, Ph, 5 H). Calcd for $C_{23}H_{35}NO_2$: C, 77.27; H, 9.87; N, 3.92. Found: C, 77.05; H, 9.95; N, 3.87.

***N*-(1-Phenylethyloxy)-1-aza-2,2-dimethyl-4-hydroxyspiro[5.6]dodecane (14).** A solution of **6** (0.67 g, 3.0 mmol) and di-*tert*-butyl diperoxyoxalate (1.04 g, 4.4 mmol) in ethylbenzene (30 mL) was stirred at 38 °C for 3 h under a nitrogen stream. Concentration of the mixture to 2−3 mL under reduced pressure and column chromatography of the concentrate on silica gel with 2:1 hexane−ethyl acetate gave **14** as a viscous oil in 85% yield (0.83 g, 2.5 mmol). This oil was purified with a recycling preparative HPLC instrument (Japan Analytical Industry, LC-908) using $CHCl_3$ as eluant. ^1H NMR: δ 0.69, 1.10, 1.23, and 1.31 (each s, $-C(C\mathbf{H}_3)_2-$, 6 H), 1.10−2.28 (m, spirocycloheptyl and piperidinyl CH_2, 16 H), 1.51 and 1.52 (each d, $J = 6.8$ Hz, $-CH(C\mathbf{H}_3)-$, 3 H), 3.92 (m, C**H**(OH), 1 H), 4.79 and 4.83 (each q, $J = 6.8$ Hz, $-C\mathbf{H}(Me)-$, 1 H), 7.23−7.33 (m, aromatic, 5 H). HR FABMS: m/z calcd for $C_{21}H_{34}NO_2$ ($M^+ + H$): 332.2591. Found: 332.2598.

General Procedure for Polymerization. Polymerizations of St were carried out in sealed Pyrex tubes. For instance, St (1.0 mL, 8.7 mmol) containing BPO (1.21 mg, 5.0×10^{-3} mmol) and **4** (1.63 mg, 6.5×10^{-3} mmol) were placed in Pyrex tubes, the contents were degassed by three freeze−pump−thaw cycles using a high-vacuum system, and the tubes were sealed off. After being heated at 120 °C for 10 min, polymerizations were carried out at 70−90 °C. After 24−240 h, the reaction mixtures were diluted with benzene (10 mL) and poured into a large excess of MeOH. Poly(St) precipitated was collected by filtration, dried at 50 °C in a vacuum oven, and weighed. M_n's and M_w/M_n's were determined by SEC. The results are summarized in Table 3.

Measurements of the Concentrations of Nitroxides by ESR. A solution of BPO (2.5×10^{-3} mmol) and nitroxide (3.3×10^{-3} mmol) in St (4.4 mmol) or alkoxyamine (5.0×10^{-3} mmol) in St (4.4 mmol) was put in an ESR tube and degassed by three freeze−pump−thaw cycles with a high-vacuum system and sealed off. The solution was then heated at 120 °C for 10 min and cooled to 80 °C, and the concentrations of nitroxide were measured at 80 °C as a function of time. For solutions of alkoxyamines they were heated at 80 °C from the beginning without heating to 120 °C.

Acknowledgment. The authors thank Dr. Yoshio Teki of Osaka City University for present of the semiempirical and ab initio MO calculations. This work was financially supported in part by a Grant-in-Aid Scientific Research No.12450376 from the Ministry of Education, Science, Sports, and Culture, Japan.

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MA0012752