JOC Article

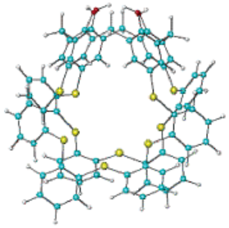
Synthesis, Conformation, and Complexation of Novel 25,26,27,28-Tetrahydroxy-5,11:17,23-bis[[2,2′-thioxydi(*o*-phenylene)dithioxy]-diphenylthio]calix[4]arene

Kyongho Yoon and Kyongtae Kim*

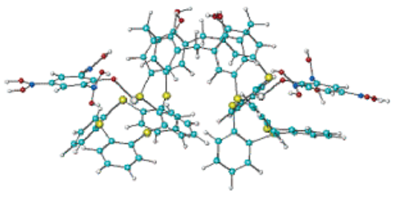
School of Chemistry and Molecular Engineering, Seoul National University, Seoul 151-742, Korea

kkim@plaza.snu.ac.kr

Received June 21, 2004



4a



4a– 2Ag$^+$ picrate

Calix[4]arenes **1a**,**b** having an electron-donating group, i.e., OH and OMe, at the lower rim reacted with thianthrene cation radical perchlorate in CH_3CN at room temperature to give the corresponding thianthrenium perchlorates **3a**,**b** in excellent yields. Treatment of **3a**,**b** comprising a mixture of conformational isomers with $NaSH{\cdot}xH_2O$ in DMF at reflux afforded the sulfur-containing cyclized compounds **4a**,**b**, respectively. Compound **4a** having a cone conformation consisted of two conformational isomers in a ratio of 0.077:1. Temperature-dependent ^1H NMR study in DMF showed that conformational isomerization between the two isomers occurred with energy barriers of 14.97 and 14.10 kcal/mol at 100 and 110 °C, respectively. The Jobs plot of **4a** against Ag^+ picrate indicated that compound **4a** strongly produced a 1:2 complex with Ag^+ ions. Molecular mechanics calculations indicated that the conformation of the energy-minimized **4a**−2Ag^+ picrate complex had two crushed pyramidal geometries made up of Ag^+ ion and four sulfur atoms, i.e., S1, S2, S4, S5 and S6, S7, S9, S10, respectively.

Introduction

Calix[4]arenes are cyclic tetramers made up of phenol and aldehyde units.[1] Numerous examples of the selective upper and lower rim functionalization of calix[4]arenes have appeared in the literature.[1] However, only a limited number of selective upper rim functionalizations doubly capped by two rings formed by linking in the para positions of two neighboring phenyl groups has been reported. For example, the octathiobis(calix[4]arene) cage molecule, prepared from 25,26,27,28-tetraethoxyethoxy-5,11,17,23-tetramercaptocalix[4]arene, CH_2I_2, and Cs_2CO_3, has been reported.[2] Reinhoudt et al.[3] reported calix[4]crown having a crown ether bridge at the positions 5 and 17. Shinkai et al.[4] obtained calix[4]arene possessing double bridges at positions 5 and 11 and 5 and 17, respectively. There are two reported compounds of cone and 1,3-alternate types having conformations immobilized by cross-linking on the upper rim.[4,5] We became interested in the reaction of calix[4]arene **1a** with thianthrene cation radical perchlorate **2** since thianthrenium perchlorate salt **3a**, which might comprise several conformational isomers because of the oxygen-through-the annulus rotation of the phenol units, would be formed in view of the formation of 5-(4-hydroxyphenyl)thianthrenium perchlorate from **2** and phenol[6] (Scheme 1).

Compound **3a** is also an interesting compound not only because such a calix[4]arene having thianthrenium perchlorate moieties at the upper rim has never been reported but also because treatment of **3a** with NaSH·

---

* To whom correspondence should be addressed. Tel: 82-2-880-6636. Fax: 82-2-874-8858.

[1] (a) Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713−1734. (b) Gutsche, C. D. *Calixarenes Revisited*; The Royal Society of Chemistry, Cambridge, 1998.

[2] Blanda, M. T.; Griswold, K. E. *J. Org. Chem.* **1994**, *59*, 4313−4315.

[3] Van Loon, J.-D.; Groenen, L. C.; Wijmenga, S. S.; Verboom, W.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 9670−9671.

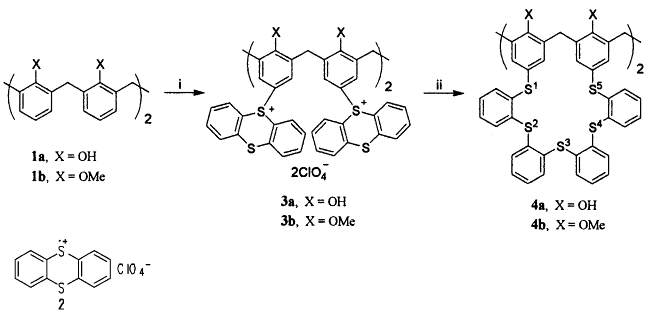
[4] Lhotak, P.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 645−648.

[5] Auduini, A.; Fanni, S.; Pochini, A.; Sicuri, A. R.; Ungaro, R. *Tetrahedron* **1995**, *51*, 7951−7958.

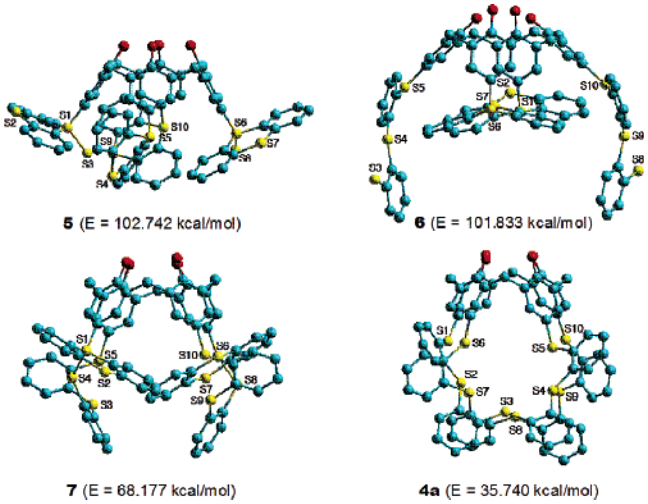
[6] (a) Silber, J. J.; Shine, H. J. *J. Org. Chem.* **1971**, *36*, 2923−2926. (b) Kim, K.; Hull, V. J.; Shine, H. J. *J. Org. Chem.* **1974**, *39*, 2534−2537.

10.1021/jo048964m CCC: $30.25

SCHEME 1[a]



[a] Reagent and conditions: (i) **2**, CH_3CN, rt, 30 min (for **3a**), 36 h (for **3b**); (ii) $NaSH\cdot xH_2O$, DMF, reflux, 3 h (for **4a**), 12 h (for **4b**).



5 (E = 102.742 kcal/mol) **6** (E = 101.833 kcal/mol)

7 (E = 68.177 kcal/mol) **4a** (E = 35.740 kcal/mol)

FIGURE 1. Molecular mechanics-calculated energy minimized conformations of sulfuran intermediates **5** and **7** and intermediate **6** (hydrogen atoms and π bonds are omitted for clarity).

xH_2O in CH_3CN/H_2O (10:1) at reflux might give a bridged compound **4a**. This compound is hitherto unknown via sequential sulfuran intermediates[7] if their formation is stereochemically and energetically favorable in view of the formation of the sulfur-containing compound[8] from the reaction of 5-(4-methoxyphenyl)thianthrenium perchlorate with the same reagent under the same conditions. It is envisaged that the reaction of **3a** with NaSH would give an intermediate **6** via a sulfuran intermediate **5** whose molecular-mechanics-calculated conformations are shown in Figure 1.[9] The energy-minimized intermediate **6** bearing two SH groups, whose thermodynamic energy is 101.833 kcal/mol, would be converted to a new sulfuran intermediate **7,** whose thermodynamic energy is 68.117 kcal/mol. The intermediate **7** rapidly undergoes a bond reorganization to give a stable compound **4a** with an energy of 35.740 kcal/mol.

Apart from a cone conformation of *tert*-butylcalix[4]-arene having C_{4v} symmetry,[10] it is difficult to predict the symmetry of **4a** because the conformations of two bridges comprising four (*o*-phenylene)dithioxy moieties per bridge may not be the same due to the conformational mobility of the phenyl groups participating in a part of the ring. In addition, one cannot rule out the possibility of oxygen-through-the annulus rotation.[11] Compound **4a** has two new cavities arising from two sulfur-containing bridges in addition to an original cavity surrounded by four phenolic moieties. The sulfur atoms in the bridges might increase the complexation ability with some heavy metal cations.[12] In this regard, it would be interesting to examine not only the extractive abilities of **4a** toward metal cations and neutral molecules but also the direction of the metal cations and the neutral molecules. If the cavities are approached for complexation in view of the observations, calix[4]arenes show $\pi-\pi$,[13] H$-\pi$,[14] or $\pi-$cation[15] interactions, depending on the guests and the structures of the host molecules. Since the cone conformation of **1** is attributable to stabilization by intramolecular H-bonding interactions among the OH groups, it is interesting to examine the activation energy according to the loss of the H-bonding of the OH groups of **4a**, which may provide information about the conformation of **4a**. With this in mind, the reaction of **1a** with **2** was studied.

Results and Discussion

Preparation and Characterization of Compounds. Treatment of **1a** with **2** (8.1 equiv) for 30 min in CH_3CN at room temperature gave a perchlorate salt **3a** and thianthrene in 80 and 93% yields, respectively. The structure of **3a** was determined on the basis of spectroscopic (^1H and ^{13}C NMR, IR) and analytical data. In particular, the ^1H NMR (300 MHz, DMSO-d_6) spectrum exhibited three broad singlets at 3.53 (2H), 3.68 (4H), and 3.91 (2H) ppm, respectively. The ^{13}C NMR (75 MHz, DMF-d_7) spectrum exhibited two singlets at 31.5 and 33.1 ppm after scanning for a prolonged period (0.032 mmol of **3a** in 1 g of DMF-d_7 for 1 h). It indicated that **3a** comprises a mixture of conformational isomers.

---

[7] (a) Qian, D.-Q.; Liu, B.; Shine, H. J.; Guzman-Jimenez, I. Y.; Whitmire, K. H. *J. Phys. Org. Chem.* **2002**, *15*, 139−147. (b) Oae, S. *Phosphorus Sulfur* **1986**, *27*, 13−29. (c) La Rochelle, R. W.; Trost, B. M. *J. Am. Chem. Soc.* **1971**, *93*, 6077−6086.

[8] (a) Shin, S. S.; Kim, M. N.; Kim, H. O.; Kim, K. *Tetrahedron Lett.* **1993**, *34*, 8469−8472. (b) Shin, S. S.; Kim, K. *Heterocycles* **1997**, *45*, 795−803.

[9] The calculations do not show the conformation of a sulfuran intermediate, formed between a molecule of NaSH and a trivalent sulfur atom of **4a**. Instead, it gives the conformation of a sulfuran intermediate **5**, formed between two molecules of NaSH and two trivalent sulfur atoms of **3a**.

[10] (a) Gutsche, C. D. *Acc. Chem. Res.* **1983**, *16*, 161−170. (b) Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.* **1985**, *107*, 6052−6059. (c) Araki, K.; Shinkai, S.; Matsuda, T. *Chem. Lett.* **1989**, 581−582. (d) Araki, K.; Murakami, H.; Ohseto, F.; Shinkai, S. *Chem. Lett.* **1992**, 539−541.

[11] (a) Araki, K.; Iwamoto, K.; Shinkai, S.; Matsuda, T. *Chem. Lett.* **1989**, 1747−1749. (b) Iwamoto, K.; Araki, K.; Shinkai, S. *J. Org. Chem.* **1991**, *56*, 4955−4962.

[12] (a) Davies, S. C.; Evans, D. J.; Hughes, D. L.; Longhurst, S.; Roger Sanders, J. *Chem. Commun.* **1999**, 1935−1936. (b) Razavet, M.; Davies, S. C.; Hughes, D. L.; Elaine, B. J.; Evans, D. J.; Fairhurst, S. A.; Liu, X.; Pickett, C. J. *J. Chem. Soc, Dalton Trans.* **2003**. 586−595. (c) Barclay, J. E.; Evans, D. J.; Davies, S. C.; Hughes, D. L.; Sobota, P. *J. Chem. Soc, Dalton Trans.* **1999**. 1533−1534.

[13] Gokel, G. W.; Barbour, L. J.; Ferdani, R.; Hu, J. *Acc. Chem. Res.* **2002**, *35*, 878−886.

[14] Lindeman, S. V.; Kosynkin, D.; Kochi, J. K. *J. Am. Chem. Soc.* **1998**, *120*, 13268−13269.

[15] (a) Lee, J. K.; Kim, S. K.; Bartsch, R. A.; Vicens, J.; Miyano, S.; Kim, J. S. *J. Org. Chem.* **2003**, *68*, 6720−6725. (b) Ungaro, R.; Casnati, A.; Ugozzoli, F.; Pochini, A.; Dozol, J.-F.; Hill, C.; Rouquette, H. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1506−1510. (c) Arduini, A.; Fabbi, M.; Mantovani, M.; Mirone, L.; Pochini, A.; Secchi, A.; Ungani, R. *J. Org. Chem.* **1995**, *60*, 1454−1457.

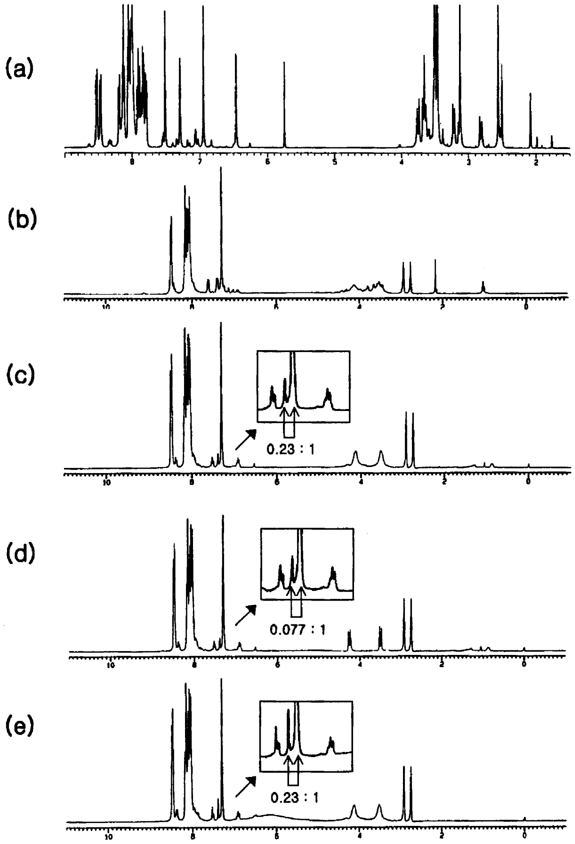


FIGURE 2. ^{1}H NMR spectra (300 MHz for **4a** and 500 MHz for **4b**) of (a) **4b** at 25 °C, (b) **4a** after demethylation of **4b** at 60 °C, (c) **4a** at 25 °C and **4a** after demethylation of **4b** at 60 °C followed by raising the temperature to 110 °C and then cooling to 25 °C, (d) **4a** at −5 °C, and (e) **4a** at 110 °C.

Treatment of **3a** with NaSH·xH$_2$O in either PhH−H$_2$O (10:1, v/v) or THF−H$_2$O (10:1, v/v) for 48 h at reflux did not yield any product. However, heating a mixture of **3a** and NaSH·xH$_2$O in DMF for 36 h at reflux gave thianthrene and compound **4a**, which were readily separated on a silica gel column using an n-hexane−CHCl$_3$ (2:1) mixture as an eluent. The chemical shifts of each proton of **4a** were determined on the basis of their HMQC and HMBC NMR spectroscopy. Interestingly, the ^{1}H NMR spectrum (300 MHz, DMF-d_7) of purified **4a** exhibited major signals along with weak minor signals (Figure 2c). We found that the ^{1}H NMR data including the integrations of the major and the minor signals were in accordance with the proposed structure of **4a**, indicating that **4a** was a mixture of two conformational isomers. The major isomer exhibited a singlet at 7.29 ppm corresponding to the characteristic calix[4]arene aromatic protons (8H), a triplet at 7.91 ppm (J = 7.8 Hz, 8 × H7), a triplet at 7.99 ppm (J = 7.3 Hz, 8 × H8), a doublet at 8.04 ppm (J = 7.8 Hz, 8 × H10), and a doublet at 8.25 ppm (J = 7.3 Hz, 8 × H11). On the other hand, a multiplet at 7.38 ppm exhibited by a minor isomer was found to correlate with the methylene carbons in its HMBC spectrum, indicating calix[4]arene aromatic protons. In addition, three weak multiplets, presumably due to the aromatic protons appearing at 6.48, 6.91, and 7.52 ppm, could not be assigned unambiguously on the basis of the HMBC spectrum. Apart from the relatively distinctive aromatic ^{1}H NMR signals exhibited by the major and the minor isomers, the ^{1}H NMR spectrum exhibited two broad singlets at 3.51 and 4.15 ppm with a weak shoulder, respectively in which the former has it at downfield side and the latter at upfield side, presumably due to the minor isomer.

Similarly, compound **3b** was prepared in 89% yield by the reaction of **1b** comprising a mixture of cone and partial cone conformers[16] with **2**. The spectroscopic and analytical data of **3b** were in accordance with the proposed structure. However, the ^{1}H NMR (300 MHz, DMF-d_7) spectrum of **3b** recorded at 25 °C exhibited two pairs of overlapped doublets 3.4 and 3.8 ppm. In addition, broad peaks ranged between 3.60 and 3.84 and between 6.31 and 6.95 ppm were observed, indicating that **3b** was a conformational mixture, including a cone conformer. Compound **3b** comprising various conformers was treated with NaSH·xH$_2$O in DMF at 110 °C as **3a** to give **4b** in 40% yield along with some unidentifiable unknown compounds.

The ^{1}H NMR (500 MHz, DMF-d_7) spectrum of **4b** measured at 25 °C exhibited three singlets at 2.55, 3.12, 3.46 ppm, assignable to the methoxy groups of the conformational isomers together with several peaks due to the methylene protons in the range of 2.81−3.22, 3.65, and 3.75 ppm (Figure 2a). Demethylation (TMSI, ZnI, CH$_3$CN, 6 h) performed at 60 °C gave **4a** in 75% yield (Figure 2b) whose melting point and analytical data were identical to those obtained from **4a** (Figure 2c) originating from **3a**. However, the ^{1}H NMR (300 MHz, DMF-d_7) spectra of **4a** obtained from the two different sources were not exactly identical. The spectrum of **4a**, obtained from demethylation of **4b**, showed additional peaks in addition to two broad methylene proton signals at 4.1 and 3.5 ppm (Figure 2b). For more information about **4a** obtained from demethylation of **4b**, the chemical shifts of each proton and ^{13}C of **4a** were unambiguously assigned based on its HMQC and HMBC spectra taken in DMSO-d_6. The HMQC spectrum exhibited a correlation of the ^{13}C NMR signals at 30.9 ppm with the broad CH$_2$ proton signals at 3.3−3.6 and 3.7−3.8 ppm. The other ^{13}C NMR signal at 31.4 ppm, presumably due to the minor conformational isomer, was correlated with the CH$_2$ proton signals at 3.3−3.5 and 3.7−3.9 ppm. In addition, the HMBC spectrum exhibited correlations of the broad CH$_2$ proton signals in the range of 3.0−3.9 ppm with the ^{13}C NMR signals at 109.2 (C3), 120.3 (C4, major), 120.4 (C4, minor), and 160.5 (C2) ppm. The observations support that the proton NMR signals in the range of 3.3−4.5 ppm are due to the methylene proton signals of the major and minor conformational isomers.

Temperature-Dependent Conformations of 4. Tempreature-dependent ^{1}H NMR (300 MHz, DMF-d_7) spectra of **4a** recorded at −5, 25, and 110 °C revealed that the spectra were nearly identical at −5 and 25 °C except for the methylene proton signals. That is, the methylene proton signals appeared as a pair of sharp doublets at 4.17 (J = 13.38 Hz) and 3.52 (J = 13.38 Hz) ppm at −5 °C (Figure 2d), whereas at 25 °C each pair of the signals coalesced to become a broad singlet, resonanced at 4.15 and 3.51 ppm, respectively. Nevertheless, the 1:0.077 integration ratio of calix[4]arene aromatic protons resonanced at 7.29 and 7.38 ppm resulting from the major

---

(16) Araki, K.; Shimizu, H.; Shinkai, S. *Chem. Lett.* **1993**, 205−206.

and the minor signals, respectively, were maintained up to near 100 °C. The integration ratio was changed to 1:0.23 at 110 °C, and a broad signal, exchanging with D_2O, appeared in the range between 4.5 and 6.4 ppm (Figure 2e). The increase in the minor peak intensity at 110 °C indicates that the conformational isomerization of the major conformer of **4a** occurs to give a conformationally less stable isomer whose thermodynamic energy which is 15.11 kcal/mol which is different from that of the major conformer of **4a**. The appearance of an exchangeable broad signal may be attributable to the loss of the strong intramolecular H-bonding among the OH groups at the lower rim at 110 °C.[10] The calculated activation energy for the bond breaking of the H-bonding (6.06−7.56 kcal/mol)[17] in water−benzyl alcohol or water−ρ-fluorobenzyl alcohol system is similar to the values reported for calix[4]arenes (5.9−7.9 kcal/mol) under the conditions (CH_3CN, DMF, 25 °C).[18] The coalescence behavior of a well-defined pair of doublets at 25 °C into two broad singlets suggests that oxygen-through-the annulus rotation of the phenolic moieties of **4a** is relatively slow at −5 °C on the NMR time scale and it speeds up at 25 °C to show the methylene hydrogens in the averaged environment. Eventually, the conformational isomerization of the major isomer takes place along with the loss of H-bonding at 110 °C. The energy-minimized conformer of **4a** (E = 35.74 kcal/mol) adopts a cone conformation and the distances between the middle of the two phenyl groups which are the farthest from the upper rim are 4.07 and 4.20 Å, respectively, which become somewhat longer for the $\pi-\pi$ stacking interactions. The calculated energy barrier of 40.21 kcal/mol at 25 °C may be too high for the conformational isomerization, which is not responsible for any changes in the integration ratios of the ^1H NMR signals corresponding to the major and the minor signals at −5 and 25 °C.

Surprisingly, upon heating the demethylated product in DMF for 6 h at 110 °C, the ^1H NMR spectrum became identical to that of **4a** (Figure 2c). Moreover, both spectra showed the same integration ratios (1:0.23) on the peaks exhibited by the foregoing major and minor conformers. These observations indicate that **4a** exists as a mixture in a definite ratio of two conformational isomers at 110 °C whether it is formed from either **3a** or **4b**. Accordingly, it is deduced that the conformational isomerization does not take place at 60 °C, at which temperature the demethylation reaction of **4b** was carried out. In the meantime, the calculated energy barriers for conformational isomerizations of the energy-minimized major conformer of **4a** in DMF were 19.35, 14.97, and 11.67 kcal/mol at 90, 100, and 110 °C, respectively. The data support that the conformational isomerization can occur at 100 °C, which in turn suggests the appearance of free OH groups arising from the breakage of the H-bonding among the OH groups at low rim at 100 °C with 14.97 kcal/mol of activation energy. The energy barrier is comparable with the free energy change of 14.1 kcal/mol for pinched-cone interconversion of calix[4]arene **1** (X = OC_8H_{17}, CO_2H) at 45 °C.[18]

TABLE 1. Extractive Abilities of 4a

metal pic	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Sr^{2+}	Ba^{2+}
extrac (%)	3	9	2	11	15	0	4
metal pic	Ag^+	Cd^{2+}	Co^{2+}	Cu^{2+}	Mn^{2+}	Ni^{2+}	Zn^{2+}
extrac (%)	165	17	32	23	1	65	11

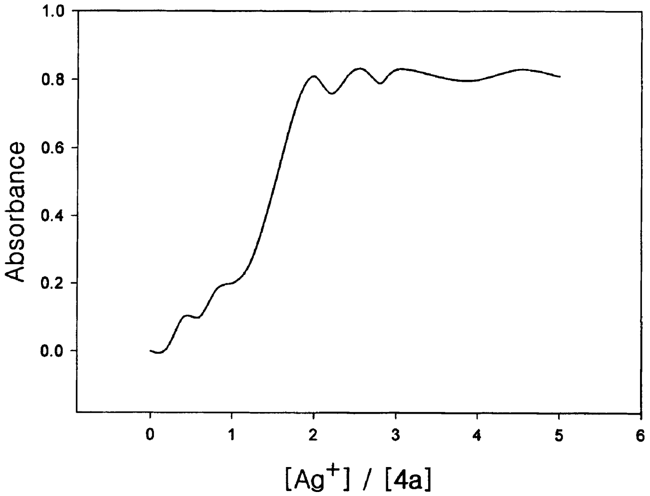


FIGURE 3. Jobs plot of **4a** agains Ag^+ picrate.

Complexations of 4a. Apart from **1**, which makes a 1:1 complex with toluene, acetone, and acetonitrile,[19] compound **4a** does not act as an acceptor for those compounds since no new ^1H NMR signals arising from the interaction between **4a** and each compound were observed when a small amount of each compound was added to the **4a** in DMF-d_7, respectively. However, **4a** showed variable affinities toward metal cations which could be demonstrated by the extractive abilities determined at 354 nm by two-phase picrate extraction.[20] The results are summarized in Table 1.

Table 1 demonstrates that a selective interaction between Ag^+ ion and **4a** is achieved. The Jobs plot[21] (Figure 3) against Ag^+ ion indicates that two Ag^+ ions are trapped by a molecule of **4a**.

It is conceivable that an Ag^+ ion interacts with each cavity made up of a (*o*-phenylene)dithioxy bridge in which the picrate counteranion assumes a position directed toward the outside of the cavity instead of the space between the two cavities. The **4a**−2Ag^+ picrate complex purified by recrystallization from $CHCl_3$−MeOH (mp 213−215 °C) showed spectroscopic and analytical data in accordance with the proposed structure whose energy-minimized conformer is shown in Figure 4. The ^1H NMR spectra of **4a** recorded in DMSO-d_6 and DMF-d_7, respectively, were almost identical to the corresponding spectra of the **4a**−2Ag^+ picrate complex. In contrast, some of the ^{13}C NMR (125 MHz) signals of **4a**−2Ag^+ picrate show

---

[17] Ahn, D. S.; Lee, S. *Bull. Korean Chem. Soc.* **2002**, *23*, 262−266.

[18] Conner, M.; Janout, V.; Regen, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 9670−9671.

[19] (a) Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* **1981**, *103*, 3192−3199. (b) Xu, W.; Puddephatt, R. J.; Manojlovic-Muir, L.; Muir, K. W.; Frampton, C. S. *Inclusion Phenom. Mol. Recognit. Chem.* **1994**, *19*, 277−280. (c) Ungaro, R.; Pochini, A.; Andreetti, G. D.; Domiano, P. *J. Chem. Soc, Perkin Trans. 2* **1985**. 197−199.

[20] Bartsch, R. A.; Yang, I. W.; Jeon, E. G.; Walkowiak, W.; Charewicz, W. A. *J. Coord. Chem.* **1992**, *27*, 75−82.

[21] Takehara, K.; Ueda, I.; Kamaya, H. *Anal. Sci.* **2001**, *17*, 1543−1546.

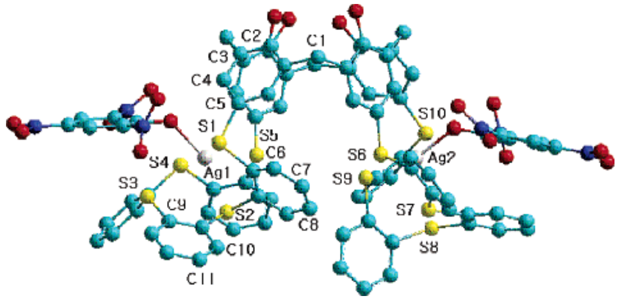


FIGURE 4. Conformation of the energy-minimized **4a**−2Ag$^+$ picrate complex (hydrogen atoms and π bonds omitted for clarity).

downfield shifts with respect to the C4−C10 atoms in both DMSO-d_6 and DMF-d_7 (refer to the Supporting Information). The values of the chemical shift differences ($\Delta\delta$) appear to be somewhat greater in DMSO-d_6 than in with DMF-d_7. This result indicates that DMSO-d_6, which is of higher polarity than DMF-d_7, would be a better solvent for the stabilization of the complex.

Molecular mechanics calculations show that nonbonded distances between Ag$^+$ ion and sulfur atoms in each cavity, i.e., S1, S2, S4, and S5 and S6, S7, S9, and S10 are in the range between 2.36 and 2.40 Å, respectively. However, those distances between Ag$^+$ ion and S3 and S8 are 2.99 and 2.88 Å, respectively, which are significantly greater than the distances between Ag$^+$ ion and other sulfur atoms. Accordingly, the S3 and S8 atoms would not participate in making **4a**−2Ag$^+$ picrate complex donor atoms. In addition, the angles of S1−Ag$^+$−S2, S2−Ag$^+$−S4, S4−Ag$^+$−S5, S1−Ag$^+$−S5, S6−Ag$^+$−S10, S6−Ag$^+$−S9, S7−Ag$^+$−S9, and S7−Ag$^+$−S10 are 98.82, 94.54, 82.10, 97.82, 92.65, 83.41, 97.81, and 82.50°, respectively. The data are indicative of a crushed square-pyramidal geometry comprising a Ag$^+$ ion and four sulfur atoms in each cavity. Furthermore, it may be envisaged that the **4a**−2Ag$^+$ picrate complex does not have C_{2v} symmetry in a strict sense despite the indication of C_{2v} symmetry in the ^{13}C NMR spectroscopic data.

Conclusion

In conclusion, calix[4]arenes having four hydroxyl groups at the lower rim reacted readily with thianthrene cation radical perchlorate to give thianthrenium perchlorate salts, which reacted with NaSH·xH$_2$O in DMF at reflux temperature, leading to the title compound via intramolecular formation of sulfuran intermediates. The ^{1}H NMR spectrum indicates that the title compound consists of two conformational isomers with cone conformations. The isomerization of the energy-minimized major conformer to the less stable one occurs at 110 °C with an energy barrier of 11.67 kcal/mol. One molecule of the title compound is found to strongly produce a 2:1 complex with two molecules of Ag$^+$ picrates.

Experimental Section

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. ^{1}H NMR, ^{13}C NMR, and 2D NMR spectra were recorded with 300 and 500 MHz instruments using CDCl$_3$, DMSO-d_6, or DMF-d_7 as the solvent. Infrared spectra were obtained as thin films on KBr plates. All reactions were monitored for completion by thin-layer chromatography (TLC), which was performed using precoated silica gel plates, and the detection was achieved with the aid of UV light. Column chromatography was performed on silica (70−230 mesh, ASTM). Melting points are uncorrected.

General Procedure for the Preparation of 25,26,27,28-Tetra(hydroxy or methoxy)-5,11,17,23-calix[4]arene Thianthrene-5-yl Perchlorate 3. To a solution of 25,26,27,28-tetra(hydroxy or methoxy)calix[4]arene (**1**) (0.117−0.151 mmol) in dried CH$_3$CN (50 mL) was added thianthrene cation radical perchlorate (**2**) (0.948−1.223 mmol). The mixture was stirred for 30 min at room temperature. Removal of the solvent in vacuo gave a residue that was chromatographed on a silica gel column (70−230 mesh, 20 × 3 cm). Elution with a mixture of CH$_2$Cl$_2$ and MeOH (9/1, v/v) gave thianthrene (0.104−0.141 mmol, 89−93%), followed by **3a** (0.093 mmol, 80%) and **3b** (0.127 mmol, 89%), respectively.

25,26,27,28-Tetrahydroxy-5,11,17,23-calix[4]arene thianthrene-5-yl perchlorate (3a): 80%; mp 275 °C dec (from acetone/MeOH); ^{1}H NMR (300 MHz, DMF-d_7) δ 3.52 (br s, 2H, ArCH_2Ar), 3.62−3.84 (br m, 4H, ArCH_2Ar), 3.89 (br s, 2H, ArCH_2Ar), 6.46−7.01 (br m, 8H), 7.40−7.71 (m, 8H), 7.83−8.06 (m, 16H), 8.06−8.16 (4H, m), 8.19−8.41 (4H, m), The OH proton (4H) signal is invisible; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.53 (br s, 2H, ArCH_2Ar), 3.68 (br s, 4H, ArCH_2Ar), 3.91 (br s, 2H, ArCH_2Ar), 6.47−7.01 (br m, 8H), 7.55−8.41 (m, 32H), the OH proton (4H) signal is invisible; ^{13}C NMR (75 MHz, DMF-d_7) δ 31.5, 33.1, 111.8, 129.2, 130.4, 131.1, 131.4, 132.3, 134.5, 135.2, 161.0, 162.0; ^{13}C NMR (75 MHz, DMSO-d_6) δ 32.7, 110.7, 130.3, 130.5, 130.8, 131.4, 132.6, 134.8, 134.9, 160.8, 162.6; IR (KBr) 3060, 2960, 2940, 2850, 1620, 1580, 1480, 1450, 1440, 1420, 1330, 1260, 1190, 1150, 1125, 1050, 1030, 930, 850 cm^{-1}. Anal. Calcd for $C_{76}H_{52}Cl_4O_{20}S_8$: C, 54.22; H, 3.11; S, 15.24. Found: C, 54.23; H, 3.21; S, 15.53.

25,26,27,28-Tetramethoxy-5,11,17,23-calix[4]arene thianthrene-5-yl perchlorate (3b): 89%; mp 284 °C dec (from acetone/MeOH); ^{1}H NMR (300 MHz, DMF-d_7) δ 3.17 (s, 3H), 3.35 (d, 6H, J = 6.75 Hz), 3.43−3.84 (br m, 8H, ArCH_2Ar), 3.60 (s, 3H), 6.31−6.95 (m, 8H), 7.69−7.97 (br m, 24H), 8.35−8.43 (m, 8H); ^{13}C NMR (75 MHz, DMF-d_7) δ 31.2, 34.2, 55.2, 61.1, 61.2, 114.1, 111.7, 119.1, 121.3, 129.8, 130.0, 130.2, 130.8, 131.1, 134.5, 134.6, 134.8, 134.9, 135.1, 135.5, 135.6, 137.7; IR (KBr) 3059, 2999, 2958, 2837, 1736, 1578, 1501, 1452, 1378, 1254, 1189, 1131, 1026 cm^{-1}. Anal. Calcd for $C_{80}H_{60}Cl_4O_{20}S_8$: C, 55.23; H, 3.48; S, 14.75. Found: C, 55.15; H, 3.57; S, 14.75.

General Procedure for the Preparation of 5,11:17,23-Bis[[2,2′-thioxydi(*o*-phenylene)dithioxy]diphenylthio]calix[4]arene (4). To a solution of **3** (0.177−0.204 mmol) in dried DMF (50 mL) was added NaSH·xH$_2$O (476−500 mg). The mixture was heated at 100−110 °C for 36−40 h and cooled to room temperature. The mixture was poured into 3% aqueous HCl solution (50 mL), which was extracted with CH$_2$Cl$_2$ (50 mL × 3). The extract was dried over anhydrous MgSO$_4$. Removal of the solvent gave a residue that was chromatographed on a silica gel column (10 × 1 cm) to give **4**.

25,26,27,28-Tetrahydroxy-5,11:17,23-bis[[2,2′-thioxydi(*o*-phenylene)dithioxy]diphenylthio]calix[4]arene (4a): 61%; mp 167−169 °C (from CHCl$_3$/n-hexane); ^{1}H NMR (500 MHz, DMF-d_7) δ 3.51 (br s, 4H, ArCH_2Ar), 3.50 (overlap, 0.3H, minor ArCH_2Ar), 4.15 (br s, 4H, ArCH_2Ar), 4.16 (overlap, 0.3H, minor ArCH_2Ar), 6.48 (m, 0.6H, minor), 6.91 (m, 0.6H, minor), 7.29 (s, 8H), 7.38 (br m, 0.6H, minor), 7.52 (br m, 1.2H, minor), 7.91 (t, 8H, J = 7.8 Hz), 7.99 (t, 8H, J = 7.3 Hz), 8.04 (d, 8H, J = 7.8 Hz), 8.25 (d, 8H, J = 7. 3 Hz), the OH proton (4H) signal is invisible; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.29 (br s, 4H, ArCH_2Ar), 3.29 (overlap, 0.6H, minor ArCH_2Ar), 4.03 (br s, 4H, ArCH_2Ar), 6.75 (m, 1.2H, minor), 7.02 (s, 8H), 7.08 (s, 0.6H, minor), 7.51 (m, 1.2H, minor), 7.90−7.93 (s, 8H, H8), 7.98−8.01 (s, 8H, H11), 8.03−8.05 (s, 8H, H7), 8.24−8.26 (s, 8H, H10), the OH proton (4H) signal is invisible; ^{13}C NMR (125 MHz, DMF-d_7) δ 31.2, 110.5, 120.7, 129.7, 130.6, 131.1, 132.6, 134.6, 135.0, 136.2, 160.8; ^{13}C NMR (75 MHz, DMSO-d_6) δ 30.9 (C1), 109.1 (C3), 120.3 (C4), 129.3 (C11), 129.8 (C8), 130.5 (C10), 131.1 (C5), 134.0 (C7), 134.1 (C6), 134.3 (C9), 160.5 (C2); IR (KBr) 3056, 2928, 1699, 1568, 1465, 1436, 1328, 1228, 1184, 1101, 1030, 931, 886, 752 cm^{-1}. Anal. Calcd for $C_{76}H_{52}O_4S_{10}$: C, 67.62; H, 3.88; S, 23.75. Found: C, 67.75; H, 3.65; S, 23.50.

4a Obtained from Demethylation of 4b: ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.00−4.50 (br m, 4H, ArCH$_2$Ar), 3.00−4.50 (br m, 0.6H, minor ArCH$_2$Ar), 6.74 (m, 1.2H, minor), 7.02 (s, 8H), 7.10 (s, 0.6H, minor), 7.32 (m, 0.6H, minor), 7.83−7.89 (m, 0.6H, minor), 7.90−7.93 (m, 8H), 7.98−8.01 (m, 8H), 8.03−8.05 (m, 8H), 8.24−8.26 (m, 8H), the OH proton (4H) signal is invisible; ^{13}C NMR (125 MHz, DMSO-d_6) δ 30.9, 31.4 (minor), 109.2, 120.3, 120.4 (minor), 129.3, 129.8, 130.0 (minor), 130.3, 130.5, 131.1, 133.5 (minor), 133.7 (minor), 134.0, 134.1, 134.3, 160.5.

25,26,27,28-Tetramethoxy-5,11:17,23-bis[[2,2′-thioxydi-(*o*-phenylene)dithioxy]diphenylthio]calix[4]arene (4b): 40%; mp 164−167 °C (from CHCl$_3$/*n*-hexane); ^{1}H NMR (500 MHz, DMF-d_7) δ 2.55 (s, 3H), 2.81−3.22 (m, 2H, ArCH$_2$Ar), 3.12 (s, 3H), 3.46 (s, 6H), 3.65 (t, 4H, J = 13.70 Hz, ArCH$_2$Ar), 3.75 (d, 2H, J = 14.44 Hz, ArCH$_2$Ar), 6.46 (s, 2H), 6.94 (s, 2H), 7.29 (s, 2H), 7.51 (s, 2H), 7.78−7.93 (m, 10H), 7.99−8.04 (m, 12H), 8.12−8.20 (m, 6H), 8.50 (dd, 4H, J = 27.35, 7.47 Hz); ^{13}C NMR (125 MHz, DMF-d_7) δ 29.4, 30.7, 34.7, 54.9, 59.5, 60.0, 61.4, 114.2, 117.5, 118.3, 118.5, 118.7, 120.1, 120.8, 121.4, 128.5, 129.5, 129.8, 129.9, 130.0, 130.1, 130.2, 130.2, 130.7, 130.9, 134.4, 134.5, 134.6, 134.7, 134.7, 134.9, 135.0, 135.1, 135.5, 135.5, 135.9, 137.7, 160.7, 161.5, 161.7; IR (KBr) 3040, 2912, 2840, 2792, 1586, 1491, 1438, 1374, 1230, 1123, 1019 cm^{-1}. Anal. Calcd for $C_{80}H_{60}O_4S_{10}$: C, 68.34; H, 4.30; S, 22.81. Found: C, 68.45; H, 4.35; S, 22.61.

4a−2Ag^{+}picrate: mp 213−215 °C (from CHCl$_3$/MeOH); ^{1}H NMR (300 MHz, DMF-d_7) δ 3.51 (br d, J = 12.39 Hz, 4H, ArCH$_2$Ar), 4.13 (br d, J = 12.39 Hz, 4H, ArCH$_2$Ar), 7.31 (s, 8H), 8.01−8.12 (m, 16H), 8.16 (dd, J = 7.49, 1.70 Hz, 8H), 8.47 (dd, J = 7.49, 1.70 Hz, 8H) 8.68 (s, 4H); ^{13}C NMR (75 MHz, DMF-d_7) δ 30.6, 110.4, 120.6, 125.0, 125.6, 129.7, 130.5, 131.1, 132.6, 134.6, 135.0, 136.1, 142.6, 160.7, 161.6; IR (KBr) 3056, 2928, 1699, 1584, 1485, 1449, 1373, 1254, 1149, 1091, 1024, 797, 742 cm^{-1}. Anal. Calcd for $C_{88}H_{56}Ag_2N_6O_{18}S_{10}$: C, 52.28; H, 2.79; N, 4.16; S, 15.86. Found: C, 52.10; H, 2.88; N, 4.18; S, 15.92.

Solvent Extraction for Metal Ions. A UV−vis spectrophotometer was used to measure extractive ability. Each metal picrate (0.5 mmol) prepared by the literature method[22] was dissolved in deionized water (100 mL), and compound **4a** (140 mg, 0.12 mmol) was dissolved in chloroform (100 mL). For the complexation test, deionized water (2 mL) containing each metal picrate (5×10^{-3} M) and chloroform (2 mL) containing **4a** (1×10^{-3} M) were mixed in each capped test tubes (5 mL). For the blank test, deionized water (2 mL) containing each metal picrate (5×10^{-3} M) and chloroform (2 mL) were mixed in each capped test tube (5 mL). The biphasic mixtures were stirred vigorously for 5 min and then kept at 25 ± 1 °C for 24 h. The amount of each metal picrate in the aqueous phase was determined via a UV−vis spectrophotometer and measured at 354 nm. The extractive abilities of **4a** were calculated by eq 1. All experiments were carried out in triplicate, and the respective results were averaged. The subtraction of the picrate transferred into the plain chloroform from the initial concentration of picrate in the aqueous phase is the [M$_{aq}$] value, and [M$_t$] is the concentration of picrate in the aqueous phase after extraction. [H$_o$] is the concentration of the host molecule.

$$\text{extractive ability (\%)} = [([M_{aq}] - [M_t])/[H_o]] \times 100 \quad (1)$$

Temperature Study, Temperature-dependent (TD) ^{1}H NMR spectra of **4a** and **4b** were measured in a sealed tube using DMF-d_7 as solvent. The temperature of the dynamic NMR changed over the range of −5 to +110 °C. The TD ^{1}H NMR spectra of **4a** were observed in NMR rotor at temperature, respectively; **4b** was observed in the spectrum by raising the temperature to 110 °C after demethylation at 60 °C in the reactor.

Molecular Mechanics Calculations. The structures of **4a**, **5**, **6**, and **7** were built and energy-minimized using the conjugate gradient method in MacroModel 5.0 with MM2^{+} force field. In addition, minimum energy configurations of the molecule in aqueous phase were identified by the Monte Carlo search method using the same force field, followed by conjugate gradient minimization to a gradient of less than 0.001 kcal/mol Å, and 5000 conformations were sampled. In these conformation searches, the GB/SA solvation model was used. The global minimum configuration is represented in Figures 1 and 4.

Acknowledgment. This work was supported by Grant No. NO R01-2002-000-00140-0 from the Korea Sciences and Engineering Foundation.

Supporting Information Available: ^{1}H NMR spectrum of **4a** (S1), HMQC spectrum of **4a** (S2), HMBC spectrum of **4a** (S3), and HMBC spectrum of **4a**−2Ag^{+}pic^{-} (S4); HMQC and HMBC spectra of **4a** obtained from demethylation of **4b** (S6, S7); table of comparison of selective ^{13}C NMR (125 MHz) data between **4a** and **4a**−2Ag^{+} picrate complex in DMSO-d_6 and DMF-d_7 (Table S1). This material is available free of charge via the Internet at http://pubs.acs.org.

JO048964M

---

[22] Sevdic, D.; Fekete, L.; Meider, H. *J. Inorg. Nuclear Chem.* **1980**, *42*, 885−889.