New Sterically Hindered Nitroxides for the Living Free Radical Polymerization: X-ray Structure of an α-H-Bearing Nitroxide

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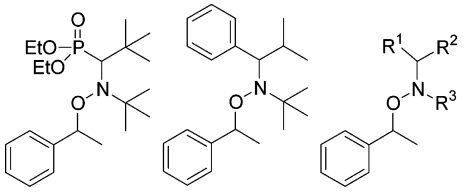
ABSTRACT: The synthesis of three new sterically hindered Hawker−Braslau type alkoxyamines for the nitroxide-mediated living radical polymerization is described. Efficient polymerizations can be performed at 105 °C. With alkoxyamine **11** controlled polymerization of *n*-butyl acrylate and styrene is possible even at 90 °C. AA and AB diblock copolymers can be prepared in a controlled manner using alkoxyamine **11**. Kinetic EPR experiments for the determination of the C−O bond activation energies of the new alkoxyamines are described. Furthermore, ^{1}H NMR alkoxyamine decomposition studies are presented. These kinetic experiments are used for the discussion of the polymerization results. Furthermore, the X-ray structure of a Hawker-Braslau type nitroxide is presented. X-ray data and ESR data are used to explain the high stability of these nitroxides.

Introduction

Controlled free radical polymerizations have gained renewed interest during the past few years. This is due to the development of nitroxide-mediated polymerizations (NMP),[1] atom transfer radical polymerizations (ATRP),[2] and RAFT polymerizations,[3] which allow the preparation of polymers with well-defined architectures. The molecular weight can be controlled, and small polydispersities are generally obtained. Furthermore, block copolymers can be prepared using these new methods. These polymerization techniques can also be used to prepare new interesting materials.[1,2] The control of the polymerization in NMP and ATRP relies on the principle of the persistent radical effect (PRE).[4] For example, in the NMP, reversible formation of a dormant alkoxyamine from the corresponding nitroxide and the chain growing polymer radical ensures a low concentration of free radicals during the entire polymerization. Low radical concentrations provide a low fraction of irreversible termination via polymer radical dimerization/disproportionation processes.

Alkoxyamines are generally used as initiators/regulators in NMP.[1] Many nitroxides have successfully been used as regulators/initiators for controlled styrene polymerization. However, controlled NMP of acrylates is still difficult to achieve. Only a few reports on successful acrylate polymerizations using alkoxyamines have appeared to date. Tordo and co-workers introduced alkoxyamine **1** as a highly efficient initiator/regulator for the polymerization of acrylates (Figure 1).[5,6] Hawker and Braslau showed that readily prepared alkoxyamine **2** is also suitable for the controlled *n*-butyl acrylate polymerization.[7] In their detailed investigations they studied the effect of the variation of the substituents R^1 and R^2 (see **3**). A *tert*-butyl group as in **2** was chosen as the R^3 substituent for most compounds. We assume that the R^3 group may heavily influence the efficiency of the polymerization (kinetics, polydispersity, etc.). Herein, we report the synthesis of new Hawker/Braslau type alkoxyamines bearing bulky tertiary R^3 substituents. Their efficiency as regulators for the polymerization of styrene and *n*-butyl acrylate will be discussed. Furthermore, the X-ray structure of a Hawker/Braslau type nitroxide will be presented.[8,9] In addition, we will discuss kinetic data of the C−O bond homolysis and alkoxyamine decomposition studies.



1 **2** **3**

Figure 1. Alkoxyamines **1** and **2** successfully used for the controlled acrylate polymerization.

Experimental Section

Materials. Benzaldehyde (Fluka, 98+%), (1-bromoethyl)-benzene (Aldrich, 97%), 2-bromopropane (Aldrich, 98%), 4,4′-di-*tert*-butyl-2,2′-bipyridyl (Aldrich, 98%), *N*,*N*-dimethylacrylamide (Fluka, 98+%), hydrazine monohydrate (Fluka, 99%), isobutyraldehyde (Aldrich, 98%), 2-nitropropane (Fluka, 96+%), pyridinium toluene-4-sulfonate (Fluka, 99+%), (trimethylsilyl)-diazomethane (Aldrich, 2 M in hexane), and Triton B (Fluka, 96+%) were used as received. Styrene (BASF) and *n*-butyl acrylate (Fluka, 99+%) were both distilled under reduced pressure from CaH_2 to remove the stabilizer. Et_2O was distilled over K/Na, benzene and THF were distilled from sodium, and CH_2Cl_2, 1,2-dimethoxyethane, and *n*-hexane were distilled from CaH_2 before use. All other chemicals were used as received.

General. ^{1}H NMR and ^{13}C NMR spectra were recorded on a AMX 500 (500 MHz, Bruker), ARX 300 (300 MHz, Bruker), or ARX 200 (200 MHz, Bruker). Chemical shifts δ in ppm relative to $SiMe_4$ as internal standard. TLC: silica gel 60 F_{254} plates (Merck); detection with UV or dipping into a solution of $KMnO_4$ (1.5 g in 333 mL of 1 *m* NaOH) or a solution of $Ce(SO_4)_2 \cdot H_2O$ (10 g), phosphormolybdic acid hydrate (25 g), concentrated H_2SO_4 (60 mL), and H_2O (940 mL), followed by heating. Flash chromatography: silica gel 60 (40−63 μm, Merck or Fluka); at ca. 0.4 bar. Melting points: 510 apparatus (Büchi); uncorrected. IR spectra of the new compounds were recorded on a IR 750 (Nicolet Magna) or a IFS-200 (Bruker).

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Mass spectra were recorded as electrospray mass spectrometry (ESI-MS) or field desorption mass spectrometry (FD-MS) on a CH7 (Varian) and as HRMS on a 95S (MAT). Size exclusion chromatography (SEC) was carried out with THF as eluent at a flow rate of 1.0 mL/min at room temperature on a system consisting of a L6200A Intelligent Pump (Merck Hitachi), a set of two Plgel 5 μm MIXED-C columns (300 × 7.5 mm, 5 μm pore size, molecular range 200−2 000 000 g/mol, Polymer Laboratories), and a RI-101 detector (Shodex). Data were acquired through a PL Datastream unit (Polymer Laboratories) and analyzed with Cirrus GPC software (Polymer Laboratories) based upon calibration curves built upon polystyrene and poly(methyl methacrylate) standards (Polymer Laboratories Polystyrene Medium MW Calibration Kit S-M-10 to determine the molecular weight of polystyrene and Polymer Laboratories Poly(methyl methacrylate) Medium MW Calibration Kit M-M-10 to determine the molecular weight of *n*-butyl acrylate) with peak molecular weights ranging from 500 to 3 000 000 g/mol. EPR spectra were recorded on a ESP 300 E (Bruker) equipped with a Nicolet Cavity (Bruker) and a B-TC 80/15 (Bruker). The nitroxide concentrations were determined by double integration of the EPR spectra and calibration with a TEMPO solution in *tert*-butylbenzene. Elemental analyses were performed on a CHN-Rapid-Elementaranalysator (Heraeus) at the University of Marburg.

***N,N*-4-Trimethyl-4-nitropentanamide** (**4**). 2-Nitropropane (15.2 mL, 168 mmol) was dissolved in 1,2-dimethoxyethane (100 mL) and heated to 70 °C. Triton B (2.3 mL, 13 mmol) and *N,N*-dimethylacrylamide (14.8 mL, 143 mmol) were added dropwise to the stirred solution in three portions. The reaction mixture was stirred at 70 °C for 3 h. 1 N HCl was added at room temperature, and the aqueous layer was extracted with CH_2Cl_2 (3×). The collected organic layers were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was dried in vacuo to afford **4** (26.87 g, 85%) as a green oil which was used without further purification. IR (film): 3478 w, 2989 w, 2939 w, 1648 s, 1536 s, 1499 m, 1472 m, 1458 m, 1399 s, 1373 m, 1348 m, 1263 w, 1143 w, 1062 w, 845 w cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.00 (s, 3H, $N(CH_3)_2$), 2.95 (s, 3H, $N(CH_3)_2$), 2.29 (s, 4H, CH_2), 1.62 (s, 6H, $C(CH_3)_2$). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 171.3 (CO), 88.0 ($C(CH_3)_2$), 37.4 (CH_2), 36.1 ($N(CH_3)_2$), 35.8 (CH_2), 29.0 ($N(CH_3)_2$), 26.2 ($C(CH_3)_2$). MS (EI): 188 (2, $[M]^+$), 142 (48), 72 (100), 44 (26). HRMS (EI) Calcd for $C_8H_{16}N_2O_3$ (M^+): 188.1161. Found: 188.1159.

[4-(Dimethylamino)-1,1-dimethyl-4-oxobutyl][2-methylpropylidene]ammoniumolate (**5**). Compound **4** (10.0 g, 53.1 mmol), isobutyraldehyde (9.6 mL, 0.1 mol), and NH_4Cl (3.12 g, 58.4 mmol) were dissolved in a mixture of Et_2O (95 mL) and H_2O (257 mL) and cooled to 0 °C. Zinc powder (13.89 g, 0.212 mol) was added in small portions over a period of 1 h at 0 °C, and the reaction mixture was vigorously stirred at room temperature for 3 days. The heterogeneous mixture was filtered through a sintered glass filter, and the residue was washed with MeOH (4×). The solution was extracted with CH_2Cl_2 (5×), and the collected organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was dried in vacuo. Purification by flash chromatography (CH_2Cl_2/MeOH, 19:1) afforded **5** (8.68 g, 72%) as a colorless oil. IR (film): 3474 w, 2964 w, 2935 w, 2872 w, 1645 s, 1577 m, 1499 m, 1467 m, 1397 s, 1357 m, 1263 w, 1169 m, 1141 w, 11103 m, 1063 w cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.61 (d, J = 7.0 Hz, 1H, NCH), 3.15 (hept, J = 7.0 Hz, 1H, $CH(CH_3)_2$), 3.01 (s, 3H, $N(CH_3)_2$), 2.92 (s, 3H, $N(CH_3)_2$), 2.30−2.06 (m, 4H, CH_2), 1.48 (s, 6H, $C(CH_3)_2$), 1.05 (d, J = 6.8 Hz, 6H, $CH(CH_3)_2$). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 172.5 (CO), 141.3 (NCH), 71.1 ($C(CH_3)_2$), 37.6 (CH_2), 35.7 ($N(CH_3)_2$), 35.6 (CH_2), 28.7 ($N(CH_3)_2$), 26.6 ($C(CH_3)_2$), 26.4 ($CH(CH_3)_2$), 19.3 ($CH(CH_3)_2$). MS (EI): 228 (8, $[M]^+$), 183 (18), 142 (74), 112 (12), 97 (10), 72 (100), 46 (22). HRMS (EI) Calcd for $C_{12}H_{24}N_2O_2$ (M^+): 228.1833. Found: 228.1835.

***N,N*-4-Trimethyl-4-[(2-methyl-1-phenylpropyl)amino]-pentanamide-*N*-oxyl Radical** (**6**). Nitrone **5** (5.00 g, 21.9 mmol) and LiBr (19.0 g, 218 mmol) were dissolved in THF (70 mL), and the solution was cooled to 0 °C. A solution of phenylmagnesium bromide (prepared using Mg (1.17 g, 48.2 mmol) and phenyl bromide (2.54 mL, 24.1 mmol) in Et_2O (25.5 mL)) was slowly added to the nitrone solution at 0 °C. The reaction mixture was allowed to warm to room temperature, and stirring was continued for 12 h. Saturated NH_4Cl and H_2O were added at 0 °C, and the mixture was extracted with Et_2O (3×). The collected organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Recrystallization from pentane/CH_2Cl_2 afforded the hydoxylamine (3.64 g, 54%) as colorless plates; mp 111 °C. IR (KBr): 3333 w, 2988 w, 2971 w, 2953 w, 2922 w, 2866 w, 1618 s, 1488 m, 1468 m, 1454 m, 1423 m, 1404 m, 1358 m, 1305 m, 1289 m, 1266 m, 1134 m, 1073 m, 951 w, 733 s, 702 s cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.43−7.22 (m, 5H, CH arom), 3.14 (d, J = 10.0 Hz, 1H, NCH), 3.06 (s, 3H, $N(CH_3)_2$), 2.99 (s, 3H, $N(CH_3)_2$), 2.62−2.02 (m, 4H, CH_2), 1.15 (dd, J = 5.5 Hz, 1H, $CH(CH_3)_2$), 1.12 (s, 3H, $C(CH_3)_2$), 0.93 (d, J = 6.8 Hz, 3H, $CH(CH_3)_2$), 0.53 (d, J = 6.8 Hz, 3H, $CH(CH_3)_2$), 0.47 (s, 3H, $C(CH_3)_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3 (CO), 143.5 (C arom), 130.4 (CH arom), 128.0 (CH arom), 126.8 (CH arom), 71.5 (NCH), 60.6 ($C(CH_3)_2$), 37.7 ($N(CH_3)_2$), 36.5 (CH_2), 36.3 ($N(CH_3)_2$), 32.0 ($CH(CH_3)_2$), 27.8 ($C(CH_3)_2$), 24.9 (CH_2), 22.5 ($CH(CH_3)_2$), 21.2 ($C(CH_3)_2$), 21.0 ($CH(CH_3)_2$). MS (EI): 306 (7, $[M]^+$), 263 (20), 247(10), 218 (40), 142 (100), 91 (38), 87 (42), 46 (49). Anal. Calcd for $C_{18}H_{30}N_2O_2$ (306.443): C, 70.55; H, 9.87; N, 9.14. Found: C, 70.17; H, 9.92; N, 9.05.

The hydroxylamine (1.70 g, 5.54 mmol) was treated with a mixture of MeOH (23 mL), concentrated NH_4OH (0.9 mL), and $Cu(OAc)_2$ (55.0 mg, 0.28 mmol). A stream of oxygen was bubbled through the solution for 1 h. The reaction mixture was treated with 2 N NH_4OH (143 mL) and extracted with CH_2Cl_2 (4×). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Drying in vacuo afforded the pure nitroxide **6** as an orange solid in quantitative yield; mp 64 °C. IR (KBr): 3441 w, 2976 w, 2964 w, 2913 w, 2871 w, 1634 s, 1492 m, 1453 m, 1415 m, 1396 m, 1365 m, 1128 m, 1068 m, 741 s, 700 s cm^{-1}. EPR data: α_N = 14.44 G, $\alpha_{H\beta}$ = 2.40 G, g = 2.006. MS (EI): 305 (2, $[M]^+$), 218 (3), 142 (100), 133 (17), 91 (20), 87 (61), 72 (44), 46 (32). HRMS (EI) Calcd for $C_{18}H_{29}N_2O_2$ (M^+): 305.2229. Found: 305.2233.

***N,N*-4-Trimethyl-4-[(2-methyl-1-phenylpropyl)(1-phenylethoxy)amino]pentane Amide** (**7**). (1-Bromoethyl)benzene (0.49 mL, 3.57 mmol), nitroxide **6** (1.20 g, 3.93 mmol), Cu powder (238 mg, 3.75 mmol), $Cu(OTf)_2$ (11.0 mg, 0.04 mmol), and 4,4′-di-*tert*-butyl-2,2′-bipyridyl (19.0 mg, 0.14 mmol) were suspended under argon in benzene (14 mL). In a sealed tube, the reaction mixture was stirred at 65−70 °C for 20 h. The solids were removed by filtration over silica gel (washing with CH_2Cl_2), and the solvent was removed under reduced pressure. Purification by flash chromatography (pentane/ethyl acetate, 3:1) afforded **7** (968 mg, 66%) as a 1:1 mixture of diastereoisomers as a colorless oil. IR (film): 3469 w, 3026 w, 2974 w, 2868 w, 1650 s, 1492 m, 1453 m, 1396 m, 1382 m, 1137 m, 1059 m, 761 s, 702 s cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, both diastereoisomers): δ = 7.50−7.17 (m, 10H, CH arom), 4.96−4.87 (m, 1H, CH), 3.42 (d, J = 10.5 Hz, 1H, CH), 3.28 (d, J = 10.7 Hz, 1H, CH), 2.95 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 2.84 (s, 3H, CH_3), 2.43−1.78 (m, 4H, CH_2), 1.65 (d, J = 6.6 Hz, 3H, CH_3), 1.57 (d, J = 6.6 Hz, 3H, CH_3), 1.35 (d, J = 6.3 Hz, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 0.80 (s, 3H, CH_3), 0.72 (s, 3H, CH_3), 0.57 (d, J = 6.6 Hz, 3H, CH_3), 0.24 (d, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, both diastereoisomers): δ = 173.9 (C), 142.6 (C), 131.3 (CH), 131.2 (CH), 128.5 (CH), 127.8 (CH), 127.7 (CH), 127.3 (CH), 126.8 (CH), 126.6 (CH), 126.5 (CH), 83.7 (CH), 83.2 (CH), 72.3 (CH), 72.2 (CH), 62.8 (C), 62.7 (C), 37.4 (CH_3), 36.7 (CH_2), 36.5 (CH_2), 35.8 (CH_3), 32.6 (CH_3), 32.2 (CH_3), 28.7 (CH_2), 28.5 (CH_2), 27.2 (CH_3), 26.9 (CH_3), 26.0 (CH_3), 25.6 (CH_3), 25.1 (CH_3), 23.7 (CH_3), 22.5 (CH_3), 22.4 (CH_3), 21.6 (CH_3), 21.4 (CH_3), 20.0 (CH_2). MS (FD): 410 (100, $[M]^+$, 305 (60), 105 (20). MS (ESI): 328 (100, $[M-C_8H_9 + Na]^+$), 285 (30), 195 (45), 165 (10), 142 (40), 109 (10). HRMS (ESI) Calcd for $C_{18}H_{29}N_2O_2$ ($M-C_8H_9^+$): 305.2229. Found: 305.2230.

(1,1-Diethylpropyl)[phenylmethylidene]ammonium-olate (9). 3-Ethyl-3-nitropentane (**8**)[10] (1.22 g, 8.41 mmol), benzaldehyde (1.34 g, 12.6 mmol), and NH_4Cl (0.50 g, 9.25 mmol) were dissolved in a mixture of Et_2O (5 mL) and H_2O (10 mL) and cooled to 0 °C. Zinc powder (2.20 g, 33.6 mmol) was added in small portions over a period of 1 h, and the reaction mixture was vigorously stirred at room temperature for 19 h. The heterogeneous mixture was filtered through a sintered glass filter, and the residue was washed with Et_2O. The solution was extracted with Et_2O (3×), and the collected organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was dried in vacuo. Purification by flash chromatography (pentane/MTBE, 9:1) afforded **9** (0.98 g, 53%) as colorless crystals; mp 38 °C. IR (KBr): 3447 w, 3019 w, 2968 w, 2944 w, 2879 w, 1574 s, 1550 s, 1447 s, 1405 s, 1378 m, 1322 m, 1124 s, 799 s, 755 m, 695 s cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 8.34−8.27 (m, 2H, CH arom), 7.45−7.36 (m, 4H, CH arom), 1.91 (q, J = 7.4 Hz, 6H, CH_2CH_3), 0.85 (t, J = 7.4 Hz, 9H, CH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 131.85 ($C(CH_2CH_3)_3$), 129.95 (C arom), 128.86 (CH arom), 128.41 (CH arom), 80.10 (NCH), 26.58 (CH_2CH_3), 8.39 (CH_2CH_3). MS (ESI): 220 (20, $[M + H]^+$), 195 (10), 176 (15), 163 (10), 154 (20), 144 (10), 123 (12), 122 (100), 99 (10), 57 (15). HRMS (ESI) Calcd for $C_{14}H_{22}NO$ (M^+): 219.1622. Found: 219.1624.

***N*-(1,1-Diethylpropyl)-α-(1-methylethyl)benzenemethanamine-*N*-oxyl Radical (10)**. Nitrone **9** (3.60 g, 16.4 mmol) was dissolved in Et_2O (40 mL) and cooled to 0 °C. A Grignard solution (prepared with Mg (1.40 g, 57.5 mmol) and 2-bromopropane (3.84 mL, 41.0 mmol) in Et_2O (38 mL)) was added dropwise to the solution at 0 °C. The reaction mixture was stirred for 2 h under reflux. Saturated NH_4Cl was added, and the aqueous layer was extracted with Et_2O (3×). The combined organic layers were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was dried in vacuo. Purification by flash chromatography (pentane/ethyl acetate, 9:1) afforded the pure hydroxylamine (2.60 g, 60%) as an orange oil. IR (film): 3465 w, 3062 w, 3026 w, 2967 w, 2938 w, 2879 w, 1643 s, 1491 m, 1455 s, 1382 m, 1166 w, 1073 w, 1029 w, 748 s, 719 w, 701 s cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 8.19 (s, 1H, CH arom.), 7.76−7.74 (m, 2H, CH arom), 7.40−7.39 (m, 2H, CH arom), 3.35 (d, J = 9.6 Hz, 1H, NCH), 2.37−2.27 (m, 1H, $CH(CH_3)_2$), 1.62 (q, J = 7.3 Hz, 4H, CH_2CH_3), 1.36−1.19 (m, 2H, CH_2CH_3), 1.13 (d, J = 9.9 Hz, 3H, $CH(CH_3)_2$), 0.83−0.74 (m, 9H, CH_2CH_3), 0.57 (d, J = 9.9 Hz, 3H, $CH(CH_3)_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.6 ($C(CH_2CH_3)_3$), 131.1 (C arom), 130.5 (CH arom), 129.3 (CH arom), 128.9 (CH arom), 128.1 (CH arom), 127.4 (CH arom), 126.9 (CH arom), 70.4 (NCH), 66.1 ($CH(CH_3)_2$), 32.6 ($CH(CH_3)_2$), 28.9 (CH_2CH_3), 27.7 (CH_2CH_3), 26.9 (CH_2CH_3), 22.0 (CH_2CH_3), 21.2 (CH_2CH_3), 9.4 (CH_2CH_3), 8.3 (CH_2CH_3). MS (EI): 262 (2, $[M-H]^+$), 134 (5), 133 (37), 122 (17), 98 (14), 89 (29), 61 (100), 54 (10). HRMS (EI) Calcd for $C_{17}H_{29}NO$ (M^+): 263.2249. Found: 263.2242.

The hydroxylamine (2.53 g, 9.60 mmol) was treated with a mixture of MeOH (40 mL), concentrated NH_4OH (1.5 mL), and $Cu(OAc)_2$ (96.0 mg, 0.48 mmol). A stream of oxygen was bubbled through the solution for 1 h. The reaction mixture was treated with 2 N NH_4OH (288 mL) and extracted with CH_2Cl_2 (3×). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Drying in vacuo afforded the pure nitroxide **10** (2.19 g, 87%) as a red oil. IR (film): 3062 m, 3026 m, 2967 w, 2879 w, 1705 m, 1643 m, 1491 m, 1454 w, 1382 s, 1155 m, 1072 m, 915 m, 748 s, 719 m, 701 s cm^{-1}. EPR data: α_N = 14.21 G, $\alpha_{H\beta}$ = 2.62 G, g = 2.006. MS (EI): 262 (2, $[M]^+$), 134 (6), 133 (50), 122 (8), 98 (24), 89 (36), 61 (100), 54 (12). HRMS (EI) Calcd for $C_{17}H_{28}NO$ (M^+): 262.2171. Found: 262.2165.

1-{1-[(1,1-Diethylpropyl)(1-phenylethoxy)amino]-2-methylpropyl}benzene (11). (1-Bromoethyl)benzene (0.85 mL, 6.25 mmol), nitroxide **10** (1.80 g, 6.88 mmol), Cu powder (417 mg, 6.57 mmol), $Cu(OTf)_2$ (20.0 mg, 0.06 mmol), and 4,4′-di-*tert*-butyl-2,2′-bipyridyl (34.0 mg, 0.25 mmol) were suspended under an argon atmosphere in benzene (15 mL). In a sealed tube, the reaction mixture was stirred under an argon atmosphere at 65−70 °C for 15 h. The solids were removed by filtration over silica gel (washing with CH_2Cl_2). Purification by flash chromatography (pentane/MTBE, 200:1) afforded **11** (1.66 g, 72%) as a 1:1 mixture of diastereoisomers as a colorless oil. IR (film): 3085 w, 3061 w, 3026 w, 2971 w, 2878 w, 1944 w, 1873 w, 1803 w, 1601 s, 1493 m, 1453 s, 1381 s, 1057 s, 1028 m, 923 m, 910 m, 890 m, 759 s, 700 s cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, both diastereoisomers): δ = 7.95−7.13 (m, 10H, CH arom), 4.88 (q, J = 6.6 Hz, 1H, CH), 3.45 (d, J = 10.8 Hz, CH), 3.32 (d, J = 10.8 Hz, CH), 2.44−2.32 (m, CH), 1.63 (d, J = 6.6 Hz, CH_3), 1.54 (d, J = 6.6 Hz, CH_3), 1.49−1.26 (m, CH_2, CH_3), 1.23 (d, J = 6.3 Hz, CH_3), 1.19−1.01 (m, CH_2, CH_3), 0.95 (d, J = 6.3 Hz, CH_3), 0.76 (t, J = 7.5 Hz, CH_3), 0.55 (t, J = 7.5 Hz, CH_3), 0.53 (d, J = 6.3 Hz, CH_3), 0.21 (d, J = 6.3 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, both diastereoisomers): δ = 145.81 (C), 143.31 (C), 131.04 (CH), 128.03 (CH), 127.21 (CH), 127.01 (CH), 126.87 (CH), 126.23 (CH), 83.94 (CH), 83.27 (CH), 71.39 (CH), 71.28 (CH), 67.61 (C), 32.77 (CH_3), 27.66 (CH_2), 24.89 (CH_3), 22.36 (CH_3), 21.53 (CH_3), 8.94 (CH_3). MS (EI): 367 (0.2, $[M]^+$), 264 (58), 262 (89), 235 (24), 221 (21), 220 (72), 174 (32), 165 (20), 164 (47), 134 (50), 133 (86), 130 (29), 122 (51), 105 (46), 99 (46), 91 (39). HRMS (ESI) Calcd for $C_{25}H_{37}NO$ (M^+): 367.2875. Found: 367.2865.

1-(2-Methyl-1-phenylpropyl)hydrazine (12). (1-Bromo-2-methylpropyl)benzene[11] (7.32 g, 34.4 mmol) was dissolved at room temperature in MeOH (75 mL). Hydrazine monohydrate (200 mL, 4.12 mol) was added dropwise to the stirred solution, and the reaction mixture was stirred for 12 h at room temperature. The solution was extracted with Et_2O (2×), and the collected organic layers were washed with brine and were dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was dried in vacuo to afford pure **12** (5.48 g, 97%) as a pale yellow oil. The product obtained was directly used in the next step. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.33−7.26 (m, 5H, CH arom.), 3.36 (d, J = 7.2 Hz, 1H, $CH(NHNH_2)$), 3.08 (bs, 3H, $NHNH_2$), 1.87 (oct, J = 7.0 Hz, 1H, $CH(CH_3)_2$), 1.00 (d, J = 6.6 Hz, 3H, $CH(CH_3)_2$), 0.75 (d, J = 6.8 Hz, 3H, $CH(CH_3)_2$). MS (EI): 164 (1, $[M]^+$), 133 (31), 121 (6), 107 (96), 91 (22), 77 (41).

1-{2-Methyl-1-[(2-methyl-1-phenylpropoxy)(1,1,3,3-tetramethylbutyl)amino]propyl}benzene (14). A suspension of PbO_2 (5.85 g, 24.4 mmol) in hexane (20 mL) was treated for 1 h by ultrasonic. A solution of nitroso-*tert*-octane **13**[12] (1.00 g, 6.98 mmol) in hexane (20 mL) was stirred for 1 h and added to the stirred PbO_2 suspension, and the reaction mixture was cooled to 0 °C. Hydrazine (**12**) (4.01 g, 24.4 mmol) was added dropwise, and the suspension was stirred for 18 h at room temperature. The mixture was filtered, and the solvent was removed under reduced pressure. Purification by flash chromatography (pentane/MTBE, 200:1) afforded **14** (1.99 g, 70%) as a 1.4:1 mixture of diastereoisomers as a colorless viscous oil. IR (film): 2955 w, 1469 m, 1452 m, 1382 m, 1364 m, 1241 w, 1072 w, 1000 m, 758 m, 733 w, 701 s cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, both diastereoisomers): δ = 7.48−7.13 (m, 10H, CH arom), 4.77 (bs, CH) 4.66 (d, J = 6.3 Hz, CH), 3.46 (d, J = 10.3 Hz, CH), 3.27 (d, J = 10.6 Hz, CH), 2.74−2.64 (m, CH), 2.59−2.46 (m, CH), 2.37−2.26 (m, CH), 1.90 (s, CH_2), 1.86 (s, CH_2), 1.66 (s, CH_2), 1.61−0.79 (m, CH_3), 0.63 (s, 3H, CH_3), 0.57 (d, J = 6.6 Hz, 3H, CH_3), 0.15 (d, J = 6.6 Hz, CH_3), 0.07 (s, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, both diastereoisomers): δ = 142.09 (C), 139.18 (C), 131.5 (CH), 131.05 (CH), 129.57 (CH), 129.20 (CH), 129.09 (CH), 128.88 (CH), 128.54 (CH), 127.94 (CH), 127.80 (CH), 127.72 (CH), 127.55 (CH), 127.48 (CH), 126.91 (CH), 126.79 (CH), 126.50 (CH), 126.09 (CH), 93.08 (CH), 91.98 (CH), 72.59 (CH), 72.42 (CH), 66.39 (C), 65.38 (C), 53.44 (CH), 51.31 (CH), 51.16 (CH), 46.18 (CH), 33.04 (CH_3), 32.94 (CH_3), 32.70 (CH_3), 32.61 (CH_3), 32.35 (CH_3), 29.15 (CH_3), 29.07 (CH_3), 28.78 (CH_3), 28.27 (CH_3), 23.07 (CH_3), 22.87 (CH_3), 22.56 (CH_3), 22.10 (CH_3), 21.64 (CH_3), 21.15 (CH_3), 21.08 (CH_3), 18.02 (CH_3), 16.73 (CH_3). MS (ESI): 410 (8, $[M + H]^+$), 298 (49), 242 (67), 227 (48), 196 (6), 195 (100), 179 (6), 163 (13), 133 (15), 65 (10). Anal. Calcd for $C_{28}H_{43}NO$ (409.647): C, 82.09; H, 10.58; N, 3.42. Found: C, 82.38; H, 10.40; N, 3.55.

Typical Procedure for the Polymerization of Styrene. A Schlenk tube was charged with the alkoxyamine initiator

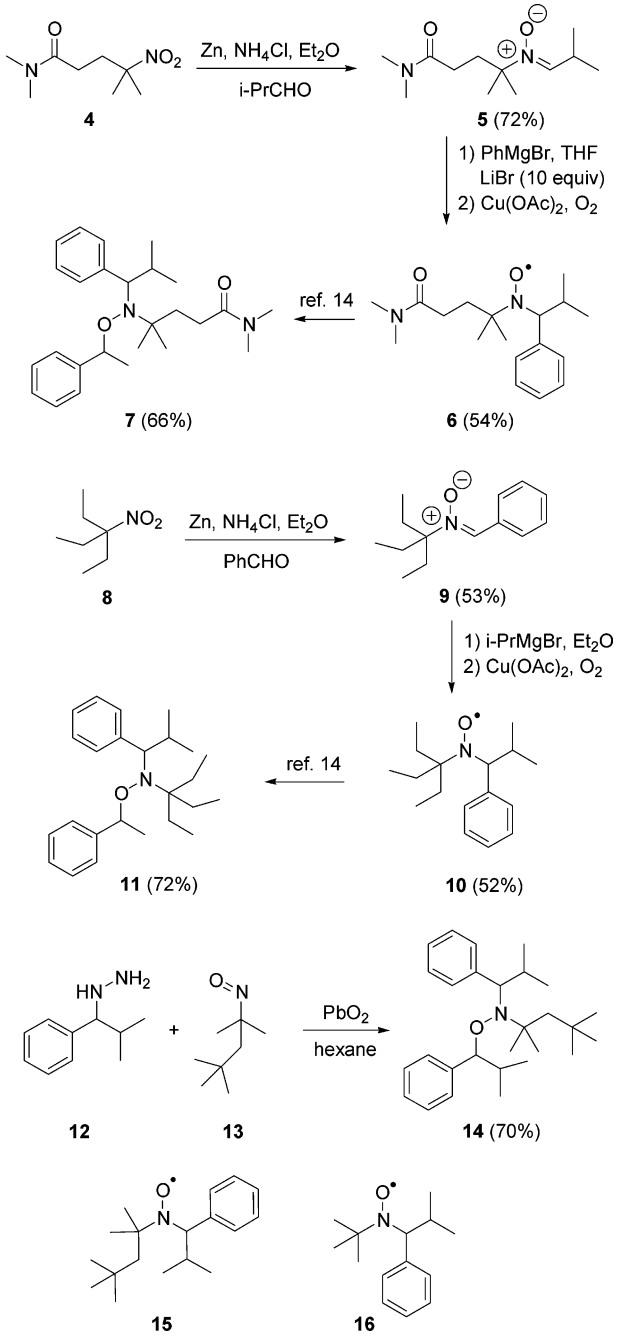
11 (53.0 mg, 0.14 mmol) and styrene (1.65 mL, 14.4 mmol). The tube was subjected to three freeze−thaw cycles and sealed off under argon. The polymerization was carried out under argon at 105 °C for 15 h. The resulting mixture was cooled to room temperature, dissolved in CH_2Cl_2, and poured into an aluminum dish, and residual monomer was removed in a vacuum-drying cabinet at 60 °C for 12 h. Conversion was evaluated gravimetrically; molecular weight and polydispersity index (PDI) were determined by size exclusion chromatography (SEC). Conversion = 76%; M_n = 7500 g mol^{-1}; PDI = 1.12.

Typical Procedure for the Polymerization of *n*-Butyl Acrylate. A Schlenk tube was charged with the alkoxyamine initiator **11** (12.0 mg, 0.03 mmol), nitroxide **10** (0.40 mg, 1.60 μmol), and *n*-butyl acrylate (1.18 mL, 8.25 mmol). The tube was subjected to three freeze−thaw cycles and sealed off under argon. The polymerization was carried out under argon at 105 °C for 14 h. The resulting mixture was cooled to room temperature, dissolved in CH_2Cl_2, and poured into an aluminum dish, and residual monomer was removed in a vacuum-drying cabinet at 60 °C for 12 h. Conversion was evaluated gravimetrically; molecular weight and polydispersity index (PDI) were determined by size exclusion chromatography (SEC). Conversion = 57%; M_n = 14 500 g mol^{-1}; PDI = 1.19.

Results and Discussion

Synthesis of the Alkoxyamines 7, 11, and 14. The tertiary nitroalkane **4** was readily prepared from 2-nitropropane and *N*,*N*-dimethylacrylamide.[13] Reduction of the nitroalkane to the corresponding hydroxylamine and subsequent nitrone formation using i-PrCHO afforded **5** in 72% yield (Scheme 1). Phenyl Grignard addition and oxidation provided nitroxide **6** (54%). Alkoxyamine formation according to a literature procedure[14] yielded alkoxyamine **7** (66%). Alkoxyamine **11** was prepared using a similar strategy. Triethylnitromethane (**8**) was readily prepared via a Ritter reaction from the corresponding tertiary alcohol.[10] Nitrone formation was achieved with activated Zn and nitroalkane **8** in the presence of benzaldehyde (→ **9**, 53%). Grignard addition and oxidation (→ **10**, 52%) followed by alkoxyamine formation afforded initiator/regulator **11** (72%). Alkoxyamine **14** was prepared in a single operation by the reaction of hydrazine (**12**)[11] with nitroso compound **13** in the presence of PbO_2 according to Corey et al. (70%).[12,15,16] Nitroxide **16** was prepared according to literature procedures,[7] and nitroxide **15** was prepared in analogy.

Scheme 1. Synthesis of the Alkoxyamines 7, 11, and 14



Polymerization Studies. The polymerization of styrene was studied first. The initial polymerizations were conducted in sealed tubes using 1% of the alkoxyamine initiator at 105 and 125 °C and were stopped after 6 or 15 h, respectively. The conversion was determined gravimetrically. The PDI and the molecular weight of the polymers were analyzed using SEC. The results are summarized in Table 1.

Styrene polymerization using alkoxyamine **7** at 125 °C afforded PS with a narrow PDI in 53% conversion (entry 1). Polymerization can also be performed at 105 °C with initiator/regulator **7** (entry 2, 56%, PDI = 1.13). With alkoxyamine **11** polymerization at 125 °C for 6 h was fast (87% conversion), however, not well controlled (PDI = 1.32, entry 3). Probably, nitroxide **10** or dormant polymer alkoxyamines derived from **10** are not sufficiently stable at 125 °C. Indeed, polymerization at 105 °C afforded PS with narrow PDI and high conversion (entry 4). Styrene polymerization using *tert*-octyl alkoxyamine **14** at 125 °C afforded PS with a PDI of 1.28 (entry 9). Again, lowering the reaction temperature to 105 °C provided a better control of the polymerization (PDI = 1.16, entry 10). With known[7] alkoxyamine **2** good control of the polymerization was obtained at 105 and 125 °C; however, compared with **11** lower conversions were obtained (entries 11 and 12).

We can conclude from these initial studies that similar results in terms of conversion and control were obtained for the Hawker/Braslau alkoxyamine **2**[7] and the amide containing alkoxyamine **7** (compare entries 1, 2 with 11, 12). The replacement of the *tert*-butyl group (R^3 substituent in **3**) by a 3-dimethylaminocarbonyl-1,1-dimethylpropyl group has no significant effect on the styrene polymerization. However, replacing the *tert*-butyl group with the 1,1-diethylpropyl group in going from alkoxyamine **2** to **11** heavily influences the polymerization outcome. As compared to the **2**-mediated styrene polymerizations, reactions with alkoxyamine **11** are faster and higher conversions can be obtained.

Table 1. Bulk Styrene Polymerization Using Alkoxyamines 7, 11, and 14[a]

entry	alkoxyamine (mol %)	temp (°C)	time (h)	conv (%)	$M_{n,th}$ (g/mol)	$M_{n,exp}$ (g/mol)	PDI
1	**7** (1%)	125	6	53	5500	3600	1.15
2	**7** (1%)	105	15	56	5800	6600	1.13
3	**11** (1%)	125	6	87	9100	10800	1.32
4	**11** (1%)	105	15	77	8000	9800	1.14
5	**11** (0.6%)	105	15	74	12800	16700	1.14
6	**11** (0.4%)	105	15	73	19000	21500	1.13
7	**11** (0.1%)	105	15	58	60400	68200	1.28
8	**11** (1%)	90	53	73	7600	9800	1.09
9	**14** (1%)	125	6	79	8200	11700	1.28
10	**14** (1%)	105	15	59	6100	8800	1.16
11	**2** (1%)	125	6	63	6600	5000	1.16
12	**2** (1%)	105	15	51	5300	6400	1.17

[a] For comparison, some polymerizations were conducted using known[7] alkoxyamine **2**.

However, an increase of the polydispersity was observed if the polymerization was conducted at 125 °C. Therefore, polymerizations using alkoxyamine **11** are best conducted at 105 °C. At 105 °C the *tert*-octyl alkoxyamine **14** is a more efficient initiator/regulator than the parent compound **2**, however, not as efficient as regulator **11**. We therefore decided to continue our studies with the most efficient initiator **11**. We first attempted to prepare higher molecular weight polystyrene (entries 5−7). Polystyrene with an M_n of 68 000 g/mol and satisfactory PDI was obtained. We found that styrene polymerization can also be performed at 90 °C (entry 8, 53 h, 73% conversion, PDI = 1.09).

To check the controlled/living character of the styrene polymerization with alkoxyamine **11**, conversion was plotted as a function of time, and the molecular weight was plotted as a function of monomer conversion (Figure 2). The linear increase of $\ln([M_0]/[M])$ vs time and molecular weight vs monomer consumption proves the controlled character of the **11**-mediated styrene polymerization.

We then started to look at the controlled polymerization of *n*-butyl acrylate using the new alkoxyamines **7**, **11**, and **14**. The polymerizations were conducted at 125 and 105 °C in neat *n*-butyl acrylate in the presence of the corresponding nitroxide (5% with respect to the alkoxyamine). The addition of nitroxide improves the control of the acrylate polymerization for other alkoxyamines.[7,17]

n-Butyl acrylate polymerization using **7** at 125 °C afforded a 41% conversion (entry 1, PDI = 1.20). With alkoxyamine **11** a higher conversion and slightly broader PDI was obtained (entry 2). Decreasing the initiator concentration under otherwise identical conditions provided poly(*n*-butyl acrylate) with a M_n of 33 400 g/mol and a PDI of 1.22 (entry 3). With the *tert*-octyl alkoxyamine **14** good control and acceptable conversion were obtained (entry 8, 49% conversion, PDI = 1.18). Polymerization using the known[7] alkoxyamine **2** provided a similar result (entry 9, 48% conversion PDI = 1.21). In analogy to the styrene polymerizations described above, alkoxyamines **7** and **14** and the parent alkoxyamine **2** provide similar results. With the triethyl derivative **11** as an initiator/regulator higher conversions were obtained. Therefore, some additional polymerizations were performed using the most efficient regulator **11**. First we tested whether polymer formation can be conducted at lower temperature. Indeed, polymerization at 105 °C for 14 h provided poly(*n*-butyl acrylate) with a narrow PDI (1.19, 57% conversion, entry 4). Decreasing the amount of added nitroxide resulted in a faster but still controlled polymerization (entry 5). A broader PDI was obtained upon targeting higher molecular weight poly(*n*-butyl acrylate) (entry 6). Controlled polymerization of *n*-butyl acrylate was achieved at 90 °C (56% conversion, 72 h, PDI = 1.16, entry 7). With the alkoxyamines **7** and **14** *n*-butyl acrylate polymerization could not be conducted at 105 °C. Conversions were low and results were not reproducible.

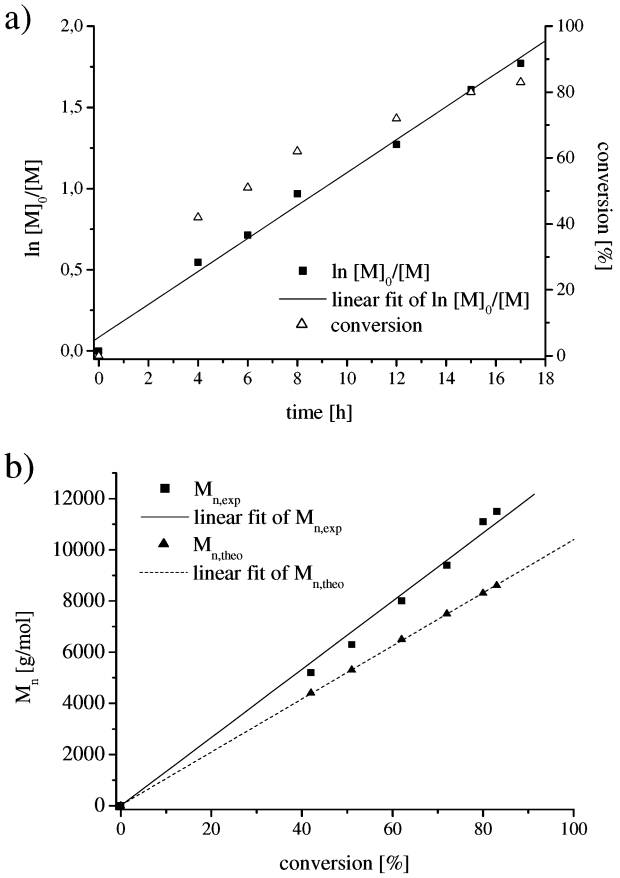


Figure 2. (a) Monomer conversion vs time (styrene, bulk, 105 °C, 1 mol % **11**). (b) Molecular weight (experimental and theoretical) vs monomer conversion (styrene, bulk, 105 °C, 1 mol % **11**, 15 h).

We then focused on the formation of block copolymers using alkoxyamine **11**. Poly(*n*-butyl acrylate) prepared with **11** (M_n = 15 100 g/mol, PDI = 1.15) was used as an initiator (0.2 mol %) for the neat styrene polymerization. Reaction for 15 h at 105 °C afforded poly(*n*-butyl acrylate)-*block*-polystyrene with good control (M_n = 40 800 g/mol, PDI = 1.26, 58% conversion). Furthermore, polystyrene (M_n = 7500 g/mol, PDI = 1.12) was successfully used as a macroinitiator for the neat styrene polymerization (105 °C, 15 h, 0.4 mol %) to provide polystyrene with a M_n of 21 800 g/mol and a PDI of 1.17. However, the formation of polystyrene-*block*-poly(*n*-butyl acrylate) using a polystyrene macroinitiator failed. Similar observations have previously been described for the diblock copolymer preparation using the parent alkoxyamine **2**.[7]

Kinetics of the C−O Bond Homolysis and Decomposition Rate Constants. Kinetic experiments to determine the C−O-bond homolysis rate constants were conducted in *tert*-butylbenzene at 403 K. Oxygen was used to scavenge the styryl radical, and the concentration of the released nitroxide was measured by EPR

Table 2. Bulk *n*-Butyl Acrylate Polymerization Using Alkoxyamines 7, 11, and 14[a]

entry	alkoxyamine (mol %)	nitroxide (mol %)	temp (°C)	time (h)	conv (%)	$M_{n,th}$ (g/mol)	$M_{n,exp}$ (g/mol)	PDI
1	**7** (1%)	**6** (0.05%)	125	6	41	5300	8000	1.20
2	**11** (1%)	**10** (0.05%)	125	6	84	10500	18000	1.23
3	**11** (0.4%)	**10** (0.02%)	125	6	82	26300	33400	1.22
4	**11** (1%)	**10** (0.05%)	105	14	57	7300	14500	1.19
5	**11** (1%)	**10** (0.02%)	105	15	84	10800	15100	1.15
6	**11** (0.6%)	**10** (0.03%)	105	14	89	19000	43400	1.45
7	**11** (1%)	**10** (0.05%)	90	72	56	7200	10200	1.16
8	**14** (1%)	**15** (0.05%)	125	6	49	6300	13500	1.18
9	**2** (1%)	**16** (0.05%)	125	6	48	6200	9500	1.21

[a] For comparison, a polymerization was conducted using known[7] alkoxyamine **2**.

Table 3. Rate Constants for the C−O Bond Homolysis and Decomposition Rate Constants of Alkoxyamines 7, 11, and 14 and EPR Parameters of the Corresponding Nitroxides

entry	alkoxyamine	k_d (s^{-1})[a]	E_a (kJ/mol)[b]	k_{dec} (s^{-1})[c]	nitroxide	α_N (G)[d]	$\alpha_{H\beta}$ (G)[d]	*g*
1	**7**	9.9×10^{-3}	126.4	4.2×10^{-5}	**6**	14.44	2.40	2.006
2	**11**	4.0×10^{-2}	121.7	9.6×10^{-5}	**10**	14.21	2.62	2.006
3	**14**	1.1×10^{-2}	126.2			14.86	2.79	2.006

[a] Measured at 403 K. [b] E_A was calculated using $A = 2.4 \times 10^{14}$ s^{-1}; see ref 18. Statistical errors between 2 and 3 kJ/mol. [c] Measured at 398 K. [d] Measured at room temperature.

spectroscopy, as previously described.[6,18−21] The experimental cleavage rate constants k_d were calculated using eq 1 (conversions up to 30%).

$$\ln\left(\frac{[\text{nitroxide}]_\infty - [\text{nitroxide}]_t}{[\text{nitroxide}]_\infty}\right) = -k_d t \qquad (1)$$

The activation energies E_a were estimated from the rate constants using $A = 2.4 \times 10^{14}$ s^{-1}.[6,18−20] The data are presented in Table 3.

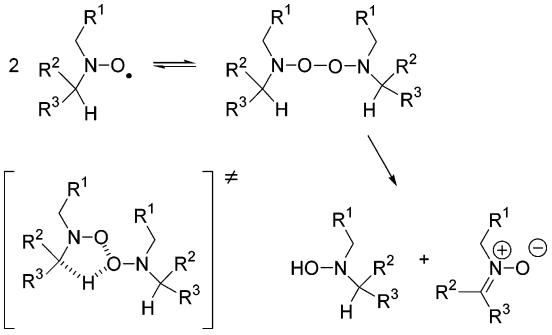
Furthermore, we also determined the rate constant for the thermal decomposition of the alkoxyamines **7** and **11** to provide styrene and the corresponding hydroxylamine. The decomposition rate constant is an important parameter to evaluate the efficiency of a new alkoxyamine initiator for the NMP.[22] The alkoxyamine was dissolved in a NMR tube in perdeuterio-*p*-xylene (0.03−0.06 M). The degassed sample was heated to 398 K within the cavity of a 500 MHz ^{1}H NMR spectrometer, and the decomposition was followed by monitoring the decrease of the alkoxyamine signals and the increase of the styrene resonances. The signal of the benzylic H atom at around 4.7 was used to estimate the alkoxyamine concentration. Similar experiments have previously been described.[20,22,23] Spectra were recorded every 5 min. The decomposition rate constants (k_{dec}) for the various alkoxyamines were determined using eq 2

$$\ln([S]/[A] + 1) = k_{dec} t \qquad (2)$$

according to Fukuda's work[23] ([S] = styrene concentration; [A] = alkoxyamine concentration) and are summarized in Table 3.

In agreement with the polymerization results described above, the lowest activation energy (E_a) for the C−O bond homolysis was measured for alkoxyamine **11** (entry 2). The replacement of the *tert*-butyl group by the larger 1,1-diethylpropyl group leads to a decrease of E_a by about 5 kJ/mol (E_a for **2** = 127.1 kJ/mol).[18] This is due to the larger steric repulsion by the 1,1-diethylpropyl group compared to the repulsion by the *tert*-butyl group. However, the sterically hindered alkoxyamine **11** turned out to be less stable than the parent regulator **2** (k_{dec} for **2**: 8.8×10^{-6} s^{-1}). Therefore, the best styrene polymerization results with **11** were obtained at 105 °C. Alkoxyamine **11** and the corresponding polymeric alkoxyamines are not sufficiently stable at 125 °C. The same was observed for the *n*-butyl acrylate polymerizations where best results have been obtained at 105 °C.

Scheme 2. Self-Reaction of Dialkyl Nitroxides



Replacement of one methyl group of the *tert*-butyl group in alkoxyamine **2** by larger alkyl substituents (→ **7**, **14**) does not alter the C−O homolysis rate constant significantly (entries 1 and 3). As expected from the homolysis rate constants, alkoxyamine **7** decomposes slower than alkoxyamine **11**.

X-ray Structure of Nitroxide 6. In general, nitroxides with a H atom α to the N atom are not stable and readily undergo disproportionation to form the corresponding hydroxylamine and nitrone. Ingold et al. carefully studied the self-reaction of dialkyl nitroxides and suggested a two-step mechanism depicted in Scheme 2.[24] Nitroxide dimerization in the first step is followed by syn-elimination to give the nitrone and the hydroxylamine. Therefore, syn-orientation of the α-H atom with respect to the nitroxide O atom is important for the decomposition; α-H-bearing nitroxides where the H atom is located anti to the nitroxide O atom should be stable. We obtained crystals of nitroxide **6** suitable for X-ray analysis. The structure is depicted in Figure 3.[25] As expected for a stable nitroxide, the H atom is located anti to the nitroxide O atom. The O(2)−N(2)−C(9)−H torsion angle in **6** is 170.8°, close to 180° where highest stability is expected. A similar result has previously been obtained by the groups of Volodarsky and Tordo for two other α-H-bearing stable nitroxides.[8] Furthermore, the C(5)-methyl group in **6** is positioned syn to the nitroxide O atom and is therefore the most important substituent for shielding of the nitroxide O atom.

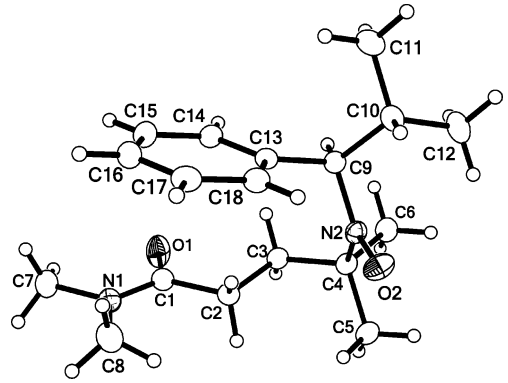


Figure 3. X-ray structure of nitroxide **6**.

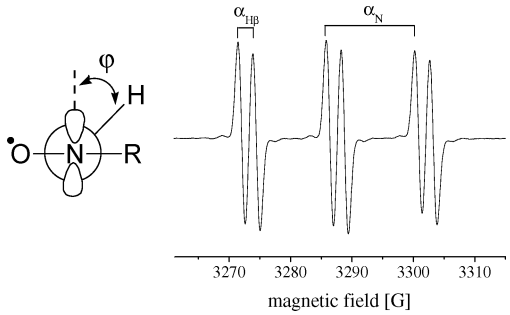


Figure 4. Room temperature ESR spectrum of nitroxide **6** ($\alpha_{H\beta} = 2.40$ G; $\alpha_N = 14.44$ G, in *t*-BuPh) and the dihedral angle φ which can be estimated from the Heller−McConnell equation.

The larger 3-dimethylaminocarbonyl-1,1-dimethylpropyl is located away from the nitroxide and has therefore no influence on the shielding of the nitroxide. This is probably the reason why alkoxyamines **7** and the parent **2** provided similar polymerization results. Thus, for efficient shielding all three methyl groups of the *tert*-butyl substituent in **2** have to be replaced. Indeed, alkoxyamine **11** bearing ethyl groups instead of methyl groups at the given position turned out to be the most efficient polymerization initiator/regulator in this series.

We decided to further study the conformation of nitroxides **6** and **10** in solution using ESR spectroscopy. Similar studies on stable α-H-bearing nitroxides have previously been published.[6,26] The hyperfine coupling constant $\alpha_{H\beta}$ can be used to determine the dihedral angle φ (see Figure 4, Table 3) using a simplified Heller−McConnell[27] equation ($\alpha_{H\beta} = B_N \cos^2(\varphi)$) with an estimated B_N of 26.55 G.[28] At room temperature, 2.40 G was measured for $\alpha_{H\beta}$, which leads to a dihedral angle φ of 72.5°. The room temperature ESR spectrum of nitroxide **6** is depicted in Figure 4. Thus, also in solution the α-H atom adopts near perfect anti alignment with the nitroxide O atom (O(2)−N(2)−C(9)−H torsion angle in solution = 162.5°). Unfortunately, because of line broadening, it was not possible to measure the $\alpha_{H\beta}$ of **6** at higher temperatures (90−125 °C). A dihedral angle φ of 71.7° was calculated from the ESR hyperfine coupling constant for the solution conformation of nitroxide **10**. As expected, a similar dihedral angle was also obtained for the nitroxide derived from alkoxyamine **14** ($\varphi = 71.1°$).

Conclusion

We have presented the synthesis of three new Hawker−Braslau type alkoxyamines. To increase the steric hindrance around the nitroxide O atom, the *tert*-butyl at the N atom in the parent alkoxyamine **2** was replaced with sterically more demanding substituents such as the 1,1-diethylpropyl group (→ **11**). The increased steric demand of the R^3 substituent in alkoxyamines of type **3** decreases the activation energies for C−O bond homolysis, as measured by kinetic ESR experiments. The C−O bond homolysis activation energy is an important parameter in the nitroxide-mediated polymerization. Compared to the parent regulator **2**, our new alkoxyamine **11** has higher activity as regulator/initiator for the controlled polymerization of styrene. Efficient polymerization could be accomplished at 105 °C. Controlled styrene polymerization can even be performed at 90 °C. However, the increased steric demand of the R^3 substituent also decreases the stability as determined by ^{1}H NMR spectroscopy. Therefore, polymerizations worked better at lower temperature. The same was also observed for the *n*-butyl acrylate polymerization where best results with alkoxyamine **11** were obtained at 105 °C. With alkoxyamine **11** controlled polymerization of *n*-butyl acrylate is possible even at 90 °C. In addition, AA and AB diblock copolymers have successfully been prepared using polystyrene and poly(*n*-butyl acrylate) macroinitiators derived from **11**.

Furthermore, we presented an X-ray structure of a Hawker−Braslau type nitroxide. As expected for a stable nitroxide, the α-H atom is located away from the nitroxide O atom. The O(2)−N(2)−C(9)−H torsion angle in **6** is 170.8°, close to 180° where highest stability is expected (Figure 3). Conformational analysis using ESR spectroscopy showed that this anti arrangement of the α-H atom with respect to the nitroxide O atom is also conserved in solution. The X-ray structure revealed that for perfect shielding of the nitroxide all three methyl groups of the *tert*-butyl group in the parent Hawker−Braslau nitroxide have to be replaced with larger substituents. Indeed, replacement of only one methyl group with larger alkyl substituents such as in **7** and in **14** has only a small effect on the polymerization regulator/initiator efficiency.

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