Controlled/Living Polymerization of Methyl Methacrylate Using New Sterically Hindered Imidazoline Nitroxides Prepared via Intramolecular 1,3-Dipolar Cycloaddition Reaction

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Received 5 August 2013; accepted 10 December 2013; published online 27 December 2013
DOI: 10.1002/pola.27071

ABSTRACT: A series of imidazoline nitroxides with bulky spirocyclic moieties at the positions 2 or 5 of imidazole ring were synthesized using intramolecular 1,3-dipolar cycloaddition in 2*H*-imidazole 1-oxides or 4*H*-imidazole 3-oxides with pent-4-enyl groups followed by isoxazolidine ring opening and oxidation. Capability of the nitroxides to control radical polymerization of methyl methacrylate (MMA) and styrene was investigated. For that purpose, alkoxyamines were synthesized from the aforementioned nitroxides and *tert*-butyl α-bromoisobutyrate. Homolysis rate constants of the alkoxyamines were measured and possible contributions of side reactions were quantified. Nitroxide-mediated polymerization of styrene and MMA was studied using the alkoxyamines as initiators. MMA polymerization was found to proceed in controlled regime up to 55% of monomer conversion and the polymer obtained was able to reinitiate the polymerization of styrene. Quota of "living" chains estimated to reach 90%. © 2013 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2014**, *52*, 929–943

KEYWORDS: block copolymers; kinetics (polym.); living radical polymerization (LRP); methyl methacrylate; NMR

INTRODUCTION Nitroxide-mediated polymerization (NMP) is a powerful technique for preparation of low polydispersity, end-functionalized polymeric materials.[1–5] The technique was first successfully applied for styrene polymerization using commercially available nitroxide 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO).[6,7] Since that many new nitroxides have been designed for the application as control agents in NMP-enabling controlled polymerization of styrenic and acrylic monomers and preparation of well-defined block copolymers.[8,9] There are a number of methods in NMP that allow for the controlled polymerization of a broad range of monomers. They include the variation of polymerization conditions, for example, temperature, pressure, solvents, or polarity of the medium.[10–14] The latter leads to protonation/deprotonation of functional substituents in alkoxyamines and nitroxides, which affects either on the initiation or polymerization rate. Methacrylates is one of monomer families which are hard to polymerize via NMP due to the side reactions of β-hydrogen atom transfer via intramolecular or radical pathway.[15–19] It should be noted that pMMA-*b*-pSty copolymers possess valuable functional properties,[20–25] so the technology for bulk production of high quality polymer of this type is of current importance. The best results on NMP of methyl methacrylate (MMA) were achieved when 2,2-diphenyl-3-phenylimino-2,3-dihydroindol-1-yloxyl nitroxide (DPAIO) was used as mediator for polymerization control.[26] No H-transfer reaction was detected for this nitroxide.[27] Polymerization of MMA using DPAIO as a mediator allowed to reach 60% of monomer conversion in bulk at 100 °C. However, DPAIO is not suitable for the controlled polymerization of styrene (Sty) due to extremely high activation energy of homolysis of corresponding alkoxyamine. Therefore, preparation of pMMA-*b*-pSty copolymers is hardly achievable using this nitroxide. Moreover, the polymer formed in NMP controlled by DPAIO nitroxide was not able to reinitiate polymerization due to side reaction of N—O bound fragmentation in corresponding alkoxyamine.[16,26] Other approach that permits NMP of MMA has been proposed by Charleux et al.[28,29] It implies addition of small amount of styrene or acrylonitrile, which allows controlled NMP of MMA with *N*-*tert*-butyl-*N*-[1-diethylphosphono-(2,2-dimethylpropyl)] nitroxide (SG1) as mediator. In this case, polymerization can be conducted at

Additional Supporting Information may be found in the online version of this article.

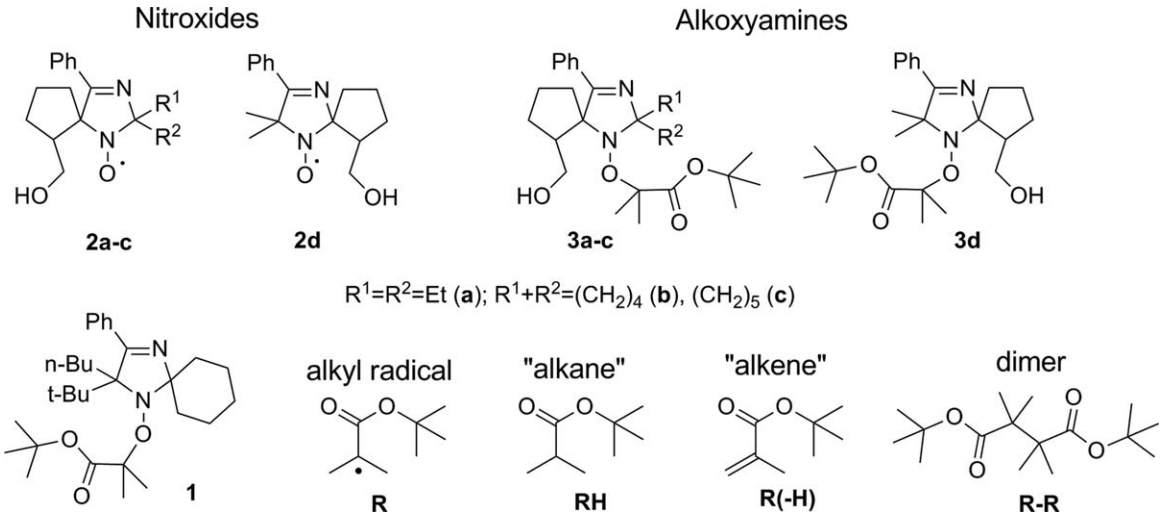


CHART 1 The structures of nitroxides, alkoxyamines, and their decomposition products.

78 °C in controlled regime up to 60% of monomer conversion with formation of perfectly "living" polymer. This approach has the only drawback that it does not allow for the preparation of pure p-MMA. Even small amount of comonomer can alter properties of the polymer formed as exemplified by the change in properties of block-like copolymers.[30] Thereby, an efficient mediator of NMP of MMA is not found yet.

Imidazoline nitroxides are known to be efficient mediators of styrene polymerization.[31–35] Recently, we reported synthesis of a series of sterically hindered imidazoline nitroxides and corresponding alkoxyamines. Studies of their thermal decomposition revealed very low rates of H-transfer reaction.[17] One of these alkoxyamines (**1**, Chart 1) has been even successfully applied for NMP of MMA although polymer formed was not "living" due to thermal degradation of the corresponding nitroxide. Mechanism of the nitroxide decomposition was shown to imply homolytic detachment of *tert*-butyl group from the α-carbon of nitroxyl group. One could expect that replacement of *tert*-butyl group with spirocyclic moiety may increase in thermal stability retaining high degree of sterical hindrance.

We have recently demonstrated that intramolecular 1,3-dipolar cycloaddition may be successfully applied to nitroxides synthesis.[36,37] Due to relatively low sensitivity of intramolecular 1,3-dipolar cycloaddition reactions to sterical hindrance, this method may help in construction of strained spiro-cyclic moieties adjacent to nitrogen atom, allowing for the synthesis of highly sterically hindered nitroxides. This approach was successfully used for preparation of nitroxides **2a–d** (Chart) from 2*H*-imidazole 1-oxide and 4*H*-imidazole 3-oxide derivatives. The nitroxides were converted to corresponding alkoxyamines **3a–d**. The thermal homolysis/reformation of the later was studied using NMR to evaluate the applicability of the nitroxides **2a–d** as mediators for NMP. The nitroxides **2a–d** were found to be efficient mediators of NMP of styrene and MMA.

EXPERIMENTAL

General

5-Bromo-1-pentene was purchased from ABC; copper (II) trifluoromethane sulfonate was obtained from Alfa Aesar; and all other chemicals were purchased from Aldrich and used as received. Monomers were distilled before use. The 2*H*-imidazole 1-oxides **4a-c**[38] and 4,4-dimethyl-5-phenyl-4*H*-imidazole 3-oxide[39] were prepared according to literature protocols.

^{1}H NMR spectra were recorded at 300 or 400 MHz, and ^{13}C NMR spectra were recorded at 75 or 100 MHz.^{1}H and ^{13}C chemical shifts (δ) were internally referenced to the residual solvent peak. IR spectra were acquired on FTIR spectrometer in KBr and are reported in wave numbers (cm^{-1}). Reactions were monitored by TLC using UV light (254 nm) and/or aqueous permanganate for visualization. Column chromatography was performed on silica gel 60 (70−230 mesh).

Synthesis

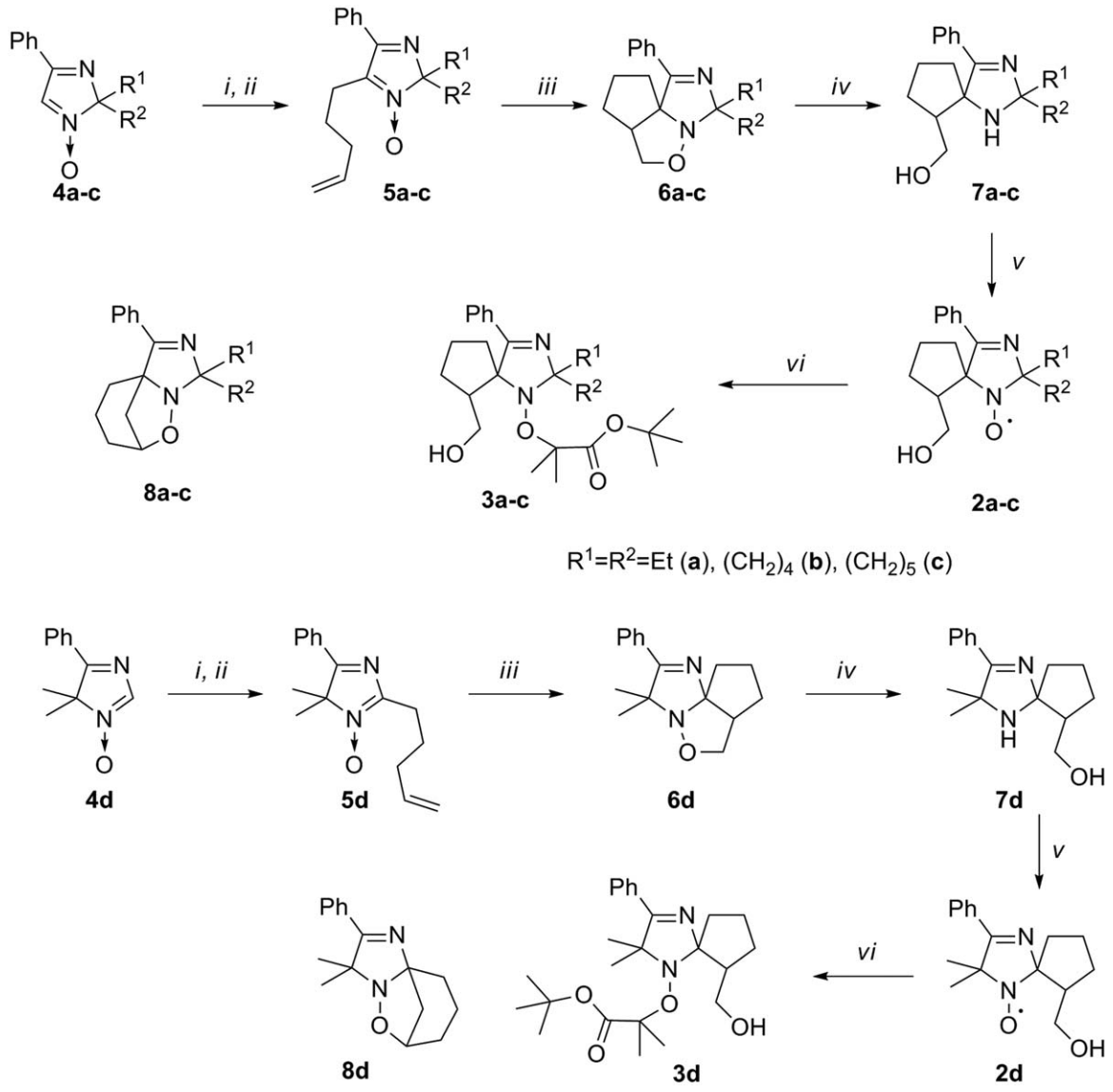
See Scheme 1.

Pent-4-enyl Nitrones 5a–d (General Procedure)

A solution of pent-4-enylmagnesium bromide was prepared via slow addition of a 5-bromopentene-1 (2.38 g, 16 mmol) and dry Et_2O (20 mL) mixture to a suspension of Mg chips (0.49 g, 20.4 mmol) in dry Et_2O (20 mL). Then a solution of nitrone **4a–d** (13.3 mmol) in a mixture of dry Et_2O (20 mL) and dry benzene (20 mL) was added dropwise. The reaction mixture was stirred for 3−5 h, quenched with water (15 mL). Organic layer was separated and manganese dioxide (10 g, 115 mmol) was added. The mixture was stirred for 2 h, the oxidant was filtered off, the solution was concentrated in vacuum, and the residue was separated using column chromatography on silica gel using hexane-diethyl ether mixture 1:1 as an eluent to give the alkenyl nitrones **5a–d**.

2,2-Diethyl-5-(pent-4-enyl)-4-phenyl-2H-imidazole 1-oxide (5a)

Yield: 70%, oil. UV (EtOH) λ_{max}(log ε), nm: 231 (3.29), 275 (3.39); IR (neat) ν, cm^{-1}: 698.2, 771.5, 914.2, 1008.7,



SCHEME 1 Synthesis of the nitroxides **2a–d** and alkoxyamines **3a–d**: (i) $CH_2{=}CH(CH_2)_3MgBr$; (ii) PbO_2; (iii) 110 °C; (iv) Zn/AcOH (Method A) or $Ti(O\text{-}iPr)_4$/EtMgBr (Method B); (v) MCPBA; (vi) $BrCMe_2COOtBu$, Cu, $Cu(OTf)_2$.

1197.8, 1278.8, 1305.8, 1350.1, 1384.9, 1448.5, 1516.0, 1564.2, 1589.3, 1641.4, 2858.4, 2879.6, 2929.8, 2974.1. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.47$ (t, $J = 7$, 6H) and 1.84–2.13 (m, 4H), (2×Et), 1.49–1.61 (m, 2H, $^6CH_2$), 1.84–2.13 (m, 2H, $^5CH_2$), 2.58–2.66 (m, 2H, $^4CH_2$), 4.79–4.89 (m, 2H, $^8CH_2$), 5.61 (tdd, $J_t = 6.7$, $J_{d1} = 10.4$, $J_{d2} = 17$, 1H, ^{7}CH), 7.32–7.41 (m, 3H) and 7.58–7.64 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 6.10$ (CH_3, Et), 29.45 (CH_2, Et), 22.94 and 24.05 ($^5CH_2$, $^6CH_2$), 33.07 ($^4CH_2$), 103.59 (^{1}C), 115.19 ($^8CH_2$), 127.04(C_o, Ph), 128.45 (C_m, Ph), 130.47 (C_p, Ph), 132.02 (C_i, Ph), 136.76 (^{7}CH), 141.64 (^{3}C), 168.09 (C═N); Anal. Calcd for $C_{18}H_{24}N_2O$: C, 76.02; H, 8.51; N, 9.85. Found: C, 76.12; H, 8.86; N 9.92.

2-(Pent-4-enyl)-3-phenyl-1,4-diazaspiro[4.4]nona-1,3-diene 1-oxide (5b)

Yield: 75%, oil; UV (EtOH) λ_{max}(log ε), nm: 218 (3.15), 269 (3.40); IR (neat) ν, cm^{-1}: 696.2, 773.4, 923.8, 992.3, 1023.1, 1211.2, 1384.8, 1448.4, 1481.2, 1515.9, 1562.2, 2871.7, 2957.6, 3062.7; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.60$–1.69 (m, 2H, $^6CH_2$), 1.96–2.11 (m, 8H) and 2.18–2.27 (m, 2H) (5×CH_2), 2.69–2.75 (m, 2H, $^4CH_2$), 4.90–4.98 (m, 2H, $^8CH_2$); 5.71 (tdd, $J_t = 6.7$, $J_{d1} = 10.2$, $J_{d2} = 17$, 1H, ^{7}CH), 7.43–7.50 (m, 3H) and 7.67–7.72 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.25$ and 23.97 ($^5CH_2$, $^6CH_2$), 25.85 and 36.92 (spiro-cyclopentane), 32.91 ($^4CH_2$), 107.20 (^{1}C), 115.10 ($^8CH_2$), 136.88 (^{7}CH), 139.45 (^{3}C), 127.13 (C_o, Ph), 128.40 (C_m, Ph), 130.32 (C_p, Ph), 139.45 (C_i, Ph); 165.69 (C═N); Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.49; H, 7.53; N 10.08.

2-(Pent-4-enyl)-3-phenyl-1,4-diazaspiro[4.5]deca-1,3-diene 1-oxide (5c)

Yield: 77%, m.p. 37 °C (hexane); UV (EtOH) λ_{max}(log ε), nm: 230 (3.18), 262 (3.35); IR (KBr) ν, cm^{-1}: 701, 779, 912,

1014, 1168.8, 1384.8, 1445.5, 1513.0, 1564.1, 1583.4, 1640.3, 2859.2, 2935.4, 3073.3; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.31–1.47$ (m, 3H), 1.80–1.94 (m, 5H), 2.00–2.08 (m, 2H) and 2.10–2.20 (m, 2H) (6×CH_2); 1.58–1.68 (m, 2H, $^6CH_2$), 2.70–2.76 (m, 2H, $^4CH_2$), 4.89–4.98 (m, 2H, $^8CH_2$), 5.71 (tdd, $J_t = 6.8$, $J_{d1} = 10.2$, $J_{d2} = 17$, 1H, ^{7}CH), 7.43–7.51 (m, 3H), and 7.68–7.75 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.36$ (CH_2), 24.38 (CH_2), 24.67 (CH_2), 23.08 (CH_2), 34.90 (CH_2), 33.20 ($^4CH_2$), 101.50 (^{1}C), 115.39 ($^8CH_2$), 127.53(C_o, Ph), 128.46 (C_m, Ph), 130.55 (C_p, Ph), 132.83 (C_i, Ph), 137.23 (^{7}CH), 139.34 (^{3}C), 166.61 (C═N); Anal. Calcd for $C_{19}H_{24}N_2O$: C, 76.99; H, 8.16; N, 9.45. Found: C, 76.85; H, 8.05; N 9.32.

4,4-Dimethyl-2-(pent-4-enyl)-5-phenyl-4H-imidazole 3-oxide (5d)

Yield: 80%; oil; UV (EtOH) λ_{max}(log ε), nm: 232 (3.10), 265 (3.39), 361 (3.82); IR (neat) ν, cm^{-1}: 991.4, 1105.2, 1238.3, 1382.9, 1463.9, 1647.2, 2875.8, 2935.6, 2979.9; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.62$ (s, 6H, 2×CH_3), 1.86 (quintet $J = 7.4$, 2H, $^5CH_2$); 2.14 (q $J = 7$, 2H, $^4CH_2$), 2.78 (t $J = 7.5$, 2H, $^6CH_2$), 4.94 (d_{br}, $J = 10.3$, 1H) and 5.02 (dd, $J_{vic} = 1.4$, $J_{hem} = 17$, 1H) ($^8CH_2$), 5.79 (tdd, $J_t = 6.7$, $J_{d1} = 10.3$, $J_{d2} = 17$, 1H, ^{7}CH); 7.38–7.49 (m, 3H) and 7.90–7.97 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.73$ (2×CH_3); 24.31 and 24.93 ($^5CH_2$ and $^6CH_2$), 33.18 ($^4CH_2$), 78.98 (^{1}C), 115.13 ($^8CH_2$), 126.90 (C_o, Ph), 128.82 (C_m, Ph), 131.53 (C_p, Ph), 130.31 (C_i, Ph), 137.50 (^{7}CH), 151.31 (^{3}C), 176.80 (C═N); Anal. Calcd for $C_{16}H_{20}N_2O$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.81; H, 7.98; N 11.01.

Intramolecular 1,3-Dipolar Cycloaddition of Nitrones 5a–d (General Procedure)

A solution of **5a–d** (0.3 mmol) in toluene (2 mL) was stirred at +110 °C during 50–70 h or heating in microwave oven at +170 °C for 30–60 min. Progress of the reaction was monitored by TLC (silica gel, Et_2O/C_6H_{14} 1:1, developing with 1% aq $KMnO_4$). The solution was concentrated in vacuum and residue was separated by column chromatography (silica gel 60, Et_2O/C_6H_{14} 1:1) to give **6a–d**, respectively. The yield was not dependent on the method of heating.

3,3-Diethyl-1-phenyl-6a,7,8,9-tetrahydro-3H,6H-cyclopenta[c]imidazo[1,5-b]isoxazole (6a)

Yield: 90%; m.p. 99–101 °C (hexane); UV (EtOH) λ_{max}(log ε), nm: 246 (2.55); IR (KBr) ν, cm^{-1}: 694.5, 771.5, 985.6, 1037.7, 1164.9, 1294.2, 1446.6, 1454.3, 1494.8, 1573.9, 1610.5, 2854.6, 2945.2, 2964.5, 2985.7; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.03$ (t $J = 7.5$, 3H) and 1.14 (t $J = 7.5$, 3H) (2×CH_3); 1.50–1.80 (m, 4H, 2×CH_2) 1.89–2.12 (m, 4H, 2×CH_2), 1.89–2.12 (m, 2H, $^4CH_2$), 3.17–3.28 (m, 2H, ^{7}CH), 3.41 (t $J = 8$, 1H), 3.97 (t $J = 8$, 1H, $^8CH_2$), 7.32–7.43 (m, 3H) and 7.81–7.89 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 8.52$ (Me), 9.28 (Me), 24.02, 25.26, 29.49 and 30.92 (2×$\underline{C}H_2$Me, $^5CH_2$, $^6CH_2$), 37.05 ($^4CH_2$), 52.68 (^{7}CH), 71.20 ($^8CH_2$), 91.84 (^{3}C), 98.85 (^{1}C), 128.09(C_o, Ph), 128.26 (C_m, Ph), 130.07(C_p, Ph), 132.00 (C_i, Ph), 168.49 (C═N); Anal. Calcd for $C_{18}H_{24}N_2O$: C, 76.02; H, 8.51; N, 9.85. Found: C, 76.10; H, 8.86; N 10.02.

1-Phenyl-6a,7,8,9-tetrahydro-6H-spiro[cyclopenta[c]imidazo[1,5-b]isoxazole-3,1'-cyclopentane] (6b)

Yield: 81%; 121–122 °C (hexane+5% $CHCl_3$); UV (EtOH) λ_{max}(log ε), nm: 248 (2.63); IR (KBr) ν, cm^{-1}: 694.4, 771.5, 1001.0, 1037.7, 1203.5, 1290.3, 1446.6, 1571.9, 1606.7, 2852.6, 2869.9, 2960.1; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.70–2.20$ (m, 12H, 6×CH_2), 1.60–1.69 (m, 1H, $^4CH_2$), 2.36–2.43 (m, 1H, $^4CH_2$), 3.28–3.37 (m, 1H, ^{7}CH), 3.42 (t $J = 8.5$, 1H) and 4.07 (t $J = 8.5$, 1H) ($^8CH_2$), 7.34–7.44 (m, 3H) and 7.85–7.90 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 24.62$ (CH_2), 24.73 (CH_2), 25.15 (CH_2), 29.73 (CH_2), 33.74 (CH_2), 35.63 (CH_2), 39.90 ($^4CH_2$), 52.08 (^{7}CH), 71.58 ($^8CH_2$), 92.34 (^{3}C), 102.79 (^{1}C), 128.10 (C_o, Ph), 128.28 (C_m, Ph), 130.23 (C_p, Ph), 131.62 (C_i, Ph), 167.99 (C═N); Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.79; H, 7.82; N 9.98.

1'-Phenyl-6a',7',8',9'-tetrahydro-6'H-spiro[cyclohexane-1,3'-cyclopenta[c]imidazo[1,5-b]isoxazole] (6c)

Yield: 75%; m.p. 110–111 °C (hexane+5% $CHCl_3$); UV (EtOH) λ_{max}(log ε), nm: 248 (2.61); IR (KBr) ν, cm^{-1}: 694.3, 771.5, 986.5, 1038.6, 1106.1, 1447.4, 1492.8, 1572.8, 1609.4, 2855.3, 2864.9, 2943.1; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.48–2.20$ (m, 16H, 8×CH_2), 3.21–3.31 (m, 1H, ^{7}CH), 3.42 (t $J = 8$, 1H) and 4.03 (t $J = 8$, 1H) ($^8CH_2$), 7.35–7.46 (m, 3H) and 7.85–7.92 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.32$ (CH_2), 23.62 (CH_2), 25.21 (CH_2), 25.56 (CH_2), 29.47 (CH_2), 31.81(CH_2), 37.11 (CH_2), 38.51 (CH_2), 52.53 (^{7}CH), 71.12 ($^8CH_2$), 91.71 (^{3}C), 95.26 (^{1}C), 128.15 (C_o, Ph), 128.32 (C_m, Ph), 130.18 (C_p, Ph), 131.95 (C_i, Ph), 168.65 (C═N); Anal. Calcd for $C_{19}H_{24}N_2O$: C, 76.99; H, 8.16; N, 9.45. Found: C, 76.96; H, 8.03; N 9.76.

3,3-Dimethyl-2-phenyl-6a,7,8,9-tetrahydro-3H,6H-cyclopenta[c]imidazo[1,2-b]isoxazole (6d)

Yield: 70%; oil; UV (EtOH) λ_{max}(log ε), nm: 243 (2.58); IR (neat) ν, cm^{-1}: 698.2, 775.4, 866.0, 966.3, 1031.9, 1172.7, 1191.9, 1224.8, 1292.3, 1365.6, 1384.9, 1446.6, 1463.9, 1494.8, 1573.9, 1608.6, 2850.7, 2866.1, 2949.1, 2968.4; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.47$ (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 1.57–1.62 (m, 1H, $^6CH_2$), 1.88–1.94 (m, 1H, $^6CH_2$); 1.88–1.94 (m, 2H, $^5CH_2$), 1.95–1.99 (m, 2H, $^4CH_2$), 3.02–3.08 (m, 1H, ^{7}CH), 3.39 (t $J = 8.5$, 1H) and 4.02 (t $J = 8.5$, 1H) ($^8CH_2$), 7.32–7.40 (m, 3H) and 7.68–7.72 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 20.52$ and 28.20 (2×CH_3), 25.68 ($^5CH_2$), 28.96 ($^6CH_2$), 36.93 ($^4CH_2$), 54.04 (^{7}CH), 70.61 ($^8CH_2$), 75.61 (^{1}C), 109.25 (^{3}C), 127.97 (C_o, Ph), 128.17 (C_m, Ph), 129.84 (C_p, Ph), 132.75 (C_i, Ph), 173.27 (C═N); Anal. Calcd for $C_{16}H_{20}N_2O$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.88; H, 8.18; N 11.09.

General Procedure for Isoxazolidine Ring Opening (Synthesis of 7a–d)

Method A

Zn powder (650 mg, 10 mmol) was added in one portion to a warm (60 °C) stirred solution containing isoxazolidines

5a–d (1 mmol), EtOH (3 mL), AcOH (60%, 6 mL) and EDTA·disodium salt (2 g). The reaction mixture was stirred at 60 °C for 3 h, and then cooled down to r.t. The mixture was basified to pH 10 with 30% NH_4OH solution and extracted with $CHCl_3$. The $CHCl_3$ extract was dried with Na_2CO_3 and concentrated in vacuum. The residue was purified by column chromatography (silica gel, Et_2O) to give amines **7a–d**.

(2,2-Diethyl-4-phenyl-1,3-diazaspiro[4.4]non-3-en-6-yl) methanol (7a)

Yield: 72%; m.p. 98–99 °C (hexane-ethyl acetate 5:1); IR (KBr) ν, cm^{-1}: 697.2, 767.6, 950.8, 1027.9, 1107.1, 1171.7, 1243.9, 1316.3, 1376.1, 1445.5, 1458.1, 1574.8, 1614.3, 1736.8, 2938.3, 2964.4; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.91$ (t $J = 7.5$, 3H, CH_3), 1.01 (t $J = 7.5$, 3H, CH_3), 1.68–1.85 (m, 6H, 3×CH_2), 1.62 and 1.90 (each qAB, $J_q = 7.5$ $J_{AB} = 14.8$, 2H, $\underline{CH_2}Me$), 1.94–2.04 and 2.10–2.20 (each m, 2H, $^4CH_2$), 2.49–2.59 (m, 1H, ^7CH), 3.60 (dd$J_1 = 4J_2 = 11.7$, 1H) and 3.80 (dd, $J_1 = 2J_2 = 11.7$, 1H) ($^8CH_2$), 7.30–7.41 (m, 3H) and 7.56–7.63 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 8.29$ and 8.31 (2×Me), 31.21 and 33.65 (2×$\underline{C}H_2Me$), 22.93 and 26.31 ($^5CH_2$ and$^6CH_2$), 41.89 ($^4CH_2$), 46.38 (^7CH), 61.17 ($^8CH_2$), 81.68 (^3C), 92.54 (^1C), 127.59 (C_o, Ph), 127.96(C_m, Ph), 129.26(C_p, Ph), 133.16 (C_i, Ph), 171.19 (C═N); Anal. Calcd for $C_{18}H_{26}N_2O$: C, 75.48; H, 9.15; N, 9.78. Found: C, 75.22; H, 8.88; N 9.45.

(13-Phenyl-6,12-diazadispiro[4.1.4.2]tridec-12-en-1-yl) methanol (7b)

Yield: 65%; oil; IR (neat) ν, cm^{-1}: 698.2, 769.6, 945.1, 1010.7, 1026.1, 1105.2, 1298.1, 1332.8, 1444.7, 1573.9, 1610.5, 2871.9, 2956.8, 3298.2; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.56$–2.10 (m, 13H, 6×CH_2, and 1/2$^4CH_2$), 2.14–2.21 (m, 1H, $^4CH_2$), 2.45–2.55 (m, 1H, ^7CH), 3.58 (dd, $J_1 = 4.3$, $J_2 = 11.7$, 1H) and 3.78 (dd, $J_1 = 2$ $J_2 = 11.7$, 1H) ($^8CH_2$), 7.32–7.40 (m, 3H) and 7.59–7.65 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.28$, 24.01, 24.12, and 26.38 ($^5CH_2$, $^6CH_2$ and 2×CH_2spiro-cyclopentane), 41.29, 41.69, 41.93 ($^4CH_2$, 2×CH_2spiro-cyclopentane), 46.46 (^7CH), 61.38 ($^8CH_2$), 81.92 (^3C), 97.40 (^1C), 127.93 (C_o, Ph), 128.27 (C_m, Ph), 129.57 (C_p, Ph), 133.26 (C_i, Ph), 170.79 (C═N); Anal. Calcd for $C_{18}H_{24}N_2O$: C, 76.02; H, 8.51; N, 9.85. Found: C, 75.82; H, 8.78; N 9.65.

(14-Phenyl-6,13-diazadispiro[4.1.5.2]tetradec-13-en-1-yl) methanol (7c)

Method B

Titanium (IV) iso-propoxide (Ti(O-*i*Pr)$_4$, 3.01 g, 10.58 mmol) was injected with a syringe into a flask with dry Et_2O (5 mL) under a stream of argon. Then 2 M solution of EtMgBr in Et_2O (5.5 mL, 11 mmol) was added dropwise within 2 min upon vigorous stirring. The solution turned black over the course of EtMgBr addition. The reaction mixture was stirred under argon for 15 min at rt and then for 15 min under reflux. A solution of **6c** (1 g, 3.4 mmol) in Et_2O (5 mL) was added dropwise, and the resulting solution was stirred under reflux for 3−5 h until consumption of the starting material occurred. Progress of the reaction was monitored by TLC (silica gel, EtOAc, developed with 1% aq $KMnO_4$). The reaction mixture was quenched with H_2O (3 mL) and stirred under reflux for 24 h. Organic layer was separated, solvent was evaporated in vacuum, and the residue was purified using column chromatography (silica gel, EtOAc) to give **7c**.

Yield: 75% (Method A), 71% (Method B); oil; IR (neat) ν, cm^{-1}: 698.2, 769.6, 950.9, 1028.0, 1105.2, 1269.1, 1315.4, 1446.6, 1573.9, 1612.4, 2856.5, 2933.6, 3281.1; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.39$–1.90 (m, 14H, 7×CH_2), 1.98–2.08 (m, 1H) and 2.12–2.19 (m, 1H) ($^4CH_2$), 2.50–2.59 (m, 1H, ^7CH), 3.58 (dd, $J_1 = 4$, $J_2 = 11.8$, 1H) and 3.79 (dd, $J_1 = 2J_2 = 11.8$, 1H) ($^8CH_2$), 7.33–7.42 (m, 3H) and 7.59–7.64 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.05$, 23.18, 23.42, 25.09, 26.14, 39.75 and 39.99 ($^5CH_2$, $^6CH_2$ and 5×(CH_2)spiro-cyclohexane), 42.73 ($^4CH_2$), 46.45 (^7CH), 61.36 ($^8CH_2$), 81.70 (^3C), 89.25 (^1C), 127.93 (C_o, Ph), 128.25 (C_m, Ph), 129.60 (C_p, Ph), 133.39 (C_i, Ph), 170.88 (C═N); Anal. Calcd for $C_{19}H_{26}N_2O$: C, 76.47; H, 8.78; N, 9.39. Found: C, 76.65; H, 8.59; N 9.25.

(3,3-Dimethyl-2-phenyl-1,4-diazaspiro[4.4]non-1-en-6-yl) methanol (7d)

Yield: 78%; m.p. 119–120 °C ($CHCl_3$); IR (KBr) ν, cm^{-1}: 700.1, 783.1, 846.7, 954.7, 1012.6, 1114.8, 1153.4, 1188.1, 1215.1, 1371.4, 1444.6, 1467.8, 1570.0, 1604.7, 1643.3, 2869.9, 2906.6, 2962.6, 2981.9, 3271.2; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.50$ (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 1.67–2.00 (m, 5H, 2×CH_2 and1/2 $^4CH_2$); 2.03–2.12 (m, 2H, 1/2$^4CH_2$ and^7CH), 3.58 (dd, $J_1 = 3J_2 = 11.5$, 1H) and 3.65 (dd, $J_1 = 8J_2 = 11.5$, 1H) ($^8CH_2$), 7.34–7.43 (m, 3H) and 7.69–7.76 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.77$ and 26.90 ($^5CH_2$and $^6CH_2$), 28.70 and 28.76 (2×CH_3), 39.65 ($^4CH_2$), 48.36 (^7CH), 64.30 ($^8CH_2$), 69.42 (^1C), 99.05 (^3C), 128.26 (C_o, Ph), 128.65 (C_m, Ph), 130.17 (C_p, Ph), 133.18 (C_i, Ph), 173.25 (C═N); Anal. Calcd for $C_{16}H_{22}N_2O$: C, 74.38; H, 8.58; N, 10.84. Found: C, 74.31; H, 8.26; N 10.75.

Nitroxides 2a–d (General Procedure)

A solution of **7a–d** (145 mg, 0.38 mmol) in $CHCl_3$ (4 mL) was cooled to −10 °C and MCPBA (65 mg, 0.38 mmol) was added in one portion. The mixture was stirred at 0 °C until the reaction was complete (control by TLC analysis, silica gel Et_2O – hexane 1:1).The solution was concentrated in vacuum, and the residue was separated by column chromatography (silica gel 60, Et_2O – hexane 1:1).

2,2-Diethyl-6-(hydroxymethyl)−4-phenyl-1,3-diazaspiro[4.4]non-3-en-1-oxyl (2a)

Yield: 69%; m.p. 95–99 °C (hexane); UV (EtOH) λ_{max}(log ε), nm: 245 (4.03); IR (KBr) ν, cm^{-1}: 695.3, 766.6, 1037.6, 1123.4, 1184.2, 1302.8, 1417.6, 1445.5, 1573.8, 1612.4, 2879.5, 2938.3, 2969.2; Anal. Calcd for $C_{18}H_{25}N_2O_2$: C, 71.73; H, 8.36; N, 9.29. Found: C, 71.58; H, 7.98; N 9.31.

1-(Hydroxymethyl)-13-phenyl-6,12-diazadispiro[4.1.4.2]tridec-12-en-6-oxyl (2b)

Yield: 75%, m.p. 77–78 °C (hexane); UV (EtOH) λ_{max}(log ε), nm: 246 (4.10); IR (KBr) ν, cm^{-1}: 650.0, 696.3, 771.5, 1006.8, 1029.9, 1176.5, 1209.3, 1313.5, 1338.6, 1446.6, 1467.8, 1494.8, 1570.0, 1598.9, 2871.9, 2958.7; Anal. Calcd

for $C_{18}H_{23}N_2O_2$: C, 72.21; H, 7.74; N, 9.36. Found: C, 72.50; H, 7.57; N 9.37.

1-(Hydroxymethyl)-14-phenyl-6,13-diazadispiro[4.1.5.2]tetradec-13-en 6-oxyl (2c)

Yield: 71%, oil; UV (EtOH) λ_{max}(log ε), nm: 244 (4.06); IR (neat) ν, cm^{-1}: 650.0, 696.3, 771.5, 906.5, 1037.7, 1112.9, 1176.5, 1284.6, 1446.6, 1494.8, 1571.9, 1600.9, 2858.4, 2935.6; Anal. Calcd for $C_{19}H_{25}N_2O_2$: C, 72.81; H, 8.04; N, 8.94. Found: C, 72.50; H, 7.91; N 8.75

6-(Hydroxymethyl)-2,2-dimethyl-3-phenyl-1,4-diazaspiro[4.4]non-3-en-1 oxyl (2d)

Yield: 79%; m.p. 86–87 °C (hexane); UV (EtOH) λ_{max}(log ε), nm: 246 (4.16); IR (KBr) ν, cm^{-1}: 702.1, 785.2, 1043.5, 1122.5, 1161.1, 1203.5, 1247.9, 1307.7, 1328.9, 1377.1, 1446.6, 1460.1, 1571.9, 1602.8, 2870.0, 1933.6, 2966.4; Anal. Calcd for $C_{16}H_{21}N_2O_2$: C, 70.30; H, 7.74; N, 10.25. Found: C, 70.15; H, 7.42; N 9.93.

Synthesis of Alkoxyamines 3a–d (General Procedure)

The alkoxyamines were prepared using method developed by Matyjaszewski et al.[40] A mixture of the nitroxide **2a–d** (2.2mmol), 2-bromo-2-methylpropionic acid *tert*-butyl ester (0.5 g, 2.25 mmol), Cu powder (140 mg, 2.25 mmol), 4,4′-di-*tert*-butyl-2,2′-bipyridine (24 mg, 0.09 mmol), $Cu(OTf)_2$ (8 mg, 0.023 mmol), and benzene (5 mL) was placed to a Schlenk flask and degassed by three freeze-pump-thaw cycles. The solution was stirred for 24 h at 50 °C. Benzene was removed in. vacuum and the residue was separated by column chromatography (silica gel, EtOAc–hexane 3:7)

tert-Butyl 2-(2,2-diethyl-6-(hydroxymethyl)-4-phenyl-1,3-diazaspiro[4.4]non-3-en-1-yloxy)-2-methylpropanoate (3a)

Yield: 60%; m.p. 113–121 °C; UV (EtOH) λ_{max}(log ε), nm: 234 (3.85); IR (KBr) ν, cm^{-1}: 700.1, 771.5, 842.9, 943.2, 970.2, 1024.2, 1130.3, 1157.2, 1290.3, 1369.4, 1448.5, 1573.9, 1618.2, 1724.3, 2873.9, 2943.3, 2972.2; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t J = 7.5, 3H, CH_3), 0.97 (t J = 7.5, 3H, CH_3),1.46 (s, 3H, $OCCH_3$); 1.49 (s, 9H, ^{t}Bu), 1.52 (s, 3H, $OCCH_3$), 1.56–1.65 (m, 2H), 1.70–1.82 (m, 2H), 1.96–2.17 (m, 5H) and 2.34–2.42 (m, 1H)(5×CH_2), 2.98–3.07 (m; 1H, ^{7}CH), 3.76 (dd, $J_1 = 7J_2 = 11$, 1H) and 3.87 (dd, $J_1 = 6J_2 = 11$, 1H) ($^8CH_2$), 7.36–7.39 (m, 3H) and 7.55–7.59 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.18 and 9.33 (2×$\underline{C}H_3CH_2$), 27.75 (2×$CH_3\underline{C}H_2$), 24.75, 25.68 and 27.87 (2×CH_3 and ^{t}Bu), 23.38, 28.46 and 29.00 (3×CH_2), 50.71 (^{7}CH), 62.23 ($^8CH_2$), 81.14, 82.44 and 84.97 (^{3}C, $\underline{C}Me_3$ and $\underline{C}Me_2$), 97.03 (^{1}C), 172.92 and 173.53 (C═N, C═O); 127.83 (C_o, Ph), 128.08 (C_m, Ph), 129.19 (C_p, Ph), 134.97 (C_i, Ph); Anal. Calcd for $C_{26}H_{40}N_2O_4$: C, 70.24; H, 9.07; N, 6.30. Found: C, 70.29; H, 8.72; N 6.76.

tert-Butyl 2-{[1-(hydroxymethyl)-13-phenyl-6,12-diazadispiro[4.1.4.2]tridec-12-en-6-yl]oxy}-2-methylpropanoate (3b)

Yield: 64%; m.p. oil; UV (EtOH) λ_{max} (log ε), nm: 232 (3.81); IR (KBr) ν, cm^{-1}: 701.7, 1134.0, 1281.3, 1368.5, 1444.1, 1450.4, 1605.9, 1639.4, 1729.0, 2867.9, 2923.1, 2963.7;^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 3H, CH_3), 1.46 (s, 9H, ^{t}Bu), 1.49 (s, 3H, CH_3), 1.45–1.57 (m, 2H), 1.63–1.81 (m, 5H), 1.83–1.96 (m, 2H); 2.00–2.09 (m, 2H), 2.21–2.29 (m, 1H), 2.39–2.48 (m, 1H) and 2.64–2.74 (m, 1H) (7×CH_2), 3.29–3.39 (m, 1H, ^{7}CH), 3.62 (dd, $J_1 = 4J_2 = 12$, 1H) and 3.78 (dd, $J_1 = 8$ $J_2 = 12$, 1H, $^8CH_2$), 7.29–7.36 (m, 3H) and 7.45–7.50 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.41, 23.13, 23.28, 27.99, 29.64 and 33.94 (5×CH_2); 24.52, 24.97 and 27.73 (2×CH_3 and^{t}Bu), 38.07 ($^4CH_2$), 49.20 (^{7}CH), 63.28 ($^8CH_2$), 81.33, 82.20 and 87.28 (^{3}C, $\underline{C}Me_3$ and$\underline{C}Me_2$), 104.28 (^{1}C), 127.75 (C_o, Ph), 128.09 (C_m, Ph), 128.94 (C_p, Ph), 135.19 (C_i, Ph), 170.97 (C═N), 171.88 (C═O); Microanalysis: Anal. Calcd for $C_{26}H_{38}N_2O_4$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.65; H, 8.49; N 6.59.

tert-Butyl 2-{[1-(hydroxymethyl)-14-phenyl-6,13-diazadispiro[4.1.5.2]tetradec-13-en-6-yl]oxy}-2-methylpropanoate (3c)

Yield: 54%; m.p. 117–120 °C; UV (EtOH) λ_{max}(log ε), nm: 231 (3.84); IR (KBr) ν, cm^{-1}: 702.1, 1136.0, 1280.7, 1367.5, 1444.6, 1452.4, 1600.9, 1641.4, 1732.0, 2869.9, 2923.9, 2964.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47 (s, 3H, CH_3), 1.49 (s, 9H, ^{t}Bu), 1.53 (s, 3H, CH_3), 1.20–1.28 (m, 2H), 1.41–1.55 (m, 1H), 1.57–1.93 (m, 10H), 1.97–2.06 (m, 1H), 2.30–2.39 (m, 1H) and 2.07–2.16 (m, 1H) (7×CH_2), 2.87 (ddd, $J_1 = 6J_2 = 7.5$, $J_3 = 9.5$, 1H ^{7}CH), 3.65 (dd, $J_1 = 6J_1 = 12$, 1H) and 3.80 (dd, $J_1 = 7.5J_1 = 12$, 1H) ($^8CH_2$), 7.33–7.38 (m, 3H) and 7.51–7.55 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.60, 25.27 and 27.82 (2×CH_3 and ^{t}Bu); 22.91, 23.46, 23.98, 25.64 and 28.21 ($^5CH_2$, $^6CH_2$ and 3×CH_2 spiro-cyclohexane), 30.11 and 33.97 (2×CH_2 spiro-cyclohexane), 37.94 ($^4CH_2$), 49.73 (^{7}CH), 63.04 ($^8CH_2$), 81.23, 82.27 and 85.79 (^{3}C, $\underline{C}Me_3$ and $\underline{C}Me_2$); 95.24 (^{1}C), 127.91 (C_o, Ph), 128.03 (C_m, Ph), 128.99 (C_p, Ph), 135.36 (C_i, Ph), 172.61 and 172.83 (C═O and C═N); Anal. Calcd for $C_{27}H_{40}N_2O_4$: C, 71.02; H, 8.83; N, 6.13. Found: C, 71.16; H, 8.56; N 6.33.

tert-Butyl 2-(6-(hydroxymethyl)-2,2-dimethyl-3-phenyl-1,4-diazaspiro[4.4]non-3-en-1-yloxy)-2-methylpropanoate (3d)

Yield: 63%; oil; UV (EtOH) λ_{max} (log ε), nm: 234 (3.83); IR (neat) ν, cm^{-1}: 698.2, 1033.8, 1134.1, 1292.3, 1367.5, 1444.1, 1462.0, 1627.9, 1728.2, 2871.9, 2935.6, 2978.3; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (s, 9H, ^{t}Bu), 1.41 (s, 3H), 1.42 (s, 3H), 1.47 (s, 3H) and 1.55 (s, 3H) (4×CH_3), 1.72–1.79 (m, 1H), 1.90–2.15 (m, 4H) and 2.33–2.44 (m, 1H) (3×CH_2), 3.48 (dt, J_d = 4.5 J_t = 11.2, 1H, ^{7}CH), 3.83 (d_b, J = 11.2, 1H) and 4.40 (d_b, J = 10, 1H)($^8CH_2$), 7.33–7.39 (m, 3H) and 7.54–7.59 (m, 2H) (Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.13, 24.32, 24.48 and 25.74 (4×CH_3), 27.80 (^{t}Bu), 20.63 and 26.73 ($^5CH_2$ and $^6CH_2$), 32.32 ($^4CH_2$), 51.16 (^{7}CH), 65.04 ($^8CH_2$), 77.67 (^{1}C), 81.51 and 82.07 ($\underline{C}Me_3$ and $\underline{C}Me_2$), 106.86 (^{3}C), 127.46 (C_o, Ph), 127.82 (C_m, Ph), 128.15 (C_p, Ph), 129.32 (C_i, Ph), 172.00 and 172.16 (C═N and C═O); Anal. Calcd for $C_{24}H_{36}N_2O_4$: C, 69.20; H, 8.71; N, 6.73. Found: C, 69.45; H, 8.51; N 6.69.

Kinetic Measurements

For kinetic measurements, 20 mM solutions of alkoxyamines (700 μL) in benzene-d_6 in conventional NMR tube were

degassed by three freeze-pump-thaw cycles, sealed under vacuum and placed into preheated probe head of the Bruker Avance – 200 MHz NMR spectrometer. ^{1}H NMR spectra were recorded at different time intervals after the beginning of heating. The NMR experiments gave series of NMR spectra resolved in time. The resulting kinetics was obtained by automatic integration of the NMR signals corresponding to initial alkoxyamine, alkane R-H, alkene R(-H).

In separate experiments, thiophenol (200 mM) was added as a radical scavenger. PhSH is known to suppress reformation of alkoxyamine via irreversible quenching of the alkyl radicals with large rate constants.[41,42] Mechanism of PhSH reaction with nitroxides is rather complicated,[43] so the reaction products were not analyzed.

Nitroxides 2a–d Thermal Stability

EPR spectra were recordered on Bruker X-band spectrometer. Solutions (10^{-4} M) of a nitroxide in chlorobenzene (300 μL) were placed into a glass tubes, degassed, and sealed. The samples were placed into preheated to 100 °C oil bath for 24 h. EPR spectra of the samples were recorded and compared to a spectrum of a standard solution of TEMPO.

Polymerization

Monomer (5 mL) was placed into round bottom two-neck flask equipped with magnetic stirrer and backflow condenser. Then precalculated amount of alkoxyamine was added. The mixture was purged with argon for 15 min to remove oxygen from the system and the reaction vessel was placed into a preheated oil bath. Samples of the polymerization mixture (typically 100 μL) were taken through definite periods of time and stored in a fridge at −18 °C. They were used to determine monomer conversion and molecular weight and polydispersity index (PDI) of polymer formed.

After the polymerization experiment the reaction mixture was diluted with cold methanol, polymer precipitate was filtered off, dried, and used as initiator for a reinitiation experiment. The later was performed similarly to the described above procedure.

Determination of the "Living" Character of the Polymerization

The "living" nature of the polymerization was confirmed by either reinitiation experiment (see above) or by decomposition of macroalkoxyamines in air saturated solutions. The weighted amount of precipitated polymer was dissolved in toluene to get 5×10^{-5} to 10^{-4} M solution. The solution was heated at 100 °C in the oil bath. ESR spectra were recorded before and in the course of heating. Quantification of the nitroxide formed allowed for the estimation of quota of "living" chains.

Sample Analysis

To determine a monomer conversion, a sample of the polymerization mixture (50 μL) was dissolved in 650 μL of chloroform-*d*. ^{1}H NMR spectra were recorded for each sample. Integration of NMR signals of the polymer and the monomer allowed to calculate of the monomer conversion.

The polymer molecular weight and PDI were determined by gel permeation chromatography. The polymer precipitated from a reaction mixture after dilution with methanol was filtered off and dried. The resulting dry polymer (3 mg) was dissolved in 1 mL of THF and analyzed on Agilent-1200 LC chromatograph equipped with isocratic pump, thermostated PL-gel Mixed C column, variable wavelength, and refractive index detectors. THF was used as eluent at 1 mL/min flow rate. Polymer fractions were quantified using refraction index. M_n and PDI values were obtained after automatic integration with the help of universal calibration curve obtained for low polydispersity polystyrene calibration standards (Agilent).

RESULTS AND DISCUSSION

Synthesis

We have recently found a new method for sterically hindered nitroxides construction, based on intramolecular 1,3-dipolar cycloaddition—isoxazolidine ring opening—oxidation sequence.[36,37] This sequence allowed for stereospecific synthesis of highly sterically hindered nitroxide from optically active aldonitrone of pyrroline series.[37] Here, we used essentially the same approach to prepare few spiro-bicyclic nitroxides of imidazoline series. Nitroxides **2a–d** and alkoxyamines **3a–d** were prepared according to Scheme 1.

Aldonitrones **4a–d** were treated with pent-4-enylmagnesium bromide. After quenching of the reaction mixture with water, products were oxidized *in situ* and α-pent-4-enyl nitrones **5a–d** were isolated with good yields. Heating of the nitrones **5a–d** in toluene either under reflux or upon microwave irradiation afforded a single product in each case. Isolated products showed shift in UV absorption wavelengths to 245 nm (typical for phenylimine absorption) from 260 to 280 nm for **5a–c** and 362 nm for **5d**, and absence of low-field signals belonging to aldonitrone and terminal alkene moieties in NMR ^{1}H spectra, indicating an intramolecular 1,3-dipolar cycloaddition occurrence. One could expect two regioisomers **6** and **8** formation in this reaction (Scheme 1). Low field signal of methylene group carbon at 70.6–71.6 ppm allowed to unambiguously discard structures **8**. Analysis of NMR ^{1}H and ^{13}C spectra revealed structural similarity to intramolecular cycloaducts formed from α-pent-4-enyl nitrones of pyrroline series[37] and allowed to assign the cyclopenta[c]imidazoisoxazole-type structures **6a–d** to the isolated products.

It should be noted that in no case 100% conversion was observed and starting compound **5** was always present in the reaction mixtures independently on conditions and reaction time. Moreover, formation of **5a** was observed by TLC and NMR upon heating of the pure cycloadduct **6a** in toluene. After 60 min of heating at 160 °C under microwave irradiation the ratio **5a**:**6a** was 1:5. These observations denote reversibility of cycloaddition reaction, which coincide with the concept of orbital-controlled mechanism.[44] The

observable amount of aldonitrones **5a–d** under conditions close to equilibrium may result from stabilization of the nitrone group due to conjugation with phenylimine system.

Recently, we have suggested a new convenient method for N—O bong cleavage in isoxazolidines by low-valence titanium (LVT) reagent prepared from $Ti(O\text{-}iPr)_4$ and EtMgBr.[36,37] Treatment of cycloadduct **6c** with the LVT reagent resulted in the selective cleavage of isoxazolidine ring to give corresponding aminoalcohol **7c** in a good yield.

It has been shown that Zn/HOAc system is an efficient reagent for reductive isoxazolidine ring opening.[45] Indeed, treatment of the cycloadducts **6a–d** with Zn/HOAc afforded corresponding aminoalcohols **7a–d**. A yield of **7c** was only a bit lower than that obtained using low-valence titanium (LVT) reagent (see Experimental section).

It is known that oxidation of highly sterically hindered amines into nitroxides with H_2O_2/Na_2WO_4 is sometimes unsuccessful and use of peracids, for example, MCPBA, gives better result.[36,37,46] Similarly, only trace amounts of corresponding nitroxides were formed in the reaction of aminoalcohols **7a–d** with hydrogen peroxide in presence of Na_2WO_4, while oxidation with MCPBA afforded **2a–d** in 69–79% yields.

The nitroxides were converted into alkoxyamines **3a–d** via standard Matyjaszewski's procedure[40] with *tert*-butyl 2-bromo-2-methylpropanoate. It has been shown that alkoxyamines prepared from imidazoline nitroxides may show double set of signals in the NMR spectra because of formation of two diastereomeric forms due to slow inversion at alkoxyamine nitrogen.[12] However, single set of signals was observed for highly sterically hindered alkoxyamines of this series,[37] presumably because bulky substituents in the asymmetric molecule make one of the invertamers strongly favorable. Similar effect occurs for alkoxyamines **3a–d**. Obviously, rigidly fixed hydroxymethyl group at spirocyclopentane moiety does not permit inversion at N1, leading to a single invertamer formation.

Nitroxides 2a–d as Mediators for NMP

Measurements of k_d and Kinetic Parameters for H-Atom Transfer Reaction

To predict a NMP result, Fischer[47] developed phase-diagram approach based on eqs (1–3), providing both a living fraction ($0 < F < 1$, F being the fraction of dead chains, eq (1)), a PDI (eq (2)), and time of polymerization ($t_{90\%}$ being the time for 90% monomer conversion, $K = k_d/k_c$, eq (3)). Monomer is characterized with two parameters: a rate constant of propagating chain radical addition to monomer double bond (k_p),and a propagating chains recombination (termination) constant (k_t).A success of the NMP experiments, that is, high livingness ($F > 0.8$) and high control (PDI < 1.5), depends primarily on k_d value for dormant species. Value of k_c is less important as its variation by 10–20 times has little effect on a position of the alkoxyamine on Fischer's diagram. Side reactions, for example, H-atom transfer, can alter controlled regime of polymerization, so possible side reactions should be determined before application of an alkoxyamine as an initiator for NMP.

$$F = \left(\frac{2k_d k_t \ln 10}{k_c k_p [I]_0}\right)^{1/2} \quad (1)$$

$$\mathrm{PDI}_\infty = 1 + \frac{[I]_0}{[M]_0} + \left(\frac{\pi k_p^3 [I]_0}{k_d k_c k_t}\right)^{1/2} \quad (2)$$

$$t_{90}\% = \frac{(2\ln 10)^{3/2}}{3{k_p}^{3/2}} \left(\frac{k_t}{K[I_0]}\right)^{1/2} \quad (3)$$

Earlier an experimental approach that makes possible to determine a value of homolysis rate constant k_d and intramolecular/radical H-atom transfer reaction rate constants k_{dD} and k_{cd}, respectively, was proposed. The approach is based on analysis of products and kinetics of decomposition of an alkoxyamine alone and in the presence of alkyl radicals scavenger/nitroxide reducing agent.[17] Reactions which may proceed under these conditions are shown in the Supporting Information Scheme 1.

When an alkoxyamine decomposes in the presence of PhSH, alkyl radicals are scavenged with formation of alkane RH (see Supporting Information Scheme 1a). Formation of alkene indicates H-atom transfer by intramolecular mechanism (reaction 4 in Supporting Information Scheme 1a). Analyzing kinetics of alkoxyamine decomposition and alkene/alkane formation one can obtain both k_d and k_{dD} values.

In another experiment, an alkoxyamine is heated alone (Supporting Information Scheme 1b). If no side reactions take place, so-called persistent radical effect is observed in the course of reversible homolysis (reactions 1, 5, 7 at Supporting Information Scheme 1b) and kinetics of alkoxyamine decomposition is described by eq (4).[4848] For alkoxyamines with tertiary alkyl fragment at oxygen atom, H-atom transfer with alkene formation may take place (Reaction 6). Kinetics of an alkoxyamine decomposition is exponential according to eqs (5) and (6). If the value of k_c is known or estimated, a rate constant of H-atom transfer can be obtained. Even though if an exact value of k_c is unknown, eq (5) allows for an estimation of factor of disproportionation f_D. This parameter is very important for NMP of methacrylates. Fischer[48] has shown that if f_D is lower that 0.7% H-atom transfer reaction has no effect on NMP.

$$[A] = [A]_0 - [A]_0^{2/3} \left(\frac{3k_d^2 2k_t}{k_c^2}\right)^{1/3} t^{1/3} \quad (4)$$

$$[A] = [A]_0 \; e^{-k_d f_D t} \quad (5)$$

$$f_D = \frac{k_{cD}}{k_c + k_{cD}} \quad (6)$$

where [A] is the alkoxyamine concentration, f_D is the fraction of disproportionation.

Experiments of these types were performed for alkoxyamines **3a–d**. Figure 1 demonstrates ^1H NMR data before

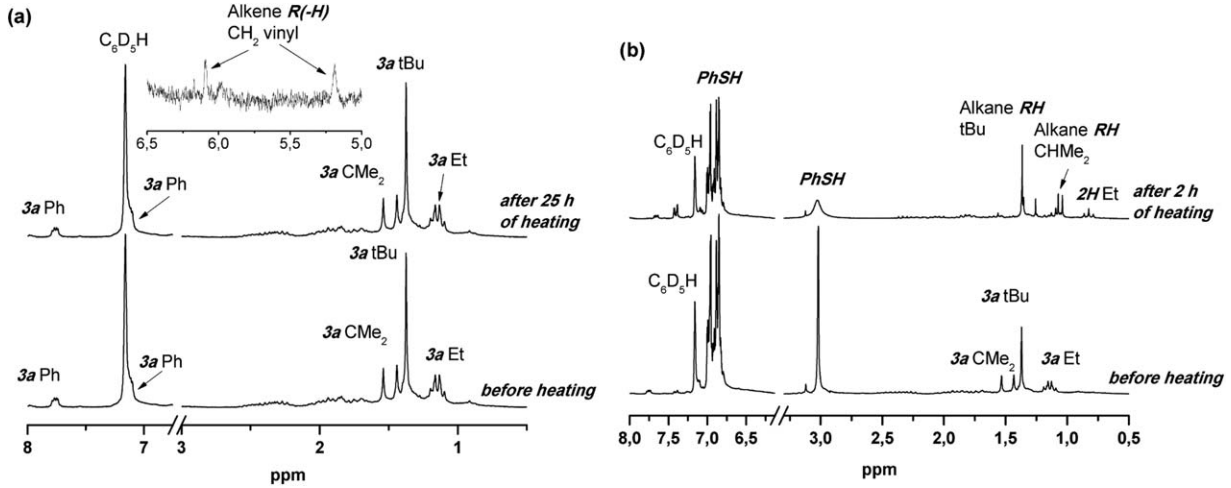


FIGURE 1 1H NMR spectra recorded before (lower) and after (upper) the decomposition of alkoxyamine **3a** alone (a) and in the presence of 20 equiv of PhSH (b). Temperature of decomposition was 70 °C, concentration of alkoxyamine was 20 mM, solvent – C6D6. Inset: NMR signals of the vinyl protons of alkene formed during decomposition of **3a** in pure solution.

and after heating of alkoxyamine **3a** in the presence and in the absence of scavenger. Noteworthily, no trace of alkene was observed upon thermolysis of this alkoxyamine in the presence of PhSH [Fig. 1(b)], clearly showing that intramolecular H-transfer does not occur. Analysis of alkoxyamines decomposition kinetics (Supporting Information Fig. 1) gave rate constants k_d for the alkoxyamines **3a–d** presented in Table 1. Values of activation energies of homolysis were obtained with average vibration factor $A_0 = 2.4 \times 10^{14}$ s^{-1}.[49–51]

There are two main parameters that contribute to the value of homolysis and H-atom transfer kinetic parameters named sterical hindrance and polarity of nitroxyl and alkyl fragment of alkoxyamine. For alkoxyamines **3**, alkyl parts are identical, and polarity of nitroxyl parts has close values. So that hereafter only steric parameters of the nitroxyl parts are discussed.

In the absence of scavenger, quantitative formation of alkene was observed for all the alkoxyamines indicating radical mechanism of H-atom transfer reaction. It should be noted that kinetics of decomposition of alkoxyamines was rather slow. The kinetics analysis made it possible to evaluate the contribution of H-atom transfer into one cycle of decomposition and recombination (disproportionation factor f_D) for alkoxyamines **3a–d** (see Table 1). As disproportionation factor is relatively low for alkoxymine **3a** that compound can be considered as possible initiator for NMP of MMA. Values of k_c for alkoxyamines **3a–d** formation were estimated by structure-reactivity correlations developed by Marque et al. as 5×10^7 $M^{-1}s^{-1}$.[52–54]

Values of f_D and of k_{cd} (Table 1) decrease in the row **2d>2b>2c>2a** clearly following the pattern of overall sterical requirements of the substituents adjacent to the nitroxide group. This fact is in agreement with general consideration that access of the nitroxide oxygen to a proper hydrogen atom of C-centered radical is a rate-limiting step in intermolecular H-transfer. Meanwhile, this row does not coincide with the row of k_d and E_a dependence on alkoxyamine structure (**3d >3c>3a>3b**). The difference may arise from nonplanar geometry of sp3 alkoxyamine nitrogen atom with a bulky alkoxy group: structures with more bulky, but more flexible diethyl (**3a**) and spiro-cyclohexane (**3c**) moieties are less strained

TABLE 1 Kinetics Parameters of Decomposition of Alkoxyamines (0.02 M) Alone and in Presence of Thiophenol (0.2 M) at 70 °C

	Decomposition in the Presence of Scavenger		Decomposition in the Absence of Scavenger		
Alkoxyamine	$k_d \times 10^4$ (s^{-1})	E_a (kJ/mol)	$k_{obs} \times 10^4$ (s^{-1})	f_D (%)	$k_{cd} \times 10^{-6}$ ($M^{-1}s^{-1}$)
3a	2.6 ± 0.2	118.0	0.035 ± 0.003	1.3	0.7
3b	3.3 ± 0.3	117.0	0.090 ± 0.005	2.7	1.4
3c	1.8 ± 0.3	119.0	0.040 ± 0.005	2.3	1.2
3d	1.0 ± 0.3	120.0	0.030± 0.005	3.0	1.6
1[a]	6.0	115.5	0.017	0.28	0[b]

[a] Data from ref. 17.

[b] Below the detection limit of the method.

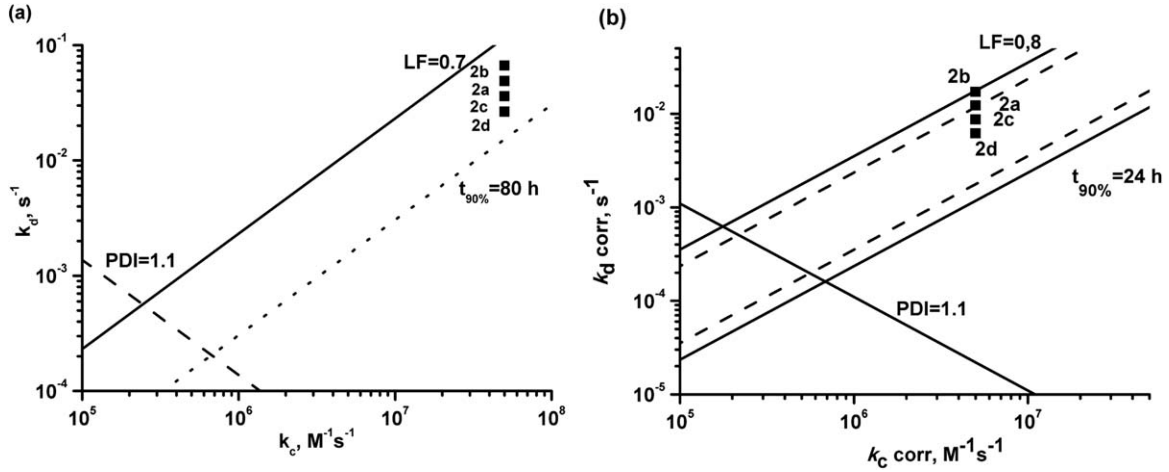


FIGURE 2 Fischer's diagram for (a) Sty polymerization at 120 °C in bulk with initiator monomer to initiator ratio 1/350; (b) for MMA polymerization at 80 °C in bulk with initiator monomer to initiator ratio 1/400 (full line) and 1/800 (dashed line). Symbols: position of nitroxides **2a–d**.

than in **3b**, where 6,12-diazadispiro[4.1.4.2]tridec-12-ene ring system is not capable of strong conformational changes.

Comparison of new alkoxyamines **3a–d** with alkoxyamine **1**[17] (see Table 1) reveals that the later showed better parameters, that is, lower E_a value and smaller f_D for the corresponding nitroxide compared to **2a–d**. A crucial obstacle which impedes the application of **1** in NMP is thermal instability of the nitroxide.

Thermal Stability

Thermal degradation of a nitroxide can alter NMP parameters decreasing the quota of "living" chains, capable of reinitiation, in a polymer formed.[17] Heating of nitroxides **2a–d** degassed solutions in chlorobenzene at 100 °C for 24 h did not lead to decay of the nitroxides EPR signals, implying that they are sufficiently stable to be used in NMP.

Fischer's Diagrams

An accurate determination of k_d in the above mentioned thermolysis experiments allowed for the use of Fischers' diagrams for evaluation of applicability for NMP. Applying eqs (1–3) for different experimental conditions (i.e., polymerization temperature, polymerization time, monomer to initiator ratio) we predicted a character of the polymerization. Values of k_p and k_t measured by Buback and coworkers were used.[55,56]

It has been shown by Guillaneuf et al.[57] that dependence of k_d and k_c on the length of polymer chain must be taken into account for correct calculation of NMP. For example, k_d, and k_c values implemented in phase diagrams in cases of MMA[58] polymerizations were corrected for the account of the penultimate effect on homolysis, as well as for the account of the chain-length effect on recombination.[59]

In this work, we used an average value of vibration factor $A_0 = 2.4 \times 10^{14}$ s^{-1} for calculation of k_d values at various temperatures. k_c values were assumed to be temperature independent. Resulting Fischer's diagrams for the polymerization of styrene and MMA are presented in Figure 2.

Application of Alkoxyamine 3a as Initiator for NMP of MMA and Sty

According to the above data, alkoxyamine **3a** showed the smallest contribution of H-atom transfer reaction among the alkoxyamines studied. It is thermally stable up to 100 °C; therefore, it was selected as initiator for NMP of MMA. The conditions of polymerization were selected according to Fischer's diagram analysis [Fig. 2(b)] that is bulk polymerization at 80 °C with initiator to monomer ratio were 1/800 and 1/350, so that target M_n was 80 and 35 kDa, respectively. Although position of alkoxyamine **2a** is on the border of "living and controlled" zone when monomer to initiator ratio is 800 to 1, it can still be tested as initiator in aforementioned conditions.

The evolution of molecular mass and polydispersity versus conversion for the polymerizations is presented in Figure 3, and the parameters of the polymerization experiments are summarized in Table 2. When the target M_n was 80 kDa [Entry 1, Table 2 and Fig. 3(a)], the growth of polymer molecular weight was linear up to 30% of monomer conversion. After that, the growth of the polymer's molecular weight stopped. The reason for that could be poor solubility of pMMA in its monomer. Furthermore, it is known that the values of homolysis and recombination rate constants depend much of the length of the polymer chain. In particular, the value of k_c decreases for nitroxide and alkyl radical with polymer residue up to 10 times, and the value of k_d increases up to 10–15 times with respect to unimolecular alkoxyamine.[60] This can also influence the controlled regime of the polymerization. Despite nonlinear growth of the molecular weight of the pMMA in the course of polymerization, the polydispersity of the polymer obtained was 1.4 which is below the limit for controlled polymerization. The polymerization was stopped at monomer conversion 45%. It

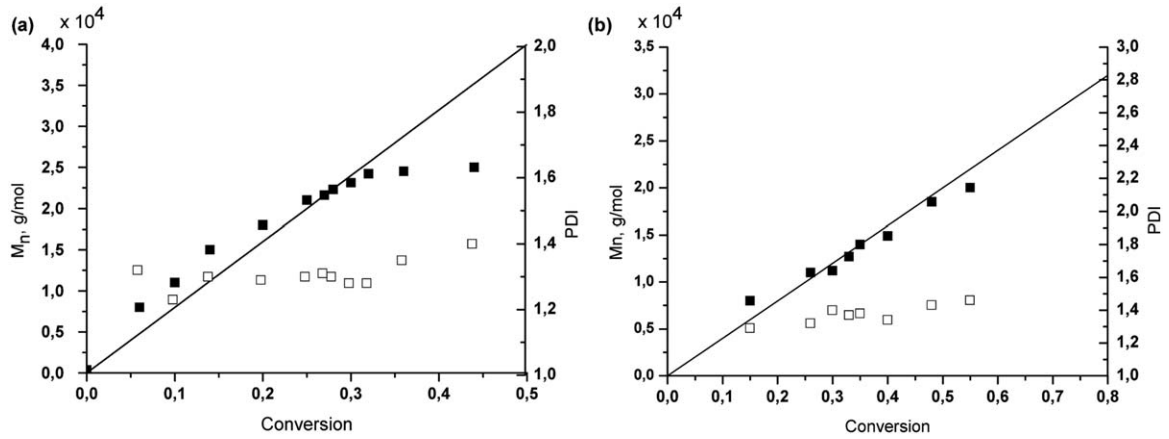


FIGURE 3 Evolution of Mn and PDI vs. monomer conversion for NMP of MMA initiated with alkoxyamine **3a** at $T = 80$ °C with different monomers to initiator (a) 800/1, (b) 350/1.

should be noted that GPC showed formation of pMMA with slightly nonsymmetrical molecular weight distribution [see Fig. 4(a)]. This could be due to slow initiation as described by Guillaneuf et al.[61]

To evaluate the quota of "living" chains in the polymer obtained the reinitiation experiment was performed. The polymeric pMMA-based alkoxyamine was used to initiate the polymerization of styrene with the following conditions: temperature 90 °C, bulk, monomer to initiator ration 40,000/1. Unfortunately, pMMA is poorly soluble in Sty.[62] Hence, only large monomer to macroinitiator ratio could be examined in the reinitiation experiment.

Despite the nonlinear growth of M_n with conversion during MMA polymerization, the polymer obtained was able to reinitiate the polymerization of styrene [Fig. 4(a)]. The investigation of the reaction mixture samples using gel permeation chromatography (GPC) showed that no polystyrene homopolymer was formed and nearly all pMMA was converted to block copolymer within 2.5 h. Integration of chromatography peaks gave estimation of the fraction of living chains as 80%. High percentage of "living" chains confirms insignificant impact of H-atom transfer reaction. Thus, the reason of the noncontrolled regime of NMP of MMA at monomer conversion higher than 30% is changes in kinetic parameters of homolysis/recombination of macroalkoxyamine with growth of polymeric chain.

Lowering the monomer to initiator ratio allowed for conducting the polymerization in controlled mode up to 55% of conversion [Entry 2, Table 2 and Fig. 3(b)]. The PDI of the polymer obtained was as low as 1.4 that is below the theoretical limit for the controlled polymerization. Reinitiation experiment was performed in the same conditions (monomer to macroinitiator ratio was 40,000/1, temperature of polymerization 90 °C) and revealed fraction of "living" chains exceeding 90% [Fig. 4(b)]. As the result of the chain extension experiment, pMMA-*b*-pSty block copolymer was obtained. The polymer exhibited $M_n = 220$ kDa and PDI = 1.45. The final conversion of the Sty was 10%. The expected molar mass of the copolymer was 230 kDa. The deviation in the molar mass of the copolymer obtained was ~10%. This allows for estimation of fraction of "living" chains as 90%, which is in a good agreement with GPC data.

To get further insight in the "living" mechanism of MMA polymerization initiated with **3a** we performed a study of polymer chain ends by means of ESR spectroscopy. It was found that, within 6 h, the macroalkoxyamine decomposes completely in solution in the presence of oxygen, which is highlighted by growth of the ESR signal of nitroxide formed.

TABLE 2 Parameters of the Polymer Obtained During Polymerization of Sty and MMA Initiated with Alkoxyamine **3a**

Entries	Monomer	Polymerization Temperature (°C)	$[M]_0/[I]_0$	Conversion	M_n[a] (kDa)	$M_{n,\ th}$ (kDa)	PDI	Time of Experiment (h)
1	MMA	80	800/1	0.44	25	35	1.40	9
2	MMA	80	400/1	0.55	20	22	1.44	6
3	MMA	90	1,900/1	0.45	30	66.5	1.35	1.2
4	Sty	120	350/1	0.25	8.7	9.1	1.27	9
5	Sty	100	800/1	0.70	60	58	1.43	45

[a] According to universal calibration with PS standards.

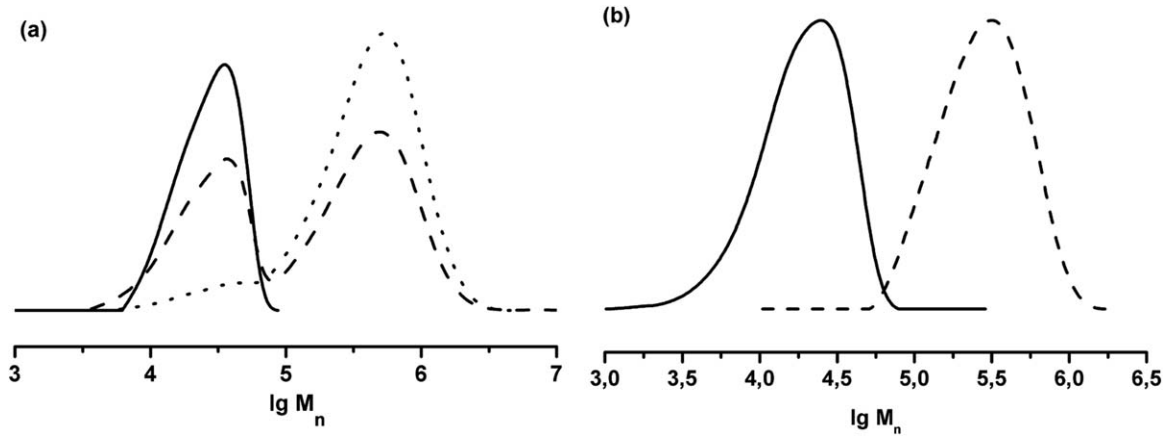


FIGURE 4 Reinitiation experiment: styrene polymerization initiated with poly-MMA-2 initiator (M/I ratio 40,000/1 by weight) at 90 °C: (a) macroinitiator pMMA from Entry 1 in Table 2 (M_n = 25 kDa, PDI = 1.40, solid line), GPC trace of reaction mixture after 1.5 h of heating (dashed line), GPC trace of reaction mixture after 2.5 h of heating (M_n = 410 kDa, PDI=1.44, dotted line) (b) macroinitiator pMMA from Entry 2 in Table 2 (M_n = 20 kDa, PDI = 1.44, full line line), GPC trace after 3.5 h of reaction (M_n = 220 kDa, PDI = 1.45, dashed line).

The quantification of the ESR signal showed that the quota of "living" chains, for example, chains capable to decompose with formation of nitroxide is more than 80%. The resulting ESR spectra are presented as Supporting Information.

To study the temperature effect, the polymerization of MMA initiated with **3a** was performed at 90 °C. The details are summarized in Table 2, Entry 3. The resulting polymerization kinetics is presented as Supporting Information. It should be mentioned that the polymerization was controlled up to about 30% of monomer conversion. The polymer obtained was able to reinitiate polymerization of Sty (see Supporting Information for details). The quota of "living" chains was estimated as 50%. It should be noted that at 90 °C the impact of H-atom transfer reaction increases. This leads to higher fraction of irreversible termination events in the course of polymerization. As a result, the polymer obtained is not "living."

The applicability of alkoxyamine **3a** for initiation of Sty polymerization was tested as well. The conditions were selected according to the Fischer's diagram (see above).The polymerization was performed at 120 °C with monomer to initiator ratio 350 to 1. It should be noted that typically NMP of styrene proceeds at elevated temperatures; however, recently new nitroxide families allowed for considerable decrease in polymerization temperatures.[63]

The evolution of M_n and PDI versus conversion for NMP of Sty initiated with alkoxyamine **3a** is presented in Figure 5(a), the parameters of experiment and characteristics of the polymer obtained are summarized in Table 2 (Entries 4 and

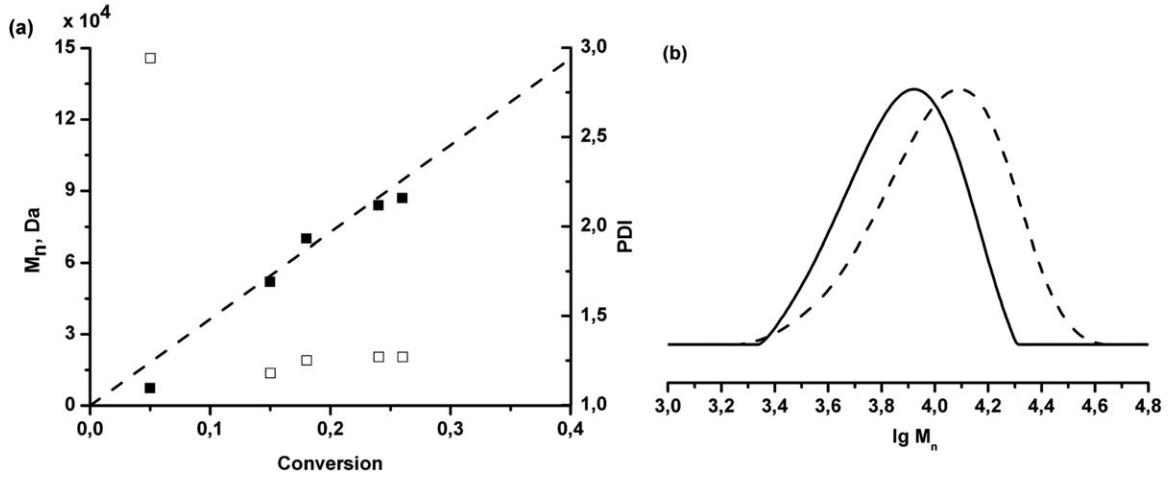


FIGURE 5 (a) Evolution of M_n and PDI versus monomer conversion for NMP of Sty initiated with alkoxyamine **3a** at T = 120 °C, [M]/[I] = 350/1. □, PDI; ■, M_n; dashed line, theoretical molecular weight; (b) GPC traces of poly-Sty sample in abovementioned polymerization experiment obtained at 25% of monomer conversion (M_n = 8.7 kDa, PDI = 1.27, solid line) and pSty-*b*-pMMA sample obtained in reinitiation experiment (M_n = 9.2 kDa, PDI = 1.30, dashed line) after 1 h of reaction.

TABLE 3 Results of the Chain Extension/Reinitiation Experiments

Entries	Macroinitiator M_n (kDa) PDI	Monomer	Monomer to Initiator Ratio	Temperature (°C)	Duration (h)	Conversion	Resulting Polymer M_n (kDa) PDI	Resulting Polymer, $M_{n,th}$[a] (kDa)	F[b]
1	pMMA 25 1.40	Sty	40,000/1	90	2.5	0.1	410 1.44	430	0.8
2	pMMA 20 1.44	Sty	22,000/1	90	3.5	0.1	220 1.45	210	0.9
3	pSty 7.0 1.25	Sty	13,000/1	120	1	>0.01	13,5 1.20	–	0.9
4	pSty 8.7 1.27	MMA	15,000/1	100	1	>0.01	9.2 1.30	–	0.9
5	pSty 21 1.17	MMA	9,000/1	100	15	0.44	390 1.93	417	0.9

[a] Molecular weight calculated on the base of monomer to initiator ratio and monomer conversion.

[b] Fraction of "living" chains.

5). Owing to relatively low temperature, the polymerization proceeded rather slowly. At $T = 120$ °C only 25% of conversion was achieved after 9 h. The polymerization was controlled which is highlighted by linear growth of polymer molecular weight with conversion and the resulting polymer had $M_n = 8.7$ kDa and PDI = 1.27 [Fig. 5(a)]. The obtained polymer had high percentage of "living" chains, which was proved by chain extension experiments. Polymer obtained at conversion 24% after about 4 h of heating was precipitated with cold methanol and filtered ($M_n = 7.0$ kDa and PDI = 1.25). The obtained polymer (5 mg) was added to 1 mL of styrene and the mixture was heated at 130 °C. In the chain extension experiment performed with styrene, one could observe the growth of molecular weight (Table 3, Entry 3). Owing to high polymerization temperature and small amount of macroinitiator, the contribution of styrene self-initiation process was not negligible; however, this did not prevent formation of high molecular weight polystyrene with relatively low PDI.

It should be noted that application of **3a** in Sty homopolymerization allows for the achievement of high monomer conversions. This was verified in polymerization experiment performed in the cavity of NMR spectrometer: the sample of 700 μL of Sty and 3 mg of **3a** (monomer to initiator ratio is 800/1) was degassed and placed into the preheated NMR cavity ($T = 100$ °C). After 45 h of heating, the monomer conversion reached 70% affording pSty with $M_n = 60$ kDa, PDI = 1.43 (Table 2, Entry 5).

It is known that sometimes the block copolymer cannot be obtained when using NMP technique with pSty macroinitiator.[64] The pSty obtained in the styrene homopolymerization initiated with **3a** ($M_n = 8.7$ kDa and PDI = 1.27) was also able to reinitiate the polymerization of MMA with formation of block copolymer of $M_n = 9.2$ kDa and PDI = 1.30 [Fig. 5(b) and Table 3, Entry 5]. The reaction was carried out for 1 h to prevent thickening of the reaction mixture. Owing to short reaction time, the increase of the M_n in reinitiation experiment was not large (only 0.5 kDa).

To prove once again the formation of block copolymer, the reinitiation experiment was conducted with the pSty sample obtained at 40% of conversion during NMR experiment ($M_n = 21$ kDa, PDI = 1.17). The precipitated pSty was added to MMA monomer (1/9000 initiator to monomer ratio) and the mixture was heated in the cavity of the NMR spectrometer at 80 °C. The results are presented as Supporting Information and summarized in Table 3. The GPC analysis showed the increase of molecular weight of the resulting polymer. The resulting block copolymer had higher PDI (Table 3, Entry 5), presumably because the polymerization was carried out without stirring.

CONCLUSIONS

In this article, we demonstrated high synthetic potential of a new methodology of sterically hindered nitroxides construction via intramolecular cycloaddition—isoxazolidine ring opening—oxidation sequence. Series of new sterically hindered imidazoline nitroxides have been prepared starting from aldonitrones of 2*H*-imidazol 1-oxide and 4*H*-imidazole 3-oxide. To study their applicability for initiation of NMP of different monomers, the values of the homolysis rate constants were determined for corresponding alkoxyamines and possible side reactions were monitored and quantified. According to Fischer's diagrams, it was found that alkoxyamines under investigation are suitable for initiation of NMP of styrene and MMA. Moreover, high steric hindrance decreases an impact of H-atom transfer reaction for this nitroxides making them potentially effective mediators of NMP of methacrylic monomers.

Application of alkoxyamine **3a** allows for controlled polymerization of Sty and MMA up to moderate conversions with formation of polymer with low polydispersity and high quota of "living" chains. Application of **3a** as initiator for NMP is beneficial. First of all, when **3a** is employed as initiator, controlled regime of two different monomers (Sty and MMA) could be achieved. As a result, block-copolymer preparation is facilitated. It should be noted that such MMA mediators as DPAIO-nitroxide[26] or *N*-phenyl nitroxides[65,66] are not suitable for NMP of Sty. Furthermore, NMP of MMA initiated by **3a** proceeds at lower temperature in comparison with DPAIO and *N*-phenylalkoxyamines and it allows for preparation of polymers with close values of M_n and PDI. Lowering polymerization temperature increases the energy efficiency of the process. In contrast to MMA polymerizations using SG1-

based initiator, no addition of Sty[16] or acrylonitrile[67] or 9-(4-vinylbenzyl)−9*H*-carbazole[68] is required to reach controlled regime of polymerization when **3a** is used as initiator, so that block copolymer with pure blocks could be prepared.

Thus, applicability of investigated nitroxides for mediation of NMP of MMA and styrene was demonstrated. Controlled polymerization for both monomers was conducted in mild reaction conditions. The polymer formed contained high fraction of "living" chains and was able to reinitiate the polymerization making preparation of block copolymer possible.

ACKNOWLEDGMENTS

This work was partly supported by the Russian Foundation for Basic Research (Grants No. 12-03-1042a, 12-03-00737a and 12-03-33010), by Russian President's foundation (program MK-1654.2013.3) and by the Ministry of Education and Science of the Russian Federation (projects 8436 and 8456). The Center of Collective utilization of NIOC SB RAS is acknowledged for the recording of NMR spectra for this work.

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