Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron 61 (2005) 8159–8166

Tetrahedron

Crowned dendron: ion-responsive flexibility of macromolecules induced by integrated crown ether moieties

Mutsuo Tanaka,[a,*] Yoshihiro Higuchi,[b] Naoki Adachi,[c] Yasuhiko Shibutani,[c] Saleh A. Ahmed,[a,†] Shinpei Kado,[b] Makoto Nakamura[b] and Keiichi Kimura[b,*]

[a]*Institute for Biological Resources and Functions, AIST, Central 5, 1-1-1, Higashi, Tsukuba, Ibaraki 305-8565, Japan*
[b]*Department of Applied Chemistry, Faculty of Systems Engineering, Wakayama University, 930, Sakae-dani, Wakayama, Wakayama 640-8510, Japan*
[c]*Department of Chemistry, Faculty of Engineering, Osaka Institute of Technology, 5-16-1, Ohmiya, Asahi-ku, Osaka 535-8585, Japan*

Received 23 May 2005; revised 14 June 2005; accepted 14 June 2005

Abstract—Polybenzyl ether type dendrons bearing the crown ether moieties at the periphery, namely, crowned dendrons were synthesized, and the effect of complex formation on their flexibility with metal-ion binding properties was examined. Upon addition of Na^+, ^1H NMR spectra of the crowned dendrons in CD_3CN were significantly broadened, reflecting the flexibility restriction of the crowned dendrons by the complex formation with Na^+. Such a significant flexibility restriction was observed only with Na^+, although ESI-MS studies revealed that the crowned dendrons formed 1:2 complexes (a metal ion:the crown ether moiety) regardless of the kind of metal ions. The flexibility restriction became significant with increasing dendron generation on the basis of ^1H NMR spectra and spin-lattice relaxation time (T_1) measurements. Binding constants of the crowned dendrons with metal ions in CD_3CN decreased with the increase of the dendron generation, reflecting an influence of the charge repulsion as well as a dendrimer effect to cause the steric hindrance. The examination of UV–vis absorption spectra for complexes of the crowned dendron with metal picrates in THF displayed the formation of a loose ion-pair complex with Na^+, namely, a typical sandwich type complex. However, in CH_3CN, all metal picrates were solvated to be in a loose ion-pair even without complex formation. These results suggested that the control of macromolecular flexibility with metal ions is feasible by the integration of crown ether moieties with a dendritic structure.

---

1. Introduction

In biological systems, the stimulation, recognition, and response are a series of events to produce biological functions, in which specific flexibility and shape persistence of macromolecules are essential factors. The molecular recognition to induce an allosterism through flexibility control of macromolecules has been considered as one of factors to produce biological functions such as non-linear response, switching, self-restoration, and so on. To understand such a biological system and to realize it artificially have been a fascinating work in chemistry.

Our interest is in the manipulation of molecular functions with metal ions in view of the molecular recognition. For example, the combination of a crown ether moiety with a photochromic molecule afforded ion-responsive photochromic materials.[1] These contexts prompted us to study flexibility behavior of macromolecules induced by complex formation of integrated crown ether moieties. Recently, dendrimer is one of the attractive macromolecules to produce various function because of its ordered structure, dendritic structure,[2] and some dendrimers, which have several molecular recognition sites have been reported.[3] Therefore, we set out to synthesize a dendrimer bearing crown ether moieties at the periphery, namely, crowned dendrimer. In this macromolecule, the crown ether moieties are integrated with a dendritic structure, and ion-responsive flexibility induced by the complex formation of the integrated crown ether moieties is expected.

Several crowned dendrimers have already been reported.[4–7] In the case of dendrimers bearing crown ether moieties at the periphery,[4,5] however, any flexibility change by the formation of metal ion complex in solution have not been found.[5] Among dendrimers bearing crown ether moieties at the core,[6,7] the first example of ion-responsive morphology was reported in a mesophase.[7] To the best of our knowledge,

---

Keywords: Dendron; Ion-responsive flexibility; Crown ether.

* Corresponding authors. Tel.: +81 72 751 9209; fax: +81 72 751 9629; e-mail: mutsuo-tanaka@aist.go.jp
† Present address: Chemistry Department, Faculty of Science, Assiut University, 71516 Assiut, Egypt

doi:10.1016/j.tet.2005.06.037

ion-responsive flexibility of crowned dendrimers in solution has not been reported yet, although there is a report on a dendrimer showing pH-responsive flexibility due to the charge repulsion in solution.[8]

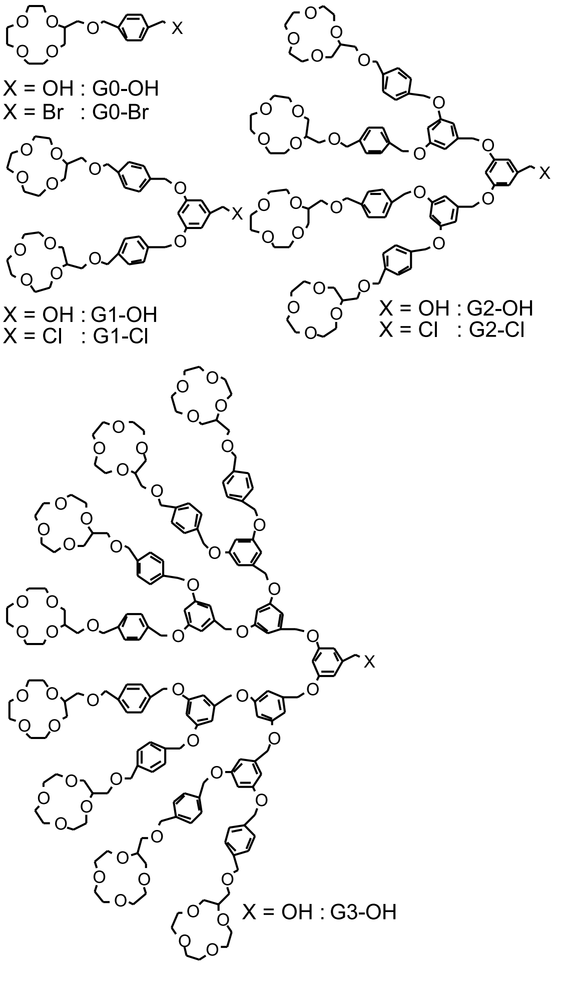
In this paper, we report the synthesis of a new macromolecule bearing crown ether moieties with a dendritic structure, and its ion-responsive flexibility induced by its metal ion binding.

2. Results and discussion

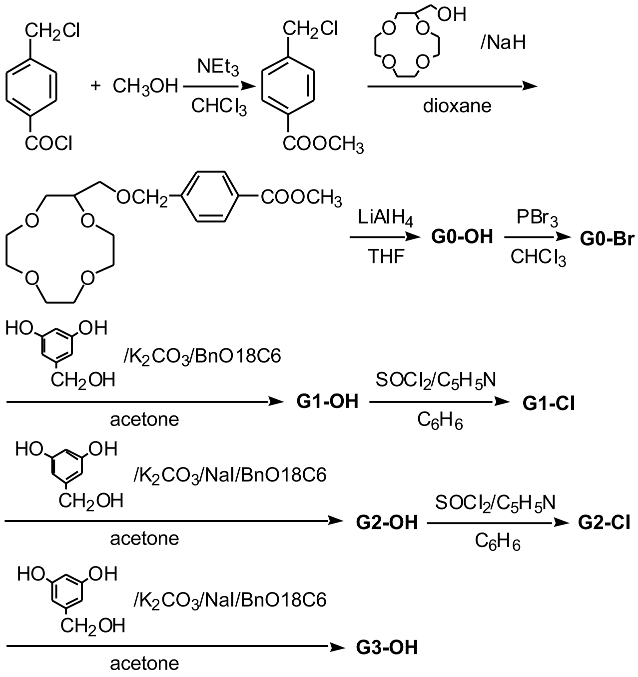
2.1. Synthesis

Crowned dendrons, Gn-X ($n=0$–3, X=OH, Cl, or Br) listed in Scheme 1 were synthesized according to a convergent approach.[9] We chose 12-crown-4 as a building block for our crowned dendrimer because assembling 12-crown-4 moieties shows marked differences from the single 12-crown-4 moiety not only in the metal-ion binding ability but also in the complex structure; the 12-crown-4 moiety forms 2:1 complexes with Na^+ and 1:1 complexes with Li^+, respectively.[10]

The adopted synthetic procedures for the crowned dendrons are summarized in Scheme 2. At the first step, 12-crown-4 moiety was introduced at the *para* position of benzyl alcohol to afford **G0-OH**. And the generation of the crowned dendron was then increased according to the synthetic procedures for Fréchet type dendrimer in the presence of benzyloxymethyl-18-crown-6 (BnO18C6) as a phase transfer catalyst.[11] The reactivity of benzyl hydroxyl group at the focal position decreased with increasing dendron generation, and finally, attempts to synthesize the fourth generation dendron and the dendrimer with **G3-OH** dendron were not successful. Therefore, we examined the flexibility of maclomolecules with a dendron structure. The structure of **G3-OH** did not seem to be too crowded to hamper the reaction on the basis of the result of molecular mechanics calculation. Some interaction of the crown ether moieties with the reactant may disturb the subsequent reaction.



Scheme 1. Synthesized crowned dendrons.



Scheme 2. Synthesis outline. BnO18C6 represents benzyloxymethyl-18-crown-6.

2.2. Flexibility of G3-OH depending on metal ions

In order to investigate the influence of complex formation on the flexibility of **G3-OH**, ^1H NMR spectra were measured in the presence of various alkali and alkaline-earth metal ions in CD_3CN at room temperature. Upon addition of alkali metal perchlorates, a drastic down-field shift in the spectra for protons of the crown ether moieties was observed, which indicated complex formation of the crown ether moieties with metal ions. The spectra of the **G3-OH** protons of the crown ether moieties in the presence of Li^+ and Na^+ are shown in Figure 1. In the case of Na^+, a significant broadening of spectra was induced. This broadening obviously suggests that the flexibility of the crowned dendron was restricted by the Na^+ complex formation in ^1H NMR time-scale. On the other hand, such a significant broadening was not observed with other alkali metal ions, although the down-field shift for the protons of the crown ether moieties appeared with all the metal ions.

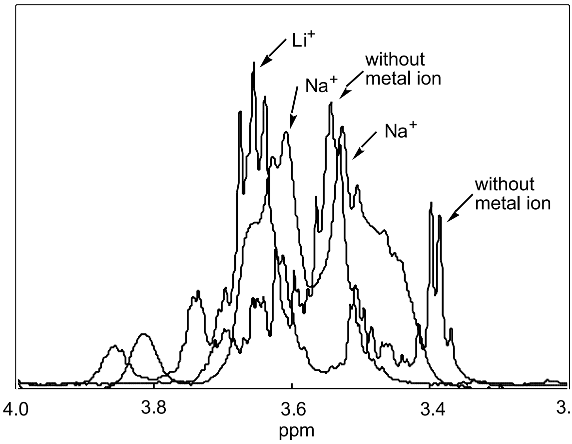


Figure 1. ^{1}H NMR spectra for crown ether protons of **G3-OH** in the presence or absence of metal ions in CD_3CN at room temperature. The concentrations of **G3-OH** and $MClO_4$ were 1×10^{-3} and 1×10^{-2} mol dm^{-3}, respectively.

The spectral change induced by the complex formation was found not only at the protons of the crown ether moieties but also at all the protons of **G3-OH**. Especially, the peaks of the **G3-OH** aromatic protons at the periphery (the protons of the aromatic ring moiety adjacent to the crown ether moiety) showed a very intriguing behavior depending on the kind of metal ions, as depicted in Figure 2. In the presence of Li^+, the shape of the peaks were sharp with a down-field shift indicating the complex formation with Li^+, and such a down-field shift was observed for all the protons in **G3-OH**. To the contrary, the addition of Na^+ induced an up-field shift with a significant broadening in the spectrum, and the up-field shift was observed for all the protons except for the protons of the crown ether moieties. At a higher temperature, 70 °C, the spectrum with Na^+ became sharp with a smaller up-field shift. Therefore, the up-field shift induced by the Na^+ complex formation seemed to reflect diamagnetic anisotropy of aromatic rings[12] caused by the flexibility restriction. In the case of K^+, a slight up-field shift was observed except for the crown ether protons. The behavior of the K^+ complexation is similar to that of the Na^+ complexation, but any broadening was not discernible.

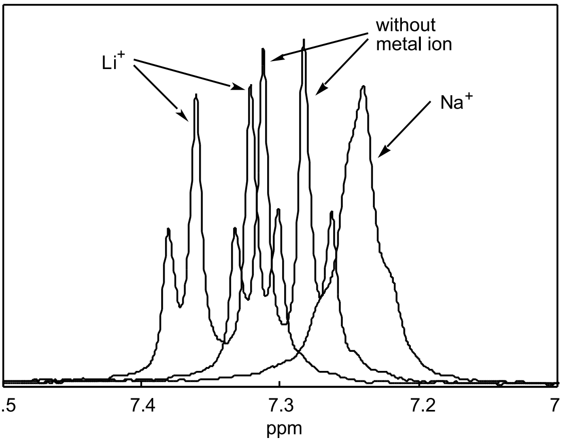


Figure 2. ^{1}H NMR spectra for aromatic protons of **G3-OH** in the presence or absence of metal ions in CD_3CN at room temperature. The concentrations of **G3-OH** and $MClO_4$ were 1×10^{-3} and 1×10^{-2} mol dm^{-3}, respectively.

Furthermore, any spectral change was hardly observed in the presence of Rb^+ and Cs^+ except for the down-field shift of the crown ether protons. In the cases of alkaline-earth metal ions, although a significant down-field shift was observed for the protons of the crown ether moieties, any spectral broadening could not be detected because of the low solubility of the complexes. Those results suggest that the complex formation affects the flexibility of **G3-OH** depending on the kind of metal ions.

In order to investigate the influence of anion on the flexibility of **G3-OH**, lithium and sodium picrates, the picrate anion, of which is known as a large counteranion, were added to **G3-OH** in CD_3CN, and ^{1}H NMR spectra were examined. In the case of sodium picrate, some broadening of ^{1}H NMR spectra was observed in a similar way to the case of $NaClO_4$. With lithium picrate, a down-field shift indicating the complex formation was discernible, but no broadening was detected. This result suggests that the difference of the metal ion size controls the flexibility of **G3-OH** rather than the difference of the anion size.

ESI-MS measurements were carried out to determine how many metal ions were captured by **G3-OH** in CH_3CN. The ESI-MS spectra showed that each **G3-OH** molecule holds four metal ions, where the peaks at *m/z* of 842 with Li^+ and at *m/z* of 858 with Na^+ were observed. Even in the presence of 100-fold excess amount of Li^+ and Na^+, each **G3-OH** molecule was found to hold four metal ions at most. The ESI-MS spectrum with Na^+ is shown in Figure 3. Additionally, the Job plots for ^{1}H NMR titration data gave a maximum close to 0.8 in the molar fraction of Li^+, which is consistent with the ESI-MS result. Therefore, the crown ether moieties tend to form 1:2 complexes (a metal ion:the crown ether moiety) regardless of the kind of metal ions. This result means that the difference between Li^+ and Na^+ complexes of **G3-OH** in ^{1}H NMR spectra was induced by the difference in the metal ion size ($Li^+ = 0.60$ and $Na^+ = 0.98$ Å) but not in the number of the captured metal ions.

In Fréchet type dendrimer, a metal ion could be attached to the benzyl ether oxygens. Upon addition of Li^+, the ^{1}H NMR spectra for **G3-OH** showed a down-field shift induced

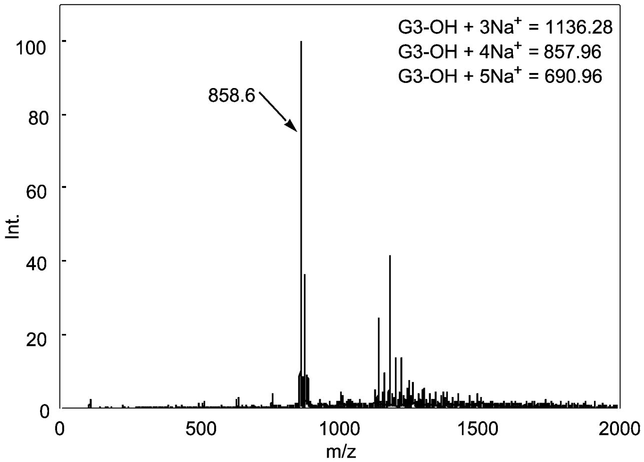


Figure 3. ESI-MS spectra of **G3-OH** in the presence of $NaClO_4$ in CH_3CN. The concentrations of **G3-OH** and $NaClO_4$ were 1×10^{-5} and 1×10^{-3} mol dm^{-3}, respectively.

by complex formation with Li^+ for all protons. The down-field shift for the crown ether protons was about 0.15 ppm but that for the benzyl protons was much smaller being between 0.05 and 0.07 ppm. Furthermore, in the case of Na^+, the down-field shift was observed only for the crown ether protons, and ESI-MS measurements revealed that the **G3-OH** can capture a maximum of four metal ions. Therefore, the metal ion captured by **G3-OH** seems to be located at the crown ether moieties.

Unfortunately, attempts to visualize the difference in flexibility between Li^+ and Na^+ complexes of **G3-OH** by atomic force microscopy (AFM) failed.

2.3. Dendrimer effect on flexibility

In order to evaluate the dendrimer effect, ^1H NMR spectra were examined for **G0-OH**, **G1-OH**, and **G2-OH** in the presence of various alkali metal ions in a similar way to **G3-OH**. The ^1H NMR spectra of the aromatic protons at the periphery in the presence of Li^+ and Na^+ are shown in Figures 4 and 5, respectively. In Figure 4, Li^+ did not induce any peak broadening in spectra for all the crowned dendrons. However, in the case of Na^+, the ^1H NMR spectral peaks became drastically broad with increasing dendron generation (Fig. 5). This result indicates that the flexibility restriction of the crowned dendron by Na^+ complex formation depends strongly on the dendron generation, that is, a dendrimer effect.

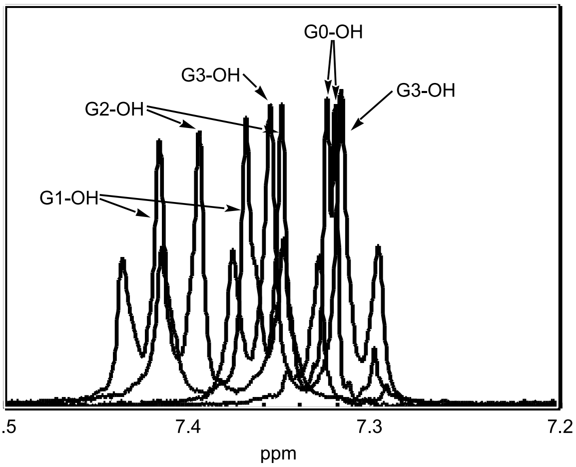


Figure 4. ^1H NMR spectra for aromatic protons of **G0~3-OH** in the presence of $LiClO_4$ in CD_3CN at room temperature. The concentrations of **G0~3-OH** and $LiClO_4$ were 8, 4, 2, 1×10^{-3}, and 1×10^{-2} mol dm^{-3}, respectively.

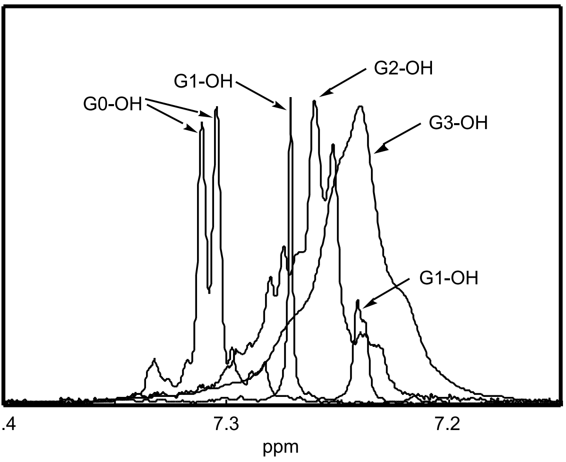


Figure 5. ^1H NMR spectra for aromatic protons of **G0~3-OH** in the presence of $NaClO_4$ in CD_3CN at room temperature. The concentrations of **G0~3-OH** and $NaClO_4$ were 8, 4, 2, 1×10^{-3} and 1×10^{-2} mol dm^{-3}, respectively.

In Figure 4, the down-field shift induced by the Li^+ complexation is increased with increasing the dendron generation from $\Delta\delta=0.01$ for **G0-OH** to $\Delta\delta=0.04$ for **G3-OH**. On the other hand, the up-field shift caused by the Na^+ complexation showed an opposite tendency. The up-filed shift induced by Na^+ is the most significant for **G1-OH** ($\Delta\delta=-0.12$) and is decreased with the increase of dendron generation, being $\Delta\delta=-0.09$ and -0.06 for **G2-OH** and **G3-OH**, respectively. As anticipated, such an up-field shift was not observed for **G0-OH**. This result again implies that the difference in the metal ion size caused a significant difference in the dendron flexibility.

In order to express the flexibility restriction of the dendron numerically, the spin-lattice relaxation time (T_1) in CD_3CN at room temperature was measured as an indicator for the flexibility restriction of the crowned dendron, where the decrease of intramolecular motion results in the T_1 reduction. It is known that the complex formation of crown ethers with metal ions reduces their T_1 value in the NMR spectra through the reduction of intramolecular motion.[13] The T_1 values of the aromatic protons at the periphery (protons of the aromatic ring moiety adjacent to the crown ether moiety) for **G0~3-OH** in the absence of metal ions were 3.5, 1.9, 1.5, and 1.3 s, respectively, which indicated the enhancement of flexibility restriction with increasing the dendron generation. When $LiClO_4$ and $NaClO_4$ were added to the **G3-OH** solution, the T_1 value decreased to 1.1 and 0.72 s, respectively. This result clearly indicates that the metal complex formation of **G3-OH** reduces the intramolecular motion, namely, the flexibility, and that Na^+ is more effective in the flexibility restriction than Li^+. This significant flexibility restriction induced by the complex formation of **G3-OH** with Na^+, as shown in the T_1 measurements, is consistent with the result of the ^1H NMR studies.

2.4. Metal-ion binding properties

The binding constants for complexes with metal perchlorates in CD_3CN at room temperature were evaluated through the binding isotherms by non-linear least-square regression[14] using the ^1H NMR titration data. The tertiary proton of the crown ether moiety was used as an indicator. The binding constants for **G1~3-OH** were determined as the average value for the binding sites, in which two crown ether moieties captured one metal ion. The obtained data are summarized in Table 1. Although the binding constants for **G0-OH** showed Li^+, Ca^{2+}, and Sr^{2+} selectivity, the selectivity was not remarkable. On the other hand, the binding constants for **G1~3-OH** indicated a clear selectivity to Na^+ and Ca^{2+}. While the metal-ion binding ability of 12-crown-4 towards Li^+ is well known to form 1:1 complex,[15] bis(12-crown-4) derivatives generally show a high binding ability towards Na^+ by the formation of

Table 1. Binding constants with metal perchlorates in CD_3CN[a]

	Li^+	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
G0-OH	14	7.7	2.3	0.66	0.28	0.34	73	110	24
G1-OH	1.3	110	3.0	1.8	0.79	0.28	460	6.5	—[b]
G2-OH	0.84	96	1.0	0.74	0.64	2.2	330	5.7	—[b]
G3-OH	0.78	90	0.96	(9.8)[c]	(19)[c]	2.1	170	(52)[c]	—[b]

[a] The unit is $10^3\ mol^{-1}\ dm^3$.

[b] The values could not be determined.

[c] The values did not reflect conceivable binding constants because of charge repulsion and steric hindrance.

sandwich-type complexes, namely, 1:2 (a metal ion:the crown ether moiety) complex.[16] In the case of polymers carrying a 12-crown-4 moiety at the side chain, high binding abilities towards Na^+ are also attained by the formation of similar sandwich-type complexes.[17] Therefore, this binding ability of **G1 ∼ 3-OH** to Na^+ is derived from the formation of sandwich-type complexes. However, the binding constants for **G1 ∼ 3-OH** generally decreased with the increase of dendron generation. The degree of decrease in the binding constants with increasing dendron generation was more significant with Ca^{2+} than with Na^+. This implies that the charge repulsion of divalent Ca^{2+} became more serious than that of monovalent Na^+ with increasing the dendron generation, since the radius of Na^+(0.98 Å) is as large as that of Ca^{2+}(0.99 Å). Thus, the dendrimer effect was also observed in the binding constants reflecting the charge repulsion.[8]

In the cases of Rb^+, Cs^+, and Sr^{2+}, the binding constants for **G3-OH** shown in parenthesis in Table 1 were extraordinary large. To determine the binding constants, **G3-OH** was regarded as a tetradentate ligand, tentatively. However, because of the charge repulsion and steric hindrance with the dendrimer effect, it is likely that **G3-OH** could not act as a tetradentate ligand with those metal ions to yield extraordinarily large binding constants.

2.5. Complexing behavior of G3-OH with metal picrates

Metal picrates are known to show significant changes in the UV–vis absorption spectra depending on the nature of ion-pair. The formation of a sandwich type complex with crown ethers to afford a loose ion-pair complex induces a red-shift in the UV–vis absorption spectra in THF.[18] Therefore, UV–vis absorption spectra with alkali metal picrates were measured in the presence or absence of **G3-OH** to evaluate its complexing behavior. The UV–vis absorption spectra of lithium and sodium picrates are shown in Figure 6. Upon the addition of **G3-OH**, while lithium picrate did not show any meaningful change in the spectrum, sodium picrate indicated a significant spectral change with 7 nm red-shift at the maximal absorption (shift from 352 to 359 nm). It is obvious that this red shift in the spectrum indicates the formation of a sandwich type complex, in which a metal ion is captured by two crown ether moieties effectively, and therefore the formation of a loose ion-pair.[18] Such a significant red-shift was only observed with sodium picrate, and other metal picrates showed only a slight red shift of less than 3 nm.

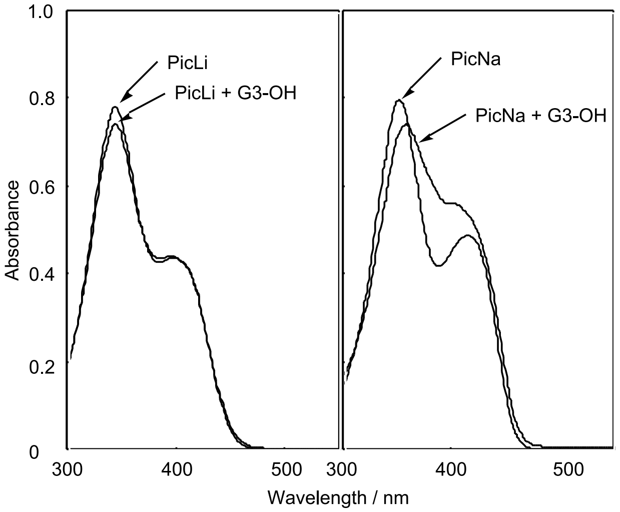


Figure 6. UV–vis absorption spectra of metal picrates in the presence of **G3-OH** in THF at room temperature. The concentrations of **G3-OH** and metal picrates were $5\times10^{-5}\ mol\ dm^{-3}$. PicLi and PicNa represent lithium and sodium picrates, respectively.

In CH_3CN, however, such a spectral change was hardly observed by addition of **G3-OH**, and all the picrates showed the maximal absorption at 375 nm. This tendency shows that all the metal picrates are in a loose ion-pair by solvation with CH_3CN even without complex formation, as the wavelength of the maximal absorption (375 nm) for the metal picrates in CH_3CN was much longer than that (359 nm) for sodium picrate in THF in the presence of **G3-OH**. These observations again support that the metal ion captured by the crown ether moieties is a crucial factor to induce the flexibility restriction of the crowned dendron.

3. Conclusions

The manipulation of macromolecular flexibility by recognition of metal ions was examined with dendrons bearing crown ether moieties at the periphery, crowned dendron, where the crown ether moieties were integrated with their dendron structure. The significant influences of metal complex formation on the flexibility demonstrate that the manipulation of macromolecular flexibility by recognition of metal ions is possible by integration of the crown ether moieties in macromolecules. A study on application of this ion-responsive flexibility of macromolecules for molecular function control to materials chemistry is in progress in due course.

4. Experimental

4.1. General

All chemicals and metal perchlorates were of available purity and used without further purification. For the UV–vis absorption spectra measurements, THF and CH_3CN of spectroscopic grade were used. Metal picrates were prepared by the reaction of equimolar amounts of aqueous picric acid and metal hydroxide, or carbonate. To avoid the explosion of metal picrates during drying, only a small amount of metal picrates was prepared each time. Gel permeation chromatography (GPC) using chloroform as an eluent was used for purification of the dendrons.

4.2. Synthesis of dendrons

4.2.1. 4-Chloromethylbenzoic acid methyl ester. Methanol (1.60 g, 50 mmol), triethylamine (1.52 g, 15 mmol), and chloroform (100 mL) were put into a three-necked flask at 0 °C. A chloroform solution (20 mL) of 4-chloromethylbenzoyl chloride (1.89 g, 10 mmol) was added dropwise to the mixture. The reaction mixture was allowed to warm at room temperature and stirred for 12 h. The reaction mixture was poured into water, and the organic layer was separated. The crude product (quantitative) obtained as a colorless liquid by solvent evaporation was used for the subsequent synthesis after drying.

4.2.2. 4-(12-Crown-4-methoxymethyl)benzoic acid methyl ester. Hydroxymethyl-12-crown-4 (2.27 g, 11 mmol), sodium hydride (720 mg, 30 mmol), and dioxane (100 mL) were put in a three-necked flask, and the mixture was refluxed. A dioxane solution (20 mL) of crude 4-chloromethylbenzoic acid methyl ester (1.85 g, 10 mmol) was added dropwise and the reaction mixture was then refluxed for 5 h. Methanol was added to the cooled reaction mixture to quench the excess sodium hydride, and the solvent was then evaporated. Aqueous hydrochloric acid (5 wt%) was added to acidify the residue, and the product was extracted with chloroform. The organic layer was separated, and the crude product (quantitative) obtained as a brownish liquid by solvent evaporation was used for the subsequent synthesis after drying.

4.2.3. Compound G0-OH. Lithium aluminum hydride (760 mg, 20 mol) and THF (100 mL) were put in a three-necked flask. A THF solution (20 mL) of crude 4-(12-crown-4-methoxymethyl)benzoic acid methyl ester (3.54 g, 10 mmol) was added dropwise at room temperature, and the reaction mixture was refluxed for 20 h. Concentrated aqueous hydrochloric acid was added dropwise to the cooled reaction mixture to quench the excess lithium aluminum hydride. The solvent was evaporated, and water was poured into the obtained residue. The product was extracted with chloroform twice, and the organic layer was separated. The crude product obtained by solvent evaporation was purified by GPC to afford a colorless liquid product (63%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.4–3.9 (17H, m, OCH_2, OCH=), 4.54 (2H, s, $PhCH_2$), 4.68 (2H, s, $PhCH_2$), 7.31 (2H, d, $J=8.4$ Hz, ArH), 7.34 (2H, d, $J=8.4$ Hz, ArH); IR (neat, cm^{-1}): 3019 (CH_2), 1219 (OCH_2); *m/z* 349 ($M+Na^+$). Anal. Calcd for $C_{17}H_{26}O_6$: C 62.56, H 8.03, found: C 62.65, H 8.07.

4.2.4. Compound G0-Br. *Compound* **G0-OH** (652 mg, 2 mmol) and chloroform (50 mL) were put in a three-necked flask at room temperature. A chloroform solution (20 mL) of phosphorus tribromide (813 mg, 3 mmol) was added dropwise, and the reaction mixture was stirred for 1 h. The reaction mixture was poured into water, and the organic layer was separated. The crude product obtained by solvent evaporation was purified by GPC to give a colorless liquid product (77%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.4–3.9 (17H, m, OCH_2, OCH=), 4.49 (2H, s, $PhCH_2$), 4.54 (2H, s, $PhCH_2$), 7.30 (2H, d, $J=8.0$ Hz, ArH), 7.37 (2H, d, $J=8.0$ Hz, ArH).

4.2.5. Compound G1-OH. Under a nitrogen atmosphere, **G0-Br** (778 mg, 2 mmol), 3,5-dihydroxybenzyl alcohol (133 mg, 0.95 mmol), benzyloxymethyl-18-crown-6 (BnO18C6, 77 mg, 0.2 mmol), potassium carbonate (556 mg, 4 mmol) and acetone (50 mL) were put in a three-necked flask, and the mixture was refluxed for 3 days under nitrogen atmosphere. The solvent was evaporated, and aqueous hydrochloric acid (5 wt%) was poured to acidify the obtained residue. The product was extracted with chloroform, and the organic layer was separated. The crude product obtained by solvent evaporation was purified by GPC to yield a colorless liquid (94%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.4–3.9 (34H, m, OCH_2, OCH=), 4.54 (4H, s, $PhCH_2$), 4.60 (2H, s, $PhCH_2OH$), 5.01 (4H, s, $PhCH_2$), 6.52 (1H, s, ArH), 6.61 (2H, s, ArH), 7.33 (4H, d, $J=7.6$ Hz, ArH), 7.38 (4H, d, $J=7.6$ Hz, ArH); IR (neat, cm^{-1}): 3020 (CH_2), 1215 (OCH_2); *m/z* 756 ($M+Na^+$). Anal. Calcd for $C_{41}H_{56}O_{13}$: C, 65.06; H, 7.46. Found: C, 65.18; H, 7.43.

4.2.6. Compound G1-Cl. *Compound* **G1-OH** (724 mg, 1 mmol), pyridine (474 mg, 6 mmol), and benzene (100 mL) were put in a three-necked flask at room temperature. A benzene solution (20 mL) of thionyl chloride (714 mg, 6 mmol) was added dropwise, and the reaction mixture was refluxed for 4 h. Concentrated aqueous hydrochloric acid was added dropwise to the cooled reaction mixture. The reaction mixture was poured into water, and the benzene layer was separated. The crude product obtained by solvent evaporation was purified by GPC to give a colorless liquid product (67%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.4–3.9 (34H, m, OCH_2, OCH=), 4.50 (2H, s, $PhCH_2Cl$), 4.55 (4H, s, $PhCH_2$), 5.02 (4H, s, $PhCH_2$), 6.55 (1H, s, ArH), 6.63 (2H, s, ArH), 7.34 (4H, d, $J=7.6$ Hz, ArH), 7.39 (4H, d, $J=7.6$ Hz, ArH).

4.2.7. Compound G2-OH. Under a nitrogen atmosphere, **G1-Cl** (1.485 g, 2 mmol), 3,5-dihydroxybenzyl alcohol (133 mg, 0.95 mmol), benzyloxymethyl-18-crown-6 (BnO18C6, 77 mg, 0.2 mmol), potassium carbonate (2.76 g, 20 mmol), catalytic amount of sodium iodide, and acetone (50 mL) were put in a three-necked flask, and the mixture was refluxed for 3 days under nitrogen atmosphere. The solvent was evaporated, and aqueous hydrochloric acid (5 wt%) was poured to acidify the obtained residue. The product was extracted with chloroform, and the organic layer was separated. The crude product obtained by solvent evaporation was purified by GPC to afford a pale-yellow liquid (39%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.4–3.9 (68H, m, OCH_2, OCH=), 4.54 (8H, s, $PhCH_2$), 4.60 (2H, s, $PhCH_2OH$), 4.96 (4H, s, $PhCH_2$), 5.02 (8H, s, $PhCH_2$), 6.51 (1H, s, ArH), 6.55 (2H, s, ArH), 6.58 (2H, s, ArH), 6.66 (4H, s, ArH), 7.33 (8H, d, $J=8.0$ Hz, ArH), 7.38 (8H, d, $J=8.4$ Hz, ArH); IR (neat, cm^{-1}): 3017 (CH_2), 1217 (OCH_2);

m/*z* 1640 (M+ Na^+). Anal. Calcd for $C_{89}H_{116}O_{27}$: C 66.07, H 7.23, found: C 66.00, H 7.13.

4.2.8. Compound G2-Cl. *Compound* **G2-OH** (1.55 g, 1 mmol), pyridine (474 mg, 6 mmol), and benzene (100 mL) were put in a three-necked flask at room temperature. A benzene solution (20 mL) of thionyl chloride (714 mg, 6 mmol) was added dropwise, and the reaction mixture was refluxed for 4 h. Concentrated aqueous hydrochloric acid was added dropwise to the cooled reaction mixture. The reaction mixture was poured into water, and the benzene layer was separated. The crude product obtained by solvent evaporation was purified by GPC to afford a pale-yellow liquid product (74%); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.4–3.9 (68H, m, OCH_2, OCH=), 4.51 (2H, s, $PhCH_2Cl$), 4.55 (8H, s, $PhCH_2$), 4.97 (4H, s, $PhCH_2$), 5.02 (8H, s, $PhCH_2$), 6.5 (3H, m, ArH), 6.62 (2H, s, ArH), 6.67 (4H, s, ArH), 7.34 (8H, d, $J=8.0$ Hz, ArH), 7.39 (8H, d, $J=8.4$ Hz, ArH).

4.2.9. Compound G3-OH. Under a nitrogen atmosphere, **G2-Cl** (3.14 g, 2 mmol), 3,5-dihydroxybenzyl alcohol (133 mg, 0.95 mmol), benzyloxymethyl-18-crown-6 (BnO18C6, 77 mg, 0.2 mmol), potassium carbonate (2.76 g, 20 mmol), a catalytic amount of sodium iodide, and acetone (50 mL) were put in a three-necked flask, and the mixture was then refluxed for 3 days under nitrogen atmosphere. The solvent was evaporated, and aqueous hydrochloric acid (5 wt%) was poured to acidify the obtained residue. The product was extracted with chloroform, and the organic layer was separated. The crude product obtained by solvent evaporation was purified by GPC to give a pale-yellow liquid (47%); ^1H NMR ($CDCl_3$, 400 MHz) δ 3.4–3.9 (136H, m, OCH_2, OCH=), 4.4–4.6 (18H, m, $PhCH_2$, $PhCH_2OH$), 4.8–5.0 (28H, m, $PhCH_2$) 6.5–6.7 (21H, m, ArH), 7.32 (16H, d, $J=6.4$ Hz, ArH), 7.38 (16H, d, $J=8.4$ Hz, ArH); IR (neat, cm^{-1}): 3015 (CH_2), 1215 (OCH_2); *m*/*z* 858.6 ((M+4Na^+)/4). Anal. Calcd for $C_{185}H_{236}O_{55}$: C, 66.53; H, 7.12. Found: C, 66.63; H, 7.11.

4.3. NMR spectra measurements

NMR measurement was carried out in the presence or absence of various metal perchlorates or picrates in acetonitrile-d3 at room temperature. The concentrations of $LiClO_4$ and $NaClO_4$ were 1×10^{-2} mol dm^{-3}, and that of **G3-OH** was 1×10^{-3} mol dm^{-3}. Because of the low solubility, the concentrations of $KClO_4$, $RbClO_4$, and $CsClO_4$ were 5×10^{-3} mol dm^{-3} and the concentration of **G3-OH** was 5×10^{-4} mol dm^{-3}. In the cases of alkaline-earth metal perchlorates, a precipitation was formed with **G3-OH** solution (1×10^{-3} mol dm^{-3}), when the concentration of metal ions was more than 1×10^{-4} mol dm^{-3}. For metal picrates, the concentration of **G3-OH** was 5×10^{-4} mol dm^{-3}, and that of lithium and sodium picrates was 2.5×10^{-3} mol dm^{-3}.

In order to examine the dendrimer effect, the concentrations of **G0∼3-OH** were 8×10^{-3}, 4×10^{-3}, 2×10^{-3}, and 1×10^{-3} mol dm^{-3}, respectively, and the concentration of lithium and sodium perchlorates was 1×10^{-2} mol dm^{-3}.

In the case of the binding constants determination, the concentrations of **G0∼3-OH** were 8×10^{-3}, 4×10^{-3}, 2×10^{-3}, and 1×10^{-3} mol dm^{-3}, respectively, for Li^+ and Na^+. On the other hand, in the cases of K^+, Rb^+, and Cs^+, the concentrations of **G0∼3-OH** were 4×10^{-5}, 2×10^{-3}, 1×10^{-3}, and 5×10^{-4} mol dm^{-3}, respectively.

The sum of the concentrations for **G3-OH** and $LiClO_4$ was 1×10^{-2} mol dm^{-3} for Job plots.

For the T_1 measurement, the concentrations of **G0∼3-OH** solutions were 8×10^{-3}, 4×10^{-3}, 2×10^{-3}, and 1×10^{-3} mol dm^{-3}, respectively. On the other hand, the concentration of metal ions was 1×10^{-2} mol dm^{-3}. A weighted average was adopted as the T_1 value of coupling peaks.

4.4. ESI-MS spectra measurements

ESI-MS measurement was carried out using acetonitrile as the solvent. The concentration of **G3-OH** was 1×10^{-5} mol dm^{-3}, and that of metal perchlorate was 1×10^{-4} or 1×10^{-3} mol dm^{-3}.

4.5. UV–vis spectra measurements

The concentrations for metal picrates and **G3-OH** were 5×10^{-5} mol dm^{-3}, and THF and CH_3CN of spectroscopic grade were used. For measurements, a quarts cell which has a 10 mm light path length was used.

4.6. AFM measurements

A CH_3CN solution of **G3-OH** whose concentration was 1×10^{-4} mol dm^{-3} was put on graphite plate, and the sample was dried for several hours. Without metal ion, thickness of the **G3-OH** layer was less than 20 nm. In the presence of an equal amount of $NaClO_4$ (1×10^{-4} mol dm^{-3}), however, **G3-OH** formed a particle, the radius, of which was several hundreds nm. The reason for why the addition of $NaClO_4$ to **G3-OH** caused such a significant morphology change of **G3-OH** under dry conditions is not understood yet.

Acknowledgements

We are very much indebted to Japan Society for Promotion of Science (JSPS) for the financial support of this work by a Grant-in-Aid for JSPS fellows. We also thank Ms. Eiko Muro and Ms. Sachiko Namba for their experimental assistance.

References and notes

1. (a) Sasaki, H.; Ueno, A.; Anzai, J.; Osa, T. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1953–1956. (b) Inouye, M.; Akamatsu, K.; Nakazumi, H. *J. Am. Chem. Soc.* **1997**, *119*, 9160–9165. (c) Kimura, K.; Yamashita, T.; Yokoyama, M. *J. Phys. Chem.* **1992**, *96*, 5614–5617. (d) Ahmed, S. A.; Tanaka, M.; Ando, H.; Iwamoto, H.; Kimura, K. *Tetrahedron* **2004**, *60*, 3211–3220. (e) Tanaka, M.; Ikeda, T.; Xu, Q.; Ando, H.;

Shibutani, Y.; Nakamura, M.; Sakamoto, H.; Yajima, S.; Kimura, K. *J. Org. Chem.* **2002**, *67*, 2223–2227. (f) Salhin, A. M. A.; Tanaka, M.; Kamada, K.; Ando, H.; Ikeda, T.; Shibutani, Y.; Yajima, S.; Nakamura, M.; Kimura, K. *Eur. J. Org. Chem.* **2002**, 655–662. (g) Tanaka, M.; Nakamura, M.; Salhin, A. M. A.; Ikeda, T.; Kamada, K.; Ando, H.; Shibutani, Y.; Kimura, K. *J. Org. Chem.* **2001**, *66*, 1533–1537.

2. *Dendric Molecules: Concepts, Synthesis, Perspectives*; Newkome, G. R., Moorefield, C. N.F, Vögtle, F., Eds.; VCH: Weinheim, 1996.
3. (a) Marchion, F.; Venturi, M.; Credi, A.; Balzani, V.; Belohradski, M.; Elizarov, A. M.; Tseng, H.; Stoddart, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 568–573. (b) Paulo, P. M. R.; Gronheid, R.; Schryver, F. C. D.; Costa, S. M. B. *Macromolecules* **2003**, *36*, 9135–9144. (c) Dirksen, A.; Hahn, U.; Schwanke, F.; Nieger, M.; Reek, J. N. H.; Vögtle, F.; Cola, L. D. *Chem. Eur. J.* **2004**, *10*, 2036–2047. (d) Langereis, S.; Lussanet, Q. G. d.; Genderen, M. H. P. v.; Backes, W. H.; Meijer, E. W. *Macromolecules* **2004**, *37*, 3084–3091.
4. (a) Launay, N.; Slany, M.; Caminade, A.; Majoral, J. P. *J. Org. Chem.* **1996**, *61*, 3799–3805. (b) Larre, C.; Bressolles, D.; Turrin, C.; Donnadieu, B.; Caminade, A.; Majoral, J. *J. Am. Chem. Soc.* **1998**, *120*, 13070–13082.
5. (a) Nagasaki, T.; Kimura, O.; Ukon, M.; Arimori, S.; Hamachi, I.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 75–81. (b) Stephan, H.; Spies, H.; Johannsen, B.; Gloe, K.; Gorka, M.; Vögtle, F. *Eur. J. Inorg. Chem.* **2001**, 2957–2963. (c) Beer, P. D.; Gao, D. *Chem. Commun.* **2000**, 443–444. (d) Fulton, D. A.; Cantrill, S. J.; Stoddart, J. F. *J. Org. Chem.* **2002**, *67*, 7968–7981. (e) Jones, J. W.; Bryant, W. S.; Bosman, A. W.; Janssen, R. A. J.; Meijer, E. W.; Gibson, H. W. *J. Org. Chem.* **2003**, *68*, 2385–2389.
6. Gitsov, I.; Ivanova, P. T. *Chem. Commun.* **2000**, 269–270.
7. (a) Percec, V.; Johansson, G.; Ungar, G.; Zhou, J. *J. Am. Chem. Soc.* **1996**, *118*, 9855–9866. (b) Percec, V.; Cho, W.; Ungar, G.; Yeardley, D. J. P. *Chem. Eur. J.* **2002**, *8*, 2011–2025.
8. Young, J. K.; Baker, G. R.; Newkome, G. R.; Morris, K. F.; Johnson, C. S., Jr. *Macromolecules* **1994**, *27*, 3464–3471.
9. Bosman, A. W.; Janssen, H. M.; Meijer, E. W. *Chem. Rev.* **1999**, *99*, 1665–1688.
10. (a) Maeda, T.; Ouchi, M.; Kimura, K.; Shono, T. *Chem. Lett.* **1981**, 1573–1574. (b) Flink, S.; Boukamp, B. A.; Berg, A.v. d.; Veggel, F.C.J.M. v.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1998**, *120*, 4652–4657.
11. (a) Sadamoto, R.; Tomioka, N.; Aida, T. *J. Am. Chem. Soc.* **1996**, *118*, 3978–3979. (b) Jiang, D.; Aida, T. *J. Am. Chem. Soc.* **1998**, *120*, 10895–10901. (c) Enomoto, M.; Aida, T. *J. Am. Chem. Soc.* **1999**, *121*, 874–875.
12. (a) Inouye, M.; Hyodo, Y.; Nakazumi, H. *J. Org. Chem.* **1999**, *64*, 2704–2710. (b) Wall, S. L. D.; Meadows, E. S.; Barbour, L.; Gokel, G. W. *J. Am. Chem. Soc.* **1999**, *121*, 5613–5614. (c) Bartoli, S.; Roelens, S. *J. Am. Chem. Soc.* **1999**, *121*, 11908–11909.
13. (a) Kleinpeter, E.; Grotjahn, E.; Klika, K. D.; Drexler, H.; Holdt, H. *J. Chem. Soc., Perkin Trans. 2* **2001**, 988–993. (b) Mizugaki, T.; Murata, M.; Ooe, M.; Ebitani, K.; Kaneda, K. *Chem. Commun.* **2002**, 52–53.
14. *Binding Constants*; Connors, K. A., Ed.; Wiley: New York, 1987.
15. (a) Pedersen, C. J.; Frensdorff, H. K. *Angew. Chem.* **1972**, *84*, 16–26. (b) Popov, A. I.; Lehn, J. M. In *Coordination Chemistry of Macrocyclic Compounds*; Nelson, G. A., Ed.; Plenum: New York, 1979. (c) Weber, E.; Vögtle, F. In *Host-Guest Complex Chemistry: Macrocycles*; Vögtle, F., Weber, E., Eds.; Springer: Berlin, 1995.
16. (a) Pedersen, C. J. *J. Am. Chem. Soc.* **1970**, *92*, 386–391. (b) Frensdorff, H. K. *J. Am. Chem. Soc.* **1971**, *93*, 600–606. (c) Bourgoin, M.; Wong, K. H.; Hui, J. Y.; Smid, J. *J. Am. Chem. Soc.* **1975**, *97*, 3462–3467. (d) Kimura, K.; Tsuchida, T.; Maeda, T.; Shono, T. *Talanta* **1980**, *27*, 801–805.
17. Allcock, H. R.; Olmeijer, D. L.; O'Connor, S. J. M. *Macromolecules* **1998**, *31*, 753–759.
18. Bourgoin, M.; Wong, K. H.; Hui, J. Y.; Smid, J. *J. Am. Chem. Soc.* **1975**, *97*, 3462–3467.