Cyclic Alkoxyamine-Initiator Tethered by Azide/Alkyne-''Click''-Chemistry Enabling Ring-Expansion Vinyl Polymerization Providing Macrocyclic Polymers

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ABSTRACT: A cyclic initiator for the nitroxide-mediated controlled radical polymerization (NMP) is a powerful tool for the preparation of macrocyclic polymers via a ring-expansion vinyl polymerization mechanism. For this purpose, we prepared a Hawker-type NMP-initiator that includes an azide and a terminal alkyne as an acyclic precursor, which is subsequently tethered via an intramolecular azide/alkyne-"click"-reaction, producing the final cyclic NMP-initiator. The polymerization reactions of styrene with cyclic initiator were demonstrated and the resultant polymers were characterized by the gel permeation chromatography (GPC) and the matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). These results prove that the ring-expansion polymerization of styrene occurred together with the radical ring-crossover reactions originating from the exchange of the inherent nitroxides generating macrocyclic polystyrenes with higher expanded rings. © 2010 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 48: 3402–3416, 2010

KEYWORDS: azide/alkyne-"click"-reaction; macrocyclics; MALDI; radical crossover reaction; radical polymerization; ring-polymer

INTRODUCTION Macrocyclic polymers represent interesting research targets for both theoretical and synthetic chemists because of their characteristic properties, which strongly differ from those of their linear counterparts.[1–6] To cite some representative recent examples, Schappacher and Deffieux reported that macrocyclic copolymer brushes prepared via living ionic polymerization methods show self-assembly to form supramolecular nano-tubes.[7,8] Another example relates to the different chain dynamics of cyclic versus linear polymers due to the absence of dangling chain ends.[1,4] In all cases, a significant synthetic effort needs to be undertaken to achieve macrocyclic polymers free of contaminant linear polymers. A common strategy to construct the macrocyclic polymers requires the process of an end-to-end cyclization using chemical reactions with high reactivities, such as coupling reactions of α,ω-polymer dianions,[9,10] addition reactions based on HX/Lewis acid initiating systems,[11] transketalizations,[12,13] azide/alkyne-click-reactions,[14–18] or ring-closing olefin metathesis.[18–21]

Another approach uses cyclic initiators to induce a ring-expansion polymerization and thus does not rely on the use of end-to-end cyclizations. Strategies based on the polyhomologation reaction of boracyclanes using an ylide dimethylsulfoxonium methylide as the monomer,[22] ring-opening metathesis polymerizations of cyclooctene via cyclic Ru-initiators,[23,24] or ring-opening polymerization of ε-caprolactone via cyclic tin-initiators[25–28] have been successfully used to this purpose. Furthermore, *N*-heterocyclic carbenes were reported to mediate the ring-expansion polymerizations of lactide and ε-caprolactone to generate cyclic polyesters.[29–31] Only few studies have been reported on the ring-expansion polymerization applicable to conventional vinyl monomers, except Pan and coworkers[32] who reported that the ^{60}Co γ-ray-induced polymerization of methyl acrylate in the presence of cyclic initiator containing two dithioester linkages producing cyclic vinylpolymers. The ring-expansion vinyl polymerization should become a promising method that easily leads to macrocyclic polymer brushes when combined with the polymerizations of macromomomers.

In this work, we report a new synthetic route potentially providing macrocyclic polymers in which the propagation of a vinyl monomer proceeds under a ring-expansion mechanism relying on a controlled radical polymerization process. The strategy is based on the featured mechanism of the nitroxide-mediated controlled radical polymerization (NMP),[33,34] where a propagation occurs by addition of a vinyl monomer to the polymerization-active radical that is derived from the homolysis and recombination of a C—ON bond of an alkoxyamine by heating. Thus, a cyclic alkoxyamine derivative in which the head and tail are covalently linked can be used to initiate the formation of cyclic vinyl polymers via the ring-expansion polymerization mechanism as shown in Chart 1. It should be noted that

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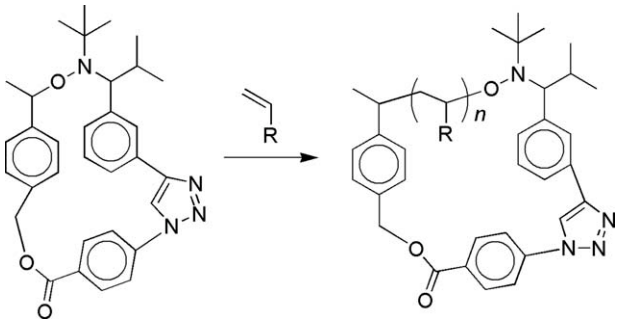


CHART 1 Concept of the ring-expansion polymerization initiated by a cyclic alkoxyamine derivative producing macrocyclic vinyl polymers.

alkoxyamine-containing ring-compounds can be further expanded via radical ring-crossover reactions as reported by Otsuka and coworkers,[35] who have focused on the polymer synthesis utilizing "dynamic covalent bonds." We first describe here that an acyclic 4-(1-(*tert*-butyl-(2-methyl-1-(3′-ethynylphenyl-propyl)aminooxy)ethyl)benzyl 4-azidobenzoate (acyclic precursor **1**, Scheme 1), in which the alkoxyamine-backbone is based on the Hawker-type initiator,[36] was prepared as a starting point for the cyclic NMP-initiator. Strategically, the azide/alkyne-"click"-reaction[37–42] of **1** was projected under high dilution conditions to produce cyclic NMP-initiator **2** as illustrated in Scheme 1. The resulting cyclic NMP-initiator **2** was then projected to serve as initiator for the NMP of styrene aiming at the generation of cyclic polystyrenes.

EXPERIMENTAL

Materials

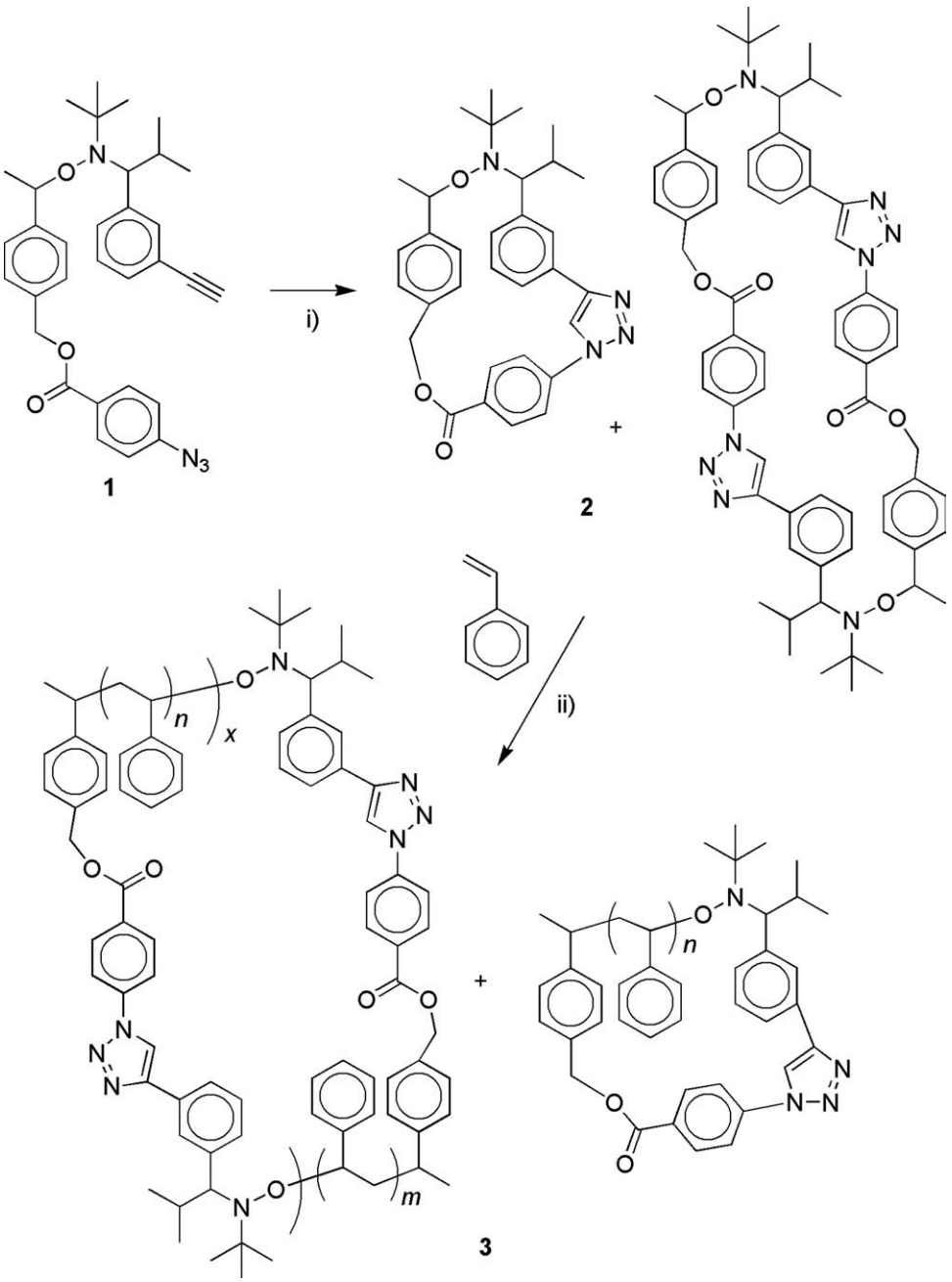
Tetrahydrofuran (THF) was refluxed over sodium and benzophenone and distilled prior to use. Dichloromethane and *N*,*N*-dimethylformamide [DMF, Fluka (Buchs, Switzerland) >99.8%] were refluxed with calcium hydride and distilled prior to use. *p*-Vinylbenzylchloride [Aldrich (Milwaukee, WI), 90%] was used after passing through aluminum oxide [Aldrich (Milwaukee, WI), activated, neutral, Brockmann I, STD grade, approx. 150 mesh, 58 Å] using toluene as an eluent. Styrene [Aldrich (Milwaukee, WI), 99.8%] was extracted with aqueous sodium-hydroxide solution, dried and distilled before use. (2-(3′-Bromophenyl)ethynyl)trimethylsilane (97%), dibromoethane (99%), magnesium (chips, 4 + 30 mesh, 99.98%), copper(II) acetate hydrate (98%), (*R*,*R*)-(−)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminomanganese(III) chloride, sodium borohydride (99%), 4-aminobenzoic acid (99%), sodium nitrate (>99.0%), sodium azide (99.5%), cesium carbonate (Cs_2CO_3, 99%), hexamethylphosphoric acid triamide (HMPA, 99%), tetrabutylammonium fluoride (TBAF, 1.0 M solution in THF), tetrakis(acetonitrile)copper(I) hexafluorophosphate ($[(CH_3CN)_4Cu]PF_6$), and *N*-ethyldiisopropylamine (DIPEA, 99%), were purchased from Aldrich (Milwaukee, WI) and used as received. Ammonium chloride (>99%), ammonium hydroxide solution (25%), and di-*tert*-butylperoxide (>95%) were purchased from Fluka (Buchs, Switzerland) and used as received. *N*-tert-Butyl-α-isopropylnitrone[36] and tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA)[43] were prepared according to literature procedures.

Instruments

^{1}H- (400 MHz) and ^{13}C-NMR (100 MHz) spectra were recorded on a Varian Gemini 2000 instrument. The ^{1}H- (500 MHz) and ^{13}C-NMR (125 MHz) spectra were recorded on a Varian Unity Inova 500 instrument. $CDCl_3$ (Isotec, 99.8 atom% D) and 1,1,1,3,3,3-hexafluoro-2-propanol-d_2 (Isotec, 99 atom% D) were used as solvents. IR spectra were recorded on a Bruker Vertex 70 FT-IR spectrometer. Electrospray ionization time-of-flight mass spectrometer (ESI-TOF MS) analysis was performed using a Bruker Daltonics Focus microTOF II. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometer (MALDI-TOF MS) and gel permeation chromatography (GPC) are described later.

2,2,5-Trimethyl-4-(3′-(trimethylsilyl)ethynyl) phenyl-3-azahexane-3-nitroxide (4)

A few drops of dibromoethane were added to magnesium (850 mg, 35.0 mmol) in dry THF (3.00 mL) and the mixture was vigorously stirred. After 10 min, a solution of (2-(3′-bromophenyl)ethynyl)trimethylsilane (5.00 g, 19.7 mmol) in dry THF (20 mL) was added dropwise over 1 h with vigorously stirring and then the mixture was refluxed for 30 min. After cooling to room temperature, the mixture was added to *N*-tert-butyl-α-isopropylnitrone (2.82 g, 19.7 mmol) with a syringe and the resulting solution was refluxed for 3 h. After cooling to room temperature, saturated ammonium chloride solution (5.00 mL) was added, the formed solids were dissolved by water (15 mL), chloroform (20 mL) was added, and the organic layer was separated. The aqueous layer was extracted with chloroform (20 mL × 3) and the combined organic layers were dried over sodium sulfate and then evaporated to dryness. The residue was redissolved in methanol (100 mL) and 25% ammonium hydroxide solution (4.00 mL) and a catalytic amount of copper(II) acetate hydrate were added. A stream of air was bubbled until the color of the mixture changed from a yellow into a dark brown (2 h). The mixture was evaporated and the residue was dissolved in a mixture of chloroform (50 mL) and 10% $KHSO_4$ solution (10 mL). The organic layer was separated and the aqueous layer was extracted with chloroform (20 mL × 3). The combined organic layers were washed with saturated sodium bicarbonate solution (20 mL), dried over sodium sulfate, and evaporated to dryness. The residue was purified by column chromatography on silica gel, eluting with 50: 1 hexane/ethyl acetate gradually increasing to 20: 1 to yield **4** (3.19 g, 51.2%) as a viscous orange oil. Data for **4**: R_f = 0.36 (hexane/ethyl acetate, 20: 1); ^{1}H NMR (400 MHz, $CDCl_3$, in the presence of pentafluorophenyl hydrazine): δ 7.24 (s, 1H, phenyl-H), 7.13 (d, 1H, ^3J = 7.5 Hz, phenyl-H), 7.08 (d, 1H, ^3J = 7.5 Hz, phenyl-H), 6.95 (m, 1H, phenyl-H), 3.11 (d, 1H, ^3J = 9.4 Hz, NCH), 2.01 (m, 1H, CH), 1.06 and 0.68 (s, 9H, $NCCH_3$), 0.86 and 0.63 (d, 6H, ^3J = 6.5 Hz, CH_3), 0.31 and 0.06 (d, 6H ^3J = 6.5 Hz, CH_3), -0.01 (s, 9H, $SiCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$, in the presence of pentafluorophenyl hydrazine): δ 134.11 (phenyl-C), 133.39 (phenyl-CH), 132.36 (phenyl-CH), 130.57 (phenyl-CH), 130.45 (phenyl-



SCHEME 1 Procedures for the generation of cyclic alkoxyamines and their use as the initiator for the polymerization: i) the "click" reaction of acyclic precursor **1** using tetrakis(acetonitrile)copper(I) hexafluorophosphate ($[(CH_3CN)_4Cu]PF_6$), *N*-ethyldiisopropylamine (DIPEA), and tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA) in *N*,*N*-dimethylformamide (DMF) at room temperature to produce cyclic initiators **2** and ii) polymerization of styrene (St) with **2** in 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanol (HFPP) to produce macrocyclic polystyrenes **3**.

CH), 129.50 (phenyl-CH), 127.82 (phenyl-CH), 127.64 (phenyl-CH), 123.15 (phenyl-C), 122.46 (phenyl-C), 105.62 (phenyl-C≡), 103.90 (phenyl-C≡), 95.55 (≡C-Si), 93.39 (≡C-Si), 73.65 (NC), 71.05 (NCH), 31.44 (CH), 31.24 (CH), 30.31 (CH_3) 26.88 (CH_3), 21.49 (CH_3), 20.48 (CH_3), 18.52 (CH_3), 18.46 (CH_3), -0.01 ($SiCH_3$), -0.15 ($SiCH_3$); IR (cm^{-1}): ν 3423, 2961, 2871, 2156, 1598, 1577, 1478, 1426, 1384, 1362, 1249, 1215, 920, 841, 760, 699, 631; ESI-TOF MS exact mass calcd. for $C_{19}H_{30}NNaOSi$ $[M + Na]^+$ 339.1988: found 338.1937.

2,2,5-Trimethyl-3-(1-(4′-chloromethyl)phenylethoxy)-4-(3′-(trimethylsilyl)ethynyl)phenyl-3-azahexane (5)

A mixture of **4** (1.70 g, 5.37 mmol), *p*-vinylbenzylchloride (1.60 g, 10.7 mmol), (*R*,*R*)-(−)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicy1idene)-1,2-cyclohexanediaminomanganese(III) chloride (680 mg, 1.07 mmol), and di-*tert*-butylperoxide (1.18 g, 8.06 mmol) in 1/1 toluene/ethanol (10 mL) was bubbled with N_2 with stirring for 10 min and then $NaBH_4$ (610 mg, 16.1 mmol) was added. After stirring for 18 h, the mixture was evaporated to dryness and portioned between chloroform (50 mL) and water (50 mL). The organic layer was separated and the aqueous layer was extracted with chloroform (20 mL × 3). The combined organic layers were dried over sodium sulfate and evaporated to dryness. The residue was purified by column chromatography on silica gel, eluting with 16:1 hexane/dichloromethane gradually increasing to 9:1 to give **5** (1.48 g, 55.6%) as a colorless oil. Data for **5**: R_f = 0.25 (hexane/dichloromethane, 9: 1); ^1H NMR

(400 MHz, $CDCl_3$) (both diastereomers): δ 7.55–7.07 (m, 16H, phenyl-H, both diastereomers), 4.91 (q, ^3J = 6.5 Hz, 2H, CHON, both diastereomers), 4.59 (s, 2H, CH_2Cl, minor diastereomer), 4.56 (s, 2H, CH_2Cl, major diastereomer), 3.40 (d, 1H, ^3J = 10.8 Hz, CH, 4.59, major diastereomer), 3.29 (d, 1H, ^3J = 10.8 Hz, CH, minor diastereomer), 2.3 and 1.3 (m, 1H, CH, both diastereomers), 1.62 (d, 3H, ^3J = 6.5 Hz, CH_3, major diastereomer), 1.54 (d, 3H, ^3J = 6.5 Hz, CH_3, minor diastereomer), 1.28 (d, 3H, ^3J = 6.4 Hz, CH_3, major diastereomer), 1.05 (s, 9H, $NCCH_3$, minor diastereomer), 0.93 (d, 3H, ^3J = 6.4 Hz, CH_3, minor diastereomer), 0.79 (s, 9H, $NCCH_3$, major diastereomer), 0.54 (d, 3H, ^3J = 6.6 Hz, CH_3), 0.26 (s, 18H, $SiCH_3$, both diastereomer), 0.22 (d, 3H, ^3J = 6.8 Hz, CH_3, minor diastereomer); ^{13}C NMR (100 MHz, $CDCl_3$) (both diastereomers): δ 145.73 (phenyl-C), 145.01 (phenyl-C), 142.35 (phenyl-C), 142.15 (phenyl-C), 136.50 (phenyl-C), 135.82 (phenyl-C), 134.58 (phenyl-CH), 134.45 (phenyl-CH), 131.30 (phenyl-CH), 131.26 (phenyl-CH), 130.11 (phenyl-CH), 129.97 (phenyl-CH), 128.40 (phenyl-CH), 128.38 (phenyl-CH), 127.34 (phenyl-CH), 127.31 (phenyl-CH), 126.52 (phenyl-CH), 122.09 (phenyl-C), 121.89 (phenyl-C), 105.92 (phenyl-C≡), 93.27 (≡C-Si), 83.20 (CH), 82.40 (CH), 71.91 (NCH), 71.82 (NCH), 60.77 (NC), 46.29 (CH_2Cl), 46.27 (CH_2Cl), 32.11 (CH), 31.78 (CH), 28.65 (CH_3) 28.47 (CH_3), 24.69 (CH_3), 23.07 (CH_3), 22.24 (CH_3), 22.05 (CH_3), 21.29 (CH_3), 21.20 (CH_3), 0.31 ($SiCH_3$), 0.29 ($SiCH_3$); IR (cm^{-1}): ν 2959, 2869, 2156, 1596, 1481, 1421, 1387, 1361, 1263, 1249, 1206, 1060, 856, 840, 797, 759, 704, 647; ESI-TOF MS exact mass calcd for $C_{28}H_{41}ClNOSi$ $[M + H]^+$ 470.2640: found 470.2613.

4-Azidobenzoic Acid (6)

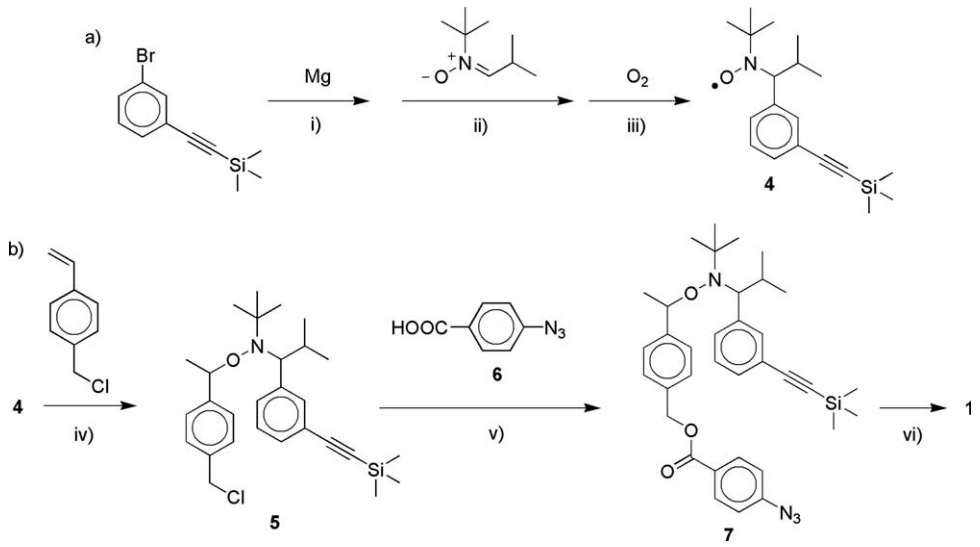
4-Azidobenzoic acid (**6**) was prepared similar to the literature procedure.[44] To a suspension of 4-aminobenzoic acid (4.50 g, 32.8 mmol) in water (25 mL) in a 2 L beaker, concentrated hydrochloric acid (5.60 mL) was added dropwise with vigorously stirring. Then an aqueous solution of sodium nitrite (2.26 g, 32.8 mmol) in water (10 mL) was slowly added with cooling in an ice bath. The color of the suspension changed to orange-yellow during the addition. After this an aqueous solution of sodium azide (2.13 g, 32.8 mmol) in water (25 mL) was slowly added, water (100 mL) and ethyl acetate (125 mL) were added, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (50 mL × 3). The combined organic layers were extracted with 1*N* sodium hydroxide aqueous solutions (40 mL × 2) and then the aqueous extracts were acidified with 1*N* hydrochloride aqueous solution (80 mL). The mixture was extracted with ethyl acetate (50 mL × 3), and the combined extracts were dried over sodium sulfate and evaporated to dryness to give **6** (4.70 g, 87.8%) as a yellow solid. Data for **6**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, ^3J = 8.4 Hz, 2H, phenyl-H), 7.09 (d, ^3J = 8.4 Hz, 2H, phenyl-H); ^{13}C NMR (100MHz, $CDCl_3$): δ 170.43 (C=O), 145.68 (phenyl-C), 132.06 (phenyl-C), 125.66 (phenyl-CH), 119.00 (phenyl-CH); IR (cm^{-1}): ν 2959, 2541, 2101, 1672, 1600, 1577, 1507, 1424, 1330, 1317, 1281, 1177, 1138, 1121, 933, 859, 831, 779, 765, 690.

*4-(1-(*tert*-Butyl-(2-methyl-1-(3′-(trimethylsilylethynyl) phenylpropyl)aminooxy)ethyl)benzyl 4-Azidobenzoate (7)*

To a solution of **5** (1.06 g, 2.66 mmol) and 4-azidobenzoic acid (**6**) (692 mg, 4.25 mmol) in hexamethylphosphoric acid triamide (HMPA, 1.0 mL), cesium carbonate (Cs_2CO_3, 953 mg, 5.32 mmol) was added and the mixture was stirred for 48 h at room temperature. The mixture was evaporated to dryness and partitioned between dichloromethane (100 mL) and water (100 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane (50 mL × 3). The combined organic layers were dried over sodium sulfate and evaporated to dryness. The residue was purified by column chromatography on silica gel, eluting with 9: 1 hexane/dichloromethane increasing to 1: 1 to give **7** (1.26 g, 79.4%) as a yellowish viscous liquid. Data for **7**: R_f = 0.47 (hexane/dichloromethane, 1: 1); ^{1}H NMR (400 MHz, $CDCl_3$) (both diastereomers): δ 8.04 (d, 4H, ^3J = 8.7 Hz, phenyl-H, both diastereomers), 7.60-7.02 (m, 20H, phenyl-H, both diastereomers), 5.34 (s, 2H, CH_2O, major diastereomer), 5.31 (s, 2H, CH_2O, minor diastereomer), 4.96 (m, 2H, CHON, both diastereomers), 3.41 (d, 1H, ^3J = 10.8 Hz, NCH, minor diastereomer), 3.29 (d, 1H, ^3J = 10.8 Hz, NCH, major diastereomer), 2.3 and 1.3 (m, 2H, CH, both diastereomers), 1.62 (d, 3H, ^3J = 6.5 Hz, CH_3, minor diastereomer), 1.54 (d, 3H, ^3J = 6.5 Hz, CH_3, major diastereomer), 1.26 (d, 3H, ^3J = 6.2 Hz, CH_3, minor diastereomer), 1.04 (s, 9H, $NCCH_3$, major diastereomer), 0.91 (d, 3H, ^3J = 6.4 Hz, CH_3, major diastereomer), 0.70 (s, 9H, $NCCH_3$, minor diastereomer), 0.54 (d, 3H, ^3J = 6.4 Hz, CH_3, minor diastereomer), 0.24 (s, 18H, $SiCH_3$, both diastereomer), 0.19 (d, 3H, ^3J = 6.4 Hz, CH_3, major diastereomer); ^{13}C NMR (100 MHz, $CDCl_3$) (both diastereomers): δ 165.59 (C = O), 165.56 (C = O), 145.61 (phenyl-C), 144.92 (phenyl-C), 144.83 (phenyl-C), 142.38 (phenyl-C), 142.20 (phenyl-C), 134.98 (phenyl-C), 134.62 (phenyl-CH), 134.50 (phenyl-CH), 134.31 (phenyl-C), 131.55 (phenyl-CH), 131.53 (phenyl-CH), 131.28 (phenyl-CH), 130.12 (phenyl-CH), 129.97 (phenyl-CH), 128.03 (phenyl-CH), 128.00 (phenyl-CH), 127.27 (phenyl-CH), 127.15 (phenyl-CH), 126.78 (phenyl-C), 126.41 (phenyl-CH), 122.08 (phenyl-C), 121.87 (phenyl-C), 118.84 (phenyl-CH), 105.90 (phenyl-C≡), 93.23 (≡C-Si), 93.01 (≡C-Si), 83.19 (CH), 82.47 (CH), 71.85 (CH), 71.76 (CH), 66.71 (CH_2O), 60.72 (NC), 32.01 (CH), 31.68 (CH), 28.54 (CH_3) 28.38 (CH_3), 24.67 (CH_3), 22.97 (CH_3), 22.15 (CH_3), 21.94 (CH_3), 21.17 (CH_3), 21.09 (CH_3), 0.16 ($SiCH_3$); IR (cm^{-1}): ν 2959, 2869, 2114, 1719, 1603, 1504, 1481, 1362, 1249, 1206, 1173, 1130, 1098, 1060, 841, 764, 734, 704, 647; ESI-TOF MS exact mass calcd for $C_{35}H_{45}N_4NaO_3Si$ $[M + Na]^+$ 619.3074: found 619.2655.

*4-(1-(*tert*-Butyl-(2-methyl-1-(3′-ethynylphenyl-propyl) aminooxy)ethyl)benzyl 4-Azidobenzoate (1)*

TBAF (1 M THF solution, 1.87 mL) was added to a solution of **7** (1.26 g, 2.40 mmol) in dry dichloromethane (10 mL). After stirring for 30 min at room temperature, water (10 mL) was added. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (20 mL × 3). The combined organic layers were dried over



SCHEME 2 a) Synthesis of a nitroxide radical with a trimethylsilyl (TMS)-protected acetylene **4** through i) the reaction of (2-(3′-bromophenyl)ethynyl)trimethylsilane with magnesium (Mg) in dry THF to prepare a Grignard reagent, ii) the reaction with *N*-tert-butyl-α-isopropylnitrone, and iii) aerial oxidation using copper(II) acetate ($Cu(OAc)_2$) in MeOH and 25% ammonium hydroxide solution and b) synthesis of the acyclic alkoxyamine derivative featuring an azide and a terminal alkyne **1** (structure; see Scheme 1) through iv) the reaction of **4** with *p*-vinylbenzylchloride using (*R*,*R*)-(−)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamino manganese(III) chloride, di-*tert*-butylperoxide, and sodium borohydride in 1:1 toluene/ethanol to prepare a alkoxyamine derivative containing chloromethyl group and trimethylsilyl (TMS)-protected acetylene **5**, v) esterification of **5** with 4-azidobenzoic acid **6** using cesium carbonate (Cs_2CO_3) in hexamethylphosphoric acid triamide (HMPA) to prepare alkoxyamine derivatives bearing 4-azidobenzoate and TMS-protected acetylene **7**, and vi) deprotection of the TMS group using TBAF in dry dichloromethane.

sodium sulfate and evaporated to dryness. The residue was purified by flush column chromatography on silica gel with 1:1 hexane/dichloromethane to give **1** (1.00 g, 79.6%) as a yellowish viscous liquid. Data for **1**: R_f = 0.39 (hexane/dichloromethane, 1: 1); ^{1}H NMR (400 MHz, $CDCl_3$) (both diastereomers): δ 8.05 (d, 2H, ^3J = 8.4 Hz, phenyl-H, minor diastereomer), 8.04 (d, 2H, ^3J = 8.4 Hz, phenyl-H, major diastereomers), 7.60-7.02 (m, 20H, phenyl-H, both diastereomers), 5.34 (s, 2H, CH_2O, major diastereomer), 5.31 (s, 2H, CH_2O, minor diastereomer), 4.93 (m, 2H, CHON, both diastereomers), 3.43 (d, 1H, ^3J = 10.4 Hz, NCH, minor diastereomer), 3.30 (d, 1H, ^3J = 10.4 Hz, NCH, major diastereomer), 3.32 (s, 1H, C≡H, major diastereomer), 3.29 (s, 1H, C≡H, minor diastereomer), 2.3 and 1.4 (m, 2H, CH, both diastereomers), 1.62 (d, 3H, ^3J = 6.8 Hz, CH_3, minor diastereomer), 1.54 (d, 3H, ^3J = 6.4 Hz, CH_3, major diastereomer), 1.27 (d, 3H, ^3J = 6.4 Hz, CH_3, minor diastereomer), 1.04 (s, 9H, $NCCH_3$, major diastereomer), 0.92 (d, 3H, ^3J = 6.8 Hz, CH_3, major diastereomer), 0.80 (s, 9H, $NCCH_3$, minor diastereomer), 0.54 (d, 3H, ^3J = 6.4 Hz, CH_3, minor diastereomer), 0.20 (d, 3H, ^3J = 6.8 Hz, CH_3, major diastereomer); ^{13}C NMR (100 MHz, $CDCl_3$) (both diastereomers): δ 165.53 (C=O), 165.50 (C=O), 145.57 (phenyl-C), 144.81 (phenyl-C), 142.47 (phenyl-C), 142.22 (phenyl-C), 134.98 (phenyl-CH), 134.75 (phenyl-C), 134.71 (phenyl-CH), 134.30 (phenyl-CH), 131.62 (phenyl-CH), 131.52 (phenyl-CH), 131.49 (phenyl-CH), 130.23 (phenyl-CH), 130.03 (phenyl-CH), 128.11 (phenyl-CH), 128.03 (phenyl-CH), 127.37 (phenyl-CH), 127.24 (phenyl-CH), 127.18 (phenyl-CH), 126.77 (phenyl-C), 126.39 (phenyl-CH), 121.04 (phenyl-C), 120.83 (phenyl-C), 118.84 (phenyl-CH), 84.37 (phenyl-C≡), 84.31 (phenyl-C≡), 83.29 (CH), 82.47 (CH), 76.52 (C≡H), 76.38 (C≡H), 71.88 (CH), 71.81 (CH), 66.77 (CH_2O), 66.75 (CH_2O), 60.74 (NC), 32.11 (CH), 31.82 (CH), 28.62 (CH_3) 28.45 (CH_3), 24.75 (CH_3), 23.10 (CH_3), 22.21 (CH_3), 22.03 (CH_3), 21.27 (CH_3), 21.16 (CH_3); IR (cm^{-1}): ν 3299, 2974, 2869, 2113, 1717, 1603, 1504, 1362, 1304, 1267, 1206, 1173, 1130, 1097, 1060, 1014, 850, 825, 765, 702; ESI-TOF MS exact mass calcd for $C_{32}H_{36}N_4NaO_3$ $[M + Na]^+$ 547.2679: found 547.2292.

Cyclic NMP-Initiator (2)

Tetrakis(acetonitrile)copper(I) hexafluorophosphate ($[(CH_3CN)_4Cu]PF_6$), 169 mg, 0.453 mmol) was added to a mixture of **1** (1.00 g, 1.91 mmol), tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-amine (TBTA, 240 mg, 0.452 mmol) and *N*-ethyldiisopropylamine (DIPEA, 1.76 g, 13.6 mmol) in DMF (60.0 mL). After stirring for 48 h, the mixture was evaporated to dryness and the residue was purified by column chromatography on silica gel with 4: 1 hexane/ethyl acetate to give **2** (191 mg, 19.1%) as a slightly yellowish solid. Data for **2**: R_f = 0.31 (hexane/ethyl acetate, 4: 1); ^{1}H NMR (500 MHz, 1,1,1,3,3,3-hexafluoro-2-propanol-d_2) (both diastereomers): δ 8.38-7.04 (m, 26H, phenyl-H and triazole-H), 5.60-4.82 (m, 6H, CH_2O and CHON), 4.04-3.80 (br, 2H, NCH), 3.30-2.10 (br, 2H, CH), 1.90-1.60 (m, 6H, CH_3), 1.50-0.80 (m, 30H, CH_3 and $NCCH_3$); ^{13}C NMR (125 MHz, 1,1,1,3,3,3-hexafluoro-2-propanol-d_2) (both diastereomers): δ 170.00-169.00 (C=O), 153.00-152.00 (triazole-C), 142.38 (phenyl-C), 142.26 (phenyl-C), 141.50 (phenyl-C),

133.80-133.20 (phenyl-CH), 132.40-131.80 (phenyl-C), 131.23 (phenyl-CH), 130.32 (phenyl-CH), 130.10-129.80 (phenyl-CH), 129.60-128.40 (triazole-CH), 127.21 (phenyl-CH), 126.07(phenyl-C), 126.03 (phenyl-C), 125.99 (phenyl-C), 125.37 (phenyl-C), 125.27 (phenyl-C), 125.18 (phenyl-C), 123.92 (phenyl-C), 123.86 (phenyl-C), 123.82 (phenyl-C), 123.06 (phenyl-C), 122.95 (phenyl-C), 122.85 (phenyl-C), 122.70 (phenyl-C), 121.74 (phenyl-C), 121.70 (phenyl-C), 121.64 (phenyl-C), 120.74 (phenyl-C), 120.63 (phenyl-C), 120.53 (phenyl-C), 70.00-69.50 (CH_2O), 31.70-30.60 (CH_3), 25.80-23.60 (CH_3), 23.00-20.20 (CH_3). IR (cm^{-1}): ν 2972, 2870, 1722, 1608, 1518, 1408, 1363, 1310, 1272, 1217, 1149, 1107, 1015, 985, 856, 812, 789, 766, 692, 663. MALDI-TOF MS exact mass calcd for $C_{32}H_{37}N_4O_3$ $[M + H]^+$ 525.3: found 524.9.

Polymerization

Typically, the cyclic initiator **2** (18.8 mg, 0.0358 mmol) was dissolved in 1,1,1,3,3,3-hexafluoro-2-phenyl-2-isopropanol (HFPP) (1.49 g) and then styrene (St) (746 mg, 7.17 mmol) was added. The mixture was subjected to three freeze-thaw cycles, sealed under argon, and immersed in an oil bath at 125 °C for 6 h with stirring. After cooling in liquid nitrogen, the mixture was diluted with THF (5 mL) and then poured into methanol (300 mL). The precipitate was purified by rep-recipitation with THF-methanol and dried in *vacuo* to give **3** (360 mg, 45.7%) as a white powder. Data for **3**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40-6.23 (br, phenyl-H), 5.45-5.23 (br, CH_2O), 2.60-1.20 (br, CH and CH_2 in the main chain), 1.20-0.06 (br, CH_3); IR (cm^{-1}): ν 3083, 3060, 3026, 2922, 2850, 1724, 1602, 1493, 1452, 1366, 1272, 1069, 1028, 755, 696; M_n = 52,200 g mol^{-1}, M_w/M_n = 2.35.

Hydrolysis

To a solution of **3** (61.1 mg) in THF (2 mL), a THF solution containing 10 wt % methanolic potassium hydroxide (KOH) (2.00 mL) was added. After stirring for 12 h at 40 °C, aqueous hydrochloric acid solution (1*N*, 5.00 mL) was added and the mixture was extracted with dichloromethane (10 mL × 2). The combined organic layers were washed with water (10 mL), dried over sodium sulfate, evaporated to dryness, redissolved in THF (1 mL), and poured into methanol (50 mL). The precipitate was filtered and dried in *vacuo* to give **8** as the main product (56.7 mg, 92.8%). Data for **8**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40-6.23 (br, phenyl-H), 4.70-4.55 (br, CH_2O), 2.60-1.20 (br, CH and CH_2 in the main chain), 1.20-0.06 (br, CH_3); IR (cm^{-1}): ν 3083, 3060, 3026, 2922, 2850, 1602, 1493, 1452, 1028, 755, 696; M_n = 13,400 g mol^{-1}, M_w/M_n = 2.08.

Radical Crossover Reaction

Acyclic alkoxyamine **5** (25.0 mg, 0.0532 mmol) and **3** (50.3 mg) were dissolved in HFPP (640 mg). The mixture was subjected to three freeze-thaw cycles, sealed under argon, and immersed in an oil bath at 125 °C for 6 h with stirring. After cooling, the mixture was diluted with THF (1 mL) and then poured into methanol (50 mL). The precipitate was filtered and dried in *vacuo* to give **9** as the main product (50.9 mg, 96.0%). Data for **9**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40-6.23 (br, phenyl-H), 5.45-5.23 (br, CH_2O), 2.60-1.20 (br, CH and CH_2 in the main chain), 1.20-0.06 (br, CH_3); IR (cm^{-1}): ν 3083, 3060, 3026, 2924, 2850, 1602, 1493, 1452, 1029, 756, 696; M_n = 13,300 g mol^{-1}, M_w/M_n = 2.12.

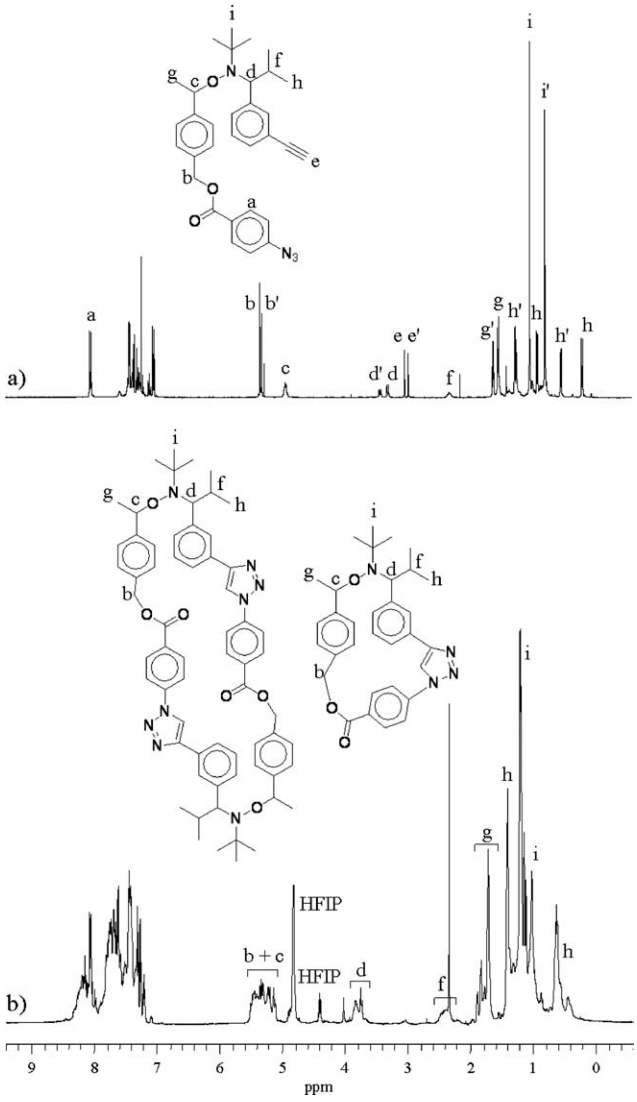


FIGURE 1 ^{1}H NMR spectra of a) **1** in $CDCl_3$ and b) **2** in 1,1,1,3,3,3-hexafluoro-2-isopropanol-d_2 (HFIP-d_2).

Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometer

MALDI-TOF-MS analyses were performed using Bruker Daltonik Autoflex III instrument. This instrument is equipped with an Nd:YAG laser (335 nm) and a delayed pulse extraction (0 or 100 ns). It was operated at an accelerating potential of 5.5 kV in a linear mode. The instrument was calibrated with a poly(ethylene glycol) (PEG) standard (M_p = 4200 g mol^{-1}, M_w/M_n = 1.02) using a four-point calibration. The solutions of **2**, **3**, and **8** in THF were prepared (2–5 g L^{-1}) in a similar manner. The matrix solution was prepared by dissolving 1,8-dihydroxy-9(10*H*)-anthracenone (dithranol) in THF (10 g L^{-1}). A silver trifluoroacetate (AgTFA) solution in THF was prepared in a concentration of (10 g L^{-1}); sodium iodide (NaI) solution in methanol was prepared in a concentration

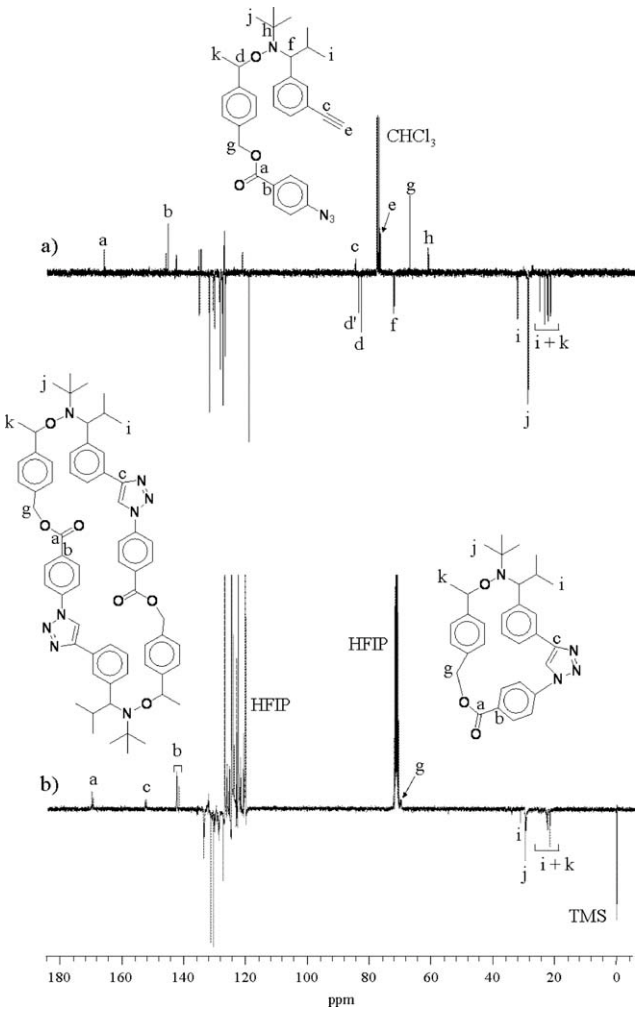


FIGURE 2 APT spectra of a) **1** in $CDCl_3$ and b) **2** in 1,1,1,3,3,3-hexafluoro-2-isopropanol-d_2 (HFIP-d_2).

of (10 g L^{-1}). The final sample solutions were prepared as follows; method I: a solution of **2** (100 μL) was mixed with the matrix solution (100 μL) and AgTFA solution (5 μL). Method II: a solution of **3** (20 μL) was mixed with the matrix solution (100 μL) and AgTFA solution (2 μL). Method III: a solution of **8** (100 μL) was mixed with the matrix solution (10 μL) and NaI solution (10 μL). A 0.5 (L portion of the respective final sample solutions has then deposited on the sample target and allowed to air-dry at room temperature. The spectra were obtained by collecting 2000–5000 shots (100 Hz repetition rate). All spectra were baseline corrected and smoothed using a three-point Savitzky-Golay algorithm.

Gel Permeation Chromatography

The number-average molecular weight (M_n), molecular weight distribution (M_w/M_n), and molecular weight at the peak top (M_p) were determined by two types of GPC apparatus in this study. Type I: A routine GPC was performed using a Viscotek VE 2001 equipped with a Viscotek VE 3580 RI detector (detector temperature, 35 °C) and a Viscotek GMH_{HR}-N column (column temperature, 22 °C; column size, 7.8 mm × 300 mm; particle size, 5 μm; exclusion limit, 4 × 10^5) using THF as an eluent at a flow rate of 1.0 mL min^{-1}. The M_n, M_w/M_n, and M_p were determined on the basis of a polystyrene calibration. Type II: Quadruple-detector GPC was performed using a Viscotek GPCmax VE-2001 equipped with a Viscotek Model 302-040 Triple Detector Array and a Well-Chrom Spectro-Photometer K-2501 (wavelength, 254 nm) and two columns consisting of a Viscotek GMH_{HR}-N Mixed Bed column (column temperature, 35 °C; column size, 7.8 mm × 300 mm; particle size, 5 μm; exclusion limit, 4 × 10^5) and a Viscotek G2500 HHR column (column temperature 35 °C, 7.8 mm × 300 mm; particle size, 5 μm, exclusion limit, 2 × 10^4) using THF as an eluent at a flow rate of 1.0 mL min^{-1}. Polystyrenes with the M_n of 6220 and 99,209 g mol^{-1} and the M_w/M_n of 1.05 and 1.02, respectively, were used for the calibrations of the detector. The M_n, M_w/M_n, and M_p were determined on the basis of a polystyrene calibration and the dn/dc of 0.185 was used for the light scattering (LS) analyses.

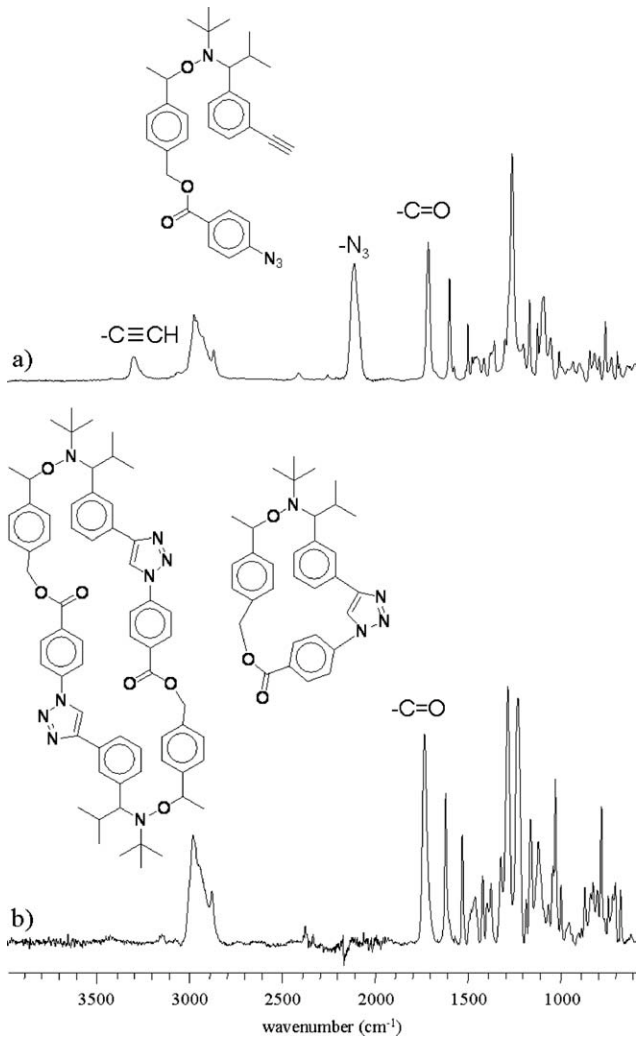


FIGURE 3 IR spectra of a) **1** and b) **2**.

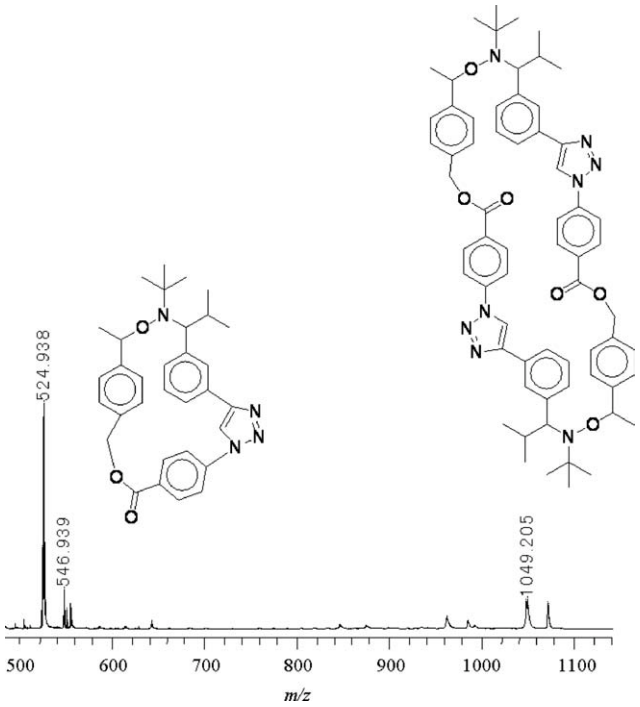


FIGURE 4 MALDI-TOF MS spectrum of **2**.

RESULTS AND DISCUSSION

Synthesis and Characterization of Cyclic NMP-Initiator

The structure of the alkoxyamine derivative featuring an azide and a terminal alkyne, acyclic precursor for azide/alkyne-"click"-reaction **1**, is illustrated in Scheme 1. To synthesize the precursor, a nitroxide radical with a trimethylsilyl (TMS)-protected acetylene **4** was first prepared through the similar reactions reported by Hawker and coworkers[36] and our group[45] (Scheme 2a). (2-(3′-Bromophenyl)ethynyl)-trimethylsilane was transformed into the Grignard reagent in dry THF and reacted with *N*-tert-butyl-α-isopropylnitrone, followed by aerial oxidations using copper(II) acetate. The target **4** could be isolated as viscous orange oils, whereas it should be noted that the prolonged refluxing during the preparation of the Grignard reagent was shown to remove the TMS-protecting group.

The obtained nitroxide radical **4** was reacted with *p*-vinylbenzylchloride using (*R*,*R*)-(−)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicy1idene)-1,2-cyclohexanediaminomanganese(III) chloride, di-*tert*-butylperoxide, and $NaBH_4$ to yield the alkoxyamine derivative **5** containing the *p*-chloromethyl group and the 3′-TMS-protected acetylene as a colorless oil (Scheme 2b). Subsequently, **5** was modified by esterification with 4-azidobenzoate **6** using cesium carbonate in hexamethylphosphoric acid triamide (HMPA) similar to a previous modification using "click"-chemistry reported in our laboratory,[45] producing the alkoxyamine derivative **7** bearing an 4-azido benzoate and TMS-protected acetylene. Afterwards, the TMS group was removed using TBAF producing the target acyclic precursor **1**. Figures 1(a) and 2(a) show the ^{1}H NMR and APT spectra for **1**, respectively, in which the characteristic signals assignable to its structure appear. The dashed alphabets in Figures 1(a) and 2(a) assign the resonances due to the minor diastereomers. Figure 3(a) shows the IR spectrum of **1**, exhibiting the strong peaks due to terminal alkyne, azide, and ester group at 3299, 2113, and 1717 cm^{-1}, respectively.

The cyclization of **1** was performed using the azide/alkyne-"click"-reaction with tetrakis(acetonitrile)copper(I) hexafluorophosphate ($[(CH_3CN)_4Cu]PF_6$) as the copper source, *N*-ethyldiisopropylamine (DIPEA) as the base, and tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA) as the cocatalyst in

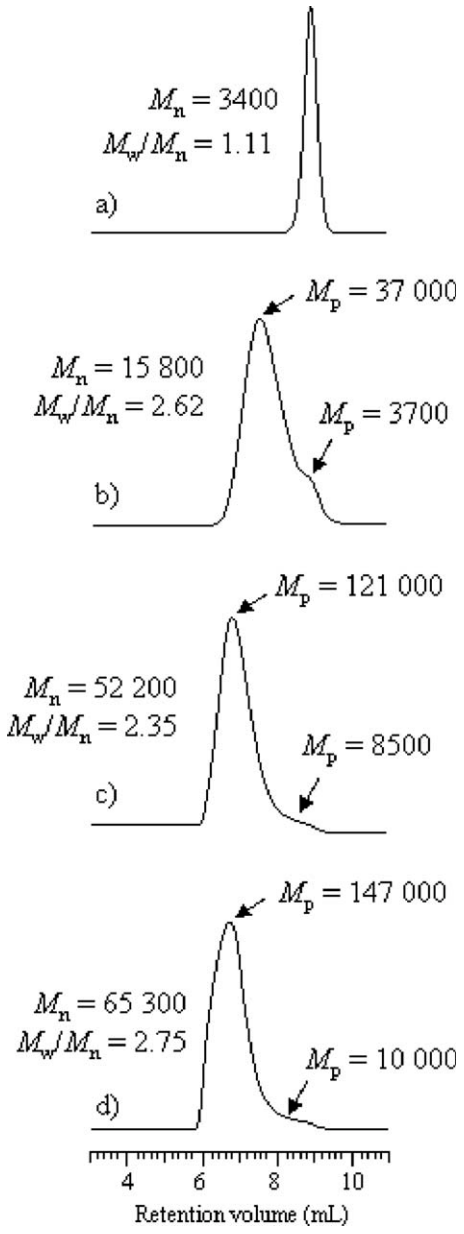


FIGURE 5 GPC traces of the products obtained by the polymerizations of styrene (St) in 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanol (HFPP) with a) **5** using the [*M*]/[*I*] of 50: 1, b) **2** using the [*M*]/[*I*] of 50:1, c) **2** using the [*M*]/[*I*] of 200:1, and d) **2** using the [*M*]/[*I*] of 1000:1.

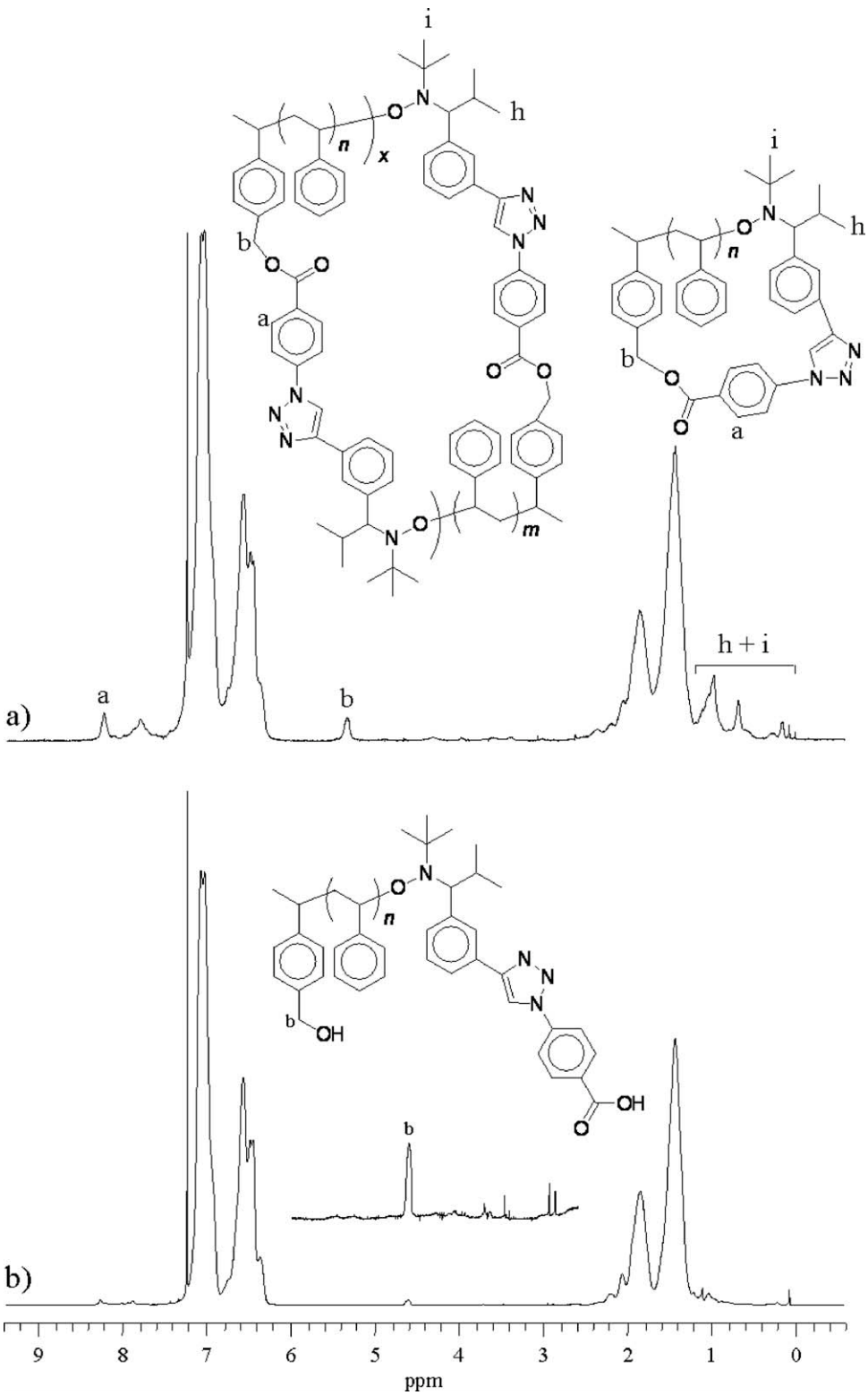
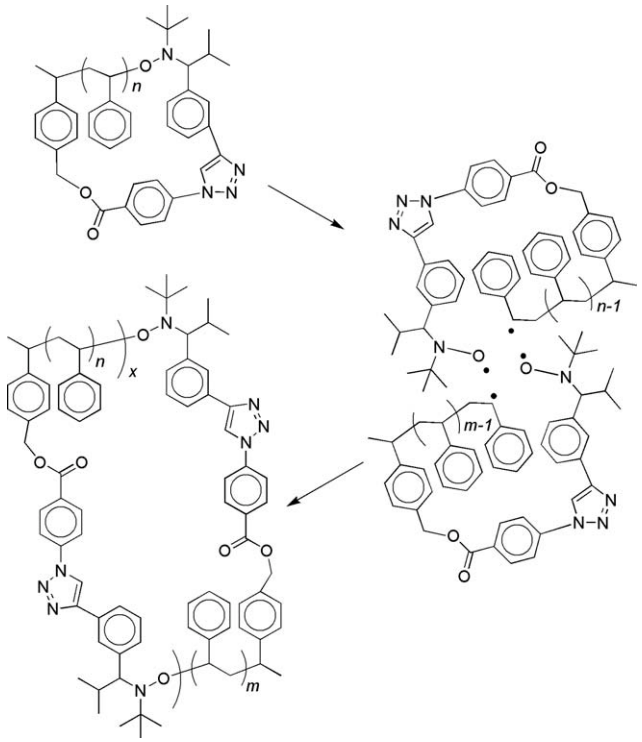


FIGURE 6 ^{1}H NMR spectra of a) the product obtained through the polymerization of styrene (St) with **2** using the [*M*]/[*I*] of 50:1 in $CDCl_3$, and b) the product after the hydrolysis of **3** with the molecular weight at the peak top (M_p) for the main peak of 121,000 g mol^{-1} using methanolic KOH in THF in $CDCl_3$.

DMF under high dilution conditions (Scheme 1). After compound **1** was consumed as judged by TLC (R_f = 0.39, hexane/dichloromethane = 1: 1), the reaction mixture was evaporated and purified by column chromatography to yield product **2** (R_f = 0.31, hexane/ethyl acetate = 4: 1) in 19.0% isolated yield. Product **2** was not soluble in common organic solvents indicative of its cyclic structure due to the restrictions of molecular mobilities within the cycle. However, **2** was found to show good solubility in fluorinated alcohols, thus enabling NMR analyses in 1,1,1,3,3,3-hexafluoro-2-propanol-d_2 (HFIP-d_2). The resonances of the ^{1}H NMR spectrum for **2** were complex, however, assignable to the target structure as displayed in



SCHEME 3 Schematic illustration for the radical ring-crossover reactions generating macrocyclic PSt with a more expanded ring. The polymer contains multiple units derived from the cyclic initiator.

Figure 1(b). Notably, the respective signals are broadened as compared to those of **1**, possibly due to the presence of restricted motions for the protons within the cyclized structures. Figure 2(b) shows the APT spectrum for **2**. The resonances due to the methine and quaternary carbons in the alkoxyamine backbones were not detected due to the low S/N ratio, whereas the resonances derived from the methyl carbons clearly appeared at the region from 32 to 20 ppm. Resonances due to the benzoate moiety were observed at the regions from 170 to 169 ppm and from 143 to 141 ppm. In addition, the resonances of the triazole-carbons appeared at the region from 153 to 152 ppm, thus proving that **2** was indeed the product formed via the azide/alkyne-"click" reaction. Figure 4 displays the MALDI-TOF MS of **2**, exhibiting the main peak at m/z = 524.9, which was consistent with the calculated $[M + H]^+$ value for the target cyclic alkoxyamine of 525.3. Another peak also appeared at m/z = 1049.2 implying that a dimeric byproduct was also generated via an intermolecular addition reaction, even though the reaction was performed using a high dilution conditions as is required for the intramolecular cyclization. However, both adsorptions due to the azide- and alkyne-moieties disappeared in the IR spectrum of **2** [Fig. 3(b)], excluding significant contaminations of **2** with acyclic byproducts. These results indicated that **2** was assignable to the target cyclic alkoxyamine tethered by the benzoate- and the 1,2,3-1*H*-triazole ring as illustrated in Scheme 1, taking into account the contamination with a small amount of the cyclic dimer.

Polymerization of Styrene with Cyclic NMP-Initiator and Characterizations of the Products to Reveal the Mechanisms of the System

We next focused on the polymerization of styrene (St) with cyclic NMP-initiator **2**. Initial experiments were tried, polymerizing St in bulk at 125 °C. However, the initiator **2** was not soluble in St even at the polymerization temperature and thus the polymerization proceeded heterogeneously and was not pursued further. As we found out that **2** was soluble in fluorinated alcohols, a fluorinated alcohol with a high boiling point, such as HFPP, was used as a solvent. To prove the influence of the fluorinated solvent on the NMP-process, St was first polymerized with the acyclic alkoxyamine **5** in HFPP using a monomer/initiator-ratio ($[M]/[I]$) of 50: 1, which afforded the PSt-polymer in 49.9% yield. Figure 5(a) shows the GPC trace of the resulting linear product, exhibiting a monodisperse peak with the number-average molecular weight (M_n) and the molecular weight distribution (M_w/M_n) of 3400 g mol^{-1} and 1.11, respectively, in which the M_n was consistent with the theoretical molecular weight ($M_{n,th}$) of 3100 g mol^{-1}. Hence, the use of HFPP as the solvent did not negatively affect the system during the polymerization reaction. However, the terminal trimethylsilyl acetylene moiety was cleaved off as indicated by the IR and ^{1}H NMR measurements, presumably due to the use of the slightly acidic solvent such as HFPP.

Subsequently similar polymerizations were performed using cyclic alkoxyamine-initiator **2** in HFPP as the solvent (Scheme 1), which now homogeneously proceeded to produce a PSt-polymer in 46.3% yield. Figure 5(b) shows the GPC trace of the PSt-product formed after initiation by the cyclic NMP-initiator **2**. It should be emphasized that the trace [Fig. 5(b)] drastically differed from that obtained by using the acyclic alkoxyamine **5** [Fig. 5(a)]. The trace of PSt-polymer via **2** exhibits bimodal peaks with the M_n = 15,800 g mol^{-1} and M_w/M_n = 2.62. The peak top (M_p)-values of the main peak and the shoulder in the lower molecular weight regions were 37,000 g mol^{-1} and 3700 g mol^{-1}, respectively. The M_p of 3700 g mol^{-1} was close to calculated value for cyclic PSt with one initiator unit of 2935 g mol^{-1}, whereas the system was shown to produce a polymer with considerably higher molecular weights. Similar results were observed for the polymerizations using a monomer/initiator-ratio of $[M]/[I]$ = 200: 1. The polymerization was demonstrated with **2** in HFPP for 6 h to produce a polymer in the 45.7%. Figure 5(c) displays the GPC trace of the product, in which the M_n and M_w/M_n were 52,200 g mol^{-1} and 2.35, respectively, with M_p values of the main peak and the shoulder of 121,000 and 8500 g mol^{-1}, respectively. Thus, the molecular weights of the products increased with the increasing $[M]/[I]$ ratios. Using a monomer/initiator-ratio of $[M]/[I]$ = 1000/1 afforded PSt-product in 43.4% yield, with M_n = 65,300 g mol^{-1} and M_w/M_n = 2.75 as shown in Figure 5(d). The M_p values of the main peak and the shoulder were 147,000 and 10,000 g mol^{-1}, respectively. Therefore, the system with the cyclic NMP-initiator produced polymers with significantly high molecular weights, indicating that this system is

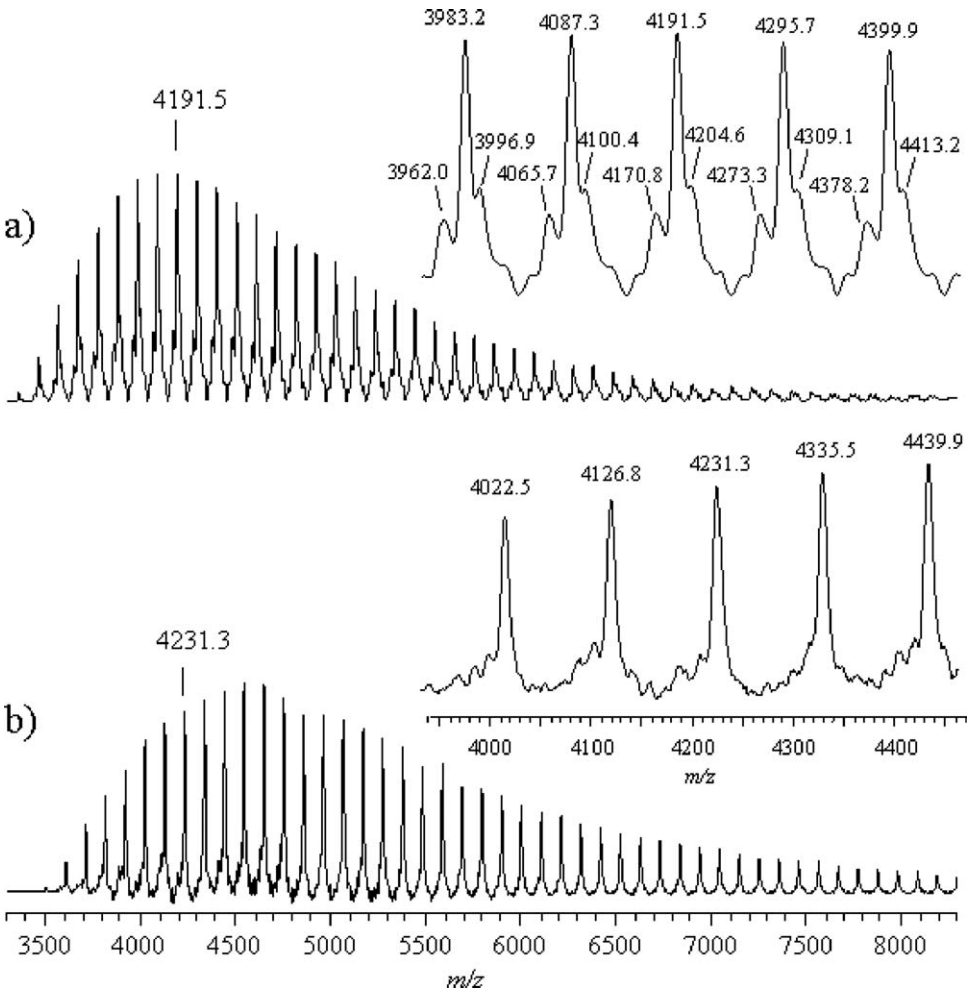


FIGURE 7 MALDI-TOF MS spectra of a) the product obtained by the polymerizations of styrene (St) in 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanol (HFPP) with **2** using [*M*]/[*I*] of 50:1 and b) the product after the hydrolysis of **3** with the molecular weight at the peak top (M_p) for the main peak of 121,000 g mol^{-1} using methanolic KOH in THF in $CDCl_3$.

accompanied with different/additional reaction-pathways as compared to that with the acyclic initiator. The pathways should include radical ring-crossover reactions, which will be later described.

Figure 6(a) shows the ^{1}H NMR of the PSt-product formed after polymerization with the [*M*]/[*I*] of 50:1. The large resonances derived from protons due to PSt appeared that included aromatic ones at the region from 7.4 to 6.2 ppm and methine and methylene ones in the main chains at the region from 2.2 to 1.2 ppm. Additionally, the characteristic signals due to the unit derived from cyclic initiator **2** clearly appeared. For examples, aromatic protons in the benzoate linkage, methylene protons adjacent to the ester group, and methyl protons in the alkoxyamine moiety were observed at the regions from 8.3 to 8.1 ppm, from 5.5 to 5.3 ppm, and from 1.2 to 0.1 ppm, respectively. In the IR spectrum of the product, the distinct peak of the carbonyl group derived from **2** appeared at 1724 cm^{-1}. These results suggested that the products were assignable to PSt's initiated by **2**. Thus, we propose that this polymerization system proceeds by the ring-expansion polymerization mechanism to produce PSt-monocycle as shown in Scheme 1. Simultaneously, radical ring-crossover reactions originating from the inherent exchange of mediated nitroxide,[35,46–48] as illustrated in Scheme 3, could occur to generate a macrocyclic PSt with a more expanded ring or linear PSt polymers.

Characterization of the Products Obtained Through the Polymerization of Styrene with Cyclic NMP-Initiator by MALDI-TOF MS

Figure 7(a) shows the MALDI-TOF MS of the product obtained through the polymerization of St with **2** using the [*M*]/[*I*] ratio of 50:1. The spectrum exhibits a series of major peaks in the area of *m/z* ranging from 3200 to 8000 with a regular interval of 104.1 corresponding to the mass of the St repeating unit. Although the observed peaks were due to the low molecular weight species considering that the M_n and M_w/M_n of this sample were 15,800 g mol^{-1} and 2.62, respectively, the *m/z* values of the peaks were consistent with those of a PSt with one initiator-unit. To state one example, the *m/z* of 4191.5 corresponds to the $[M + Na]^+$ of 35-mer PSt-monocycle, which completely agrees with the calculated value for $C_{312}H_{315}N_4O_3Na$ of 4191.5. In addition, one of the series of minor peaks was also assignable to PSt-monocycle. As an example, the *m/z* of 4170.8 was derived from the $[M + H]^+$ of a 35-mer PSt, being consistent with the calculated value for $C_{312}H_{316}N_4O_3$

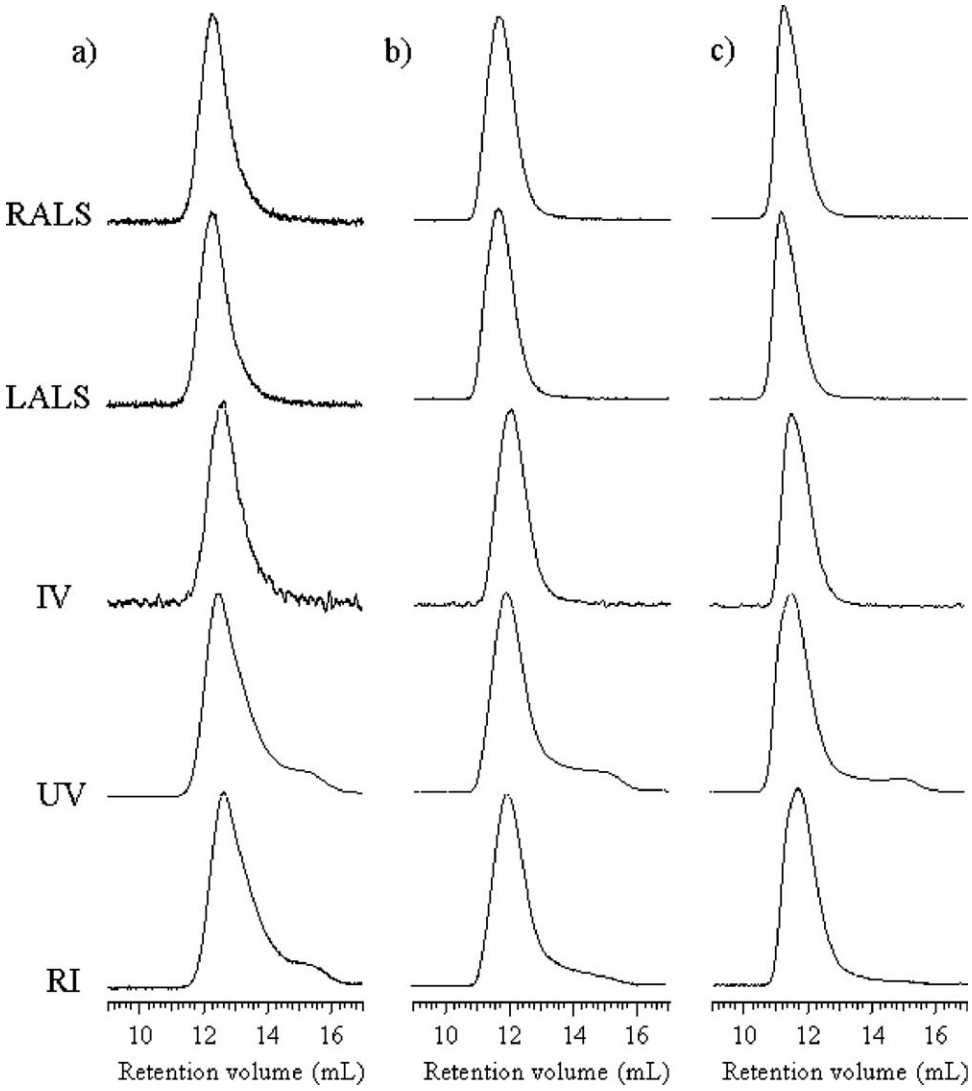


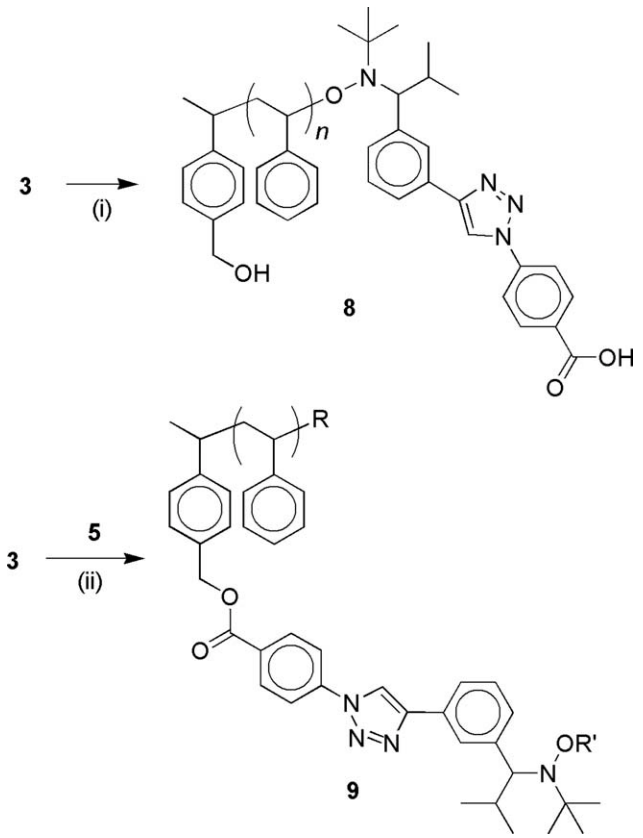
FIGURE 8 GPC traces of macrocyclic polystyrenes **3** obtained by the polymerizations of styrene (St) in 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanol (HFPP) with **2** using the [*M*]/[*I*] ratios of a) 50:1, b) 200:1, and c) 1000:1, which were detected by the RI, UV, IV, and LALS, and RALS detectors.

of 4170.9. Therefore, PSt's with cyclic structures should be produced in the present system via the mechanism as shown in Chart 1. Other series of small peaks are not assigned because various possible peaks that include those derived from cyclic PSt's with two initiator units will overlap to obscure their original peak tops; however, one of them could be due to PSt-monocycle with a potassium salt. Unfortunately, despite many efforts, the high molecular weight species could not be desorbed testing nearly 20 available MALDI-matrices.

TABLE 1 Summary for the Synthesis of Macrocyclic Polystyrenes 3[a] and Their Characterizations by GPC Equipped with RI, UV, IV, and LS Detectors, Quadruple-detector GPC

			Characterization by Quadruple-Detector GPC							
	Synthesis		RI		UV		IV		LS	
Entry	[*M*]/[*I*][b]	Yield (%)	M_w (M_w/M_n)[c]	M_p[d]	M_w (M_w/M_n)[c]	M_p[d]	M_w (M_w/M_n)[c]	M_p[d]	M_w (M_w/M_n)[c]	M_p[d]
1	50	46.3	41,400 (2.62)	49,000	29,700 (2.52)	38,500	30,700 (3.01)	36,900	37,400 (2.49)	44,700
2	200	45.7	130,000 (3.45)	126,000	63,500 (3.01)	76,500	117,000 (1.95)	96,300	120,000 (2.58)	127,000
3	1,000	43.4	238,000 (3.16)	222,000	97,500 (3.24)	112,000	202,000 (3.64)	176,000	216,000 (1.97)	219,000

[a] Prepared through the polymerizations of styrene (St) with cyclic initiator **2** in 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanol (HFPP) at 125 °C for 6 h.
[b] Monomer/initiator ratio in the feed.
[c] Weight-average molecular weight (molecular weight distribution) determined by GPC in THF using polystyrene standards.
[d] Molecular weight at the peak top determined by GPC in THF using polystyrene standards.



SCHEME 4 Ring-opening reactions of **3** by (i) the hydrolysis using methanolic KOH in THF or (ii) the radical crossover reaction with an excess amount of acyclic alkoxyamine **5** in 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanol (HFPP), producing linear polystyrene **8** or **9**.

Characterization of the Macrocyclic Polystyrenes by the Quadruple-Detector GPC

Figure 8 shows the GPC traces of **3** obtained by the polymerizations of St with **2** using the $[M]/[I]$ ratios of 50:1, 200:1, and 1000:1, which were detected by the refractive index (RI), ultraviolet-visible (UV) intrinsic viscosity (IV), and low-angle light scattering (LALS) as well as right-angle light scattering (RALS) detectors. The differences were that the shoulders in the low molecular weight regions, which were observed with the RI and UV, were almost undetected by the IV and LS; however, these are not unusual results. However, the UV-trace plausibly as the most molecular weight-independent system clearly shows the shoulder at an elution volume of about ~15 mL, which should be the monocyclic PSt being assigned by MALDI-TOF-MS.

Table 1 summarizes the results that include weight-average molecular weights (M_w) determined by the respective detectors. The M_w determined by the LS would reflect exact molecular weights for cyclic polymers; thus, we concluded that the polymerizations of St with **2** using the $[M]/[I]$ ratios of 50:1, 200:1, and 1000:1 produce macrocyclic polystyrene **3** with the M_ws of 37,400, 120,000, and 216,000 g mol^{-1} in the yields of 46.3, 45.7, and 43.4%, respectively. The respective M_ps were 44,700, 127,000, and 219,000 g mol^{-1}. The shift to increasing molecular weight with higher $[M]/[I]$ ratio can be detected, indicative of a living character of the polymerization, however, obscured by the radical crossover-reaction. We state that the present analysis would reach the limit of currently achievable polymer analytics to characterize the products of this study.

Ring-Opening of Macrocyclic PSt

To provide further insights into the mechanism by other approaches, we performed ring-opening reactions for **3** with the M_p for the main peak of 121,000 g mol^{-1} (determined by a routine GPC). The ring-opening was demonstrated by cleaving the inherent benzoate linkages using methanolic KOH in THF to produce product **8** (Scheme 4). Figure 9(a) shows the GPC trace of **8** with the M_n and M_w/M_n of 13,400 g mol^{-1} and 2.08. The M_p of 14,000 g mol^{-1} was significantly shifted to the lower molecular weight regions as compared to the starting **3**, which was relatively close to the calculated value of 10,062 g mol^{-1}. A shoulder was observed for the GPC trace of **8** in the higher molecular weight

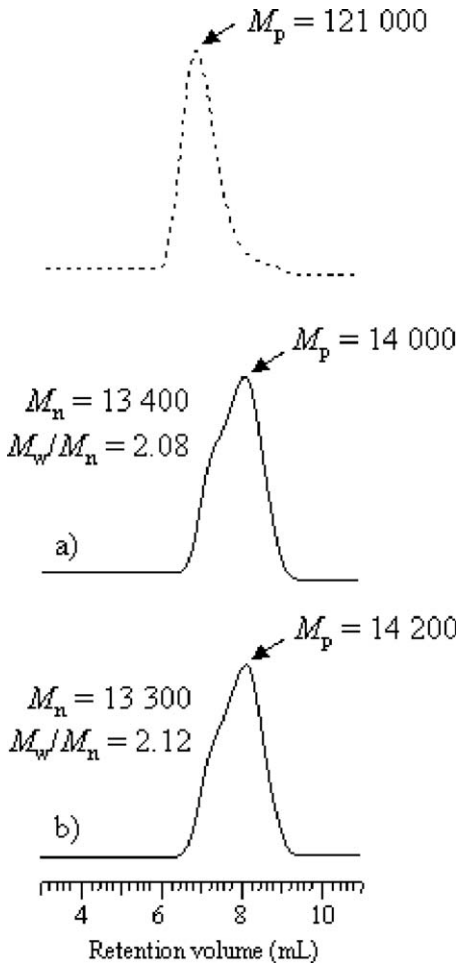


FIGURE 9 GPC traces of the products after the ring-opened reactions by a) the hydrolysis and b) the radical crossover reaction. The upper dashed line is the GPC trace of the macrocyclic polystyrene **3** before the ring-opened reactions.

regions. However, in the ^{1}H NMR spectrum of **8** [Fig. 6(b)], the signals due to the methylene protons adjacent to the ester linkage at 5.5-5.3 ppm disappeared. Alternatively, the signals assignable to methylene protons in the neighborhood of a hydroxyl group were observed at 4.7–4.5 ppm. The MALDI-TOF MS spectrum of **8** showed a series of the peaks with the *m/z* values assignable to ring-opened species [Fig. 7(b)]. As an example, the *m/z* of 4231.3 corresponds to the $[M + 2Na - H]^+$ of 35-mer PSt with bearing a triazole ring and chain-ends of a hydroxyl and a carboxylic acid groups, which agrees with the calculated value for $C_{312}H_{316}N_4O_4Na_2$ of 4231.9. Thus, the hydrolysis reaction obviously proceeded and the main species after the hydrolysis was assignable to the ring-opened PSt **8** as illustrated in Scheme 4. The results to be emphasized here should be that the molecular weight of the product drastically decreased after the hydrolysis as stated above, indicating that macrocyclic PSt **3** contained multiple benzoate linkages in the main chain. This supports the proposed mechanisms.

Another possible ring-opening reaction is based on radical crossover reactions; thus cyclic PSt **3** was heated in HFPP at 125 °C for 6 h in the presence of an excess amount of the acyclic alkoxyamine **5**. Figure 9(b) displays the GPC trace of the product with the M_n and M_w/M_n of 13,300 g mol^{-1} and 2.12, respectively. The M_p was 14,200 g mol^{-1}, therefore also significantly reduced as compared to that of the starting macrocyclic PSt **3**. Interestingly, the GPC trace was quite similar to that for **8** shown in Figure 9(a). Consequently, the main product after the reaction should be assignable to the ring-opened linear PSt **9** in which the end-groups were exchanged with those originating from **5**. Furthermore, this result strongly supported the occurrence of radical crossover reactions occurred in the system. Notably, the GPC trace of the product after the radical crossover ring-opening reaction also showed shoulders in the high molecular weight regions [Fig. 9(b)]. This motivated us to check the GPC trace after both ring-opening reactions; the product after the radical crossover reaction was treated with KOH to obtain product **10**. There were no significant differences between the GPC traces of **10** and those of **8** and **9**; hence, we could not exclude the possibility of the occurrences of side reactions, such as those caused from chain transfer reactions or recombinations linked through C—C bonds. However, the results of these ring-opening reactions agree with the proposed mechanisms of the present study.

CONCLUSIONS

A cyclic alkoxyamine that can initiate the NMP was tethered via intramolecular azide/alkyne-"click"-reaction and subsequently used for the initiation of the NMP-polymerization of styrene (St). The polymerization by such cyclic alkoxyamine-initiator enabling the ring-expansion vinyl polymerization was demonstrated for the first time. The experimental results suggested that the ring-expansion vinyl polymerizations occurred for this system producing PSt-monocycles, which is accompanied with the radical ring-crossover reactions originating from the exchange of mediated nitroxide generating macrocyclic PSt's. The occurrence of the radical ring-crossover reactions was experimentally proven, whereas the polymerization-products contain linear or catenane-like species. Thus, ongoing research is directed to the polymerization of macromonomers to prepare grafted polymeric cycles. The polymerization mechanisms with cyclic NMP-initiator can then be further supported by microscopy data.

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