Macromolecules **1993,** *26,* 3227–3229

Notes

Synthesis and Polymerization of 4-(Glycidyloxy)-2,2,6,6-tetramethylpiperidine-1-oxyl

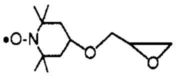
Takeshi Endo,* Keiichi Takuma, Toshikazu Takata, and Chiaki Hirose

Research Laboratory of Resources Utilization, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama 227, Japan

Received November 23, 1992
Revised Manuscript Received March 8, 1993

Stable nitroxyl radicals, which often have bulky substituents, are quite useful compounds in the studies of spin trappings, spin labelings, polymer ferromagnetism, and so on.[1–3] Nitroxyl radicals such as 4-substituted 2,2,6,6-tetramethylpiperidine-1-oxyl (1) are known to form a reversible redox system (Scheme I) with an oxoaminium salt (2) as the oxidized form and hydroxylamine (3) as the reduced form.[4–6]

It has already been demonstrated that the oxoaminium salt (2) is an excellent selective oxidant for primary and secondary monoalcohols, diols, and polyols to the corresponding carbonyl compounds and that the nitroxyl radical (1) can be regarded as an efficient mediator for the oxidations of these alcohols.[7–9] We have reported the synthesis and utility of polymer-supported nitroxyl radicals as polymeric mediator for the oxidation.[10,11] The polymeric nitroxyl radical has some advantages of not only the easy handling and separation but also the enhanced mediator activity presumably owing to the prevention by polymer effect of the reaction between the mediators. However, the control of the incorporation ratio of the nitroxyl radical function in the polymer was very difficult, because the polymer was synthesized via a polymer reaction. The difficulty should be averted by using the monomers which have the nitroxyl radical structure and thus are quite suitable for the preparation of a variety of poly(nitroxyl radical)s and for the control of the nitroxyl radical content in it. Among several ionically polymerizable groups, the epoxy group has been chosen as the polymerizing moiety of monomers with the nitroxyl radical function, because high solubility is expected for the polymer which is formed. In this paper, the synthesis and polymerization of an epoxy group-containing nitroxyl radical (4) are described.



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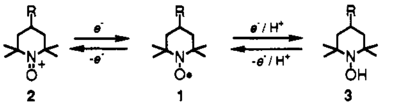
Experimental Section

Measurement. ESR (X-band) spectra of nitroxyl radicals were recorded on a Varian ESR-E12 in a 5-mm-ϕ quartz cell without degassing, and the determination of the g value was performed by using the signal of Mn^{2+} as the external standard. Mass spectra were measured by an electron impact method using a Hitachi M-80. IR spectra were recorded on a Jasco FT/IR-3. Number- and weight-average molecular weights ($\bar{M}_n$ and $\bar{M}_w$) were estimated by gel permeation chromatography (GPC) which was carried out with a Toyo Soda CCP & 8000 system (polystyrene standards). Gas chromatograms (GC) were obtained with a Shimadzu GC-8A equipped with an SE-30 column, using N_2 as the carrier gas.

Scheme I



Materials. Commercial-grade sodium tungstate, 4-hydroxy-2,2,6,6-tetramethylpiperidine (5), epichlorohydrin, sodium hydride (55% in oil), sodium dithionite, acetic acid, potassium iodide, methanol, and tetrahydrofuran (THF) were used without further purification. Potassium *tert*-butoxide was purified by sublimation. Glycidyl phenyl ether (GPE), BF_3OEt_2, methanesulfonic acid, tin tetrachloride, and CH_2Cl_2 were purified by distillation.

Preparation of 4-Hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (6). A mixture of 5 (40.0 g, 254 mmol), 80 mL of 30% hydrogen peroxide, and 30 mg of sodium tungstate in 200 mL of methanol was stirred overnight at room temperature. To the reaction mixture was added 100 mL of a saturated NaCl solution, and the resulting mixture was extracted with ether. After the combined extract was dried over anhydrous magnesium sulfate and evaporated, the orange residue was purified by column chromatography (dichloromethane/silica gel): yield 42.1 g (96.1%); mp 68.5–70.0 °C (lit.[12] mp 72–73 °C); IR (KBr) 3414, 2978, 2948, 2859, 1474, 1424, 1377, 1362, 1294, 1240, 1161, 1090, 1067, 1032, 991, 963, 939, 677 cm^{-1}.

Preparation of 4-(Glycidyloxy)-2,2,6,6-tetramethylpiperidine-1-oxyl (4). To a solution of 26.0 g (151 mmol) of 6 in 100 mL of THF was added 7.5 g (170 mmol) of NaH (55% in oil). The mixture was stirred at room temperature for 30 min under nitrogen and evaporated under reduced pressure. To the residue was added 100 g of epichlorohydrin, and the mixture was stirred at 50 °C for 20 h under nitrogen. Excess epichlorohydrin was distilled off from the reaction mixture under reduced pressure. The residual oil was purified by column chromatography (chloroform/silica gel). The collected product was purified by repeated vacuum distillation: bp 136–138 °C (4 mmHg); yield 24.5 g (71.1%). Vermilion solid: mp 38.3–38.6 °C; ESR (benzene) $g = 2.0059$, $a_N = 1.5$ mT; IR (KBr) 3479, 2997, 2977, 2939, 2900, 2868, 1461, 1386, 1362, 1339, 1257, 1243, 1192, 1177, 1104, 914, 894, 857, 768, 684 cm^{-1}; EI-MS *m/z* (relative intensity) 228 (M^+, 34), 154 (28), 41 (100). Anal. Calcd for $C_{12}H_{22}NO_3$: C, 63.13; H, 9.71; N, 6.13. Found: C, 62.88; H, 9.85; N, 6.04.

Cationic Polymerization of 4. A solution of 0.50 g (2.2 mmol) of 4 in 1.5 mL of dichloromethane under an argon atmosphere was cooled to −78 °C. A cationic initiator (3.5–3.0 mol %) was added to the solution, and the mixture was warmed up to 0 °C or room temperature and vigorously stirred for 24 or 48 h. Conversions of 4 and the molecular weight of the polymer in the polymerization mixture were estimated by GC and GPC. The results obtained are shown in Table I.

Cationic Polymerization of GPE in the Presence of a Nitroxyl Radical. To a cooled solution of GPE (1.50 g, 10 mmol) and 0.18 g (1.0 mmol) of 4-methoxy-2,2,6,6-tetramethylpiperidine-1-oxyl (7) in 2.0 mL of dichloromethane under an argon atmosphere at −78 °C was added 71 mg (0.5 mmol) of BF_3OEt_2. The mixture was warmed up to 0 °C and vigorously stirred for 24 h. Conversion of GPE was determined to be 15% by GPC.

Anionic Polymerization of 4. A Typical Procedure. A mixture of 0.50 g (2.2 mmol) of 4 and 10 mg (0.09 mmol) of potassium *tert*-butoxide in a glass tube was evacuated, sealed off, and heated at 80 °C for 2 h. The mixture was dissolved in dichloromethane, and the solution was washed with water. The

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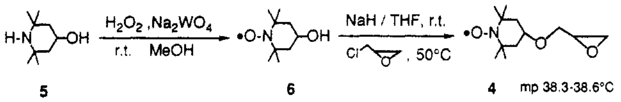
Table I. Cationic Polymerization of 4[a]

run	initiator (mol %)	temp (°C)	time (h)	conv (%)[b]
1	BF_3OEt_2 (3.0)	0	24	<5
2	$SnCl_4$ (3.5)	0	24	<5
3	CH_3SO_3H (3.0)	0	24	<5
4	$SnCl_4$ (3.5)	rt	48	<5
5	CH_3SO_3H (3.0)	rt	48	<5

[a] Carried out at the concentration of 4 at 1.5 M in CH_2Cl_2. [b] Estimated by GC.

Scheme II



organic layer was poured into *n*-hexane, and the obtained oily precipitate was separated by decantation. The viscous vermilion product was purified by dissolving in a minimum quantity of THF and reprecipitating the THF solution with *n*-hexane. The residual polymer (8) was dried at room temperature under reduced pressure. Conversion of 4 was 83%: yield 0.35 g (70%); $\bar{M}_n$ = 5800, $\bar{M}_w/\bar{M}_n$ = 1.62; ESR (benzene) *g* = 2.0060; IR (KBr), 3449, 2974, 2936, 2871, 1441, 1377, 1363, 1243, 1191, 1101 cm^{-1}. Anal. Calcd for $C_{12}H_{22}NO_3$: C, 63.13; H, 9.71; N, 6.13. Found: C, 59.58; H, 9.15; N, 5.68.

Anionic Copolymerization of 4 with GPE. A mixture of 0.50 g (2.2 mmol) of 4, 0.33 g (2.2 mmol) of GPE, and 20 mg (0.18 mmol) of potassium *tert*-butoxide in a glass tube was evacuated, sealed off, and heated at 60 °C for 20 h. The mixture was dissolved in dichloromethane, and the solution was washed with water. The organic layer was poured into *n*-hexane, and the oily precipitate obtained was separated by decantation. The viscous vermilion product was purified by dissolving in a minimum quantity of THF and reprecipitating the THF solution with *n*-hexane. The residual polymer (9) was dried at room temperature under reduced pressure: yield 0.76 g (91%); $\bar{M}_n$ = 6100, $\bar{M}_w/\bar{M}_n$ = 1.96.

Determinaton of the Content of the Nitroxyl Radical. To a solution of the polymer 8 (27.8 mg) in 10 mL of acetic acid was added 2 mL of 25% aqueous potassium iodide. The solution was stirred for 15 min at room temperature under argon, and the resultant brown solution was titrated with a 0.01 M $Na_2S_2O_3$ standard solution. The end point of the titration was the complete disappearance of the brown. At the end point, 15.30 mL of the $Na_2S_2O_3$ standard solution was consumed. The radical content of the polymer was calculated to be 100%.

Results and Discussion

Synthesis of an Epoxy Group-Containing Nitroxyl Radical (4). Commercially available 4-hydroxy-2,2,6,6-tetramethylpiperidine (5) was treated with 30% hydrogen peroxide in the presence of sodium tungstate as a catalyst[13] at room temperature in methanol to give the corresponding nitroxyl radical 6 in 96% yield (Scheme II). Reaction of 6 with epichlorohydrin was carried out in the presence of sodium hydride at 50 °C, and the corresponding nitroxyl radical-containing glycidyl ether (4) was obtained as vermilion solid in 71% yield (mp 38.3–38.6 °C). The structure of 4 was determined by IR, mass, and ESR spectra and elemental analysis. In the IR spectrum a typical absorption of nitroxyl radical at 1363 cm^{-1}, epoxy absorptions at 1243, 914, 894, 857, and 768 cm^{-1}, and an absorption of linear ether at 1104 cm^{-1} were observed other than large C-H bond absorptions (Figure 1). The mass spectrum and elemental analysis data strongly supported the nitroxyl radical structure. Thus, 4 was confirmed to be the epoxy monomer having the nitroxyl radical moiety.

Polymerization of 4. The epoxy group is generally susceptible to cationic initiators, and we first examined the cationic polymerization of 4 with BF_3OEt_2, methanesulfonic acid, and tin tetrachloride. However, no polymer was obtained and the conversion of 4 was less than 5% in any case under the conditions with 3 mol % of initiator for 24–48 h in CH_2Cl_2 ([C] = 1.5 M) at room temperature or 0 °C (Table I). Meanwhile, under the same conditions glycidyl phenyl ether (GPE) as a nitroxyl free monomer was completely consumed. Because lack of the cationic polymerizability of 4 was considered to come from the inhibition effect of the nitroxyl radical group of 4, cationic polymerization of GPE with BF_3OEt_2 (3 mol %) in the presence of 4-methoxy-2,2,6,6-tetramethylpiperidine-1-oxyl (7; 10 mol %) under the same conditions was carried out (Scheme III). In fact, the conversion of GPE was only 15%, indicating a strong suppression of the cationic polymerization by the addition of 7, probably due to the effect of the nitroxyl radical moiety as a basic function.[14,15] Thus, the polymerization of 4 under the cationic conditions is not the method suitable for the preparation of poly(nitroxyl radical) (8).

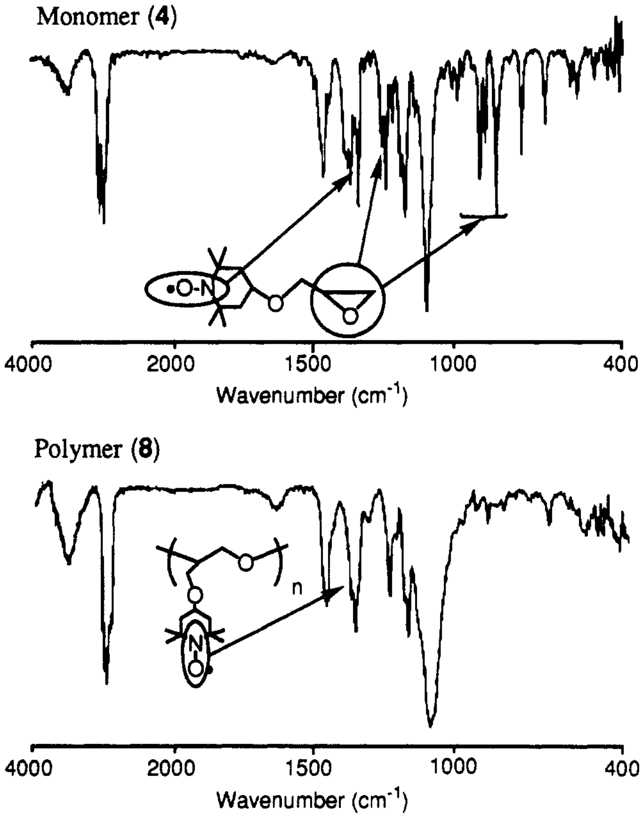
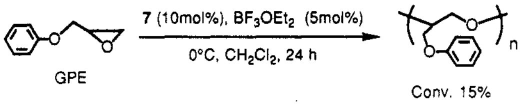
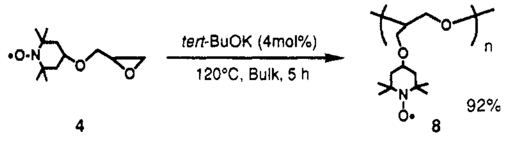


Figure 1. IR spectra of monomer 4 and polymer 8 (prepared by run 5, Table II).

Scheme III



Scheme IV



When the anionic polymerization of 4 with potassium *tert*-butoxide (4 mol %) in bulk was carried out at 120 °C for 5 h, highly viscous polymer ($\bar{M}_n$ 4900) was obtained in 92% yield (Scheme IV). The IR spectrum of the polymer showed an absorption at 1363 cm^{-1} based on the nitroxyl radical function in addition to a strong ν_{C-O} absorption corresponding to the ether bond at 1101 cm^{-1}. The nitroxyl

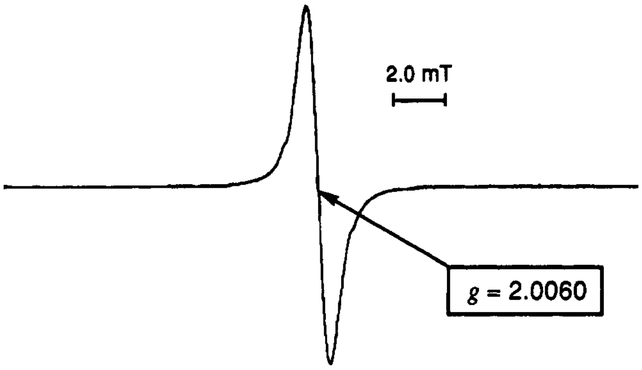


Figure 2. ESR spectrum of poly(nitroxyl radical) (8) (prepared by run 5, Table II) observed in benzene solution.

Table II. Anionic Polymerization of 4 with Potassium *tert*-Butoxide

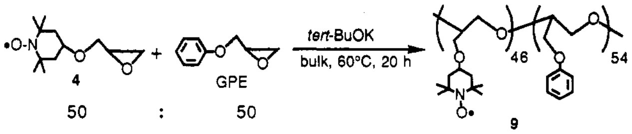
run	initiator (mol %)	temp (°C)	time (h)	conv (%)[a]	yield (wt %)[b]	$\bar{M}_n$ ($\bar{M}_w/\bar{M}_n$)[c]	radical content (mol/unit)[d]
1	4	120	5	90	92	4900 (2.29)	
2	4	60	5	90	67	3800 (4.19)	
3	8	60	3	87	66	4000 (1.90)	0.98
4	2	60	24	65	62	6600 (1.92)	
5	4	80	2	83	70	5800 (1.62)	1.00
6[e]	4	60	20		91	6100 (1.96)	0.46

[a] Estimated by GPC. [b] *n*-Hexane-insoluble part. [c] Estimated by GPC (based on polystyrene standards). [d] Determined by titration with a 0.01 M sodium dithionite standard solution in acetic acid. [e] Copolymerization with an equimolar GPE.

radical structure of the polymer produced was confirmed by the ESR spectrum (Figure 2) in which a singlet signal with $g = 2.0060$ was clearly observed. The singlet signal rather than a triplet may be spin-exchange interaction which often is observed in solid or at high radical concentration in solution. Thus, the polymer was further concluded to have the proposed nitroxyl radical structure (8).

The results of the polymerizations under various conditions are summarized in Table II. Although the yield of the polymer slightly decreased at 60 and 80 °C (runs 2–5), similar polymers were obtained. The content of the nitroxyl radical moiety was estimated to be ca. 100% by the titration with sodium dithionite for two of these polymers (Table II). Further, elemental analysis data of the polymer were satisfactory.

Scheme V



To examine the incorporation ratio of the nitroxyl radical function into the polymer, the copolymerization of 4 with GPE was carried out under anionic conditions similar to those above (Scheme V; Table I, run 6). An equimolar mixture of 4 and GPE underwent an efficient copolymerization at 60 °C for 20 h to give the corresponding copolymer 9 in 91% yield ($\bar{M}_n$ 6100). The unit ratio 4:GPE in 9 as calculated from the radical contents which were determined by the titration was 46:54, in close agreement with the feed ratio of 50:50, suggesting a very efficient introduction of the nitroxyl radical moiety with the ratio controlled by the feed ratio.

References and Notes

(1) Rozantsev, E. G. *Free Nitroxyl Radicals*: Plenum, New York, 1970.
(2) Moad, G.; Rizzardo, E.; Solomon, D. H. *Makromol. Chem., Rapid Commun.* 1982, *3*, 533.
(3) Ovchinnikov, A. A.; Korsak, Y. V.; Medvedeva, T. V.; Spector, V. N *Nature* 1987, *326*, 370.
(4) Miyazawa, T.; Endo, T. *J. Mol. Catal.* 1985, *31*, 217.
(5) Miyazawa, T.; Endo, T. *J. Mol. Catal.* 1985, *32*, 357.
(6) Golubev, V. A.; Rozantsev, E. G.; Neiman, M. B. *Bull. Acad. Sci. U.S.S.R.* 1965, 1898.
(7) Semmelhack, M. F.; Cortes, D. A.; Chou, C. S. *J. Am. Chem. Soc.* 1983, *105*, 4492.
(8) Semmelhack, M. F.; Schmidt, C. R.; Cortes, D. A.; Chou, C. S. *J. Am. Chem. Soc.* 1984, *106*, 3374.
(9) Yamaguchi, M.; Miyazawa, T.; Takata, T.; Endo, T. *Pure Appl. Chem.* 1990, *62*, 217.
(10) Miyazawa, T.; Endo, T.; Okawara, M. *J. Polym. Sci., Polym. Chem. Ed.* 1985, *23*, 1527.
(11) Miyazawa, T.; Endo, T. *J. Polym. Sci., Polym. Chem. Ed.* 1985, *23*, 2487.
(12) Kurosaki, T.; Lee, K. W.; Okawara, M. *J. Polym. Sci., Polym. Chem. Ed.* 1982, *20*, 3015.
(13) Rozantsev, E. G.; Neiman, M. B. *Tetrahedron* 1964, *20*, 131.
(14) Golbev, V. A.; Rozantsev, E. G.; Neiman, M. B. *Bull. Acad. Sci. U.S.S.R.* 1965, 1898.
(15) Golbev, V. A.; Rozantsev, E. G.; Neiman, M. B. *Izv. Ross. Akad. Nauk* 1965, 1927.