Supporting Information

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

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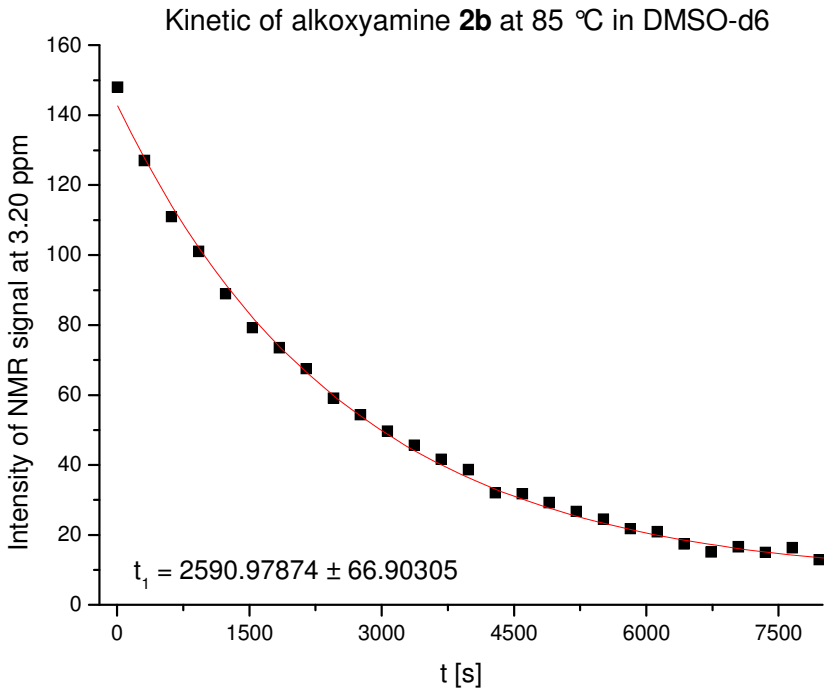
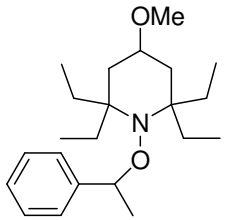
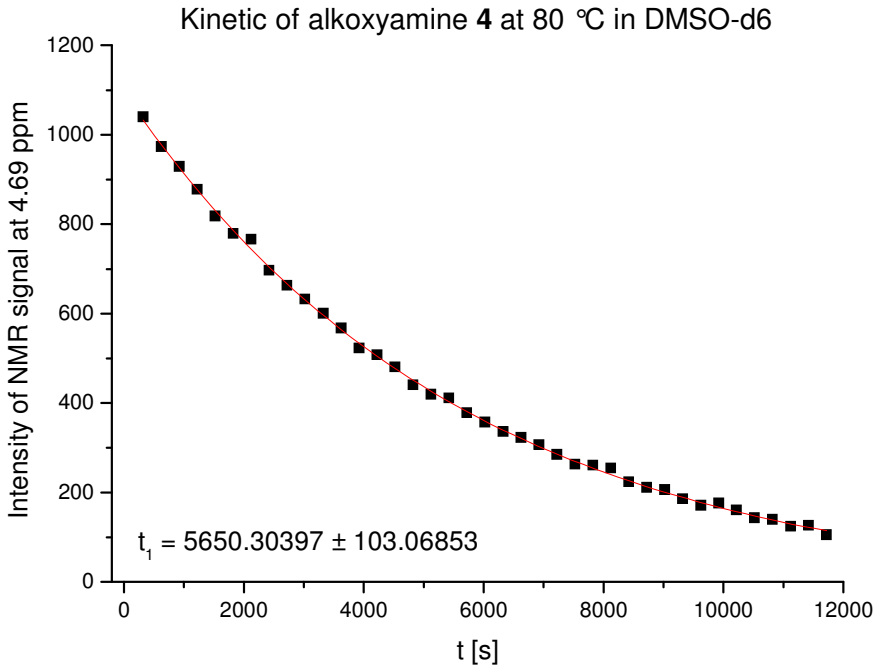
1 Kinetic Studies by NMR.

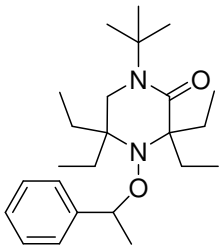
1.1 in DMSO-d6.



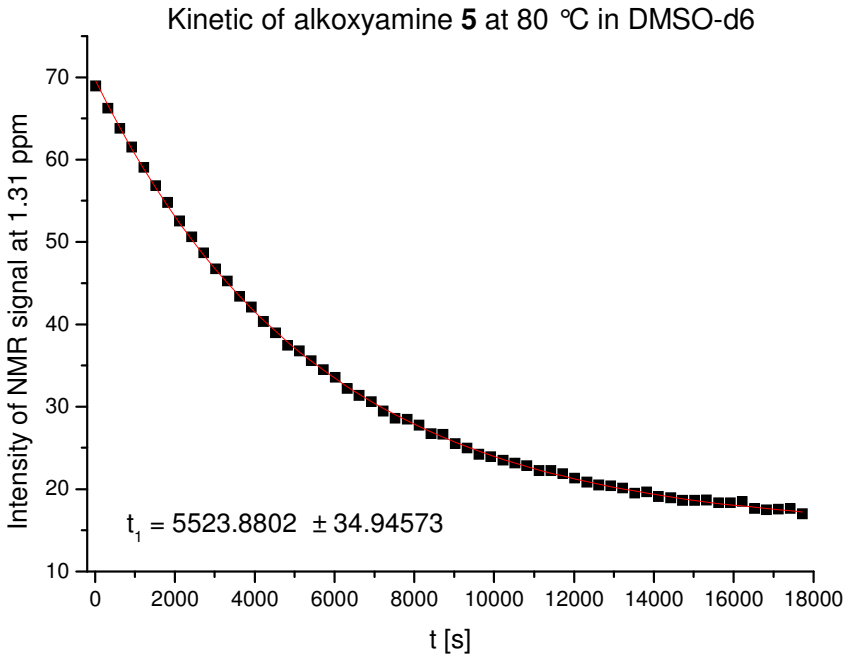


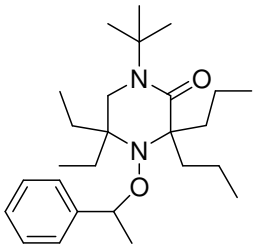
$k_d = 1/t_1 = 3.86 \times 10^{-4}\ s^{-1}$, $E_a = 122.0$ kJ/mol



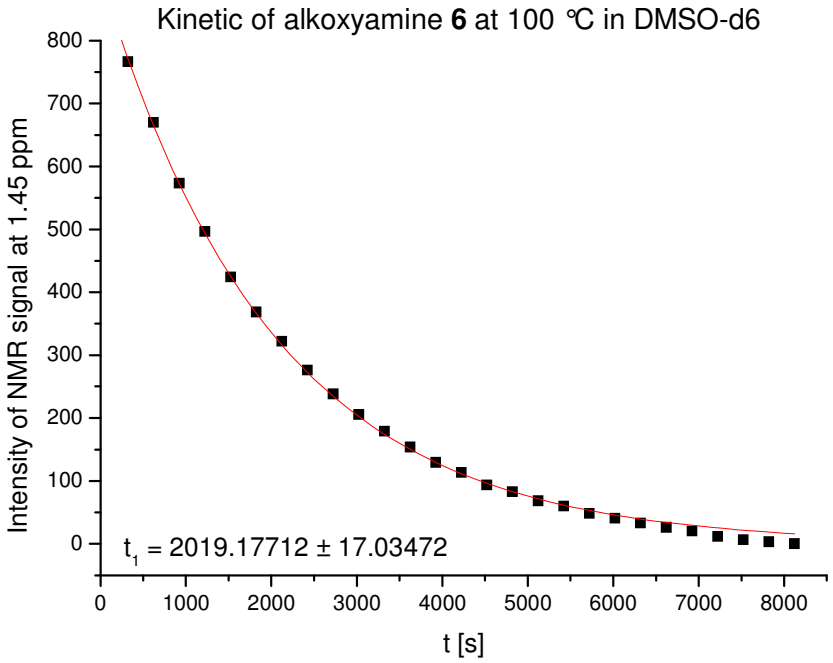


$k_d = 1/t_1 = 1.77 \times 10^{-4}\ s^{-1}$, $E_a = 122.6$ kJ/mol



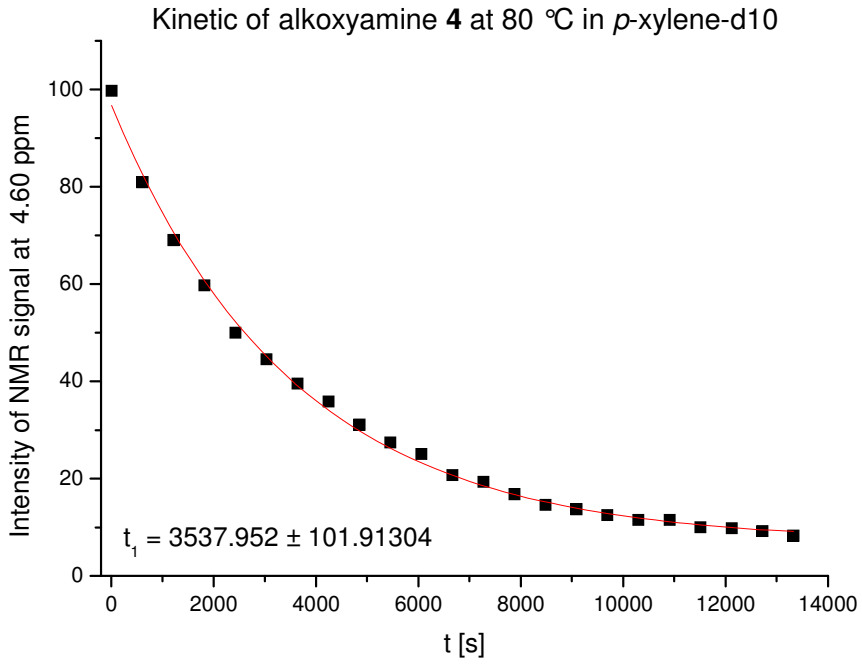


$k_d = 1/t_1 = 1.81 \times 10^{-4}\ s^{-1}$, $E_a = 122.5$ kJ/mol



$k_d = 1/t_1 = 4.95 \times 10^{-4}\ s^{-1}$, $E_a = 126.3$ kJ/mol

1.2 in *p*-Xylene-d10.

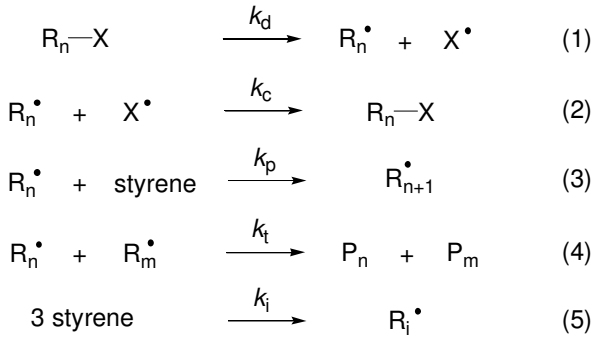


$k_d = 1/t_1 = 2.83 \times 10^{-4}\ s^{-1}$, $E_a = 121.2$ kJ/mol

2 Simulations.

The equilibrium constant *K* was estimated by simulation of the polymerization process and fitting the simulated data to the experimental data. The simulations were performed using *Presto*, a program for modeling nonlinear dynamics.[1] The following reactions were considered in the simulations: Homolysis of the nitroxide-capped dormant polymer chains into the persistent nitroxide radicals $X^{\bullet}$ and transient carbon-centered radicals $R_n^{\bullet}$ with n monomer units (*equation 1*, experimentally determined rate constant $k_d = 1.9 \times 10^{-2}\ s^{-1}$ at 125 °C was used in the simulation). Trapping of the polymeric radicals $R_n^{\bullet}$ with the nitroxide $X^{\bullet}$ to afford dormant polymeric alkoxyamines R_n-X (*equation 2*, rate constant k_c unknown to be fitted). To simplify the simulation, we assume that all the rate constants remain constant during the polymerization. This is a valid assumption as long as conversions are low and

viscosity effects play a minor role. Furthermore, k_d is set equal to the rate constant for the homolysis of the initiator alkoxyamine R_o-X (**4**) and k_c is set equal to the rate constant of the trapping of the styryl radical derived from the initiator with the nitroxide **10** ($X^{\bullet}$). Chain propagation occurs with the rate constant k_p (*equation 3*, k_p = 2318 $M^{-1}s^{-1}$).[2] Dimerization and/or disproportionation of two polymeric radicals $R_n^{\bullet}$ and $R_m^{\bullet}$ leading to chain termination are also considered in the simulation (*equation 4*, rate constant k_t = 1.73 x 10^8 $M^{-1}s^{-1}$).[3] Moreover, for the important auto polymerization of styrene we assumed the widely accepted initiation third order in styrene as first suggested by Hui and Hamielec (*equation 5*, rate constant k_i = 3.78 x 10^{-10} $M^{-2}s^{-1}$).[4] Since disproportionation of the nitroxide $X^{\bullet}$ and the growing polymeric radical $R_n^{\bullet}$ to form H-X and the corresponding terminal polymeric olefin $R_mCH{=}CHPh$ occurs only to a small extent in nitroxide mediated styrene polymerization,[5] this side reaction was not included into the kinetic scheme to simplify the simulation.



3 Experimental Part for the Synthetic Route to Alkoxyamines 5 and 6.

***N-tert*-Butyl-(2-metyl-2-nitro-propyl)-amine.** *tert*-Butylamine (5.8 ml, 0.56 mol, 1.00 eq) was added to 3-nitropropane (5.0 mL, 0.56 mol, 1.00 eq). Aqueous formaldehyde (37%, 42 ml, 0.56 mol, 1.0 eq) was added over 10 minutes while keeping the temperature between 20-30 °C and the mixture was stirred at 50 °C for 18 h. Pentane (20 mL) was added to the cooled mixture, the organic layer was separated, washed with water (2 × 30 mL) and dried over $MgSO_4$. After filtration the solvent was evaporated *in vacuo* and the crude product was

purified by distillation (49-51 °C, 0.1 mbar). The amine was obtained as a white solid (6.57 g, 37.7 mmol, 68%). Mp: 33 °C. IR (neat): 2966 m, 1534 vs, 1498 w, 1437 w, 1373 m, 1344 m, 1291 w, 1232 m, 1208 w, 1109 m, 771 m, 753 m, 718 w cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 2.90 (s, 2 H, CH_2), 1.54 (s, 6 H, 2 × CH_3), 1.02 (s, 9 H, 3 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 89.1 (C), 51.3 (CH_2), 50.3 (C), 29.2 (CH_3), 24.4 (CH_3). ESI-MS: 175 $[M + H]^+$. HRMS (ESI): calcd for $[M + H]^+$ 175.1441; found 175.1445. Anal. calcd for $C_8H_{18}N_2O_2$: C 55.15, H 10.62, N 16.08; found: C 55.08, H 10.62, N 15.91.

***N-tert*-Butyl-(2-ethyl-butane)-1,2-diamine.** *N-tert*-Butyl-(2-metyl-2-nitropropyl)-amine (1.70 g, 9.76 mmol, 1.00 eq) was stirred in a mixture of AcOH and H_2O (1:1.5, 35 mL). Zinc powder (5.12 g, 78.3 mmol, 8.00 eq) was added The reaction 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 (20 mL), treated with aq. conc. NH_3 (2 mL → pH = 9) and extracted with Et_2O (3 × 40 mL). The organic layer was dried over K_2CO_3, filtrated, and the solvent was evaporated *in vacuo*. The diamine was obtained as a colourless oil (1.35 g, 9.34 mmol, 96%) after FC (CH_2Cl_2:MeOH, 10:1). IR (neat): 2968 w, 1608 s, 1578 s, 1207 w, 1065 m,1014 m, 988 m, 925 w, 672 vs cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 4.21 (br s, 1 H, NH_2), 2.50 (s, 2 H, CH_2), 1.20 (s, 6 H, 2 × CH_3), 1.11 (s, 9 H, 3 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 52.7 (CH_2), 51.7 (C), 51.4 (C), 28.9 (CH_3), 27.2 (CH_3). ESI-MS: 145 $[M + H]^+$. HRMS (ESI): calcd for $[M + H]^+$ 145.1669; found 173.1700.

General Procedure for the Synthesis of Piperazinones (GP 2)

The diamine (1 eq) was dissolved in $CHCl_3$ (1.5 eq) and the respective ketone (12.3 eq) was added. Powdered KOH (5 eq) was added over 10 min at 10 °C. The reaction mixture was stirred for 18 h at rt and filtrated.

1-*tert*-Butyl-3,3-dipropyl-5,5-diethyl-2-piperazinone. According to GP 2 diamine **8** (0.50 g, 2.9 mmol, 1.0 eq) was dissolved in $CHCl_3$ (0.35 mL, 4.4 mmol, 1.5 eq) and 3-heptanone (5.0 mL, 36 mmol, 12 eq) was added. Powdered KOH (0.812 g, 14.5 mmol, 5.00 eq) was

added. The filtrate was evaporated to dryness and the crude product was purified with FC (pentane:Et_2O, 10:1). The piperazinone was obtained as a yellow oil (430 mg, 1.45 mmol, 50%). IR (neat): 2962 m, 2933 w, 1639 m, 1461 w, 1314 w, 1203 w, 906 vs, 727 vs, 646 s cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 300 K): δ = 1.53-1.18 (m, 12 H, 6 × CH_2), 1.36 (s, 9 H, 3 × CH_3), 0.83 (t, 6 *J* = 7.3 Hz 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 = 174.8 (C), 61.8 (C), 59.3 (C), 53.7 (C), 51.2 (CH_2), 43.0 (CH_2), 29.0 (CH_3), 28.5 (CH_3), 28.5 (CH_2), 17.1 (CH_2)14.8 (CH_2), 7.9 (CH_3). ESI-MS: 297 $[M + H]^+$, 319 $[M + Na]^+$, 616 $[2M + Na]^+$. HRMS (ESI): calcd for $[M + H]^+$ 297.2900; found 297.2901.

1-*tert*-Butyl-3,3-diethyl-5,5-methyl-2-piperazinone. According to GP 2 1,1-dimethyl-2-*tert*-butylaminopropylamine (220 mg, 1.53 mmol, 1.00 eq) was dissolved in $CHCl_3$ (186 µL, 2.3 mmol, 1.50 eq) and 3-pentanone (1.96 mL, 18.5 mmol, 12.3 eq) was added. Powdered KOH (428 mg, 7.65 mmol, 5.00 eq) was added. The filtrate was evaporated to dryness and the crude product was purified with FC (pentane:Et_2O, 10:1). The piperazinone was obtained as a colourless oil (0.21 g, 0.86 mmol, 56%). IR (neat): 2968 w, 1650 m, 1635 s, 1462 w, 1380 w, 1363 w, 1306 s, 1216 s, 1192 m, 1143 w cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 300 K): δ = 3.13 (s, 2 H, CH_2), 1.72-1.46 (m, 4 H, 2 × CH_2), 1.39 (s, 9 H, 3 × CH_3), 1.12 (s, 6 H, 2 × CH_3), 0.84 (t, *J* = 7.5 Hz, 6 H, 2 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 174.3 (C), 62.7 (C), 57.3 (CH_2), 55.1 (C), 49.3 (C), 32.8 (CH_2), 28.5 (CH_3), 8.5 (CH_3). ESI-MS: 241 $[M + H]^+$, 263 $[M + Na]^+$, 503 $[2M + Na]^+$. HRMS (ESI): calcd for $[M + H]^+$ 241.2274; found 241.2268.

General Procedure for the Synthesis of Piperazinon-4-oxyl compounds (GP 3)

Peroxyacetic acid (39% in AcOH, 1.5 eq) was added dropwise over a period of 20 min to a solution of the corresponding piperazinone (1 eq) in EtOAc at 0 °C. After stirring for 2.5 h the reaction mixture was hydrolyzed with water, the phases were separated, and the aqueous layer was extracted with pentane (3 ×). The organic layer was washed with $NaHCO_3$ (aq, sat., →

pH = 7) and was dried over $MgSO_4$. After filtration solvents were evaporated *in vacuo*. The crude product was purified with FC (pentane:EtOAc, 5:1).

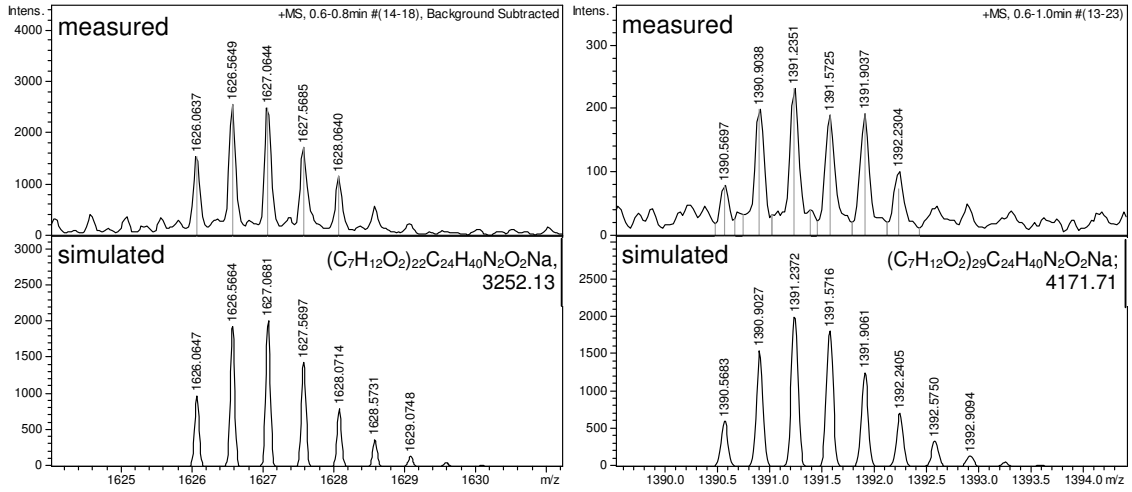
1-*tert*-Butyl-3,3-dipropyl-5,5-diethyl-2-piperazinon-4-oxyl. According to GP 3 peroxyacetic acid (388 µL, 2.02 mmol, 1.50 eq) was added to a solution of 1-*tert*-butyl-3,3-dipropyl-5,5-diethyl-2-piperazinone (400 mg, 1.35 mmol, 1.00 eq) in EtOAc (5 mL). The reaction mixture was hydrolyzed with water (5 mL), the phases were separated, and the aqueous layer was extracted with pentane (10 mL). The organic layer was washed with $NaHCO_3$ (aq, sat., 5 mL) and was dried over $MgSO_4$. The nitroxide was obtained as a red solid (380 mg, 1.22 mmol, 90%). 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 $[2M + Na]^+$. 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.

1-*tert*-Butyl-3,3-diethyl-5,5-methyl-2-piperazinon-4-oxyl. According to GP 3 peroxyacetic acid (240 µL, 1.25 mmol, 1.50 eq) was added to a solution of 1-*tert*-butyl-3,3-diethyl-5,5-methyl-2-piperazinone (0.20 g, 0.83 mmol, 1.0 eq) in EtOAc (3 mL). The reaction mixture was hydrolyzed with water (3 mL), the phases were separated, and the aqueous layer was extracted with pentane (6 mL). The organic layer was washed with $NaHCO_3$ (aq, sat., 3 mL) and was dried over $MgSO_4$. The nitroxide was obtained as a red solid (195 mg, 763 µmol, 92%). 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 $[2M + Na]^+$. 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.

4 Evidence of Livingness of the Polymer Chains with Alkoxyamine 4 by Mass Spectrometry.

Livingness of the *n*-butyl acrylate polymerization was also proofed for alkoxyamine **4** in the same way as described in the paper. After 5 h polymerization was stopped and the crude product was analyzed by mass spectrometry and by using the simulation software *PolyCalc*. The spectra obtained (Figure 1a, c) clearly showed that all the chains were end-functionalized by the nitroxide moiety. M_n and PDI were determined by *PolyCalc* (M_n = 2600, PDI = 1.28) being in good agreement with GPC results (M_n = 2900, PDI = 1.47). The polymeric alkoxyamine was used as a macroinitiator (1 mol%) for reinitiation of *n*-butylacrylate polymerization (5 h). Mass analysis proved that reinitiation was successful and that the elongated poly-*n*-butylacrylate still carried nitroxide moieties at the chain terminus (Figure 1b, d). M_n and PDI were determined by *PolyCalc* (M_n = 6100, PDI = 1.26) and by GPC (M_n = 7800, PDI = 1.30).

a) b)



c) d)

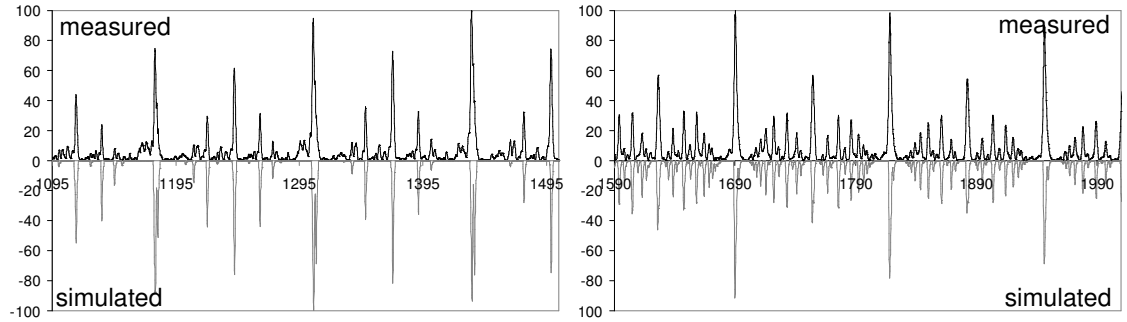


Figure 1. Characteristic region of a high resolution ESI-TOF mass spectrum and the corresponding simulated spectrum: a) after 5 h polymerization. b) after reinitiation and further polymerization for 5 h.

Comparison of the measured (upper part) and simulated (lower part) spectrum after parameter optimization: c) after 5 h polymerization. b) after reinitiation and further polymerization for 5 h.

5 References.

1. M. Wulkow, *Presto-Kinetics* 3.30.2a, CiT, 2006.
2. M. Buback, R. G. Gilbert, R. A. Hutchinson, B. Klumperman, F. D. Kuchta, B. G. Manders, K. F. Odriscoll, G. T. Russell, J. Schweer, *Macromol. Chem. Phys.* **1995**, *196*, 3267.
3. M. Buback, F. D. Kuchta, *Macromol. Chem. Phys.* **1997**, *198*, 1455.
4. A. W. Hui, A. E. Hamielec, *J. Appl. Polym. Sci.* **1972**, *16*, 749.
5. G. S. Ananchenko, H. Fischer, *J. Polym. Sci., Part A : Polym. Chem.* **2001**, *39*, 3604.