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Synthesis, Structures and Ion Selectivity of Homocalix[3]arene Thioketals derived from Homocalix[3]arene Ketones

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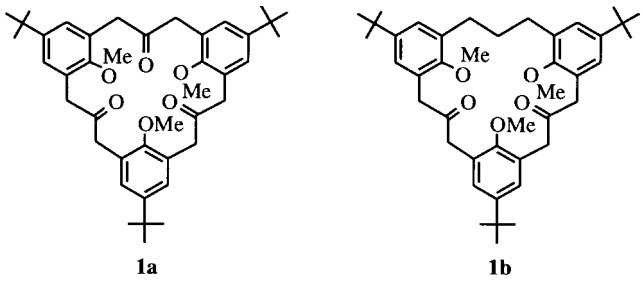
Abstract

The ^{1}H NMR spectrum of [3.3.3]metacyclophane triketone **1a** showed its flexible structure even at −80 °C in $CDCl_3$-CS_2 (1:3 v/v). In contrast, the cyclic thioketal derivative **2a** is fixed with a "partial-cone" conformation below −10 °C by the observation of the splitting pattern for the benzylic protons (J = 14.2 Hz), besides other changes in both the aromatic and aliphatic regions of the ^{1}H NMR spectrum. The coalescence temperature (T_c) for the benzylic methylene protons is 0 °C and the free energy of activation for ring inversion is estimated as 13.2 kcal mol^{-1}. Titration of the cyclic thioketal derivative **2a** with $AgSO_3CF_3$ in acetone-d_6-$CDCl_3$ (3:1 v/v) monitored by ^{1}H NMR clearly demonstrates that a 1:1 complex is formed with retention of the original symmetry. A 1:1 complexation of **2a** with Ag^+ was also confirmed by the experiment using the mole ratio method. The two-phase solvent extraction data indicated that the cyclic thioketal derivatives **2a** and **2b** show a strong Ag^+ affinity and a high Ag^+ selectivity was observed. On the contrary, the triketone **1a** shows a poor Ag^+ affinity. Thus, the synergism of the cyclophane moiety and two or three ethanedithia groups play a significant role on the complexation of tris- and bis-thioketals **2a** and **2b** with Ag^+ cation.

Introduction

Calixarenes can, in principle, be chemically modified at the three reacting sites: the hydroxy groups, aromatic rings and the methylene bridges. While the functionalization of the calixarenes at both rims has been extensively studied in the last decade [1–3], there has been a relatively small number of researches describing the modification of the methylene group owing to the relatively inert reactivity on this site. Moshfegh *et al.* [4] reported that calixarene esters react with chromic acid to undergo oxidation at the methylene bridges to give ketones, although the products are not well characterized. Ninagawa and coworkers have made similar observations and have identified the product ketones [5]. Therefore, the selective preparation of calixarene ketones using the direct oxidation method is difficult because of its low yield as well as the difficulty of the product separation from the other macrocyclic oligoketones. Therefore, it has been very difficult to obtain sufficient amounts of the above compounds to investigate their chemical behaviour.

Recently, Böhmer *et al.* [6] reported the selective replacement of the carbonyl group at a single methylene bridge of calix[4]arene by cyclocondensation of the appropriate monohydroxymethylated linear precursors in yields of 40–60%. However, the preparative routes of monohydroxymethylated linear precursors from easily available compounds seems to be too long for practical purposes.



1a **1b**

Chart 1.

Therefore, functionalization of the methylene bridges of calixarenes have been very limited.

As another direction for the modification of the methylene moiety the syntheses of calixarene analogs have been described, which were constructed by changing the methylene bridges to trimethylene bridges or dimethylene heteroatom bridges such as homooxa-, homoaza-, and homothiacalixarenes [7–9]. Recently, we reported [10] the preparation of carbocyclic [3.3.3]MCP (MCP = metacyclophane) ketones **1a** and **1b** using (*p*-tolylsulfonyl)methyl isocyanide (TosMIC) [11] as the cyclization reagent, which was applied in a new cyclization procedure without phase-transfer conditions (Chart 1) [12].

Cyclophanes with aromatic rings linked through $-CH_2COCH_2-$ bridges are of special interest because of the ease with which the carbonyl groups can be converted into other functional groups. For example, the conversion of the

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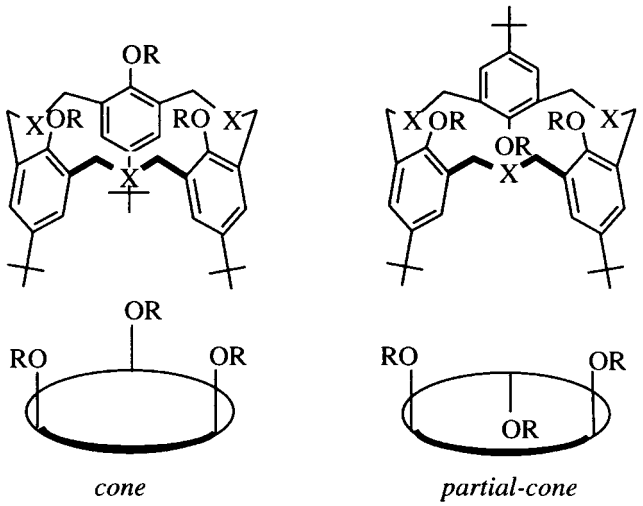


Figure 1. Two possible conformers of [3.3.3]metacyclophanes.

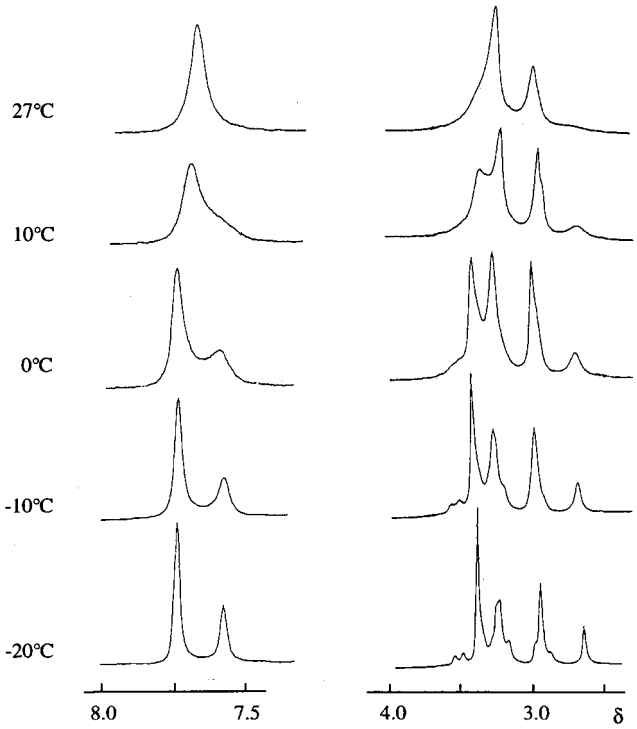


Figure 2. Dynamic ^{1}H NMR spectra of **2a** ($CDCl_3$–CS_2 1/3; 270 MHz).

carbonyl groups into dithio groups yields hosts with sulfur atoms which can serve as further binding units for molecular recognition. In this paper, we describe the functionalization of carbonyl groups of [3.3.3]MCP ketones having C_2 or C_3 symmetry, synthesized by an improved TosMIC method and their conformational and inclusion properties.

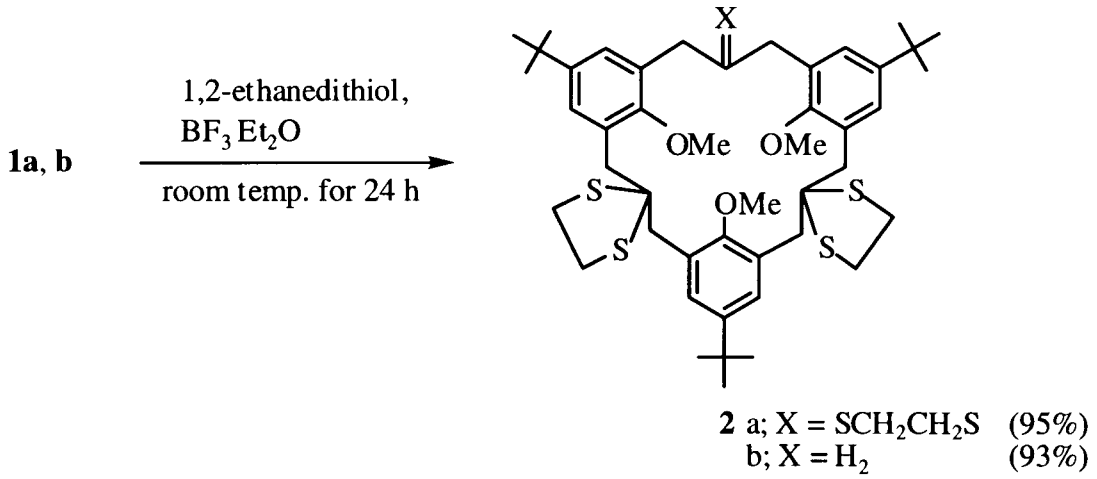
Results and discussion

The preparation of 6,15,24-tri-*tert*-butyl-9,18,27-trimethoxy[3.3.3]MCP-2,11,20-trione (**1a**) and 6,15,24-tri-*tert*-butyl-9,18,27-trimethoxy[3.3.3]MCP-2,11-dione (**1b**) using (*p*-tolylsulfonyl)-methylisocyanide (TosMIC) as the cyclization reagent was previously reported [10]. In an attempted conversion of the flexible [3.3.3]MCP ketones **1a** and **1b** into rigid host compounds to be used for complexation studies, sulfurization reactions were carried out on them. Thus triketone **1a** and diketone **1b** were converted into cyclic thioketal derivatives **2a** and **2b** in 95 and 93% yields, respectively.

The structures of **2a** and **2b** have been elucidated by elemental analyses and spectral data. For instance, the mass spectral data for **2a** and **2b** (M^+ = 882 and 792) strongly support thioketal structures, respectively. The IR spectra of **2a** and **2b** show the disappearance of absorption of the carbonyl stretching vibration around 1706 and 1720 cm^{-1}, respectively. On the other hand, there are only two possible conformations in [3.3.3]MCPs as shown in Figure 1 [10].

The ^{1}H-NMR spectrum (in $CDCl_3$) of **2a** at room temperature exhibits two broad singlets at δ 3.0 and 3.3 for the ArCH_2C(SCH_2)$_2$$CH_2$Ar methylene protons, and ethanedithia groups and the internal methoxy groups and a broad singlet for the aromatic protons at δ 7.69. This observation strongly indicates the cyclophane ring to be flexibly the same as in the parent triketone **1a** at this temperature. However, at −20 °C in $CDCl_3$–CS_2 (1:3 v/v) the two broad singlet signals at around δ = 2–4 exibited the split pattern, of which a set of doublets (J_{AB} = 14.2 Hz) at δ 3.21 and 3.50 for ArCH_2C(SCH_2)$_2$$CH_2$Ar methylene protons were observed, the aromatic protons are also observed to be split at δ 7.59 and 7.74 as broad singlets (relative intensity, 1:2) (Figure 2).

Thus, these findings are rationalized by the frozen rigid structure of macrocycle **2a**. In macrocycle **2a**, two kinds of methoxy groups were observed with one showing up at a higher field, δ 2.69 and the other at δ 3.37 in a ratio of 1:2. The former is, most likely, the methoxy group on the inverted aromatic which lies in the shielding zone of the other two benzene rings. The splitting pattern in the low temperature ^{1}H NMR also shows that tris(thioketal) derivative **2a** adopts a partial-cone conformation. The temperature of coalescence is 0 °C and the free energy of activation for inversion is estimated to be 13.2 kcal mol^{-1}. The rate of conformational ring flipping of **2a** is faster than the NMR time scale above this temperature. The value of the free energy of activation for inversion is larger than that of triketone **1a** (T_c < −80 °C in $CDCl_3$–CS_2 (1:3 v/v)) [10]. Thus this indicates that the tris(thioketal) **2a** is more rigid than the triketone **1a** due to the conversion of ketone to the sp^3-spiro skeleton. On the other hand, in the ^{1}H-NMR spectrum (in $CDCl_3$-CS_2 (1:3 v/v)) of bis(thioketal) derivative **2b** the *tert*-butyl protons and the aromatic protons appeared as two singlets at δ 1.30, 1.34 (relative intensity 2:1) and a set of doublets at δ = 7.06, 7.56 (J = 2.4 Hz) and a singlet at δ = 7.78 (relative intensity 2:1) at room temperature. Although 2-partial-cone or 3-partial-cone conformers are possible in the *partial-cone*-**2b**, these patterns correspond to the former conformer due to the C_2 symmetric structure but not the unsymmetric structure (Figure 3). It was also found that the inverted benzene protons are observed at δ = 7.78 as a singlet which is in a strongly deshielding region of the sulfur atoms of two ethanedithia groups. In contrast to **2a** the protons of the benzylic protons around δ 3.30–3.37 only appear as a



Scheme 1.

Table 1. Extraction (%) of silver picrate in CH_2Cl_2[a]

Ionophore	Extraction (%)
2a	82
2b	62
6	18
8	7

[a]Extraction (%) of alkali metal picrates by ionophores in CH_2Cl_2. Extraction conditions; 2.5×10^{-4} M of ionophore in CH_2Cl_2; 2.5×10^{-4} M of picric acid in 0.1M of $AgNO_3$ at 25 °C. Ionophore solution (5.0 mL) was shaken for 2 h with picrate solution (5.0 mL) and the % extraction was measured by the absorbance of picrate in CH_2Cl_2. Experimental error was ±2%.

broad singlet even below −80 °C and the rate of conformational ring flipping of **2b** is faster than the NMR time scale above this temperature. This indicates that the bis(thioketal) derivative **2b** is much more flexible than the tris(thioketal) derivative **2a**.

Organosulfur compounds are known to bind strongly to gold surfaces, thus making it possible for several self-assembled monolayers of absorbates with a surface-active sulfur group, an alkyl chain, and a terminal functional group to be synthesized [13]. Reinhoudt and his co-workers have recently reported the synthesis of various resorcin[4]arene absorbates with four dialkyl sulfide chains underneath, a receptor which they used in detecting a specific gas [14]. It is thus interesting to assess what kind of ionophoric cavity the tris(thioketal) (**2a**) and bis(thioketal) derivative **2b** provide. To the best of our knowledge, however, no precedent exists for the molecular design of such propane-bridged calixarene analogous metacyclophane-based ionophores. The cation binding properties of **2a** and **2b** were examined by the liquid–liquid extraction method.

Although tris(thioketal) (**2a**) and bis(thioketal) derivative **2b** both hardly extracted alkali metal cations and *n*-butylammonium cation under the experimental conditions used, high extractability for Ag^+ was observed for tris(thioketal) **2a** and bis(thioketal) **2b** (Table 1). The present extractability for Ag^+ (extraction %: 82%) are superior than that of commercially available dibenzopyridino-18-crown-6 (extraction %: 65%) [15]. In contrast, the parent triketone **1a** hardly extracted Ag^+ cation in these experimental conditions (extraction %: less than 1%). It was also found that the reference compound 1,3-bis[(5-*tert*-butyl-2-methoxy-3-methyl)phenyl]-2-(ethanedithia)propane **6**, which was prepared by treatment of ketone **5** with 1,2-ethanedithiol in 85% yield, shows only low extractability for Ag^+ cation in these experimental conditions (extaraction %: 18%).

In order to study the synergism of the cyclophane moiety in more detail, we have also prepared the corresponding bis(thioketal) **8**, which was prepared by treatment of 6,15-di-*tert*-butyl-9,18-dimethoxy[3.3]MCP-2,11-dione **7** [12b] with 1,2-ethanedithiol in 49% yield. Bis(thioketal) **8** also shows only low extractability for Ag^+ cation in these experimental conditions (extraction %: 7%). Therefore, the synergism of the cyclophane moiety and the sulfur atoms in the ethanedithia groups on the propane bridges plays a significant role on the complexation of tris(thioketal) derivative **2a** with Ag^+ cation.

Recently, Shinkai *et al.* [16] reported that the 1,3-alternate conformer of calix[4]arene tetraester can form both a 1:1 and a 2:1 metal/calixarene complex and the two metal-binding sites display negative allostericity by ^1H NMR titration experiment. In the present systems, due to the existence of three metal-binding sites of the thioketal moiety there are several possibilities for the metal complexation mode. Thus, a 1:1, 2:1 and 3:1 metal complexation of **2a** might be possible.

As shown in Figure 4, the percent extractions reach maximum at 0.5 mole fraction for this cation. This fact clearly indicates that Ag^+ forms a 1:1 complex with **2a**. Thus we could prove the synergism of the cyclophane moiety and the three thioketal moieties in the complexation. In order to prove the synergism between the cyclophane moiety and the three thioketal moieties on the propane bridges in more detail, we examined the ^1H NMR chemical shift differences between those before and after the addition of an equimolar $AgSO_3CF_3$, and the composition of the ion-ionophore complex. Titration of cyclic tris(thioketal) derivative **2a** with $AgSO_3CF_3$ in acetone-d_6-$CDCl_3$ (3:1 v/v), monitored by ^1H NMR, clearly demonstrated that a 1:1 complex with a

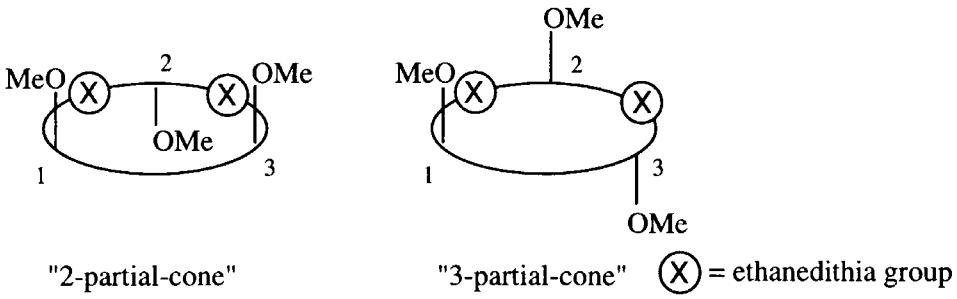
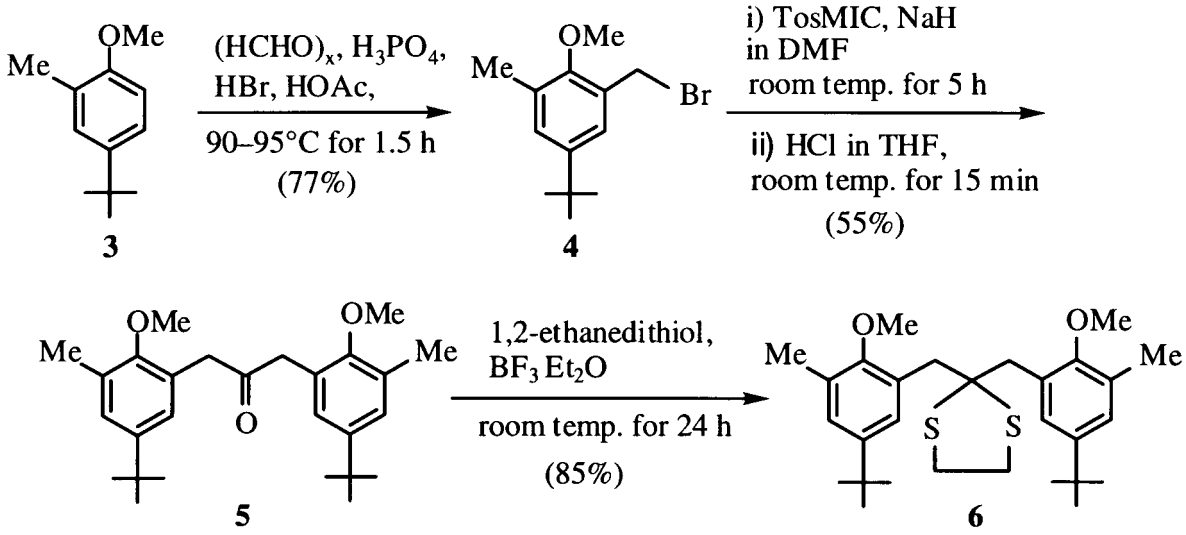


Figure 3. Conformers possible for *partial-cone*-**2b**.



Scheme 2.

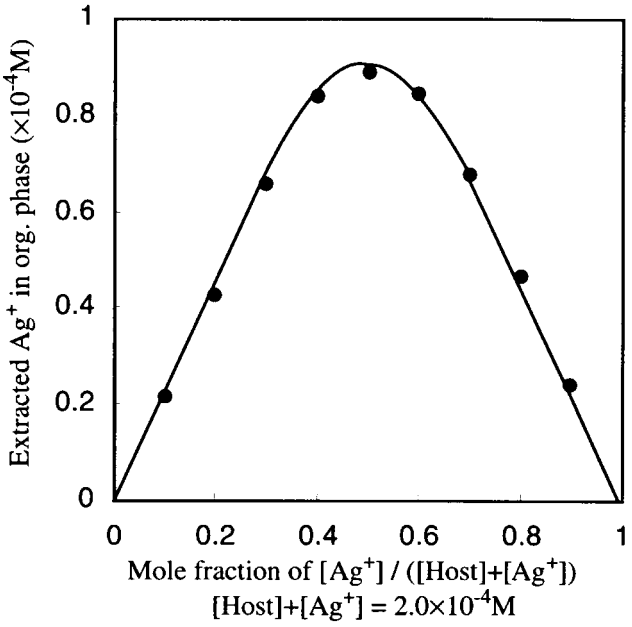
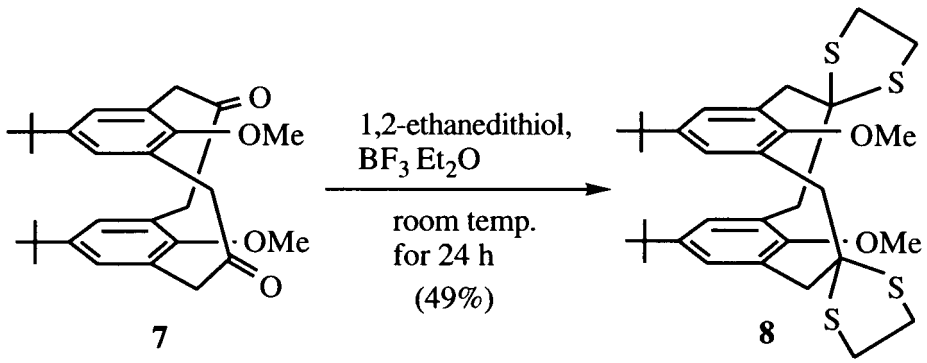


Figure 4. Job plots of the extractions of Ag^+ with host **2a**.

partial-cone conformation might be formed which is stable on the NMR time scale.

In fact, the chemical shifts of a broad singlet around δ 7.69 for the aromatic protons of **2a** were altered by titration with $AgSO_3CF_3$: i.e., a 1:3 mixture of **2a** and $AgSO_3CF_3$ showed a completely different ^1H NMR spectrum with three broad lines at δ 7.58, 7.67 and 7.84 (relative intensity, 1:1:1) becoming evident for these protons. The upper field shift for the aromatic protons might indicate the contribution of the π-electrons of the benzene ring to the complexation by the cation-π interactions [18]. Interestingly, the two broad singlet signals around at δ = 2–4 exhibited the split pattern even at room temperature, which are similar to those for the original ^1H NMR spectrum below −20 °C in the absence of Ag^+. This phenomenon indicates that the conformation ring flipping of the flexible thioketal derivative **2a** could be frozen in the process of the complexation with Ag^+ cation at this temperature. The lone pairs of electrons on the sulfur atoms and the π-electrons of the benzene ring might be responsible for the binding of the silver cation. Thus these two groups arrange themselves in a manner forming pockets into which the silver cation enters. These findings strongly support the contribution of the sulfur atoms of thioketal moieties to Ag^+-binding as well as the cation-π interaction [17, 18] demonstrated by Shinkai *et al.* in the high Ag^+ affinity of 1,3-alternate-calix[4]arene [19]. They have also reported the intramolecular tunnelling of Ag^+ through the cavity of the 1,3-alternate conformer of calix[4]arene, a motion that they named "Metal Tunnelling" [19].

Interestingly, the ^1H-NMR spectrum of a 1:1 mixture of **2a** and Ag^+ in acetone-d_6-$CDCl_3$ (3:1 v/v) at room temperature exhibits a broad singlet for the aromatic protons at δ 7.63 (Figure 5). This observation strongly indicates



Scheme 3.

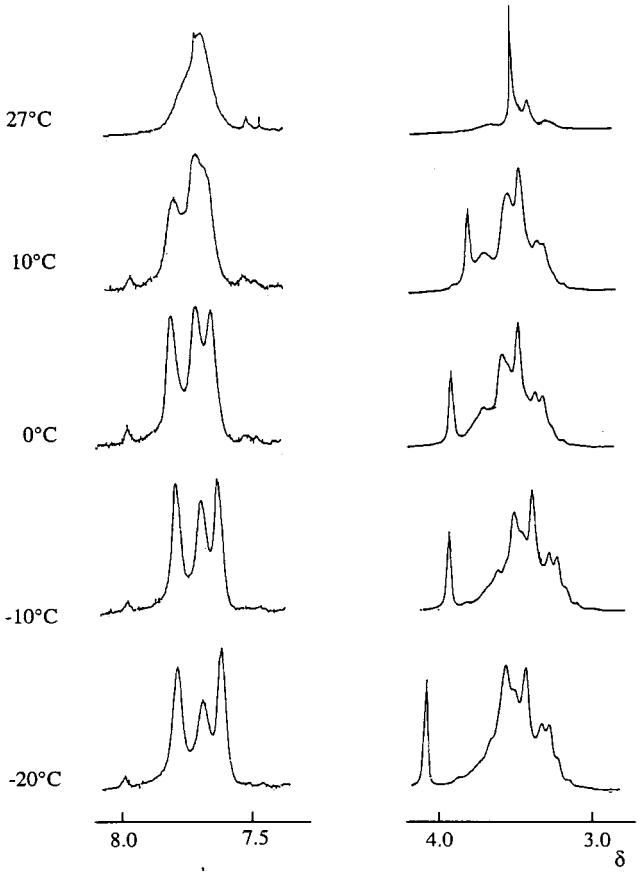


Figure 5. Partial VT ^{1}H NMR spectra of a 1:1 mixture of **2a** and $AgSO_3CF_3$ (acetone-d_6-$CDCl_3$ 3/1; 270 MHz).

that the cyclophane ring is still as flexible as in **2a** at this temperature. Upon decreasing the temperature, the broad singlet signal split to three singlet signals around δ 7.61, 7.69 and 7.78 in the integral ratio of 1:1:1. This behaviour is rationalized by the three non-equivalent aromatic protons in the partial-cone conformation with C_2 symmetry. In other words, the conformational ring flipping with Ag^+ cation in the ionophilic cavity of the host molecule **2a** occurred above room temperature, but it was frozen below 0 °C.

More detailed examination of the chemical shift change in the ^{1}H NMR titration experiment of tris(thioketal) derivative **2a** with $AgSO_3CF_3$ suggests that Ag^+ should be bound to the ionophoric cavity, which is composed of three phenolic oxygens, three sulfurs of ethanedithia groups and three benzene rings. Interestingly, the inverted methoxy protons at δ 2.69 disappeared and shifted to lower field after complexation with Ag^+. This finding strongly suggests that the methoxy group on the inverted aromatic might be deviated from the shielding zone of the other two benzene rings. However, in this complex the assignment around δ 3–4 for the benzylic protons, methoxy protons and ethanedithia protons is very complicated. Hence, it is difficult to obtain useful information from the δ values for these protons. Further experiments on these metal complexations are currently in progress in our laboratory.

Conclusion

An interesting result was obtained by conversion of carbonyl groups of [3.3.3]MCP ketones into ethanedithia groups. We have demonstrated for the first time that the functionalization of the flexible macrocycles **1** with 1,2-ethanedithiol gave bis- and tris(ethanedithia) derivatives **2** with partial-cone conformation. A two-phase solvent extraction experiment identified that the cyclic thioketal **2a** shows a strong Ag^+ affinity thus making it possible for a high Ag^+ selectivity to be observed. Titration of the cyclic thioketal **2a** with $AgSO_3CF_3$ in acetone-d_6-$CDCl_3$ (3:1 v/v) monitored by ^{1}H NMR clearly demonstrates that a 1:1 complex with a "partial-cone" conformation is formed which is stable on the NMR time scale below 0 °C. The synergism of the cyclophane moiety and two or three ethanedithia groups on the bridged chains play a significant role in the complexation of bis- and tris(ethanedithia) derivatives **2a** and **2b** with Ag^+ cation. These results consistently suggest that [3.3.3]MCP ketones are useful basic skeletons for the design of artificial receptors, particularly those with C_3 symmetry.

Experimental

All mps (Yanagimoto MP-S_1) are uncorrected. NMR spectra were determined at 270 MHz with a Nippon Denshi JEOL FT-270 NMR spectrometer with $SiMe_4$ as an internal reference: *J*-values are given in Hz. IR spectra were measured for samples as KBr pellets or a liquid film on NaCl plates in

a Nipon Denshi JIR-AQ2OM spectrophotometer. UV spectra were measured by a Shimadzu 240 spectrophotometer. Mass spectra were obtained on a Nippon Denshi JMS-01SA-2 spectrometer at 75 eV using a direct-inlet system through GLC. Elemental analysis: Yanaco MT-5.

Materials

6,15,24-Tri-*tert*-butyl-9,18,27-trimethoxy[3.3.3]metacyclophane-2,11,20-trione (**1a**) and 6,15,24-tri-*tert*-butyl-9,18,27-trimethoxy[3.3.3]metacyclophane-2,11-dione (**1b**) were prepared as previously described [10b]. 6,15-Di-*tert*-butyl-9,18-trimethoxy[3.3]metacyclophane-2,11-dione (**7**) was prepared according to the reported procedure [12b].

Synthesis

Preparation of 2,11,20-[tris(ethanedithia)]-6,15,24-tri-tert-*butyl-9,18,27-trimethoxy[3.3.3]metacyclophane (***2a***)*

To a solution of 204 mg (0.312 mmol) of **1a** and 1,2-ethanedithiol (0.5 mL, 5.96 mmol) in acetic acid (10 mL) was added boron trifluoride etherate (BF_3OEt_2) (0.1 mL, 0.392 mmol) under nitrogen and the reaction mixture stirred at room temperature for 24 h. The reaction mixture was poured into ice-water (50 mL), extracted with CH_2Cl_2 (2 × 50 mL). The combined extracts were washed with water (2 × 50 mL), dried (Na_2SO_4) and condensed under reduced pressure. The residue was chromatographed on silica gel (Wako C-300, 100 g) with chloroform as an eluent to give crude **2a**. Recrystallization from hexane gave the *title compound* **2a** (261 mg, 95%) as colorless prisms; m.p. 254–255 °C; ν_{max}(KBr)/cm^{-1} 2960, 2923, 2867, 2822, 1603, 1540, 1481, 1463, 1429, 1392, 1361, 1333, 1296, 1276, 1246, 1203, 1174, 1118, 1016, 956, 883; δ_H($CDCl_3$) (27 °C) 1.30 (27 H, s), 3.01 (9 H, broad s), 3.3 (24 H, broad s), 7.69 (6 H, broad s); δ_H(CS_2–$CDCl_3$ 3:1) (−20 °C) 1.29 (18 H, s), 1.34 (9 H, s), 2.69 (3 H, broad s), 2.98 (8 H, broad s), 3.21 (8 H, d, *J* 14.2), 3.19–3.24 (4 H, m), 3.37 (6 H, broad s), 3.50 (4 H, d, *J* 14.2), 7.59 (2 H, broad s), 7.74 (4 H, broad s); *m/z*: 882 (M^+); Found: C, 64.97; H, 7.27. Calcd. for $C_{48}H_{66}O_3S_6$: requires C, 65.26; H, 7.53%.

The splitting pattern in ^{1}H NMR shows that the isolated compound is *partial-cone*-**2a**.

Similarly, compound **2b** was obtained in 93% yield.

2,11-[Bis(ethanedithia)]-6,15,24-tri-*tert*-butyl-9,18,27-trimethoxy[3.3.3]metacyclophane (**2b**) was obtained as colorless prisms (from hexane); m.p. 168–169 °C; ν_{max}(KBr)/cm^{-1} 2955, 2925, 2866, 2824, 1503, 1500, 1481, 1453, 1392, 1352, 1331, 1295, 1276, 1244, 1202, 1174, 1115, 1016, 968, 825, 809; δ_H($CDCl_3$) 1.30 (18 H, s), 1.34 (9 H, s), 1.27–1.34 (4 H, m), 1.86–2.00 (2 H, m), 2.64 (6 H, broad s), 3.14 (3 H, broad s), 3.30–3.37 (16 H, m), 7.06 (2 H, d, *J* 2.4), 7.56 (2 H, d, *J* 2.4), 7.78 (2 H, s); *m/z*: 792 (M^+); Found: C, 69.81; H, 8.11. Calcd. for $C_{46}H_{64}O_3S_4$: requires C, 69.65; H, 8.13%.

*Preparation of 2-bromomethyl-4-*tert-*butyl-6-methylanisole (***4***)*

A mixture of 4-*tert*-butyl-2-methylanisole (**3**) (4.0 g, 22.4 mmol), paraformaldehyde (2.4 g), acetic acid (6 mL), H_3PO_4 (85%, 6 mL), and concentrated HBr (48%, 14 mL) was heated at 85–90 °C with vigorous stirring for 90 min. The reaction mixture was extracted with benzene (3 × 50 mL). The combined extracts were neutralized with a 10% aqueous Na_2CO_3 solution, washed with water, dried with Na_2SO_4, and the solvent was evaporated *in vacuo* to leave a residue, which was chromatographed on silica gel with hexane as the eluent to give the *title compound* **4** (4.7 g, 77%) as a colorless oil; δ_H($CDCl_3$) 1.29 (9 H, s), 2.30 (3 H, s), 3.85 (3 H, s), 4.58 (2 H, s), 7.15 (1 H, s), 7.20 (1 H, s).

*Preparation of 1,3-bis[(5-*tert*-butyl-2-methoxy-3-methyl)phenyl]-2-propanone (***5***)*

To a solution of bromide **4** (2 g, 7.4 mmol) and TosMIC (723 mg, 7.4 mmol) in DMF (40 mL) was added a suspension of NaH (400 mg, 10 mmol) in DMF (12 mL) dropwise over a period of 30 min. After the suspension was stirred for an additional 5 h at room temperature, it was quenched with ice-water (100 mL). The reaction mixture was extracted with CH_2Cl_2 (3 × 50 mL) and washed with water (100 mL), dried with Na_2SO_4 and concentrated. The residue was dissolved by THF (20 mL) and conc. HCl (7 mL) was added. Then the solution was stirred for 15 min. The organic layer was again extracted with CH_2Cl_2 (3 × 50 mL), washed with water (50 mL × 2), dried with Na_2SO_4, and concentrated under reduced pressure. The residue was chromatographed on silica gel using benzene-$CHCl_3$ (1:1) as eluent to give the *title compound* **5** (843 mg, 55.4%) as a pale yellow oil; δ_H($CDCl_3$) 1.27 (18 H, s), 2.29 (6 H, s), 3.63 (6 H, s), 3.75 (4 H, s), 6.96 (2 H, s), 7.08 (2 H, s); *m/z*: 410 (M^+); Found: C, 78.73; H, 9.57. Calcd. for $C_{27}H_{38}O_3$: requires C, 78.98; H, 9.33%.

*Preparation of 1,3-bis[(5-*tert*-butyl-2-methoxy-3-methyl)phenyl]-2-(ethanedithia)propane (***6***)*

To a solution of 100 mg (0.24 mmol) of **5** and 1,2-ethanedithiol (0.35 mL, 4.27 mmol) in acetic acid (6 mL) was added boron trifluoride etherate (BF_3OEt_2) (0.1 mL, 0.392 mmol) under nitrogen and the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was poured into ice-water (50 mL), extracted with CH_2Cl_2 (2 × 50 mL). The combined extracts were washed with water (2 × 50 mL), dried (Na_2SO_4) and condensed under reduced pressure. The residue was chromatographed on silica gel (Wako C-300, 100 g) with chloroform as an eluent to give the *title compound* **6** (100 mg, 85%) as colourless oil; ν_{max}(KBr)/cm^{-1} 2963, 2920, 1482, 1262, 1203, 1100, 1018, 799; δ_H($CDCl_3$) 1.29 (18 H, s), 2.29 (6 H, s), 2.88 (4 H, s), 3.31 (4 H, s), 3.63 (6 H, s), 7.06 (2 H, d, *J* 2.4), 7.53 (2 H, d, *J* 2.4); *m/z*: 486 (M^+); Found: C, 71.79; H, 8.67. Calcd. for $C_{29}H_{42}O_2S_2$: requires C, 71.56; H, 8.7%.

*Preparation of 2,11-[bis(ethanedithia)]-6,15-di-*tert*-butyl-9,18-dimethoxy[3.3]metacyclophane (***8***)*

To a solution of 100 mg (0.23 mmol) of 6,15-di-*tert*-butyl-9,18-dimethoxy[3.3]metacyclophane-2,11-dione (**7**) and 1,2-ethanedithiol (0.37 mL, 4.45 mmol) in acetic acid (6.0 mL) was added boron trifluoride etherate (BF_3OEt_2) (0.1 mL, 0.392 mmol) under nitrogen and the reaction mixture stirred at room temperature for 24 h. The reaction mixture was poured into ice-water (50 mL), extracted with CH_2Cl_2 (2 × 50 mL). The combined extracts were washed with water (2 × 50 mL), dried (Na_2SO_4) and condensed under reduced pressure. The residue was chromatographed on silica gel (Wako C-300, 100 g) with chloroform as an eluent to give crude **8**. Recrystallization from hexane gave the *title compound* **8** (66 mg, 48.9%) as prisms; m.p. 288–290 °C; ν_{max}(KBr)/cm^{-1} 2963, 2920, 1482, 1262, 1203, 1100, 1018, 799; δ_H($CDCl_3$) 1.14 (18 H, s), 3.09 (4 H, d, *J* 13.7), 3.39 (6 H, s), 3.48–3.50 (8 H, m), 3.91 (4 H, d, *J* 13.7), 7.23 (4 H, s); *m/z*: 588 (M^+); Found: C, 65.17; H, 7.42. Calcd. for $C_{32}H_{44}O_2S_4$: requires C, 65.26; H, 7.53%.

Picrate extraction measurements

Alkali metal picrates (2.5 × 10^{-4} M) were prepared *in situ* by dissolving the alkali metal hydroxide (0.01 mol) in 2.5 × 10^{-4} M picric acid (100 mL); triply distilled water was used for all aqueous solutions. Similarly, silver picrate was prepared *in situ* by dissolving silver nitrate in 2.5 × 10^{-4} M picric acid. Two-phase solvent extraction was carried out between water (5 mL, [alkali picrate] = 2.5 × 10^{-4} M) and CH_2Cl_2 (5 mL, [ionophore] = 2.5 × 10^{-4} M). The two-phase mixture was shaken in a stoppered flask for 2 h at 25 °C. We confirmed that this period is sufficient to attain the distribution equilibrium. This was repeated 3 times, and the solutions were left standing until phase separation was complete. The extractability was determined spectrophotochemically from the decrease in the absorbance of the picrate ion in the aqueous phase as described by Pedersen[20].

^{1}H NMR complexation experiment

To a $CDCl_3$ solution (5 × 10^{-4} M) of **2** in the NMR tube was added an acetone-d_6 solution (5 × 10^{-4} M) of $AgSO_3CF_3$. The spectrum was registered after addition and the temperature of the NMR probe kept constant at 27 °C.

References

1. (a) C.D. Gutsche: *Calixarenes*, Royal Society of Chemistry, Cambridge, 1989. (b) J. Vicens and V. Böhmer: *Calixarenes: A Versatile Class of Macrocyclic Compounds*, Kluwer Academic Publishers, Dordrecht, 1990. (c) C.D. Gutsche: *Calixarenes Revisited*, Royal Society of Chemistry, Cambridge, 1998.
2. C.D. Gutsche, B. Dhawan, K.H. No, and R. Muthukrishnan: *J. Am. Chem. Soc.* **103**, 3782 (1981).
3. (a) C.D. Gutsche: *Acc. Chem. Res.* **16**, 161 (1983). (b) C.D. Gutsche and L.J. Bauer: *J. Am. Chem. Soc.* **107**, 6052 (1985). (c) J.D. van Loon, L.C. Groenen, S.S. Wijmenga, W. Verboom, and D.N. Reinhoudt: *J. Am. Chem. Soc.* **113**, 2378 (1991). (d) L.C. Groenen, J.D. van Loon, W. Verboom, S. Harkema, A. Casnati, R. Ungaro, A.Pochini, F. Ugozzoli, and D.N. Reinhoudt: *J. Am. Chem. Soc.* **113**, 2385 (1991).
4. (a) A.A. Moshfegh, R. Badri, M. Hojjatie, M. Kaviani, B. Naderi, A. H. Nazmi, M. Ramezanian, B. Roozpeikar, and G.H. Hakimelahi: *Helv. Chim. Act.* **65**, 1221 (1982). (b) A.A. Moshfegh, B. Mazandarani, A. Nahid, and G.H. Hakimelahi: *Helv. Chim. Act.* **65**, 1229 (1982). (c) A.A. Moshfegh, E. Beladi, L. Radnia, S. Tofigh, and G.H. Hakimelahi: *Helv. Chim. Act.* **65**, 1264 (1982).
5. A. Ninagawa, K. Cho, and H. Matsuda: *Makromol. Chem.* **186**, 1379 (1985).
6. (a) M. Tabatabai, W. Vogt, and V. Böhmer: *Tetrahedron Lett.* **31**, 3295 (1990). (b) C. Grüttner, V. Böhmer, W. Vogt, I. Thondorf, S.E. Biali, and F. Grynszpan: *Tetrahedron Lett.* **35**, 6267 (1994). (c) S.E. Biali, V. Böhmer, S. Cohen, G. Ferguson, C. Grüttner, F. Grynszpan, E.F. Paulus, I. Thondorf, and W. Vogt: *J. Am. Chem. Soc.* **118**, 12938 (1996). (d) V. Böhmer: *Liebigs Ann.* 1997, 2019.
7. (a) M. Bergamaschi, F. Bigi, M. Lanfranchi, R. Maggi, A. Pastorio, M.A. Pellinghelli, F. Peri, C. Porta, and G. Sartori: *Tetrahedron* **53**, 13037 (1997). (b) K. Araki, K. Akao, H. Otsuka, K. Nakashima, F. Inokuchi, and S. Shinkai: *Chem. Lett.* 1994, 1251. (c) H. Otsuka, K. Araki, and S. Shinkai: *J. Org. Chem.* **59**, 1542 (1994). (d) H. Otsuka, K. Araki, H. Matsumoto, T. Harada, and S. Shinkai: *J. Org. Chem.* **60**, 4862 (1995). (e) H. Otsuka and S. Shinkai: *J. Am. Chem. Soc.* **118**, 4271 (1996). (f) Y. Suzuki, H. Otsuka, A. Ikeda, and S. Shinkai: *Tetrahedron Lett.* **38**, 421 (1997).
8. (a) Y. Ohba, K. Irie, F. S. Zhang, and T. Sone: *Bull. Chem. Soc. Jpn.* **66**, 828 (1993). (b) K. Ito, S. Izawa, T. Ohba, Y. Ohba, and T. Sone: *Tetrahedron Lett.* **37**, 5959 (1996). (c) B. Dhawan and C.D. Gutsche: *J. Org. Chem.* **48**, 1536 (1983). (d) I.U. Khan, H. Takemura, M. Suenaga, T. Shimyozu, and T. Inazu: *J. Org. Chem.* **58**, 3158 (1993). (e) J. Breitenbach and F. Vögtle: *Synthesis* 1992, 41. (f) J. Breitenbach, F. Ott, and F. Vögtle: *Angew. Chem*. **104**, 360 (1992); *Angew. Chem. Int. Ed. Engl.* **31**, 307 (1992). (f) F. Ott, J. Breitenbach, M. Nieger, and F. Vögtle: *Chem. Ber.* **126**, 97 (1993).
9. (a) M. Tashiro, A. Tsuge, T. Sawada, T. Makishima, S. Horie, T. Arimura, S. Mataka, and T. Yamato: *J. Org. Chem.* **55**, 2404 (1990). (b) A. Tsuge, T. Sawada, S. Mataka, N. Nishiyama, H. Sakashita, and M. Tashiro: *J. Chem. Soc.*, *Perkin Trans. 1* 1992, 1498.
10. (a) T. Yamato, L.K. Doamekpor, H. Tsuzuki, and M. Tashiro: *Chem. Lett.* 1995, 89; (b) T. Yamato, L.K. Doamekpor, K. Koizumi, K. Kishi, M. Haraguchi, and M. Tashiro: *Liebigs Ann.* 1995, 1259. (c) T. Yamato, M. Haraguchi, J. Nishikawa, and S. Ide: *J. Chem. Soc. Perkin Trans. 1* 1998, 609.
11. (a) O. Possel and A.M. van Leusen: *Tetrahedron Lett.* 1977, 4229; (b) D. van Leusen and A. M. van Leusen: *Tetrahedron Lett.* 1977, 4233.
12. (a) K. Kobiro, M. Takashi, N. Nishikawa, K. Kikuchi, Y. Tobe, and Y. Odaira: *Tetrahedron Lett.* **28**, 3825 (1987). (b) K. Kurosawa, M. Suenaga, T. Inazu, and T. Yoshino: *Tetrahedron Lett.* **23**, 5335 (1982). (c) T. Shinmyozu, Y. Hirai, and T. Inazu: *J. Org. Chem.* **51**, 1551 (1986). (d) K. Sako, T. Hirakawa, N. Fujimoto, T. Shinmyozu, T. Inazu, and H. Horimoto: *Tetrahedron Lett.* **29**, 6275 (1988). (e) T. Meno, K. Sako, M. Suenaga, M. Mouri, T. Shinmyozu, T. Inazu, and H. Takemura: *Can. J. Chem.* **68**, 440 (1990). (f) K. Sako, T. Meno, H. Takemura, T. Shinmyozu, and T. Inazu: *Chem. Ber.* **123**, 630 (1990). (g) K. Sako, T. Shinmyozu, H. Takemura, M. Suenaga, and T. Inazu: *J. Org. Chem.* **57**, 6536 (1992).
13. (a) C.D. Bain, E.B. Troughton, Y.-T. Tao, J. Evall, G. M. Whitesides, and R.G. Nuzzo: *J. Am. Chem. Soc.* **111**, 321 (1989). (b) P.E. Laibinis, G.M. Whitesides, D.L. Allara, Y.-T. Tao, A.N. Parikh, and R.G. Nuzzo: *J. Am. Chem. Soc.* **113**, 7152 (1991).
14. (a) E.U.T. van Velzen, J.F.J. Engbersen, and D.N. Reinhoudt: *Synthesis* 1995, 989. (b) E.U.T. van Velzen, J.F.J. Engbersen, and D.N. Reinhoudt: *J. Am. Chem. Soc.* **116**, 3597 (1994). (c) T. Weib, E.U.T. van Velzen, J.F.J. Engbersen, D.N. Reinhoudt, and W. Göpel: *Science* 1994, 265.
15. (a) S. Inokuma, S. Yasuda, S. Araki, S. Sakai, and J. Nishimura: *Chem. Lett.* 1994, 201. (b) M. Ouchi, Y. Inoue, K. Wada, S. Iketani, T. Hakushi, and E. Weber: *J. Org. Chem.* **52**, 2420 (1987). (c) H. Tsukube, T. Yamashita, M. Iwashido, and M. Zenki: *J. Org. Chem.* **56**, 268 (1991).
16. K. Iwamoto and S. Shinkai: *J. Org. Chem.* **57**, 7066 (1992).
17. (a) M. Iyoda, Y. Kuwatani, T. Yamauchi, and J. Oda: *J. Chem. Soc.*, *Chem. Commun.* 1988, 65. (b) R. Leookes and F. Vögtle: *Chem.*

Ber. **116**, 215 (1983). (c) J.-L. Pierre, P. Baret, P. Chautemps, and M. Armand: *J. Am. Chem. Soc.* **103**, 2986 (1981). (d) H.C. Kang, A.W. Hanson, B. Eaton, and V. Boekelheide: *J. Am. Chem. Soc.* **107**, 1979 (1985). (e) F.R. Heirtzler, H. Hopf, P.G. Jones, P. Bubenitschek, and V. Lehne: *J. Org. Chem.* **58**, 2781 (1993). (f) J.E. Gano, G. Subramaniam, and R. Birnbaum: *J. Org. Chem.* **55**, 4769 (1990).

18. (a) M. Nishio and M. Horita: *Tetrahedron* **45**, 7201 (1989). (b) C.D. Andreetti, R. Ungaro, and A. Pochini: *J. Chem. Soc.*, *Chem. Commun.* 1979, 1005. (c) R. Ungaro, A. Pochini, C.D. Andreetti, and O. Domiano: *J. Chem. Soc.*, *Perkin Trans. 2* 1985, 197. (d) M.A. McKervey, E.M. Seward, G. Ferguson, and B.L. Ruhl: *J. Org. Chem.* **51**, 3581 (1986). (e) D.J. Cram, S. Karbach, H.-E. Kim, C.B. Knobler, E.F. Marverick, J.L. Ericson, and R.C. Helgeson: *J. Am. Chem. Soc.* **110**, 2229 (1988). (f) P. Soncini, S. Bonsignore, E. Dalcanale, and F. Ugozzoli: *J. Org. Chem.* **57**, 4608 (1992). (g) J.L. Atwood, S.G. Bott, C. Jones and C.L. Raston: *J. Chem. Soc.*, *Chem. Commun.* 1992, 1349. (h) K. Kobayashi, Y. Asakawa, Y. Kikuchi, H. Toi, and Y. Aoyama: *J. Am. Chem. Soc.* **115**, 2648 (1993). (i) T. Yamato, A. Miyazawa, and M. Tashiro: *J. Chem. Soc.*, *Perkin Trans. 1* 1993, 3127.
19. (a) A. Ikeda and S. Shinkai: *Tetrahedron Lett.* **33**, 7385 (1992). (b) A. Ikeda and S. Shinkai: *J. Am. Chem. Soc.* **116**, 2229 (1994). (c) M. Takeshita and S. Shinkai: *Bull. Chem. Soc. Jpn.* **68**, 1088 (1995). (d) A. Ikeda and S. Shinkai: *Chem. Rev.* **97**, 1713 (1997).
20. C.J. Pedersen: *J. Am. Chem. Soc.* **89**, 2495 (1967).