A New Sterically Highly Hindered 7-Membered Cyclic Nitroxide for the Controlled Living Radical Polymerization

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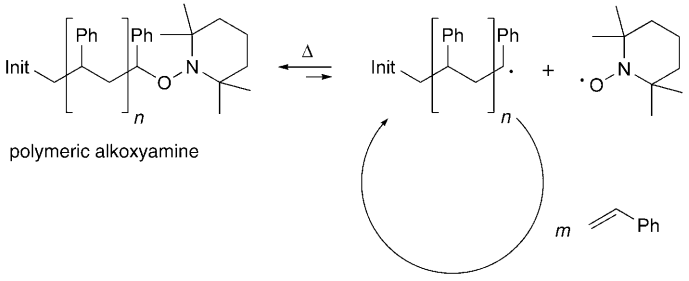
In memoriam Professor *Hanns Fischer*

The synthesis of a new sterically highly hindered 7-membered alkoxyamine, 2,2,7,7-tetraethyl-1-(1-phenylethoxy)-1,4-diazepan-5-one (**4**), starting from known 2,2,6,6-tetraethyl-1-(1-phenylethoxy)piperidin-4-one (**3**) *via* a *Beckmann*-type rearrangement is presented. It is shown that ring-enlargement by insertion of an NH moiety in going from **3** to **4** leads to a more efficient regulator for nitroxide-mediated controlled living radical styrene (=ethenylbenzene) and butyl acrylate (=butyl prop-2-enoate) polymerization. In addition to the polymerization experiments, kinetic data on the reversible C–O bond homolysis of alkoxyamines **3** and **4** are presented.

Introduction. – During the last 10 years, controlled radical polymerizations have been intensively investigated. Different methods such as nitroxide-mediated polymerizations (NMP) [1], atom-transfer radical polymerizations (ATRP) [2] and reversible addition-fragmentation chain transfer (RAFT) polymerizations [3] have been developed for the synthesis of polymers with defined molecular masses and narrow polydispersities. These methods allow the preparation of polymers with well-defined architectures and are, therefore, highly useful for the preparation of new interesting materials [1][2]. Control of polymerization in NMP and ATRP relies on the principle of the *Fischer–Ingold* persistent radical effect (PRE) [4]. In NMP, chain-growing polymer radicals and the corresponding nitroxides are reversibly formed *via* clean thermal C–O bond homolysis. As example, a 2,2,6,6-tetramethylpiperidin-1-yloxy radical-mediated (TEMPO-mediated) styrene (=ethenylbenzene) polymerization is presented in *Scheme 1*. Importantly, the equilibrium between the dormant polymeric alkoxyamine and the polymeric radical and nitroxide, respectively, lies far on the left side. Hence, a low concentration of radicals is ensured during the entire polymerization process. Consequently, irreversible terminations *via* polymer radical dimerization and disproportionation processes are suppressed due to low radical concentrations [4a].

In NMP, alkoxyamines are applied as initiators/regulators [1]. In the early work, TEMPO was used as nitroxide component to regulate radical polymerization of styrene and styrene derivatives. Unfortunately, controlled NMP of acrylates (=prop-2-enoates) could not be achieved with TEMPO as a regulator [1c]. However, in the meantime, a few reports on successful acrylate polymerizations in the presence of cyclic and noncyclic alkoxyamines have appeared [5–8]. *Hawker* and *Braslau* showed that readily pre-

Scheme 1. *TEMPO-Mediated Radical Polymerization.* Init = initiating radical.



pared alkoxyamine **1** is suitable for controlled butyl acrylate polymerization [5], and *Tordo* introduced alkoxyamine **2** as a highly efficient initiator/regulator for polymerization of acrylates (*Fig. 1*) [6]. We have introduced alkoxyamine **3** derived from a cyclic 6-membered tetraethylpiperidin-1-yloxy radical as a highly efficient initiator/regulator for controlled acrylate polymerization [7]. Moreover, it is known that in cyclic nitroxides the ring size influences the properties of the nitroxides to mediate NMP [9]. In general, 7-membered cyclic nitroxides are more efficient regulators than the corresponding 6-membered congeners [10]. Herein, we report the synthesis of a new alkoxyamine **4** bearing a sterically highly hindered 7-membered cyclic nitroxide moiety. Polymerizations of styrene and butyl acrylate by using **4** will be presented. These results are compared with those reported for the analogous polymerizations conducted with alkoxyamine **3**. In addition, we will discuss kinetic data on the reversible C–O bond homolysis of alkoxyamine **4** and of its lower homologue **3**.

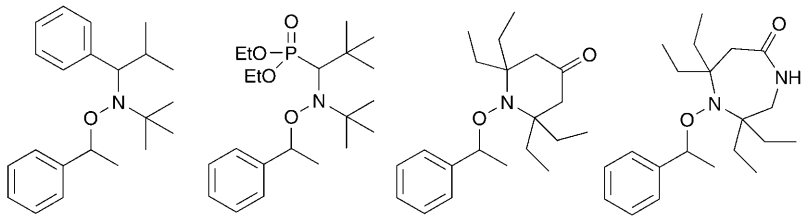
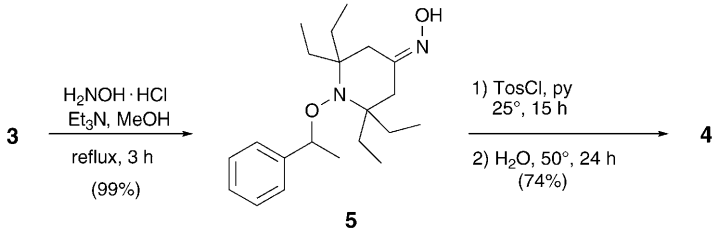


Fig. 1. *Various alkoxyamines for the controlled nitroxide-mediated acrylate polymerization*

Results and Discussion – Synthesis of Alkoxyamine 4 and Polymerization Studies. – Alkoxyamine **4** is readily prepared starting from known [7b] alkoxyamine **3** *via* a *Beckmann* ring-enlargement reaction according to a procedure recently described by *Nesvadba* and co-workers [9b]. Treatment of **3** in MeOH with the hydrochloride salt of hydroxylamine in the presence of Et_3N provided oxime **5** in quantitative yield (*Scheme 2*). Tosylation and subsequent rearrangement afforded the desired lactam **4** in a good yield (74%).

Polymerizations were conducted in sealed tubes in neat styrene or butyl acrylate in the presence of 1% of alkoxyamine initiator **4** at 70, 90, 105, and 125° and were stopped

Scheme 2. *Synthesis of Alkoxyamine* **4**



after 3 to 72 h. The polydispersity index (*PDI*) and molecular mass of the polymers were analyzed by size-exclusion chromatography (SEC), and conversion was determined gravimetrically. Results are summarized in *Tables 1* and *2*. To document the effect of the ring enlargement in the nitroxide moiety of the alkoxyamine on the polymerization process, previously reported results [7a] of the **3**-mediated styrene and acrylate polymerizations are also included into *Tables 1* and *2*.

Table 1. *Living Styrene Polymerization Using 1 mol-% of Alkoxyamines* **3** *and* **4** *as Initiators/Regulators at Different Temperatures*

Entry	Alkoxyamine	Temp. [°]	Time [h]	$M_{n,th}$[a]) [g/mol]	$M_{n,exp}$ [g/mol]	*PDI*	Conversion [%]
1	**4**	125	6	9500	10000	1.22	91
2	**4**	125	3	7900	8500	1.16	73
3	**4**	105	6	6800	6400	1.13	65
4	**4**	90	24	6500	6200	1.14	59
5	**4**	70	26	1400	1200	1.29	13
6[b])	**3**	125	6	8200	10900	1.12	79
7[b])	**3**	105	24	7200	9400	1.09	69
8[b])	**3**	90	56	7600	10500	1.08	73

[a]) $M_{n,th}$ (theoretically determined M_n) $= M_{alkoxyamine} + [\text{styrene}]_o \cdot \text{conversion} \cdot 104.15/[\text{alkoxyamine}]_o$. [b]) See [7a].

Table 2. *Living Butyl Acrylate Polymerization using 1 mol-% of Alkoxyamines* **3** *and* **4** *as Initiators/Regulators at Different Temperatures*

Entry	Alkoxyamine	Temp. [°C]	Time [h]	$M_{n,th}$[a]) [g/mol]	$M_{n,exp}$ [g/mol]	*PDI*	Conversion [%]
1	**4**	125	3	9800	13500	1.21	74
2	**4**	105	5	8300	9000	1.24	62
3	**4**[b])	90	24	5600	6600	1.25	45
4	**4**[b])	70	72	2600	3400	1.32	19
5[c])	**3**	125	9	11400	20500	1.18	89
6[c])	**3**	105	32	10600	18600	1.12	83
7[c])	**3**	90	96	9000	12300	1.13	70

[a]) $M_{n,th}$ (theoretically determined M_n) $= M_{alkoxyamine} + [\text{butyl acrylate}]_o \cdot \text{conversion} \cdot 128.17/[\text{alkoxyamine}]_o$. [b]) 1.1 mol-% of alkoxyamine **4** was used. [c]) See [7a].

Styrene polymerization at 125° for 6 h provided polystyrene in a 91% conversion and a *PDI* of 1.22 (*Table 1*, *Entry 1*). With the lower homologue **3** as an initiator/regulator, a lower conversion was achieved under identical conditions (*Entry 6*). We found that a high conversion by using **4** can be obtained in just 3 h at 125° (73%, *Entry 2*). More dramatically is the ring-enlargement effect if the polymerizations are conducted at lower temperatures. Hence, the **4**-initiated styrene polymerization at 105° for 6 h delivered polystyrene in 65% conversion with a low *PDI*, whereas, to get a similar conversion, 24 h were necessary under the same conditions by using alkoxyamine **3** (compare *Entries 3* and *7*). Styrene polymerization in the presence of **4** can be conducted at 90°, however, reaction time has to be increased to 24 h to get acceptable conversions (*Entry 4*). Polymerization with the parent **3** under identical conditions is far slower (*Entry 8*). We could show that even at 70°, controlled styrene polymerization occurs by using alkoxyamine **4**, however, reaction is very slow under these conditions (*Entry 5*). Importantly, controlled polymerization with alkoxyamine **3** did not occur at 70°, clearly documenting the benefit of the ring enlargement.

The controlled living radical polymerization of butyl acrylate in the presence of **4** at 125° for 3 h provided poly(butyl acrylate) in a high conversion with a low *PDI* (*Table 2*, *Entry 1*). Only a slightly higher conversion was achieved with **3** in 9 h (*Entry 5*). A similar outcome was obtained for the reactions conducted at 105° (*Entries 2* and *6*). Pleasingly, rather efficient acrylate polymerization was achieved at 90° with the ring-enlarged alkoxyamine **4** (*Entry 3*). However, at 70°, controlled acrylate polymerization by using **4** is very slow, and the *PDI* increased (*Entry 4*). It is important to note that additional nitroxide which is often mandatory for controlled nitroxide-mediated polymerization is not necessary for the **3**- and **4**-initiated acrylate polymerizations [5][11].

Kinetic Studies – Simulations. – The C–O bond homolysis rate constant k_d of **4** was determined in (*tert*-butyl)benzene at 378 K by kinetic EPR experiments. Oxygen was used to scavenge the styryl radical generated after C–O bond homolysis, and the concentration of the released nitroxide was measured by EPR spectroscopy, as previously described [12]. An experimental rate constant k_d of $9.4 \cdot 10^{-3}$ s^{-1} was obtained for **4**. The activation energy $E_a = 118.7 \pm 2$ kJ/mol of **4** was calculated from the experimentally determined rate constant k_d by using an *Arrhenius* factor A of $2.4 \cdot 10^{14}$ s^{-1} [12]. In agreement with the polymerization results described above, activation energy for the C–O bond homolysis of alkoxyamine **4** is smaller than E_a of **3** ($E_a = 123.7 \pm 2$ kJ/mol [7a]). This is also in agreement with semiempirical calculations predicting that the bond-dissociation energy of the C–O bond in alkoxyamines is decreasing with increasing ring size [13]. Steric congestion around the alkoxyamine N-atom obviously leads to weaker C–O bonds [9][10][13]. It is well known that E_a of the C–O bond homolysis of a regulator correlates well with the polymerization results; however, the equilibrium constant K between the nitroxide-terminated alkoxyamine and the polymer radical and nitroxide is a more valuable parameter to describe the efficiency of a nitroxide to act as a regulator for the controlled living radical polymerization ($K = k_d/k_c$; k_c = rate constant for the trapping of the macroradical with the nitroxide). Therefore, we decided to determine K values for alkoxyamines **3** and **4** by a method previously described [14].

To this end, conversions of bulk styrene polymerizations at 105° in the presence of 1 mol-% of **3** or **4** were determined after defined polymerization times (*Fig. 2*). The equi-

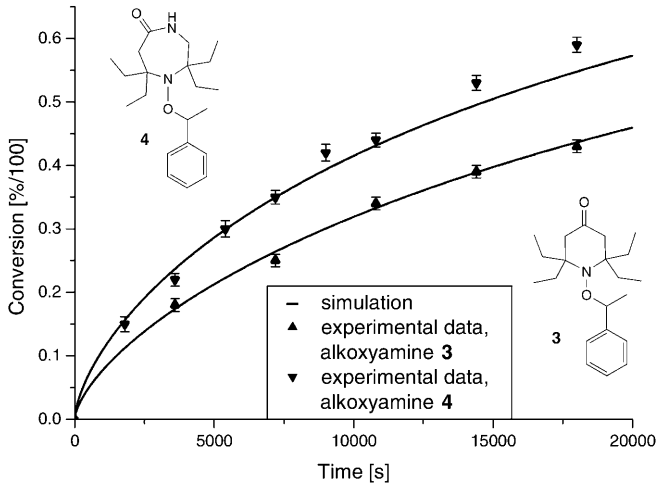


Fig. 2. *Determination of the equilibrium rate constant* K *for the* **3**- *and* **4**-*initiated styrene polymerization at 105°*

librium constant K was then estimated by simulation of the polymerization process and fitting the simulated data to the experimental data. The simulations were performed with Powersim, a program for modeling nonlinear dynamics [15]. 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 C-centered radicals $R^{\bullet}_n$ with n monomer units (*Eqn. 1*, experimentally determined rate constants k_d of **3** and **4** were used). Trapping of the polymer radicals $R^{\bullet}_n$ with the nitroxide X$^{\bullet}$ to afford dormant polymeric alkoxyamines R_n–X (*Eqn. 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, and k_c is set equal to the rate constant of the trapping of the styryl radical derived from the initiator with the nitroxide X$^{\bullet}$. Chain propagation occurs with the rate constant k_p (*Eqn. 3*, $k_p = 1.4 \cdot 10^3$ M^{-1}s^{-1} [16]). Dimerization and/or disproportionation of two polymer radicals $R^{\bullet}_n$ and $R^{\bullet}_m$ leading to chain termination are also considered in the simulation (*Eqn. 4*, rate constant $k_t = 1.4 \cdot 10^8$ M^{-1}s^{-1} [17]). 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* (*Eqn. 5*, rate constant $k_i = 3.0 \cdot 10^{-11}$ M^{-2}s^{-1} ([18a], see also [18b])). Since disproportionation of the nitroxide X$^{\bullet}$ and the growing polymeric radical $R^{\bullet}_n$ to form H–X and the corresponding terminal polymeric olefin R_mCH=CHPh occurs only to a small extent in nitroxide-mediated styrene polymerization [19], this side reaction was not included into the kinetic scheme to simplify the simulation.

$$R_n\text{–X} \xrightarrow{k_d} R^{\bullet}_n + X^{\bullet} \quad (1)$$

$$R^{\bullet}_n + X^{\bullet} \xrightarrow{k_c} R_n\text{–X} \quad (2)$$

$$R^{\bullet}_n + \text{styrene} \xrightarrow{k_p} R^{\bullet}_{n+1} \quad (3)$$

$$R^{\bullet}_n + R^{\bullet}_m \xrightarrow{k_t} P_n + P_m \quad (4)$$

$$3 \text{ styrene} \xrightarrow{k_i} R^{\bullet}_i \quad (5)$$

For alkoxyamine **3** with an experimentally determined k_d of $1.9 \cdot 10^{-3}$ s^{-1}, the best fit was achieved for $k_c = 7.6 \cdot 10^6$ $M^{-1}s^{-1}$providing an equilibrium constant K of $2.5 \cdot 10^{-10}$ M (*Fig. 2*). A K value of $7.7 \cdot 10^{-10}$ M at 105° was obtained for alkoxyamine **4** by using a k_c of $1.2 \cdot 10^7$ $M^{-1}s^{-1}$ as best fit and the above described experimentally determined k_d value of $9.4 \cdot 10^{-3}$ s^{-1}. Hence, the ring-enlargement in going from alkoxyamine **3** to **4** leads to an increase of K by a factor of *ca.* 3. This is in agreement with the styrene-polymerization experiments described above, where alkoxyamine **4** delivered better results than **3**. It is important to note that alkoxyamine **3** has been shown to be one of the most efficient alkoxyamines for NMP known to date [7].

We continued our studies by determining the equilibrium constant K for the butyl acrylate polymerization initiated/regulated by alkoxyamines **3** and **4** by means of the method first applied by *Lacroix-Demazes* and co-workers [20]. Based on theoretical work, *Fukuda* and co-workers [21] and *Souaille* and *Fischer* [11d] suggested that the conversion of NMP in the presence of large quantities of additional nitroxide can be described by *Eqn. 6* ($[I]_0$ = initial alkoxyamine concentration; $[Y]_0$ = concentration of added nitroxide; $[M]_0$ = initial monomer concentration; [M] = concentration of unreacted monomer; k_p = propagation rate constant = $7.1 \cdot 10^4$ $M^{-1}s^{-1}$ [20b]). Hence, the K value can readily be obtained by determining the conversion of NMP with different concentrations of added nitroxide at a fixed reaction time or by using a fixed concentration of added nitroxide and varying the reaction time. The latter approach was applied in the present study.

$$\ln([M]_0/[M]) = k_p K([I]_0/[Y]_0)t \quad (6)$$

To this end, polymerizations of butyl acrylate were performed in the presence of 1 mol-% of alkoxyamine **3** or **4** and 0.5 mol-% of the corresponding nitroxide **6** or **7**, respectively. The polymerizations were stopped after 9, 12, 15, 18, 21, or 24 h. The conversions were determined gravimetrically and set into relation with the reaction time (*Fig. 3*). With the experimental data and *Eqn. 6*, K was readily obtained from the slope.

Nitroxide **6** was synthesized according to our recently published procedure [8b], and nitroxide **7** was obtained by heating alkoxyamine **4** in (*tert*-butyl)benzene in the presence of oxygen (*Scheme 3*). For the **7**-mediated acrylate polymerization, we obtained a K value of $9.6 \cdot 10^{-12}$ M at 105°. As expected from the polymerization experiments, K for the **6**-mediated butyl acrylate polymerization at 105° is smaller ($K = 4.1 \cdot 10^{-12}$ M).

Hence for sterically highly hindered 2,2,6,6-tetraalkylpiperidin-1-yloxy radicals such as **6**, ring enlargement by insertion of an NH moiety leads to a more efficient nitroxide to regulate polymerization. This is in agreement with results recently reported by *Nesvadba* and co-workers for a similar system [9b]. However, ring enlargement from 6- to 7-membered rings does not necessarily always lead to more efficient systems. We

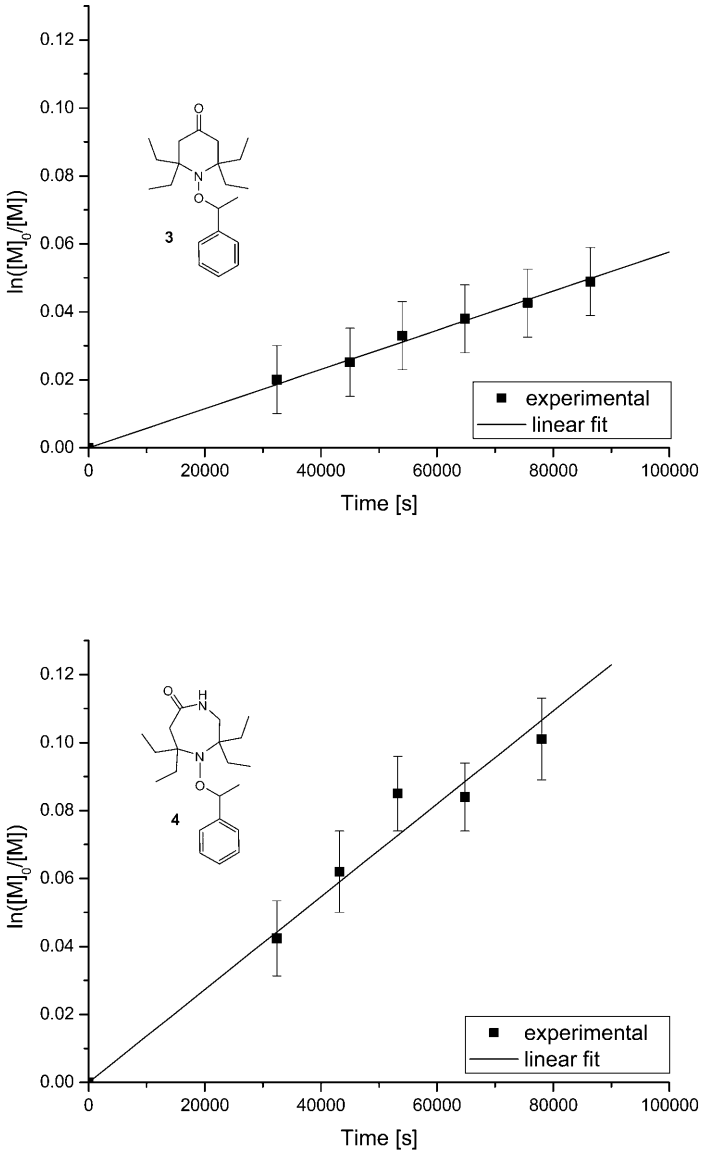
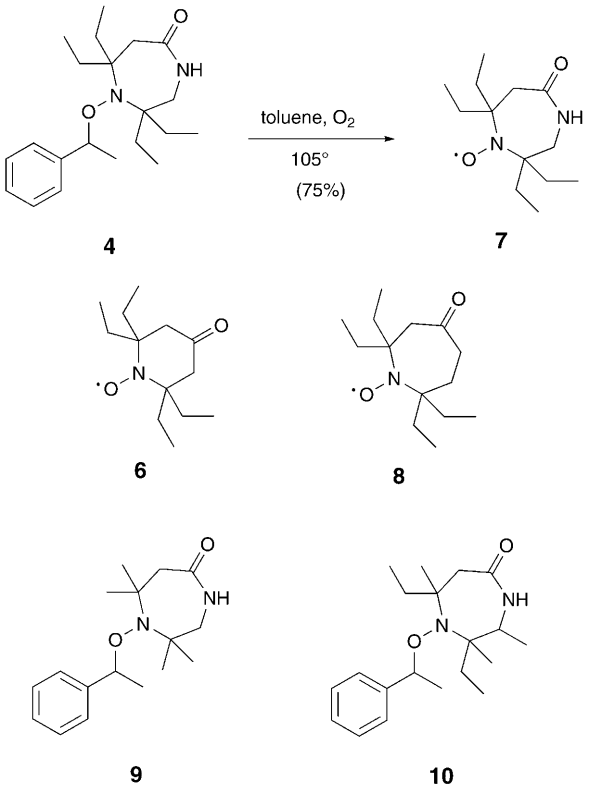


Fig. 3. *Determination of the equilibrium constant* K *for the* **3***- and* **4***-initiated butyl acrylate polymerization at 105°*

have already shown that nitroxide **8**, readily obtained from **6** by a methylene-group insertion, is unexpectedly a less efficient regulator for the controlled living radical polymerization of styrene and butyl acrylate than parent **6** [7a]. The reason for this surprising outcome is currently not understood. Conformation and also polar effects [22] have to be considered for the interpretation of the results and for the design of new even more efficient nitroxides for NMP. Work along this line is under way.

Scheme 3. *Various Systems Studied*



As expected based on previous results, the size of the 2,2- and 7,7-substitutents at the nitroxide moiety in 7-membered cyclic nitroxides heavily influences the reactivity of the nitroxide. The activation energy for the C–O bond homolysis of the tetramethyl derivative **9** is 132 kJ/mol. Replacement of two Me groups by two Et groups (→ **10**) results in a decrease of the activation energy by 10 kJ/mol [23]. As reported in the present paper, replacement of all four Me groups by Et groups leads to a further decrease of the activation energy by 3 kJ/mol.

Conclusions. – We have shown that 7-membered alkoxyamine **4** can readily be synthesized from the known 6-membered-ring alkoxyamine **3** by a *Beckmann*-type rearrangement. The ring-enlarged alkoxyamine **4** was shown to be a more efficient initiator/regulator for controlled living radical polymerization of styrene and butyl acrylate than its lower homologue **3**. Alkoxyamine **4** currently belongs to the best initiator/regulators known to date. The polymerization results are further corroborated by kinetic experiments. The equilibrium constant K between the nitroxide-terminated alkoxyamine and the polymer radical and nitroxide, which defines the efficiency of an alkoxyamine to act as a regulator for the controlled living radical polymerization [4a], is 3 times larger for the **4**-initiated styrene polymerization and *ca.* 2 times larger for the

4-initiated butyl acrylate polymerization as compared to the corresponding **3**-initiated polymerizations. Importantly, ring enlargement of nitroxide **6** by insertion of a methylene group leads to a less efficient polymerization regulator **8**.

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Experimental Part

General. Styrene (BASF) and butyl acrylate (*Fluka*, 99%) were both distilled from CaH_2 under reduced pressure to remove the stabilizer and were stored at 4° under Ar. CH_2Cl_2 was distilled from P_2O_5, pyridine from Na, and MeOH from Mg. All other chemicals were used as received. TLC: silica gel *60* F_{254} plates (*Merck*); detection with UV or dipping into a soln. of $KMnO_4$ (1.5 g in 333 ml of 1M NaOH) or a soln. of $Ce(SO_4)_2 \cdot H_2O$ (10 g), phosphomolybdic acid hydrate (25 g), conc. H_2SO_4 (60 ml), and H_2O (940 ml), followed by heating. Flash chromatography (FC): silica gel *60* (40–63 μm, *Merck* or *Fluka*); at 0.1–0.4 bar. Size exclusion chromatography (SEC): THF as eluent, flow 1.0 ml/min, at r.t.; system consisting of a *L-6200A-Intelligent* pump (*Merck Hitachi*) and two *PLgel-5μm-MIXED-C* columns (300×7.5 mm; *Polymer Laboratories*, linear range of molecular mass: 200–2000000 g/mol), *Knauer* differential refractometer (λ 950±30 nm) detector; data analysis with PSS WinGPC compact V 7.20 software based upon calibration curves built upon polystyrene standards (*Polymer Laboratories*, polystyrene medium-MW calibration kit *S-M-10*) or polymethylmethacrylate standards (*Polymer Laboratories*, polymethylmethacrylate medium-MW calibration kit *M-M-10*) with peak molecular masses ranging from 500–3000000 g/mol or 1000–1500000 g/mol, resp. Melting points: *SMP 10* (*Bibby-Stuart Scientific*); uncorrected. IR Spectra: *Digilab-FTS-4000* equipped with a *MKII-Golden-Gate* single reflection ATR system; in cm^{-1}. ^1H- (500, 400, and 300 MHz) and ^{13}C-NMR (125, 100, and 75 MHz) Spectra: *Bruker AMX-500*, *ARX-300*, or *ARX-200* spectrometer; chemical shifts δ in ppm rel. to $SiMe_4$ as internal standard, *J* in Hz. ESI-MS and HR-MS: *Bruker MicroTof*, in *m*/*z* (rel. %). Elemental analysis was performed with a *Vario EL III* (*Elementar*).

2,2,6,6-Tetraethyl-1-(1-phenylethoxy)piperidin-4-one Oxime (**5**). Et_3N (409 μl, 2.94 mmol, 2.20 equiv.) and hydroxylamine hydrochloride (186 mg, 2.67 mmol, 2.00 equiv.) were added to a soln. of alkoxyamine **3** (422 mg, 1.34 mmol, 1.00 equiv.) in MeOH (3 ml). The mixture was heated to reflux for 3 h. The solvent was evaporated, the residue dissolved in AcOEt (100 ml), the soln. washed with H_2O (3×20 ml), the combined org. layer dried ($MgSO_4$), the solvent evaporated, and the crude product purified by FC (^{t}BuOMe/pentane 1:8 → 1:6): **5** (467 mg, 99%). White solid. M.p. 100°. IR (neat): 3269*w* (OH), 3187*w*, 2967*m*, 2937*w*, 2879*w* (C–H), 1451*w*, 1330*w*, 1059*w*, 1002*w*, 931*m*, 881*w*, 759*m*, 696*s*. ^1H-NMR (400 MHz, $CDCl_3$): 9.12 (br. *s*, OH); 7.54–7.33 (*m*, 5 arom. H); 4.86 (*q*, *J*=6.8, PhC*H*Me); 2.46–1.63 (br. *m*, 8 H); 1.57 (*d*, *J*–6.8, PhCH*Me*); 1.36–0.57 (br. *m*, 16 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 157.1 (C); 145.6 (C); 127.9 (2 CH); 126.8 (CH); 126.1 (2 CH); 82.6 (CH); 65.8 (2 C); 36.1 (CH_2); 30.8–27.2 (br., 5 CH_2); 24.0 (Me); 9.8–7.8 (br., 4 Me). ESI-MS (pos.): 347 (100, $[M+H]^+$), 369 (46, $[M+Na]^+$). HR-ESI-MS (pos.): 347.2692 ($[M+H]^+$; calc. 347.2693); 369.2508 ($[M+Na]^+$; calc. 369.2512). Anal. calc. for $C_{21}H_{34}N_2O_2$ (346.26): C 72.79, H 9.89, N 8.08; found: C 72.46, H 9.87, N 8.20.

2,2,7,7-Tetraethyl-1-(1-phenylethoxy)-1,4-diazepan-5-one (**4**). To a soln. of **5** (1.38 g, 4.00 mmol, 1.00 equiv.) in pyridine (8 ml) was added *p*-toluenesulfonyl chloride (915 mg, 4.80 mmol, 1.20 equiv.). The mixture was stirred at r.t. for 15 h. H_2O (8 ml) was added, and the mixture was heated to 50° for another 24 h. The yellow soln. was diluted with H_2O (50 ml) and extracted with AcOEt (5×50 ml). The combined org. layer was washed with 4% aq. HCl soln. (2×50 ml), dried ($MgSO_4$), and concentrated in vacuo. The crude residue was purified by FC (AcOEt/pentane 1:1): **4** (1.02 g, 74%). Off-white solid. IR (neat): 3123*w* (NH), 3084*w*, 2970*w*, 2934*w*, 2885*w*, 1678*s* (C=O), 1462*w*, 1376*w*, 1058*w*, 921*w*, 764*m*, 702*m*. ^1H-NMR (400 MHz, $CDCl_3$): 7.24–7.13 (*m*, 5 arom. H); 6.31 (br. *s*, NH); 4.73–4.62 (*m*, PhC*H*Me); 3.37–1.42 (br. *m*, 4 CH_2); 1.38 (*d*, *J*–6.4, PhCH*Me*); 1.15–0.43 (br. *m*, 16 H, CH_2, Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 176.1 (C); 146.0 (C); 127.9 (2 CH); 126.8 (CH); 125.7 (2 CH); 82.6 (CH); 67.6 (br., C);

66.0 (br., C); 45.1 (CH_2); 40.6 (br., CH_2); 30.9–26.5 (br., 4 CH_2); 25.0 (Me); 10.2–7.5 (br., 4 Me). ESI-MS (pos.): 369 ($[M+Na]^+$). HR-ESI-MS (pos.): 369.2511 ($[M+Na]^+$; calc. 369.2512). Anal. calc. for $C_{21}H_{34}N_2O_2$ (346.26): C 72.79, H 9.89, N 8.08; found: C 72.49, H 9.86, N 8.12.

2,2,7,7-Tetraethyl-5-oxo-1,4-diazepan-1-yloxy (**7**). Alkoxyamine **4** (120 mg, 350 μmol, 1.0 equiv.) was dissolved in toluene (5 ml) and heated to 105° while O_2 gas was bubbled through the soln. After 7 h, the mixture was allowed to cool to r.t., the solvent was evaporated and the crude product was purified by FC (pentane/AcOEt 1:2): **7** (63 mg, 75%). Red solid. M.p. 157°. IR (neat): 3208*w*, 3176*w*, 3089*w*, 2969*m*, 2935*m*, 2883*m*, 1679*s*, 1458*m*, 1435*m*, 1411*m*, 1383*m*, 1366*m*, 1218*m*, 807*m*, 787*m*. ESI-MS (pos.): 264 ($[M+Na]^+$). HR-ESI-MS (pos.): 264.1801 ($[M+Na]^+$; calc. 264.1808).

Typical Procedure for the 4-Mediated Polymerization of Styrene. Alkoxyamine **4** (32.2 mg, 92.9 μmol, 1.00 equiv.) was suspended in styrene (1.07 ml, 9.29 mmol, 100 equiv.) in a sealed tube. The mixture was degassed in three freeze-thaw cycles and heated to 125° for 3 h. The soln. was cooled to r.t., and remaining monomer was removed in a high-vacuum cabinet at 60° overnight. Conversion was determined gravimetrically and the *PDI* was determined by SEC (conversion 73%; $M_{n,exp}$ 8500, *PDI* 1.16).

Typical Procedure for the **4***-Mediated Polymerization of Butyl Acrylate.* Alkoxyamine **4** (24.4 mg, 70.4 μmol, 1.00 equiv.) was suspended in butyl acrylate (1.01 ml, 7.04 mmol, 100 equiv.) in a sealed tube. The mixture was degassed in three freeze-thaw cycles and heated to 125° for 3 h. The soln. was cooled to r.t., and remaining monomer was removed in a high-vacuum cabinet at 60° overnight. Conversion was determined gravimetrically, and the *PDI* was determined by SEC (conversion 74%; $M_{n,exp}$ 13500, *PDI* 1.21).

Typical Procedure for the **4***-Mediated Polymerization of Butyl Acrylate for the Determination of* K. Alkoxyamine **4** (26.8 mg, 77.3 μmol, 1.00 equiv.) and the corresponding nitroxide **7** (9.3 mg, 38.7 μmol, 0.50 equiv.) were suspended in butyl acrylate (1.11 ml, 7.73 mmol, 100 equiv.) in a sealed tube. The mixture was degassed in three freeze-thaw cycles and heated to 105° for 12 h. The soln. was cooled to r.t., and remaining monomer was removed in a high-vacuum cabinet at 60° overnight. Conversion was determined gravimetrically (conversion 6.0%).

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