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Control of Living Free-Radical Polymerization by a New Chiral Nitroxide and Implications for the Polymerization Mechanism

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Use of nitroxide radicals such as TEMPO in living free-radical polymerizations is of current interest in polymer synthesis.[1−4] In this Communication, we wish to report that asymmetric nitroxide, 2,5-dimethyl-2,5-diphenylpyrrolidin-1-oxyl (DDPO, **1**, Scheme 1), mediates effectively free-radical polymerization of styrene. The polymerization is faster, gives better molecular weight (MW) control compared to TEMPO-mediated polymerization, but, unlike the latter, does not require addition of external strong acids. The amount of the nitroxide (NO) rather than benzoyl peroxide (BPO) controls the MW.[3c] We also provide some mechanistic evidence that propagation indeed occurs from the fully dissociated radicals.

DDPO was synthesized as outlined in Scheme 1.[5,6] Even though formation of both *cis* and *trans* isomers is possible, only the latter can be optically resolved. Hence, we subjected the isolated product to chiral HPLC and observed two peaks of equal intensity. The first peak corresponded to an isomer with $[\alpha]_D = +155°$ and the second one to an isomer with $[\alpha]_D = -164°$ ($c = 1$, CH_2Cl_2, 21 °C).[6] These results confirm that the isolated product is indeed the *trans* isomer. Although the yield (unoptimized) is low, the intermediate nitrone could be easily recovered and recycled.[5e]

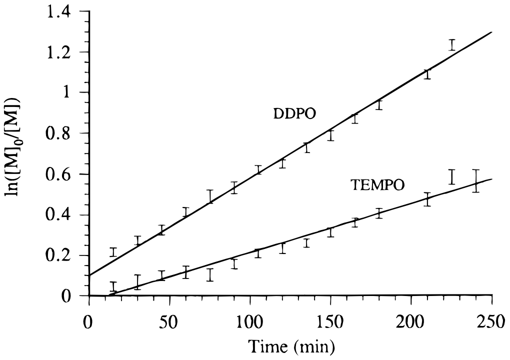


Figure 1. Plot of $\ln([M]_0/[M])$ versus time (min) for bulk polymerization of styrene in the presence DDPO and TEMPO at 137 °C: [BPO] = 0.041 M and [NO] = 0.053 M.

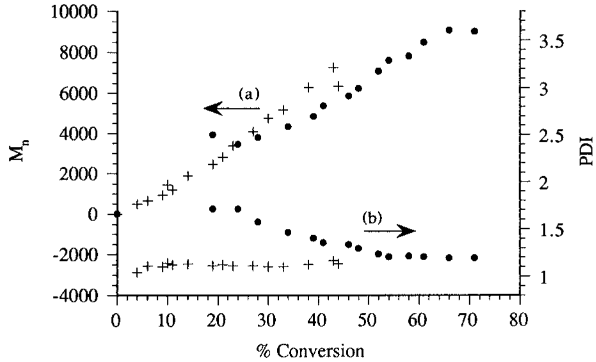
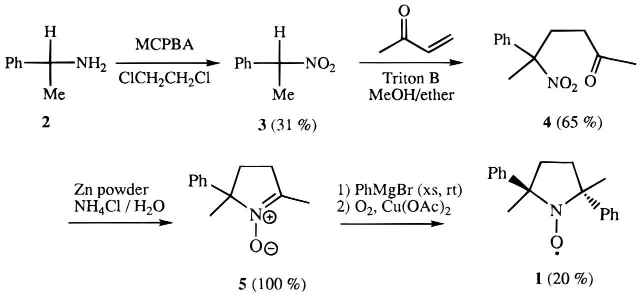


Figure 2. Dependence of M_n (a) and polydispersity index (PDI) (b) on percent conversion for bulk polymerization of styrene in the presence of DDPO (●) and TEMPO (+).

Scheme 1. Synthesis of Racemic DDPO



The polymerization results are summarized in Table 1. The following general deductions can be made: (1) DDPO mediates bulk polymerization of styrene to give polymer in high yields with fairly low polydispersity (PDI) and good MW control. (2) The MW is controlled by the amount of NO, and DDPO gives better MW control than does TEMPO. (3) $[NO]/[BPO] \geq 1$ is required for MW control and lower PDI (entries 1−6). At $[NO]/[BPO] < 1$ the amount of BPO affects the MW and PDI.[2,3] (4) The polymerization, as expected, is extremely slow and requires several days at high [NO]/[BPO]. However, the MW is still controlled by the amount of NO, and the PDI remains low (entry 5). This suggests that, during the initiation period, styryl radicals are formed not only via the expected reaction with BPO but also thermally (autoinitiation) and that the trapping by the excess NO is quite efficient. It further indicates that exchange between active and dormant chains is fast. (5) DDPO gives faster polymerization compared to TEMPO as evidenced by viscosity changes (not shown) and higher yields (entry 3 vs 6).[7a] This is evident from the first-order plots (Figure 1). The observed rate constants, k_{obs}, are 4.6×10^{-3} and 2.4×10^{-3} s^{-1} for DDPO and TEMPO, respectively.[7b] In both cases, the M_n increased linearly with conversion (Figure 2a). However, the PDI in the case of DDPO started high and decreased as the conversion increased (Figure 2b). In contrast, the PDI for TEMPO-mediated polymerization remained essentially constant over the same period. These suggest that TEMPO is a more efficient radical trapping agent but a slower polymerization mediator than DDPO is. Hence, the initial radical concentration might be relatively high in the case of DDPO, leading to a somewhat less controlled polymerization at the early stages. These results are consistent with the slightly lower $\Delta H^{\ddagger}$ for radical trapping and the slightly lower preequilibrium constant in the case of TEMPO compared to DDPO (*vide infra*).

Since the intrinsic reactivity of styrene with the growing radical is the same in both cases, the measured rate difference reflects the difference in equilibrium radical concentrations, $[P^\bullet]$. Using $k_p = 3.8 \times 10^3$ M^{-1} s^{-1} and the above k_{obs} values, we calculated $[P^\bullet]$ as 1.2×10^{-6} and 6.3×10^{-7} M for DDPO and TEMPO, respectively.[7c] From the initial nitroxide concentration $[NO]_0 = 5.3 \times 10^{-2}$ M and the expression $K_d = [P^\bullet][NO^\bullet]/[PON] = [P^\bullet]^2/[PON]$, where $[NO^\bullet]$ and [PON] are the equilibrium concentrations of the nitroxyl radical and the dormant adduct, respectively, we estimated the dissociative equilibrium constants, K_d's, to be 2.7×10^{-11} (DDPO) and 7×10^{-12} (TEMPO). Even though these are upper limits, they are still extremely small, suggesting that the polymer chains are predominantly in the dormant form. The preequilibrium, rather than

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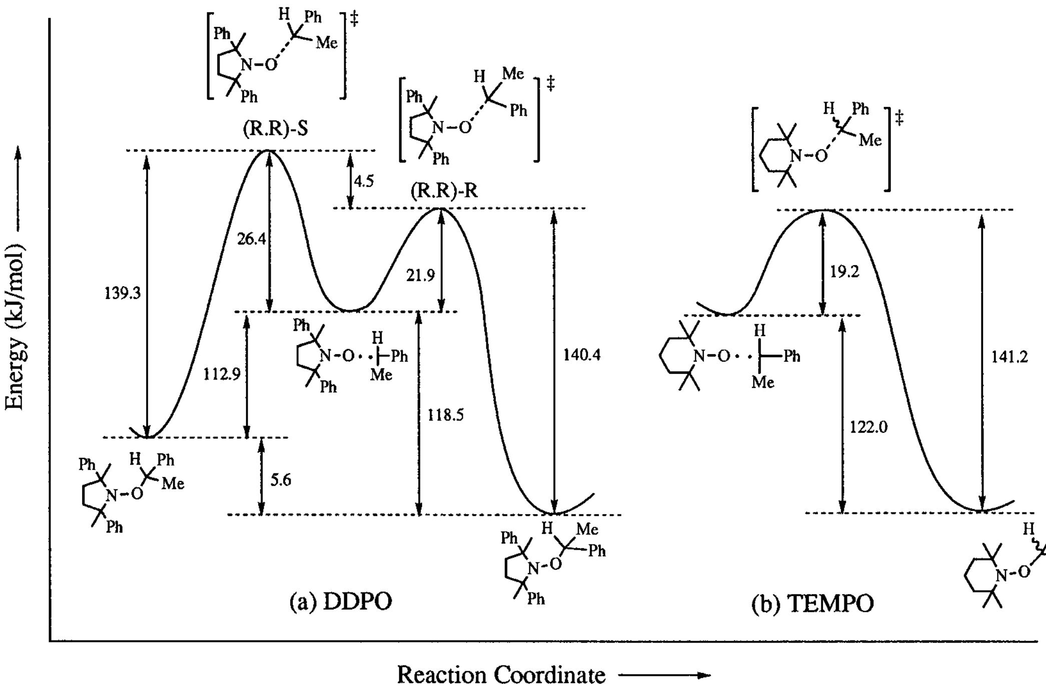

Figure 3. Reaction coordinate diagrams for dissociation and radical recombination of (a) (*R*,*R*)-DDPO−styrene diastereomeric adducts and (b) TEMPO−styrene adduct.

Table 1. Polymerization Results

entry[a]	NO[b]	[NO] (M)	[NO]/[BPO]	[CSA][c] (M)	yield (%)	M_n(calc)[d] × 10^{-3}	M_n(GPC)[e] × 10^{-3}	PDI[f]	temp (°C)	time (h)
1	DDPO	0.024	0.5		91	34.2	16.5	1.51	130	13
2	DDPO	0.049	1.0		89	16.8	14.6	1.30	130	13
3	DDPO	0.064	1.3		84	12.3	12.6	1.21	130	11
4	DDPO	0.046	1.7		58	11.9	13.2	1.22	130	36
5	DDPO	0.506	10.0		43	1.2	1.9	1.8	130	147
6	TEMPO	0.065	1.3		58	8.5	12.9	1.16	130	13
7	DDPO	0.065	1.3		36	5.4	7.0	2.17	100	13
8	TEMPO	0.063	1.3		0				90	12
9	DDPO	0.066	1.3		32	4.8	9.5	1.95	90	12
10	DDPO	0.064	1.3		0				75	13
11	DDPO	0.065	1.3		78	10.9	12.6	1.17	130	7
12	DDPO	0.064	1.3	0.005	85	12.4	13.9	1.17	130	7
13	DDPO	0.065	1.3	0.03	86	12.4	11.3	1.19	130	7
14	DDPO	0.068	1.3	0.06	78	10.8	12.3	1.21	130	7
15	TEMPO	0.064	1.3		34	5.0	7.8	1.09	130	7
16	TEMPO	0.065	1.3	0.03	79	11.4	20.2	1.20	130	7
17	TEMPO	0.063	1.3	0.06	92	13.6	21.9	1.73	130	7
18	(−)-DDPO	0.044	1.3		75	16.0	16.7	1.29	130	12

[a] Polymerizations performed in bulk styrene. [b] NO = nitroxide. [c] (+)-Camphorsulfonic acid. [d] Calculated molecular weight based on the styrene/nitroxide molar ratio. [e] Gel permeation chromatography using polystyrene standards. [f] Polydispersity index.

monomer addition (since k_p is constant), appears to be the dominant factor that controls the relative rates of these nitroxide-mediated polymerizations. Hence, any efforts directed to controlling the process must undoubtedly include finding conditions to control the preequilibrium.

The observed difference in reactivity is more pronounced at lower temperatures (entries 7−10). Thus, while at 90 °C (entries 8 and 9) DDPO-mediated reaction gave 36% yield (after 11 h) of polymer and did not become completely inhibited until the temperature reached 75 °C (entry 10), the corresponding TEMPO-mediated reaction gave none.[2a] The increase in PDI at lower temperatures is consistent with the expected slower initiation, slower exchange between active and dormant species, and the finding that PDI is high at low conversions.

It has been reported that addition of (+)-camphorsulfonic acid ((+)-CSA) to TEMPO-mediated polymerizations increased the rate and broadened the PDI of the isolated polymer.[2b] We have surprisingly found that addition of (+)-CSA to DDPO-mediated polymerization had no significant effect on the MW, the yield, and the PDI (entries 11−14). The rate, as can be judged from the yields, also appeared unaffected.[8] The yields remained high and the PDI low over the range of [CSA] studied. However, as expected, the TEMPO-mediated reaction solidified faster and gave higher yield, higher MW, and higher PDI than obtained in the absence of CSA (entries 15−17). The reasons for the lack of CSA effect on DDPO-mediated polymerization are not clear to us. However, the results suggest that CSA does more than just simply prevent autoinitiation,[2] and studies to clarify this are in progress.

In order to shed more light on the observed reactivity differences, we performed semiempirical calculations.[9] Thus, the ground state enthalpy Δ*H*° for C−ON bond homolysis (Figure 3a) for DDPO−styrene adduct was found to be 118.5 kJ/mol for (*R*,*R*)-*R* diastereomer and 112.9 kJ/mol for (*R*,*R*)-*S* diastereomer. For TEMPO−

styrene adduct (Figure 3b), we calculated $\Delta H°$ to be 122 kJ/mol, in contrast to the recently reported value of 109 kJ/mol.[2c] Similarly, $\Delta H^{\ddagger}$ for dissociation of TEMPO−styrene adduct was calculated as 141.2 kJ/mol, which agrees quite well (within 10%) with a recent experimentally measured $\Delta H^{\ddagger}$ value of 130 ± 4 kJ/mol.[7b] Our calculations gave 19.2 kJ/mol for $\Delta H^{\ddagger}$ of the reverse reaction (radical trapping) for TEMPO. We are not aware of any previous calculated $\Delta H^{\ddagger}$ values for such systems.[10] The above calculated values are consistent with the finding that the DDPO-mediated reaction is only about twice as fast as the TEMPO-mediated one.

The above results are consistent with a mechanism involving dissociated free radicals as the actual propagating species.[2c] In order to shed light on the extent to which dissociative and associative (insertion) mechanisms are involved, we probed the effect of the chirality of DDPO on the stereochemical outcome of the reaction. We first employed semiempirical calculations to locate the transition state structures and then compared the actual polymerization results using the optically active and racemic DDPO.[9] Figure 3 summarizes the results of our calculations. The $\Delta H^{\ddagger}$ for dissociation of the diastereomeric DDPO−styryl adducts are approximately the same: 140.9 and 139.3 kJ/mol, respectively, for (*R*,*R*)-*R* and (*R*,*R*)-*S* adducts. The corresponding $\Delta H^{\ddagger}$ values for the reverse processes are 26.4 and 21.9 kJ/mol for the (*R*,*R*)-*S* and (*R*,*R*)-*R* diastereomers, respectively. These are consistent with the recent report by Ingold and co-workers, who showed that rates of nitroxide radical trapping, obtained by laser flash photolysis for sterically hindered nitroxides and stabilized α-methylbenzyl and cumyl radicals (among others), are considerably lower than diffusion-controlled rates.[11] At 25 °C, our calculated $\Delta(\Delta H^{\ddagger})$ of 4.5 kJ/mol is equivalent to about a 6-fold difference in rate, while at 130 °C the rate difference will be 3- or 4-fold in favor of the (*R*,*R*)-*R* diastereomer. This suggests that under appropriate conditions chiral DDPO may have an influence on the stereochemical outcome of the polymerization if the propagation step significantly involves insertion directly into the NO−styryl adduct, which would be favored by the more stable (*R*,*R*)-*R*-diastereomer (Figure 3a). We found that polymerization of styrene using (−)-DDPO gave results similar to those reported above (entry 18).[6,8] Furthermore, polystyrene samples obtained using (−)-DDPO, (±)-DDPO, TEMPO (with or without (+)-CSA), or just BPO (no nitroxide) gave essentially the same tacticity distributions determined by ^{13}C-NMR. Hence, propagation, indeed, appears to occur predominantly or exclusively from the state where the nitroxide dissociates completely from the growing polymer chain. We are currently investigating the stereochemical and electronic effects in DDPO- and substituted DDPO-mediated reactions together with other 5-membered-ring nitroxide-controlled free-radical polymerizations.

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Supporting Information Available: MOPAC archive files and ball-and-stick models for minimum energy conformations of ground and transition states for both TEMPO and DDPO (24 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the Journal, can be ordered from the ACS, and downloaded from the Internet; see any current masthead page for odering information and Internet access instructions.

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(6) Characteristics of DDPO (**1**): Mp 132−133 °C (bright yellow crystals). ^{1}H-NMR ($CDCl_3$): δ (without phenylhydrazine) 1.4 (s, broad), 9 (s, broad); δ (with added phenylhydrazine)[12] 1.53 (s, 6H), 2.14 (m, 2H), 2.45 (m, 2H), 7.1−7.8 (m, 10H). ^{13}C-NMR ($CDCl_3$): δ (with phenylhydrazine) 27.1, 35.3, 68.7, 125.9, 126.3, 127.7, 147.3, 150.9. GC/MS: 266 (M^+), 252 ($M + H - CH_3$), 236 ($M - NO$). HRMS(EI): Calcd for $C_{18}H_{20}NO$, 266.1545; found 266.1545. GC: 1 peak. RPHPLC (H_2O/CH_3CN 30/70 v/v): 1 peak. Chiral HPLC: 2 peaks of equal intensity. First enantiomer: $[\alpha]_D = +155°$ ($c = 1$, CH_2Cl_2, 21 °C). GC: 1 peak. Second enantiomer: $[\alpha]_D = -164°$ ($c = 1$, CH_2Cl_2, 21 °C). GC: 1 peak. Calcd for $C_{18}H_{20}NO$: C, 81.15; H, 7.58; N, 5.26. Found: C, 81.07; H, 7.50; N, 5.41.

(7) (a) After our studies were completed, Kazmaier and co-workers (*Macromolecules* **1995**, *28*, 1841) reported that di-*tert*-butyl nitroxide increased the polymerization rate compared to TEMPO. Since actual rates were not reported, we presume their conclusions were based upon molecular weight, which is a dubious method for rate comparisons. (b) Between submission of our manuscript and receipt of the reviewers comments, the same authors published their rate constant for the TEMPO-mediated polymerization of styrene, which is about 2 orders of magnitude lower than our value (Veregin, R. P. N.; Georges, M. K.; Hamer, G. K.; Kazmaier, P. M. *Macromolecules* **1995**, *28*, 4391). However, the results cannot be directly compared since [TEMPO]/[BPO] ratios are different and the exact spin densities are not known. (c) *Polymer Handbook*, 3rd ed.; Brandrup, J., Immergut, E. H., Eds.; Wiley-Interscience: New York, 1989; pp 67−79.

(8) The polymerizations were carried out following literature procedures.[2] Since the reactions are performed in bulk, the system almost completely solidifies and stirring is inhibited when conversion reaches about 75%. Hence, the high yields (89−90%) are essentially the same within experimental error.

(9) See Supporting Information provided.

(10) After our manuscript was submitted, the following article dealing with detailed semiempirical calculations on non-styrenic systems and several nitroxides appeared in print: Moad, G.; Rizzardo, E. *Macromolecules* **1995**, *28*, 8722.

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