1-*tert*-Butyl-3,3,5,5-tetraalkyl-2-piperazinon-4-oxyls: Highly Efficient Nitroxides for Controlled Radical Polymerization

Saskia Miele,[†] Peter Nesvadba,[‡] and Armido Studer*,[†]

Institute of Organic Chemistry, Department of Chemistry, Westfälische Wilhelms-Universität Münster, Corrensstrasse 40, 48149 Münster, Germany, and Research Center Polymerization and Curing Agents, Ciba Inc., Schwarzwaldallee 215, CH-4002 Basel, Switzerland

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ABSTRACT: The paper describes nitroxide-mediated radical polymerization of styrene and *n*-butyl acrylate by using four sterically highly hindered 6-membered cyclic nitroxides. The syntheses of the corresponding alkoxyamine initiators are described, and also rate constants for C−O bond homolysis of these systems are discussed. It is shown that rate constants of alkoxyamines can readily be determined by ^{1}H NMR experiments. Polymerization results obtained are compared with data previously achieved with highly efficient nitroxides. Since this class of nitroxides is readily accessible, the 1-*tert*-butyl-3,3,5,5-tetraalkyl-2-piperazinon-4-oxyl radicals bearing alkyl groups that are ethyl or larger *n*-alkyl groups are probably the most efficient cyclic 6-membered nitroxides known to date for mediating NMP.

Introduction

Controlled living radical polymerization has received great attention during the past 10 years. Several methods that allow controlled polymerization of various monomers by radical chemistry have been developed. ATRP (atom transfer radical polymerization),[1] RAFT (reversible addition−fragmentation chain transfer polymerization),[2] I-group transfer polymerization,[3] Te-, Sb-, and Bi-group transfer polymerization,[4] cobalt-mediated polymerization,[5] and NMP (nitroxide-mediated polymerization)[6] are all very promising. These new methods allow the synthesis of various polymers with defined molecular weights and polydispersities below the theoretical limit (PDI < 1.5). By using either of these methods, we meanwhile reached a stage where almost every monomer can be polymerized by radical chemistry with high control.

ATRP, NMP, and some cobalt-mediated polymerizations are controlled by the persistent radical effect (PRE).[7,8] Importantly, in contrast to ATRP and the cobalt-mediated polymerization no metal is used in NMP.[9] In the present full paper we will focus on NMP where alkoxyamines are generally used as monocomponent initiators. During polymerization dormant alkoxyamine species are reversibly formed from the corresponding nitroxides and the growing macroradical. Various nitroxides have been prepared and tested as mediators in NMP. It has been found that the structure of the nitroxide moiety heavily influences properties of a nitroxide to control the polymerization process. H-bonding,[10−15] polar,[16] and steric effects[17−22] have been shown to alter the equilibrium constant between nitroxide-capped polymer and free nitroxide and polymer radical.[16−23] A larger equilibrium constant in most of the cases leads to a more efficient polymerization.[7]

We showed that in cyclic 6-membered nitroxides the installation of substituents in α-position to the nitroxide N atom that are larger than methyl groups leads to "steric pressure". The corresponding alkoxyamines such as **1**[13] and **2a**[17] turned out to be highly efficient initiators/regulators for NMP (see Figure 1). However, if substituents in that position become too large (see **3**),[19] control of polymerization is lost. As compared to noncyclic nitroxides,[24] cyclic 6-membered systems are generally more stable due to reversible β-elimination. For the noncyclic systems, β-elimination leads to nitroso compounds which upon leaving solvent cage generally do not reform the corresponding nitroxide. Therefore, we regard 6-membered nitroxides bearing ethyl groups in α-position to the N atom as prime candidates to control NMP. Although alkoxyamines **1** and **2** delivered excellent results, their application in NMP is hampered due to their tedious multistep synthesis. Herein we present in full details[25] the synthesis of piperazinone-based alkoxyamines **4**−**6**. Moreover, polymerization results and kinetic data will be provided.

Experimental Section

Materials. All reactions were performed under an argon atmosphere using the standard Schlenk technique. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-300 (^{1}H: 300 MHz; ^{13}C: 75 MHz), a Varian Inova 500 (^{1}H: 500 MHz; ^{13}C: 125 MHz), or a Varian Unity plus 600 (^{1}H: 600 MHz; ^{13}C: 150 MHz). Chemical shifts δ in ppm are referenced to the solvent residual peak. Thin layer chromatography was carried out on Merck silica gel 60 F_{254} plates; detection by UV or dipping into a solution of $KMnO_4$ (1.5 g), $NaHCO_3$ (5.0 g) in H_2O (400 mL), followed by heating. Flash chromatography (FC) was carried out on Merck or Fluka silica gel 60 (40 − 63 μm) at about 1.4 bar. Melting points (uncorrected) were determined on a SMP 10 apparatus (Stuart Scientific). IR spectra were recorded on a Varian 3100 FT-IR equipped with a MKII Golden Gate Single Reflection ATR unit. ESI-MS (*m*/*z*) and HRMS (*m*/*z*) were performed using a Bruker MicroTof and a Waters-Micromass Quattro LCZ (ESI-MS). Mass spectra of poly(*n*-butyl acrylate) before and after reinitiation for proving the livingness of the polymer chain were analyzed using the simulation software PolyCalc.[26] Size exclusion chromatography (SEC) was carried out with degassed THF as eluent at a flow rate of 1.0 mL/min at rt 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, Polymer Laboratories), and a Knauer RI differential refractometer detector. Data were analyzed with PSS WinGPC Compact V.7.20 software (Polymer Standards Service) based on 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 styrene and Poly(methyl methacrylate) Medium MW Calibration Kit M-M-10 to determine the molecular weight of poly(*n*-butyl acrylate)) with peak molecular weights ranging from 1660 to 1 000 000 g/mol. Elemental analyses were performed on a Vario EL III (Elementar-Analysensysteme GmbH). Styrene (Acros, 99%) and *n*-butyl

* Corresponding author. E-mail: studer@uni-muenster.de.
[†] Westfälische Wilhelms-Universität Münster.
[‡] Ciba Inc.

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acrylate (Acros, 99%) were distilled under reduced pressure from CaH_2 to remove stabilizer. Et_2O was distilled from K/Na, benzene was distilled from Na, THF was distilled from K, and CH_2Cl_2 was distilled from P_2O_5. The following chemicals were purchased and used as received: acetic acid (Acros, 99.8%), ammonia solution (Acros, 25% in water), (1-bromoethyl)benzene (Alfa Aesar, 97%), 3-bromopentane (Sigma-Aldrich, 95%), chloroform (Fisher Scientific, ≥99%), copper powder (Sigma-Aldrich, <10 μm, 99%), copper(II) trifluoromethanesulfonate (Alfa Aesar, 98%), dimethyl sulfoxide (Acros, 99.8%), 4,4′-di-*tert*-butyl-2,2′-bipyridyl (Sigma-Aldrich, 98%), ethyl acetate (Acros, 99.6%), formaldehyde (Acros, 37% solution in water, stabilized with 10−15% methanol), 4-heptanone (Acros, 98%), 3-pentanone (Sigma-Aldrich, 98%), peroxyacetic acid (Acros, 35% solution in diluted acetic acid), potassium hydroxide (Fluka, powder, ≥90%), 3-nitropropane (Acros, 96%), sodium nitrate (Acros, ≥98.5), *tert*-butylamine (Acros, 99%), zinc powder (Acros, 99.99%, 40 mesh).

3-Nitropentane. 3-Bromopentane (95%, 244 g, 1.54 mol, 1.00 equiv) was added to a suspension of sodium nitrite (134 g, 1.94 mmol, 1.26 equiv) in DMSO (1.2 L) and stirred at 33−35 °C for 21 h. After addition of ice water (1.5 L) the mixture was extracted with pentane (3 × 200 mL). The extracts were washed with water (2 × 50 mL) and dried over $MgSO_4$. After filtration pentane was evaporated in vacuo, and a slight yellow liquid was obtained containing 80% 3-nitropentane and 20% 3-pentylnitrite (yield of 100% 3-nitropentane: 141 g, 1.20 mol, 78%). The crude product was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 4.40−4.27 (m, 1 H, CH), 2.01−1.81 (m, 2 H, CH_2), 1.81−1.63 (m, 2 H, CH_2), 0.89 (t, J = 7.4 Hz, 6 H, 2 × CH_3).

***N*-*tert*-Butyl-(2-ethyl-2-nitrobutyl)amine (7).** *tert*-Butylamine (127 mL, 1.20 mol, 1.00 equiv) was added to crude 3-nitropentane (176 g, mixture of 80% 3-nitropentane and 20% 3-pentylnitrite, 1.20 mol, 1.00 equiv). Aqueous formaldehyde (37%, 90 mL, 1.2 mol, 1.0 equiv) was added over 10 min while keeping the temperature between 20−30 °C, and the mixture was stirred at 50 °C for 18 h. After the reaction was finished pentane (200 mL) was added to the cooled mixture; the organic layer was separated, washed with water (2 × 50 mL), and dried over $MgSO_4$. After filtration the solvent was evaporated in vacuo, and the crude product was purified by distillation (63−66 °C, 0.1 mbar). Amine **7** was obtained as colorless oil (169.5 g, 833.5 mmol, 70% calculated for pure starting material). IR (neat): 2970 m, 1530 vs, 1462 m, 1384 w, 1362 m, 1231 w, 1210 w, 1112 w, 828 w, 786 m, 769 m, 739 w cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 2.91 (s, 2 H, CH_2), 1.94 (q, J = 7.5 Hz, 4 H, 2 × CH_2), 1.03 (s, 9 H, 3 × CH_3), 0.83 (t, J = 7.5 Hz, 6 H, 2 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 96.1 (C), 50.5 (C), 45.9 (CH_2), 29.3 (CH_3), 26.5 (CH_2), 8.2 (CH_3). ESI-MS: 203 $[M + H]^+$, 225 $[M + Na]^+$, 427 $[2 M + Na]^+$. HRMS (ESI): calcd for $[M + H]^+$ 203.1754; found 203.1752. Anal. Calcd for $C_{10}H_{22}N_2O_2$: C 59.37, H 10.96, N 13.85. Found: C 59.33, H 11.10, N 13.85.

***N*-*tert*-Butyl-(2-ethylbutane-1,2-diamine (8).** Nitro compound **7** (20.0 g, 92.5 mmol, 1.00 equiv) was stirred in a mixture of AcOH and H_2O (1:1.5, 370 mL). Zinc powder (88.9 g, 741 mmol, 8.00 equiv) was added. The mixture was stirred at 80 °C for 2 h and was filtrated directly. The filtrate was evaporated to dryness, and the precipitate was dissolved in H_2O (200 mL), treated with NH_3 (5 mL → pH = 9), and extracted with Et_2O (3 × 100 mL). The organic layer was dried over K_2CO_3 and filtrated, and the solvent was evaporated in vacuo. The crude product was purified by distillation (85 °C, 4 mbar), and diamine **8** was obtained as a colorless oil (15.8 g, 91.6 mmol, 99%). Alternatively, the diamines were prepared by hydrogenation (4 bar) with Raney nickel. IR (neat): 2968 w, 1579 vs, 1462 w, 1377 vs, 1324 s, 1207 w, 1065 m, 1014 m, 988 m, 925 w, 672 vs, 617 m cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 2.25 (s, 2 H, CH_2), 1.35−1.08 (m, 4 H, 2 × CH_2), 0.96 (s, 9 H, 3 × CH_3), 0.72 (t, J = 7.5 Hz, 6 H, 2 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 53.3 (C), 49.7 (C), 49.4 (CH_2), 29.7 (CH_2), 29.1 (CH_3), 7.7 (CH_3). ESI-MS: 173 $[M + H]^+$, 195 $[M + Na]^+$. HRMS (ESI): calcd for $[M + H]^+$ 173.2012; found 173.2017.

1-*tert*-Butyl-3,3,5,5-tetraethyl-2-piperazinone (9). Diamine **8** (21.5 g, 0.125 mol, 1.00 equiv) was dissolved in $CHCl_3$ (15.1 mL, 0.187 mol, 1.50 equiv), and 3-pentanone (163 mL, 1.54 mol, 12.3 equiv) was added. Powdered KOH (35.0 g, 625 mmol, 5.00 equiv) was added over 10 min at 10 °C. The reaction mixture was stirred for 18 h at rt and was filtrated. The filtrate was evaporated to dryness, and product **9** was obtained after purification by FC (pentane:Et_2O, 10:1) as a yellow oil (18.5 g, 68.8 mmol, 55%). IR (neat): 2965 w, 2937 w, 1647 s, 1458 w, 1362 w, 1309 w, 1206 m, 1327 s, 1206 m, 986 w, 702 w cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 3.21 (s, 2 H, CH_2), 1.55 (q, J = 7.5 Hz, 4 H, 2 × CH_2), 1.44−1.29 (m, 13 H, 2 × CH_2, 3 × CH_3), 0.83 (t, J = 7.5 Hz, 6 H, 2 × CH_3), 0.80 (t, J = 7.5 Hz, 6 H, 2 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 174.5 (C), 61.9 (C), 57.0 (C), 53.4 (C), 51.0 (CH_2), 32.3 (CH_2), 28.8 (CH_3), 8.1 (CH_3), 7.8 (CH_3) ESI-MS: 269 $[M + H]^+$, 291 $[M + Na]^+$, 559 $[2 M + Na]^+$. HRMS (ESI): calcd for $[M + H]^+$ 269.2587; found 269.2590.

1-*tert*-Butyl-3,3,5,5-tetraethyl-2-piperazinon-4-oxyl (10). Peroxyacetic acid (39% in AcOH, 5.45 mL, 26.3 mmol, 1.50 equiv) was added dropwise over a period of 20 min to a solution of piperazinone **9** (4.64 g, 17.3 mmol, 1.00 equiv) in EtOAc (40 mL) at 0 °C. After stirring for 2.5 h the reaction mixture was hydrolyzed with water (50 mL), the phases were separated, and the aqueous layer was extracted with pentane (3 × 50 mL). The organic layer was washed with $NaHCO_3$ (aq, sat., 50 mL → pH = 7) and was dried over $MgSO_4$. After filtration solvents were evaporated in vacuo. The crude product was purified by FC (pentane:EtOAc, 5:1). Nitroxide **10** was obtained as a red solid (4.34 g, 15.3 mmol, 89%); mp: 33−37 °C. IR (neat): 2970 w, 2938 w, 1653 m, 1632 m, 1579 m, 1459 m, 1381 s, 1327 s, 1205 m, 1123 m, 1065 w, 989 w, 673 m cm^{-1}. ESI-MS: 306 $[M + Na]^+$, 589 $[2 M + Na]^+$. HRMS (ESI): calcd for $[M + Na]^+$ 306.2278; found 306.2277. Anal. Calcd for $C_{16}H_{31}N_2O_2$: C 67.80, H 11.02, N 9.88. Found: C 67.76, H 11.04, N 9.81.

1-*tert*-Butyl-3,3′-diethyl-5,5′-dimethyl-2-piperazinon-4-oxyl. was prepared in analogy to nitroxide **10** as described in the Supporting Information; mp: 49−50 °C. IR (neat): 2968 m, 2937 m, 2880 w, 1460 m, 1380 m, 1343 m cm^{-1}. ESI-MS: 256 $[M + H]^+$, 278 $[M + Na]^+$, 533 $[2 M + Na]^+$. HRMS (ESI): calcd for $[M + Na]^+$ 278.1965; found 278.1963. Anal. Calcd for $C_{14}H_{27}N_2O_2$: C 65.84, H 10.66, N 10.97. Found: C 65.83, H 10.69, N 10.91.

1-*tert*-Butyl-3,3′-dipropyl-5,5′-diethyl-2-piperazinon-4-oxyl. was prepared in analogy to nitroxide **10** as described in the Supporting Information; mp: 64−66 °C. IR (neat): 2962 w, 2931 w, 2875 w, 1650 s, 1456 m, 1421 w, 1361 w, 1202 m, 1139 m, 751 w cm^{-1}. ESI-MS: 312 $[M + H]^+$, 334 $[M + Na]^+$, 646 $[2 M + Na]^+$. HRMS (ESI): calcd for $[M + Na]^+$ 334.2591; found 334.2590. Anal. Calcd for $C_{18}H_{35}N_2O_2$: C 69.41, H 11.33, N 8.99. Found: C 69.43, H 11.36, N 8.99.

General Procedure for the Synthesis of 4-(1-Phenylethoxy)piperazin-2-ones (GP 1). (1-Bromoethyl)benzene (1.00 equiv), the corresponding nitroxide (1.05 equiv), copper powder (1.05 equiv), $Cu(OTf)_2$ (1 mol %), and 4,4′-di-*tert*-butyl-2,2′-bipyridyl (4 mol %) were suspended in benzene in a sealed tube. The reaction mixture was stirred at 75 °C for 24 h. Solids were removed by filtration over silica gel, followed by evaporation of the solvents in vacuo. Purification by FC (MTBE:pentane, 1:20) afforded the alkoxyamine.

1-*tert*-Butyl-3,3,5,5-tetraethyl-4-(1-phenylethoxy)piperazin-2-one (4). According to GP 1 (1-bromoethyl)benzene (0.46 mL, 3.4 mmol, 1.0 equiv), nitroxide **10** (1.00 g, 3.53 mmol, 1.05 equiv), copper powder (224 mg, 3.53 mmol, 1.05 equiv), $Cu(OTf)_2$ (12 mg, 34 μmol, 1 mol %), and 4,4′-di-*tert*-butyl-2,2′-bipyridyl (36 mg, 14 μmol, 4 mol %) were suspended in benzene (5.0 mL). The reaction afforded alkoxyamine **4** as a white solid (1.20 g, 3.09 mmol, 92%); mp 85−90 °C. IR (neat): 2975 w, 2939 w, 1642 s, 1457 m, 1416 w, 1364 w, 1344 w, 1208 m, 1153 w, 1057 w, 989 w, 914 w, 763 m, 702 s cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 7.38−7.16 (m, 5 H, Ar−H), 4.78−4.57 (m, 1 H, C*H*CH_3), 3.23−2.88 (m, 2 H, CH_2N), 2.28−2.02, 2.02−1.19, 1.19−0.36 (each m, 32 H, 4 × CH_2, 8 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$,

300 K): double set of resonance obtained: δ = 173.2 (C), 173.0 (C), 144.5 (C), 144.3 (C), 128.3 (CH), 127.8 (CH), 127.4 (CH), 127.2 (CH), 126.9 (CH), 82.9 (CH), 73.7 (C), 73.3 (C), 62.8 (C), 62.5 (C), 57.3 (C), 47.2 (CH_2), 46.4 (CH_2), 34.8 (CH_2), 33.4 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 28.4 (CH_3), 27.0 (CH_2), 26.8 (CH_2), 24.8 (CH_2), 23.2 (CH_3), 22.2 (CH_3), 11.8 (CH_3), 11.4 (CH_3), 9.8 (CH_3), 9.5 (CH_3), 9.3 (CH_3), 8.4 (CH_3), 7.8 (CH_3). ESI-MS: 389 $[M + H]^+$, 411 $[M + Na]^+$, 800 $[2\ M + Na]^+$. HRMS (ESI): calcd for $[M+ H]^+$ 389.3163; found 389.3162. Anal. Calcd for $C_{24}H_{40}N_2O_2$: C 74.18, H 10.38, N 7.21. Found: C 74.13, H 10.33, N 7.16.

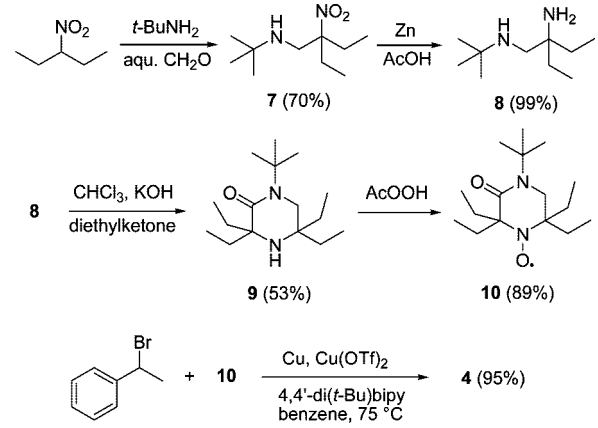
1-*tert*-Butyl-3,3-dipropyl-5,5-diethyl-4-(1-phenylethoxy)-piperazin-2-one (5). According to GP 1 (1-bromoethyl)benzene (0.62 mL, 3.2 mmol, 1.0 equiv), 3,3-dipropyl-5,5-diethyl-2-piperazinon-4-oxyl (1.09 g, 3.50 mmol, 1.10 equiv), copper powder (212 mg, 3.33 mmol, 1.05 equiv), $Cu(OTf)_2$ (11 mg, 31 μmol, 1 mol %), and 4,4′-di-*tert*-butyl-2,2′-bipyridyl (33 mg, 12 μmol, 4 mol %) were suspended in benzene (8.0 mL). Alkoxyamine **5** was obtained as colorless oil (1.25 g, 2.29 mmol, 94%). IR (neat): 2961 m, 2934 w, 1650 s, 1456 w, 1362 w, 1208 m, 1149 w, 1061 w, 760 w, 700 w cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 300 K): δ = 7.35−7.19 (m, 5 H, Ar−H), 4.74−4.59 (m, 1 H, C*H*CH_3), 3.23−2.90 (m, 2 H, CH_2N), 2.08−1.19, 1.19−0.81, 0.81−0.48 (each m, 36 H, 6 × CH_2, 8 × CH_3).^{13}C NMR (125 MHz, $CDCl_3$, 298 K): double set of resonance obtained: δ = 173.1 (C), 172.9 (C), 144.0 (C), 128.0 (CH), 127.9 (CH), 127.4 (CH), 127.1 (CH), 126.9 (CH), 126.6 (CH), 82.8 (CH), 82.4 (CH), 72.9 (C), 72.5 (C), 62.5 (C), 62.3 (C), 56.9 (C), 46.6 (CH_2), 45.9 (CH_2), 45.2 (CH_2), 43.7 (CH_2), 39.3 (CH_2), 39.0 (CH_2), 28.4 (CH_3), 26.5 (CH_2), 24.3 (CH_2), 22.9 (CH_3), 22.0 (CH_3), 19.7 (CH_2), 19.4 (CH_2), 17.7 (CH_2), 17.5 (CH_2), 15.1 (CH_3), 14.9 (CH_3), 14.5 (CH_3), 14.1 (CH_3), 9.4 (CH_3), 9.2 (CH_3), 8.1(CH_3), 7.5 (CH_3). ESI-MS: 417 $[M + H]^+$, 439 $[M + Na]^+$, 856 $[2\ M + Na]^+$. HRMS (ESI): calcd for $[M + H]^+$ 417.3476; found 417.3474. Anal. Calcd for $C_{26}H_{44}N_2O_2$: C 74.95, H 10.64, N 6.72. Found: C 74.95, H 10.64, N 6.63.

1-*tert*-Butyl-3,3-diethyl-5,5-dimethyl-4-(1-phenylethoxy)-piperazin-2-one (6). According to GP 1, (1-bromoethyl)benzene (0.33 mL, 1.2 mmol, 1.0 equiv), 3,3-dimethyl-5,5-diethyl-2-piperazinon-4-oxyl (0.50 g, 1.4 mmol, 1.1 equiv), copper powder (84.0 mg, 1.32 mmol, 1.05 equiv), $Cu(OTf)_2$ (4.5 mg, 13 μmol, 1 mol %), and 4,4′-di-*tert*-butyl-2,2′-bipyridyl (13 mg, 50 μmol, 4 mol %) were suspended in benzene (5.0 mL). Alkoxyamine **6** was obtained as a colorless oil, which solidified upon standing (0.418 g, 1.16 mmol, 92%); mp: 49−51 °C. IR (neat): 2973 w, 2934 w, 1647 s, 1459 w, 1363 m, 1310 m, 1195 m, 1150 m, 1061 w, 760 w, 699 s cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 300 K): δ = 7.34−7.12 (m, 5 H, Ar−H), 4.74−4.56 (m, 1 H, C*H*CH_3), 3.16−2.71 (m, 2 H, CH_2N), 2.19−1.20, 1.19−0.74, 0.73−0.49 (each m, 28 H, 2 × CH_2, 8 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): double set of resonance obtained: δ = 173.1 (C), 144.0 (C), 128.0 (CH), 127.6 (CH), 127.2 (CH), 127.0 (CH), 82.9 (CH), 71.7 (C), 57.4 (C), 57.2 (C), 57.0 (C), 56.9 (C), 52.2 (CH_2), 52.0 (CH_2), 34.2 (CH_2), 33.6 (CH_2), 28.7 (CH_2), 28.1 (CH_3), 22.5 (CH_3), 21.9 (CH_3), 19.9 (CH_3), 19.8 (CH_3), 11.7 (CH_3), 11.5 (CH_3), 9.1 (CH_3), 9.0 (CH_3). ESI-MS: 361 $[M + H]^+$, 383 $[M + Na]^+$, 744 $[2\ M + Na]^+$. HRMS (ESI): calcd for $[M + H]^+$ 361.2850; found 361.2853. Anal. Calcd for $C_{22}H_{36}N_2O_2$: C 72.25, H 9.70, N 8.43. Found: C 72.30, H 10.17, N 8.46.

Typical Procedure for the Polymerization of Styrene. A Schlenk tube was charged with alkoxyamine **4**, **5**, **6**, or **2b** and styrene (0.50 mL, 4.4 mmol). The tube was subjected to three freeze−thaw cycles and then sealed. The polymerization was carried out under argon at 105 °C for 4−24 h. The resulting mixture was cooled to rt and dissolved in CH_2Cl_2 (2 mL). The solvent was removed under reduced pressure, and residual monomer was removed in a vacuum-drying cabinet at 60 °C for at least 12 h. Conversion was determined gravimetrically; molecular weight and polydispersity index (PDI) were determined by size exclusion chromatography.

Typical Procedure for the Polymerization of *n*-Butyl Acrylate. A Schlenk tube was charged with alkoxyamine **4**, **5**, **6**, or **2b** and *n*-butyl acrylate (0.50 mL, 3.5 mmol). The tube was subjected to three freeze−thaw cycles and then sealed under argon. Polymerizations were carried out under argon at 105 or 125 °C for 4−24 h. The resulting mixture was cooled to rt and dissolved in CH_2Cl_2 (2 mL). The solvent was removed under reduced pressure, and residual monomer was removed in a vacuum-drying cabinet at 60 °C for at least 12 h. Conversion was determined gravimetrically; molecular weight and polydispersity index (PDI) were determined by size exclusion chromatography.

Scheme 1. Synthesis of Alkoxyamine 4



Results and Discussion

Synthesis of Alkoxyamine 4. Treatment of 3-nitropentane with *tert*-butylamine in the presence of aqueous formaldehyde afforded the nitro-Mannich product **7** in 70% yield (Scheme 1). Reduction of the nitro functionality was readily achieved with zinc in acetic acid to give diamine **8** in quantitative yield. Diamine **8** was then converted to 1-*tert*-butyl-3,3,5,5-tetraethyl-2-piperazinone (**9**) according to the procedure introduced by Lai (53%).[27] Peracid oxidation afforded the sterically hindered nitroxide **10** (89%) which was eventually converted to alkoxyamine **4** by using a known literature procedure.[28] Alkoxyamines **5** and **6** were prepared in analogy. The synthesis of alkoxyamine **2b** was previously reported by us.[20]

Polymerization Studies. Polymerizations with alkoxyamines **2b**, **4**, **5**, and **6** were performed in sealed tubes in neat styrene or *n*-butyl acrylate. Styrene polymerizations were conducted at 105 °C. Polymerizations of *n*-butyl acrylate were studied at 105 and 125 °C. Alkoxyamine concentration was systematically varied. Conversion was determined gravimetrically; PDI and molecular weight of the polymers were analyzed by using size exclusion chromatography (SEC). Results are summarized in Tables 1 and 2.

Polymerization of styrene with **4** at 105 °C occurred efficiently and well controlled (Table 1, entry 1). After 24 h a 77% conversion was achieved, and polystyrene (PS) with a narrow PDI (1.07) was isolated. PS with larger molecular weight was obtained upon systematically reducing alkoxyamine loading from 0.5 to 0.125 mol % (entries 2−4). At low initiator loading conversion slightly decreased (50−67%); however, polymerization remained well controlled (PDI < 1.20). All these experiments were repeated by running polymerizations for 6 h (entries 5−8). As expected, polymerizations occurred well controlled and conversions of 30−40% were achieved clearly, documenting that nitroxide **10** is a highly efficient regulator. We next tested whether replacing two ethyl groups in alkoxyamine **4** by two *n*-propyl groups (→ **5**) leads to a more efficient initiator/regulator. The whole series of experiments conducted with **4** were performed with **5** under otherwise identical conditions. We found only minor differences in the polymerization outcome for these two systems (compare entries

Table 1. NMP of Styrene at 105 °C with 2b and 4−6 under Different Conditions (Results Previously Obtained with 2a were Included for Comparison)

entry	alkoxyamine (mol %)	time (h)	conversion (%)	$M_{n,th}$ (g/mol)	$M_{n,exp}$ (g/mol)	PDI
1	**4** (1)	24	77	8 000	10 400	1.07
2	**4** (0.5)	24	72	15 000	15 100	1.09
3	**4** (0.25)	24	57	23 600	26 800	1.15
4	**4** (0.125)	24	50	45 000	31 200	1.19
5	**4** (1)	6	37	3 900	4 500	1.11
6	**4** (0.5)	6	33	6 900	7 400	1.11
7	**4** (0.25)	6	30	12 500	12 800	1.11
8	**4** (0.125)	6	29	24 500	20 700	1.12
9	**5** (1)	24	98	10 200	13 900	1.20
10	**5** (0.5)	24	81	17 600	22 900	1.09
11	**5** (0.25)	24	**5**9	25 500	31 600	1.15
12	**5** (0.125)	24	**5**9	57 600	61 800	1.18
13	**5** (1)	6	33	3 000	4 000	1.15
14	**5** (0.5)	6	24	4 400	9 200	1.13
15	**5** (0.25)	6	25	9 200	19 000	1.14
16	**5** (0.125)	6	25	18 900	28 900	1.17
17	**6** (1)	24	66	6 900	10 900	1.11
18	**6** (0.5)	24	79	16 900	14 500	1.14
19	**6** (0.25)	24	88	37 800	32 600	1.17
20	**6** (0.125)	24	67	58 000	46 500	1.22
21	**6** (1)	6	25	2 600	2 600	1.18
22	**6** (0.5)	6	21	4 300	5 100	1.25
23	**6** (0.25)	6	19	7 700	8 200	1.31
24	**6** (0.125)	6	22	18 000	14 200	1.29
25[a]	**2b** (1)	24	81	8 800	8 500	1.13
26	**2b** (0.5)	24	75	16 300	17 900	1.10
27	**2b** (0.25)	24	61	25 200	26 000	1.20
28	**2b** (0.125)	24	53	44 300	46 100	1.26
29	**2b** (1)	6	47	5 000	5 300	1.10
30	**2b** (0.5)	6	49	10 300	12 200	1.09
31	**2b** (0.25)	6	47	19 600	13 700	1.18
32	**2b** (0.125)	6	40	33 500	20 700	1.23
33[b]	**2a** (1)	24	69	7 200	9 400	1.09

[a] Reference 20. [b] Reference 17.

1−8 with entries 9−16), indicating that replacing the ethyl groups by larger linear *n*-alkyl groups does not influence polymerization outcome to a large extent. We next investigated the lower homologous diethyl,dimethyl-alkoxyamine **6** where two of the ethyl groups of the parent alkoxyamine **4** were replaced by smaller methyl groups. Also, the smaller congener **6** showed excellent ability to control styrene polymerization (entries 17−24).

To study the effect of the amide moiety within the ring on the polymerization, we ran polymerization of styrene with our previously reported sterically highly hindered alkoxyamine **2b**.[20] Again, a similar reaction outcome resulted for the **2b-**initiated polymerizations as compared to the results obtained with alkoxyamine **4** if polymerizations were allowed to proceed for 24 h (entries 25−28). For the 6 h experiments, slightly higher conversions were achieved for the **2b-**mediated styrene polymerizations (entries 29−32). Thus, the two sp^2-hybridized atoms of the lactam do not influence styrene polymerization. This result compares well with previously reported styrene polymerizations by using alkoxyamine **2a** bearing a ketone functionality within the ring (entry 33).[17] Hence, for styrene polymerization polar effects induced by the nitroxide moiety in piperazinones, piperidinones, and piperidines are obviously less important than steric effects.

We proved the controlled character of the **4-**mediated styrene polymerization by determining the conversion as a function of time and by analyzing the molecular weight as a function of monomer conversion (Figure 1). Both plots showed typical behavior expected for a controlled process.

We then decided to systematically study polymerization of *n*-butyl acrylate by using alkoxyamines **2b** and **4**−**6** (Table 2). Polymerizations were conducted without adding any additional free nitroxide[17] at different initiator loading (1, 0.5, 0.25, and 0.125 mol %, respectively). At 125 °C all polymerizations mediated by **4** went to high conversion (entries 1−4). However, at lower initiator loading the process was not controlled, and large PDIs resulted (2.32, entry 4). Therefore, polymerizations were repeated at lower temperature (105 °C). Pleasingly, acceptable conversions were still achieved after 24 h, and PDI remained low even upon using low initiator loading (entries 5−8). To study the effect of the replacement of two ethyl by *n*-propyl groups in alkoxyamine **4**, experiments were repeated with **5** (entries 9−16). As for the styrene polymerization discussed above, similar results were obtained for the **5-** and **4-**mediated acrylate polymerizations (compare entries 1−8 with entries 9−16). However, with alkoxyamine **6** bearing smaller methyl groups in place of ethyl substituents we were not able to control acrylate polymerization. Reactions at 125 °C and also at 105 °C were not controlled (entries 17 and 18). Better results were obtained upon increasing reaction temperature to 145 °C (entries 19 and 20). These results are not unexpected since it is known that acrylate polymerization is far more difficult to control than styrene polymerization.[17] For efficient NMP of *n*-butyl acrylate in the absence of any sacrificial nitroxide, sterically highly hindered nitroxides are requested. Indeed, with the larger tetraethylpiperidine derivative **2b** polymerization occurred well controlled (entries 21−28). Results obtained with **2b** compared well with those achieved using **4**. We already reported that *n*-butyl acrylate can be polymerized in a controlled manner with alkoxyamine **2a** (entry 29).[17] We then ran the whole series at 105 °C for 6 h (entries 30−42). At higher alkoxyamine loading (1 mol %) rather high conversions were achieved with the efficient alkoxyamines (up to 54%). However, reducing initiator loading did lead to a lowering of the conversion, and this in turn led to an increase of PDI.

We can conclude that controlled acrylate polymerization can be achieved with the cyclic 6-membered 3,3,5,5-tetraethyl-2-piperazinon-4-oxyl derived alkoxyamine **4**. Replacement of ethyl by larger *n*-alkyl groups did not influence polymerization. However, if smaller methyl groups were installed instead of ethyl substituents in the α-position to the N atom of the alkoxyamine, uncontrolled polymerization resulted. Polar effects exerted by the the nitroxide moiety did not influence acrylate polymerization outcome to a large extent since piperazinones, piperidinones, and piperidines delivered similar results as long as they bear four ethyl groups in the α-position to the alkoxyamine N atom.

Controlled character of the **5-**mediated acrylate polymerization was proved by determining conversion as a function of time and by analyzing molecular weight as a function of monomer conversion (Figure 3). Moreover, to prove the living character of the polymerization, the process was analyzed by ESI−mass spectrometry as previously shown.[29] Polymerization was conducted under the standard conditions and was stopped at low conversion after 2.5 h, and the crude product was analyzed by mass spectrometry. A characteristic peak group of the high-resolution ESI-TOF mass spectrum (Figure 4a, upper part) and the corresponding simulated isotopic pattern for a nitroxide-terminated oligomer (Figure 4a, lower part) correlated very well. All the chains were end-functionalized by the nitroxide moiety. Analysis using the simulation software PolyCalc[26] allows the determination of homopolymer characteristics. ESI is a much softer ionization/sample introduction procedure than matrix-assisted laser desorption ionization (MALDI). Therefore, ESI was chosen to prevent photolytic reactions which may occur with laser desorption. Comparison of a measured (Figure 4c, upper part) and a simulated (Figure 4c, lower part) part of the spectrum showed high similarity. Within the error limit no olefin-terminated or H-terminated chains formed by

Table 2. NMP of *n*-Butyl Acrylate at 105 and 125 °C with 2b and 4−6 under Different Conditions for 6 or 24 h (Results Previously Obtained with 2a were Included for Comparison)

entry	alkoxyamine (mol %)	temperature (°C)	time (h)	conversion (%)	$M_{n,th}$ (g/mol)	$M_{n,exp}$ (g/mol)	PDI
1	**4** (1)	125	24	96	12 300	15 000	1.20
2	**4** (0.5)	125	24	91	23 300	27 700	1.36
3	**4** (0.25)	125	24	89	45 700	51 200	1.34
4	**4** (0.125)	125	24	87	71 200	81 300	2.32
5	**4** (1)	105	24	68	8 700	9 700	1.11
6	**4** (0.5)	105	24	70	18 000	17 200	1.14
7	**4** (0.25)	105	24	71	36 500	33 900	1.20
8	**4** (0.125)	105	24	74	75 900	72 100	1.53
9	**5** (1)	125	24	90	11 600	9 700	1.21
10	**5** (0.5)	125	24	90	23 100	26 100	1.51
11	**5** (0.25)	125	24	85	34 700	39 600	1.42
12	**5** (0.125)	125	24	82	83 300	78 700	2.15
13	**5** (1)	105	24	59	7 600	12 300	1.15
14	**5** (0.5)	105	24	57	14 600	19 800	1.19
15	**5** (0.25)	105	24	54	27 800	44 500	1.28
16	**5** (0.125)	105	24	62	63 500	64 900	1.29
17	**6** (1)	125	24	96	12 300	12 200	2.40
18	**6** (1)	105	24	17	2 200	4 600	5.07
19	**6** (1)	145	6	65	8 300	15 800	1.50
20	**6** (0.5)	145	6	80	20 500	23 800	1.59
21	**2b** (1)	125	24	96	12 300	12 100	1.24
22	**2b** (0.5)	125	24	90	23 200	27 700	1.47
23	**2b** (0.25)	125	24	84	42 600	41 200	1.62
24	**2b** (0.125)	125	24	89	91 300	83 600	1.89
25	**2b** (1)	105	24	48	6 100	8 900	1.14
26	**2b** (0.5)	105	24	49	12 700	18 200	1.09
27	**2b** (0.25)	105	24	47	23 900	27 100	1.28
28	**2b** (0.125)	105	24	49	49 800	48 000	1.36
29[a]	**2a** (1)	105	24	83	10 600	18 600	1.12
30	**4** (1)	105	6	54	6 900	5 000	1.29
31	**4** (0.5)	105	6	31	8 000	9 800	1.29
32	**4** (0.25)	105	6	26	13 300	17 800	1.26
33	**4** (0.125)	105	6	20	20 100	22 900	1.25
34	**5** (1)	105	6	42	5400	8300	1.30
35	**5** (0.5)	105	6	24	6200	11 800	1.36
36	**5** (0.25)	105	6	28	14 100	18 300	1.30
37	**5** (0.125)	105	6	22	22 800	38 900	1.45
38	**6** (1)	105	6	30	3 800	4 600	5.26
39	**2b** (1)	105	6	29	3 700	5 300	1.22
40	**2b** (0.5)	105	6	26	6 700	9 300	1.17
41	**2b** (0.25)	105	6	22	11 300	15 500	1.18
42	**2b** (0.125)	105	6	23	23 900	24 100	1.28

[a] Reference 17; polymerization time was 32 h.

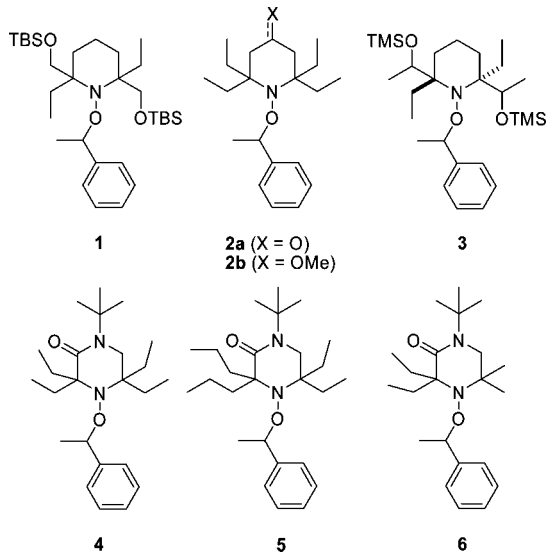


Figure 1. Sterically hindered alkoxyamines **1**−**6**.

disproportionation or hydroxylamine elimination were identified by either method.[29] Furthermore, by recursive iteration molecular weights (M_n = 1500) and PDI (1.19) were obtained by using PolyCalc. Values accorded well with GPC results (M_n = 1600, PDI = 1.38).

To further support the living character, we used the polymeric alkoxyamine as a macroinitiator (1 mol %) for reinitiation of *n*-butyl acrylate polymerization (2.5 h). Careful mass spec analysis proved that reinitiation was successful and that the elongated poly(*n*-butyl acrylate) still carried the nitroxide moiety at the chain terminus (Figure 4b,d). M_n and PDI were again determined by PolyCalc (M_n = 2900, PDI = 1.24), being in good agreement with GPC results (M_n = 2600, PDI = 1.35).

Kinetics of the C−O Bond Homolysis Determined by NMR Studies. Activation energies of the C−O bond homolysis E_A were determined by NMR spectroscopy according to a recently reported literature procedure.[30] To this end, the alkoxyamine was heated in perdeuterated dimethyl sulfoxide or perdeuterated *p*-xylene in the presence of a 10-fold excess of thiophenol to 80−100 °C in the NMR cavity. The nitroxide generated during C−O bond homolysis was quantitatively trapped by reduction with thiol so that nitroxide trapping of the secondary benzyl radical to re-form the starting alkoxyamine was completely suppressed. Reaction was monitored by following consumption of the alkoxyamine by ^{1}H NMR spectroscopy watching at an appropriate H resonance (see Supporting Information). Experimental C−O bond homolysis rate constants were calculated by means of eq 1 with [alkoxyamine]$_0$ = initial

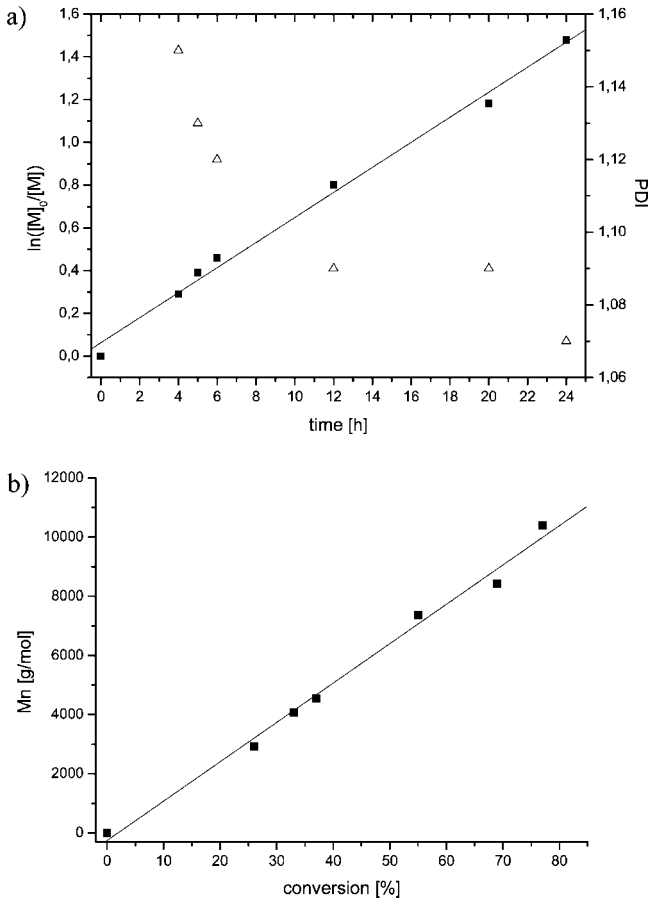


Figure 2. (a) Monomer conversion vs time and PDI evolution vs time (neat styrene, 105 °C, 1 mol % **4**; triangles = PDI; squares = $\ln([M]_0/[M])$). (b) Molecular weight vs monomer conversion (neat styrene, 105 °C, 1 mol % **4**).

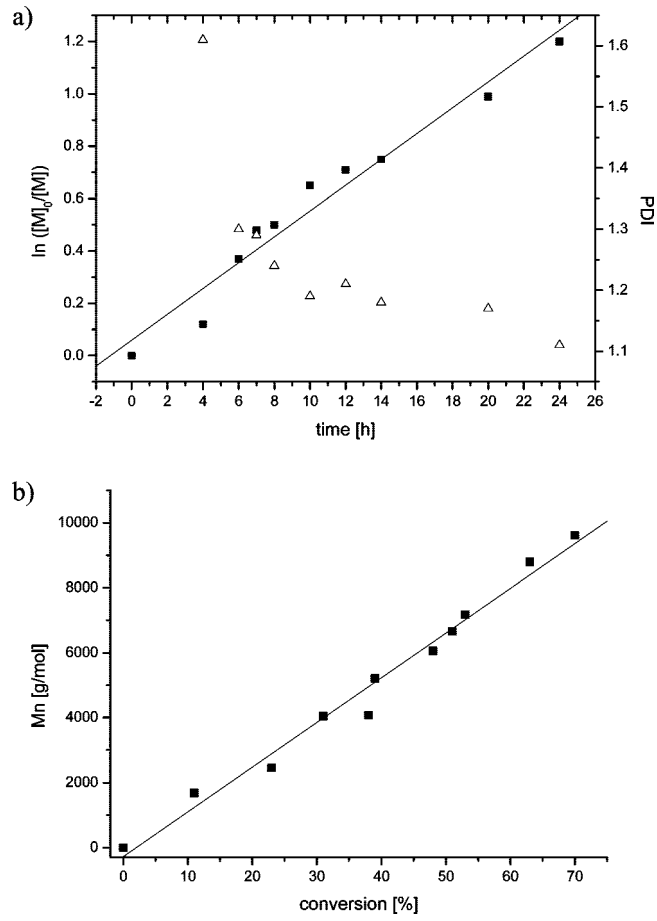


Figure 3. (a) Monomer conversion vs time and PDI vs time (neat *n*-butyl acrylate, 105 °C, 1 mol % **4**; triangles = PDI; squares = $\ln([M]_0/[M])$). (b) Molecular weight vs monomer conversion (neat *n*-butyl acrylate, 105 °C, 1 mol % **4**).

alkoxyamine concentration. Activation energies E_a were then estimated from the rate constants, whereby Arrhenius factor $A = 2.4 \times 10^{14}$ s^{-1}.[10,31] Results are summarized in Table 3.

$$\ln([\text{alkoxyamine}]_t/[\text{alkoxyamine}]_0) = -k_d t \qquad (1)$$

In agreement with the polymerization results discussed above, all α-tetraethyl-substituted alkoxyamines **4**, **5**, **2a**, and **2b** showed similar activation energies for C−O bond homolysis, indicating that polar effects do not heavily influence the rate constant of the C−O bond homolysis.[17−22] Steric effects are more important as shown for alkoxyamine **6** where a higher activation energy for C−O bond homolysis was determined. For alkoxyamine **4** rate constant for C−O bond homolysis was also determined in perdeuterated *p*-xylene. A similar value (within experimental error) was obtained showing that solvent effects play only a marginal role. Results in Table 3 document that the NMR method[30] used for determining rate constants is a valuable alternative to the more established EPR method since similar activation energies were obtained. This is useful since NMR apparatus are available in most of the departments whereas EPR machines are not always available.

Determination of the Equilibrium Constants *K*. For alkoxyamine initiator **4** the equilibrium constant *K* between the dormant alkoxyamine and the macroradical and nitroxide, respectively, was estimated for the polymerization of styrene and *n*-butyl acrylate. For styrene polymerization conversions of bulk polymerizations at 125 °C were determined after defined polymerization times by using 0.2 mol % of **4** in neat styrene. Recombination rate constant k_c was then estimated by fitting theoretical calculations to the experimental data as previously described by using $k_d = 1.9 \times 10^{-2}$ s^{-1} at 125 °C as homolysis rate constant (calculated assuming $A = 2.4 \times 10^{14}$ s^{-1} with the experimentally determined $E_A = 122.6$ kJ/mol; see Supporting Information).[19,21,32] Interestingly, we found that conversion as a function of time does not change dramatically for k_c values ranging from 5×10^7 to 1×10^8 M^{-1} s^{-1} (simulations were conducted with $k_c = 1.2 \times 10^7$, 5×10^7, 7.5×10^7, 1×10^8, and 1×10^9 M^{-1} s^{-1}; see Figure 5). Hence, these simulations do not allow distinguishing between these k_c values. Therefore, we estimated the *K* value for the **4**-mediated styrene polymerization at 125 °C to lie in between 3.8×10^{-10} and 1.9×10^{-10} M. This *K* value range estimated for the polymeric alkoxyamine agrees with the *K* value experimentally determined for the low molecular weight alkoxyamine initiator **4** ($K = 1.4 \times 10^{-10}$ M at 120 °C).[18] As expected for a highly efficient alkoxyamine, equilibrium constant *K* is similar to *K* values reported for sterically highly hindered efficient systems (*K* for **2a** = 2.5×10^{-10} M at 105 °C).[21]

For *n*-butyl acrylate polymerization the equilibrium constant *K* was estimated by using a method introduced by Lacroix-Demazes.[33] The method is based on findings by Fukuda[34] and Fischer,[35] who showed that in the presence of large quantities of additional nitroxide the conversion of the polymerization can be described by eq 2 (k_p = propagation rate constant; K = equilibrium constant between active and dormant chains ($K = k_d/k_c$); k_d = dissociation rate constant for the C−O bond homolysis; k_c = rate constant for the cross

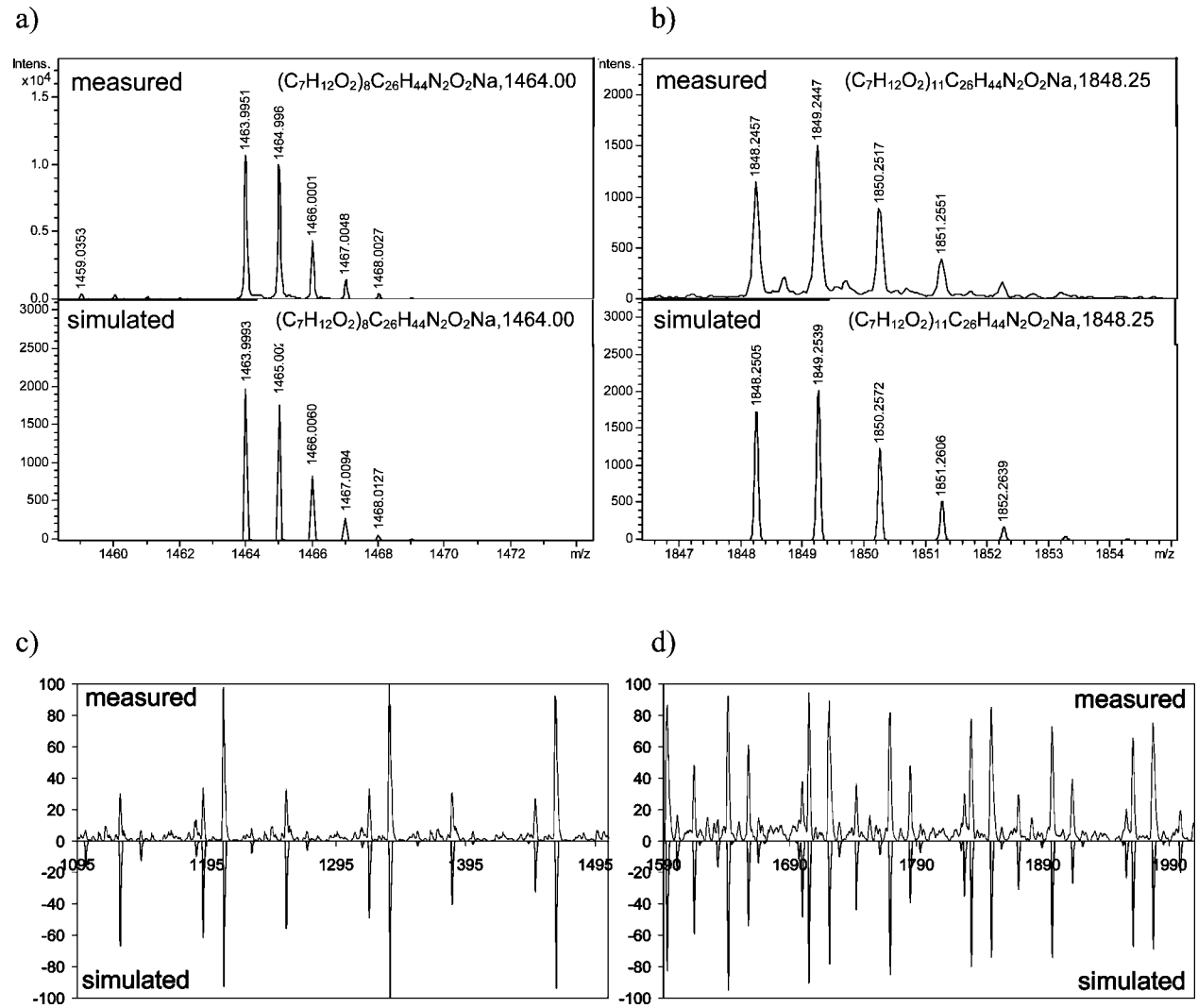


Figure 4. Characteristic region of a high-resolution ESI-TOF mass spectrum and the corresponding simulated spectrum: (a) after 2.5 h polymerization; (b) after reinitiation and further polymerization for 2.5 h. Comparison of the measured (upper part) and simulated (lower part) spectrum after parameter optimization: (c) after 2.5 h polymerization; (d) after reinitiation and further polymerization for 2.5 h.

Table 3. Kinetic Data on the C−O Bond Homolysis

alkoxyamine	E_A[a,b] (NMR) [kJ/mol]	k_d[c] (NMR) [s^{-1}] (°C)	E_A[a,b] (EPR) [kJ/mol]	k_d[c] (EPR) [s^{-1}] (°C)
4	122.6	1.7×10^{-4} (80)[d]	123.9	8.1×10^{-3} (120)[e]
5	122.5	1.8×10^{-4} (80)		
6	126.3	5.0×10^{-4} (100)	129.2	1.6×10^{-3} (120)[e]
2a			123.7	2.2×10^{-2} (130)[f]
2b	122.0	3.9×10^{-4} (85)		

[a] E_A = activation energy of C−O bond homolysis calculated using Arrhenius factor $A = 2.4 \times 10^{14}$ s^{-1} and the rate constant measured in DMSO-d_6. [b] Statistical errors between 2 and 3 kJ/mol. [c] Rate constant of homolysis at the given temperature in parentheses. [d] 2.8×10^{-4} at 80 °C in *p*-xylene-d_{10}. [e] Reference 25. [f] Reference 17.

coupling of the C-centered radical with the nitroxide; $[I]_0$ = initial alkoxyamine concentration; $[Y]_0$ = concentration of added free nitroxide):

$$\ln([M]_0/[M]) = k_p K([I]_0/[Y]_0)t \quad (2)$$

To determine the equilibrium constant *K*, several bulk polymerizations of *n*-butyl acrylate were performed by using 1 mol % of alkoxyamine **4** in the presence of 0.5 mol % of the corresponding free nitroxide **10** at 105 °C. Polymerizations were stopped after 8, 12, 14, 16, 20, 22, or 24 h. Conversions were determined gravimetrically and set into relation with reaction time as previously shown (Figure 6).[13,19] By applying eq 2, *K* for *n*-butyl acrylate polymerization controlled by **4** was obtained from the slope ($K = 3.4 \times 10^{-12}$ M at 105 °C). This value fits well with the *K* value previously measured for *n*-butyl acrylate polymerization mediated by **2a** ($K = 4.1 \times 10^{-12}$ M at 105 °C).[21] In cyclic systems, the introduction of electron-withdrawing groups near the nitroxide functionality normally leads to an increase of the C−O bond dissociation energy of the corresponding alkoxyamine.[36] In our system polar effects in going from the piperidinone (**2a**, cyclic ketone) to the piperazinone derivative (**4**, cyclic lactam) do not play a significant effect on the equilibrium constant *K* for *n*-butyl acrylate polymerization. However, we cannot rule out that

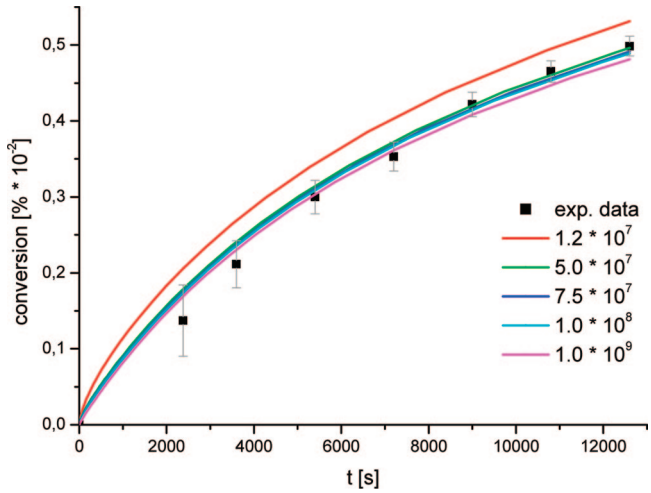


Figure 5. Conversion as a function of time for the experimental (bulk styrene polymerization, 0.2 mol % **4** at 125 °C) and simulated values for styrene polymerization using alkoxyamine **4** at 125 °C by using different k_c values and $k_d = 1.9 \times 10^{-2}$ s^{-1}.

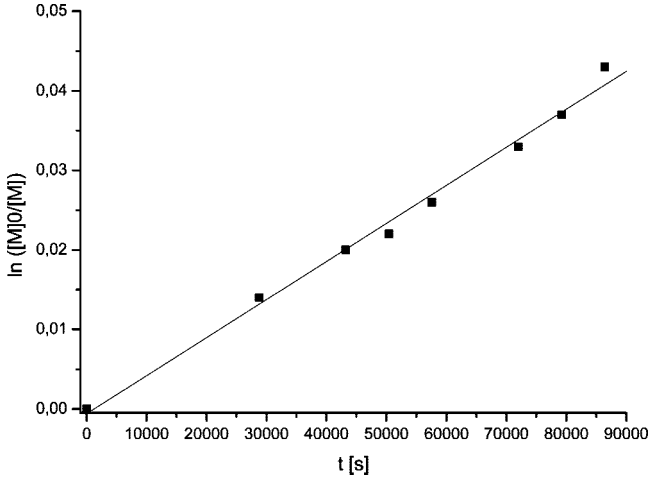


Figure 6. ln([M]$_0$/[M]) as a function of time for the determination of K according to eq 2 ($k_p = 7.1 \times 10^4$ M^{-1} s^{-1})[37] at 105 °C.

conformational effects do compensate polar effects exerted by the amide moiety in the piperazinone derivatives.

Conclusions

We presented experimental data on styrene and *n*-butyl acrylate polymerizations by using sterically highly hindered 6-membered cyclic alkoxyamines. Polymerization results were further supported by kinetic data. We showed that 6-membered cyclic nitroxides bearing four ethyl groups at the α-position of the nitroxide N atom are highly efficient regulators for NMP. Replacing ethyl groups by *n*-propyl groups did not influence reaction outcome to a large extent. However, if two ethyl groups were substituted by methyl groups, the corresponding nitroxides did not efficiently mediate polymerization of *n*-butyl acrylate. Styrene polymerization was less sensitive toward steric effects exerted by the nitroxide moiety. Polar effects in 6-membered cyclic nitroxides which bear four ethyl substituents in α-positions are less important. Hence, piperazinone, piperidinone, and piperidine derived α,α,α′,α′-tetraethyl nitroxides delivered similar results. It is important to note that alkoxyamine **4**, which delivered similar polymerization results as our most efficient alkoxyamines **2a** and **2b**, is far easier to prepare, and gram quantities are readily available. Therefore, we suggest to use in future highly efficient alkoxyamine **4** in place of our previously reported congener **2a**.

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Supporting Information Available: Graphs of the kinetic studies by NMR in DMSO-d_6 and *p*-xylene-d_{10} as well as further explanation of the simulation measurements; experimental part for the synthetic route to alkoxyamines **5** and **6** and the evidence of livingness for polymer chains bearing alkoxyamine **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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