

were very intense (37 to 100%) in all spectra of [4.2.1] isomers but trace or undetectable in spectra of their corresponding [3.3.1] isomers, thus readily distinguishing [4.2.1] isomers from [3.3.1] isomers. On the contrary all of the [3.3.1] isomers yielded characteristic $[M-101]^+$ ions of higher intensity, which correspond to the six-membered N-substituted piperidine ring cations.¹⁰ However, they were present at comparatively lower abundance in the spectra of [4.2.1] isomers which were thus easily differentiated from [3.3.1] isomers.

Besides these characteristic fragment ions, m/z 68 ions were found to be more intense in the spectra of the [4.2.1] isomers than the [3.3.1] isomers, particularly in the spectra of sulfonamides. Another characteristic $[M-43]^+$ ions were observed in all spectra of [3.3.1] isomers, but were barely or not detectable in the spectra of the corresponding [4.2.1] isomers. $[M-43]^+$ ions and m/z 68 ions appear to be useful in further confirmation of the desired [4.2.1] isomers predistinguished from [3.3.1] isomers by comparing the abundances of $[M-115]^+$ and $[M-101]^+$ fragment ion peaks.

The formation of $[M-115]^+$ ions present only in [4.2.1] isomers may be explained by the favored cleavage of the C 5-C6 bond next to C-N bond, leading to five-membered intermediates **a** (Figure 2). Subsequently they decompose by cleavage of the C1-C2 linkage with migration of a hydrogen (C8) to the carboxyl oxygen, yielding the five-membered $[M-115]^+$ ions **b**. Further loss of R function from **b** accompanied by migration of a hydrogen atom to the ring may yield diagnostic ion at m/z 68 **c** which loses a hydrogen atom to form m/z 67 ion. Less abundant $[M-101]^+$ ions **d** may be formed by the less favored cleavage of C2-C 3 bond instead of C1-C2 bond.

Similar ring cleavage process (C4-C5 cleavage) for [3.3.1] isomers may yield six-membered intermediates **e** which decompose to form $[M-101]^+$ ions **f** (Figure 3). The characteristic $[M-43]^+$ fragment ions **g** occurring only in [3.3.1] isomers are assumed to be formed by loss of $\text{CH}_2\text{CH}_2\text{CH}_3$ from molecular ions through the cleavage of C 1-C8 and C5-C6 bonds with migration of a hydrogen atom from C4.

Acknowledgment. This work was supported by the Ministry of Science and Technology (HAN project).

References

1. Carmichael, W. W.; Biggs, D. F. *Can. J. Zool.* **1978**, *56*, 510.
2. Spivak, C. E.; Wikop, B.; Albuquerque, E. X. *Mol. Pharmacol.* **1980**, *18*, 284.
3. Oh, C. Y.; Kim, K. S.; Ham, W. H. *Tetrahedron Letters* **1998**, *38*, 2133.
4. Bastable, J. W.; Hobson, J. D.; Riddell, W. D. *J. Chem. Soc., Perkin I* **1972**, 2205.
5. Bax, A.; Freeman, R.; Morris, G. *J. Magn. Reson.* **1981**, *42*, 164.
6. Bax, A.; Freeman, R. *J. Magn. Reson.* **1981**, *44*, 542.
7. Koshinen, A. M. P.; Rapoport, H. *J. Med. Chem.* **1985**, *28*, 1305.
8. Blossey, E. C.; Budzikiewicz, H.; Ohashi, M.; Fodor, G.; Djerassi, C. *Tetrahedron* **1964**, *20*, 585.
9. Bryant, W. M.; House, H. O.; Pitt, C. G.; Tefertiller, B. *A. J. Org. Chem.* **1966**, *31*, 3120.
10. Bastable, J. W.; Hobson, J. D.; Riddell, W. D. *J. Chem. Soc., Perkin I* **1972**, 2205.

Synthesis and Anion Binding Properties of Urea Derivatized *p*-*tert*-Butylcalix[6]arenes

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Received May 28, 1998

In comparison with the large variety of ligands which have been described for cation receptors,¹⁻³ the development of selective host molecules for anions is still in its infancy. The ligands for complexation of anions need to have comparatively large cavities, which have so far proved difficult to be synthesized. In addition, as the charge density of anions is low, the electrostatic forces with them are weaker than those with cations. Selective complexation of anions is more demanding than that of cations in the view of the higher free energies of solvation of anions and the frequently occurring pH dependency of anion complexation.^{4,5} Anions have a wide variety of geometries⁶ which have to be taken into account in the development of selective anion receptors.

Reinhoudt and co-workers have reported that a selective

complexation of Cl^- over Br^- and I^- can be achieved by the neutral urea receptors derived from the lower rim of calix[4]arene⁷ and that three urea groups at the lower rim of calix[6]arene are well suited for complexation of tricarboxylate.⁸ Both systems complex anions exclusively through hydrogen bonding. The use of hydrogen bonding as sole interaction for the binding of anions implies that recognition is most pronounced in non-competitive solvents. The advantage of using hydrogen bond is that a hydrogen bond is highly directional in character. Correct orientation of the hydrogen bond donors and/or acceptors can provide selective anion recognition. The urea moiety is a powerful hydrogen bond donor as was recently shown by Hamilton *et al.*⁹ in the complexation of dicarboxylate anion.

In order to develop the selective anion receptors, here we

report the synthesis and complexation behavior of three calix[6]arene based anion receptors **4a**, **4b**, and **5a**. Particularly receptors **4a** and **5a** have four OH groups near the two urea units, thus providing additional binding sites of the anion guest. The binding study was conducted with proton NMR titration with the various anions such as Cl^- , Br^- , I^- , CH_3CO_2^- , HSO_4^- , ClO_4^- , and H_2PO_4^- .

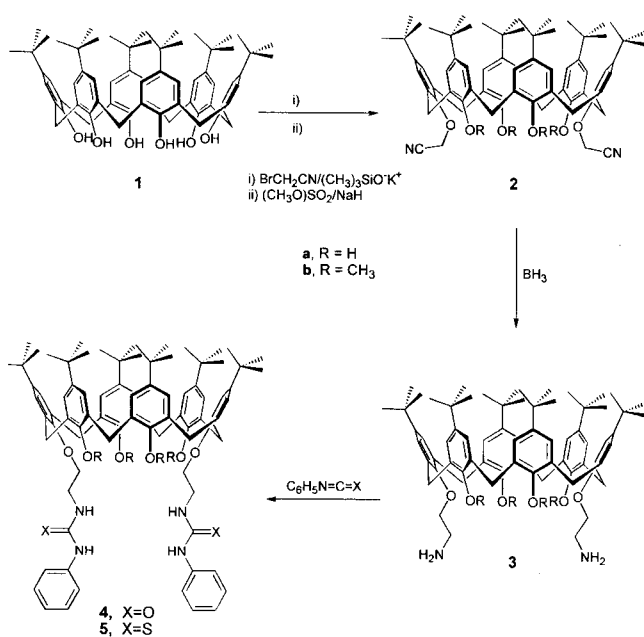
Results and Discussion

The key intermediate for the synthesis of the bidentate phenylurea calix[6]arenes is the 1,4-bis(2-aminoethoxy)calix[6]arene **3**, which was obtained by the diborane reduction of the 1,4-bis(cyanomethoxy)calix[6]arene **2**. The 1,4-bis(cyanomethoxy)calix[6]arene **2** was prepared selectively by the reaction of *p*-tert-butylcalix[6]arene **1** with bromoacetonitrile in the presence of $(\text{CH}_3)_3\text{SiO}^- \text{K}^+$.¹⁰⁻¹² Treatment of aminocalix[6]arene **3** with phenylisocyanate produced the urea derivatives of calix[6]arene **4** as shown in Scheme 1. Thiourea derivative **5a** was prepared similarly by treating aminocalix[6]arene **3** with phenylisothiocyanate. For the investigation of the effect of calixarene OH groups on anion binding, O-methylated host **4b** was also synthesized. Since it is known that Cl^- and Br^- anions are good hydrogen bond acceptors and the urea moiety is a powerful hydrogen bond donor, Cl^- and Br^- would lead to complexation.

The anion coordination properties were investigated by the proton NMR titration in CD_2Cl_2 solution in the presence of various anions such as tetrabutylammonium (TBA) chloride, bromide, iodide, dihydrogen phosphate, hydrogen sulfate, acetate, and perchlorate. In proton NMR experiments a large downfield shift of NH proton resonance and the moderate downfield shift of ortho protons of the phenyl group were observed upon addition of TBA anions to host solution as shown in Figure 1. Particularly a broad singlet at δ 6.4 for amide NH signal shifted rapidly at

around δ 9.5 upon addition of 1 equivalent TBA Cl^- . Further addition of Cl^- caused a only slight downfield shift. The ^1H NMR spectra of **4a** became broad in the beginning, but turned into a well resolved spectral pattern when complexed with chloride ion. That is, the aromatic region consists of two singlets, two triplets and a doublet. This observation could be attributed to the conformational changes of **4a**, that is, chloride ion locking the calixarene into a cone conformation by complexing strongly with the amide protons. Any further significant change was not observed after one equivalent of TBA Cl^- , suggesting that **4a** complexed with chloride ion 1:1 solution stoichiometry. The position of hydroxy protons was not clear at this moment, but a broad signal at δ 6.5 upon addition of Cl^- could be assigned as OH protons. Upon addition of anion to host solution, sometimes the NH signal was disappeared and reappeared, in this occasion, the signal from ortho proton of the phenyl ring near urea unit was used for the stability constant calculation. Large chemical shift change of the NH protons in the presence of anion suggests that the anions bind the urea protons directly. Calixarene aromatic signals became two singlets without much change of the position, indicating that the anions bind at the opposite side of aromatic protons *i.e.* at the lower rim of calixarenes, but fix the motion of calixarene framework upon complexation. The association constants of the various anions to the receptors are calculated from the resulting titration curves using EQ-NMR¹³ and these values are presented in Table 1.

The receptor **4a** exhibits remarkable thermodynamic stability and selectivity preference for chloride anion over $\text{H}_2\text{PO}_4^- > \text{Br}^- > \text{CH}_3\text{CO}_2^- > \text{HSO}_4^-$.¹⁴ The ^1H NMR titration curves of **4a** indicate 1:1 complex stoichiometry (Figure 1), suggesting that **4a** forms the intramolecular complexation with two urea units. In order to investigate the effect of OH protons upon binding of anions, **4b** which has no OH protons was also titrated with the various anions. It showed



Scheme 1. Synthesis of Urea Derivatized Calix[6]arenes.

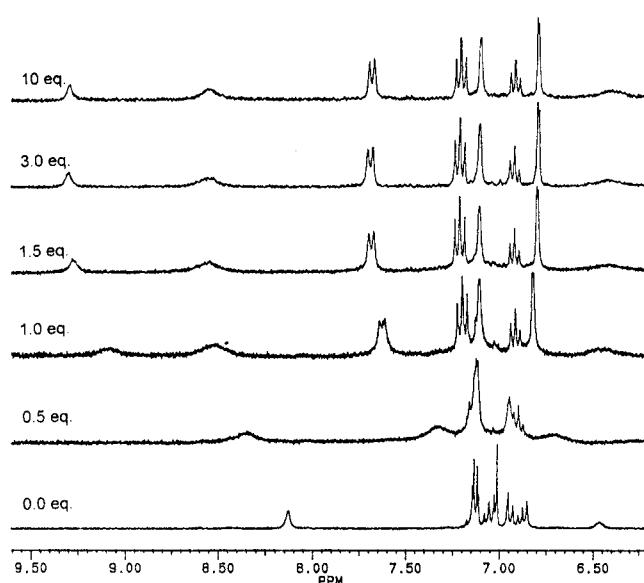


Figure 1. The partial ^1H NMR spectra of **4a** in the presence of TBA (tetrabutylammonium) Cl^- in CD_2Cl_2 . Numbers at the left side indicate the equivalent amounts of Cl^- added.

Table 1. Stability constant data (K_{ass}, M^{-1}) of urea derivatives of calix[6]arenes

ligand	Cl ^{-a}	Br ⁻	H ₂ PO ₄ ⁻	CH ₃ CO ₂ ⁻	HSO ₄ ⁻
4a	2030	780	830	680	150
5a	250	40	290	210	220
4b	50	- ^b	60	- ^b	- ^b

^aTetrabutylammonium salts. Concentration of host is 5 mM in CD₂Cl₂. Estimated error <10%. ^bVery weak binding, a stability constant value could not be calculated in this solvent.

a limited binding for Cl⁻ and H₂PO₄⁻ and virtually no binding was observed with Br⁻, CH₃CO₂⁻ and HSO₄⁻. Preference for Cl⁻ with receptor **4a** suggests that the four urea NH protons as well as four calixarene OH protons could participate on the anion binding to provide the spherical binding site for Cl⁻.

In an attempt to further increase the strength of the anion complexation the phenylthiourea derivative **5a** was synthesized. Due to the increased acidity of the NH protons of thiourea compared to urea (thiourea $pK_a=21.0$; urea $pK_a=26.9$),¹⁵ the anion complexation was expected to be stronger. However, only much weaker binding and virtually no selectivity over the anion were observed. The reason for the weaker binding properties might be that the enhanced hydrogen donating ability of the thiourea groups more strongly promotes the competing intra and intermolecular hydrogen bonding than the anion binding affinity.⁸

Experimental

5,11,17,23,29,35-Hexa-tert-butyl-37,40-bis(cyanomethoxy)-38,39,41,42-tetra-hydroxycalix[6]arene (2a). To a solution of 9.8 g (10 mmol) of *t*-butylcalix[6]arene **1** and 7.8 g of (CH₃)₃SiOK in 700 mL of THF and 60 mL of DMF, 2.4 mL of BrCH₂CN in 50 mL of THF was added for a period of 30 min under ice bath. After 1h ice bath was removed and the solution stirred for 2h at room temperature. The solvents were removed and the residue was treated with 600 mL of 1 N HCl solution. The precipitate was collected and dried. The crude products were treated with MeOH. Most of them was soluble and then quickly filtered and from the methanol solution 8.1 g (77%) of **2a** was obtained. ¹H NMR (CDCl₃) δ 7.10 (d, 4H, ArH, $J=2.3$ Hz), 6.99 (d, 4H, ArH, $J=2.3$ Hz), 6.94 (s, 4H, ArH), 4.54 (s, 4H, -OCH₂CN), 3.93 and 2.92 (two s, 12H, ArCH₂Ar), 1.21 and 1.09 (two s, 54H, -C(CH₃)₃). ¹³C NMR (CDCl₃) δ 150.02, 148.85, 148.74, 143.39, 132.34, 127.26, 126.81, 126.34, 125.83, 125.62 and 115.54 (Ar and -CN), 58.78 (-OCH₃), 34.24, 33.94, 32.50, 31.61, 31.48, 31.13 and 30.31 (ArCH₂Ar and -C(CH₃)₃). MAS-FAB m/z 1074 [M+Na]⁺. Anal. Calcd for C₇₀H₈₆N₂O₆: C, 80.00; H, 8.19; N, 2.67. Found: C, 80.09; H, 8.28; N, 2.45.

5,11,17,23,29,35-Hexa-tert-butyl-37,40-bis(cyanomethoxy)-38,39,41,42-tetramethoxy-calix[6]arene (2b). To a solution of 4.0 g of **2a** and 1.12 g of NaH (60% oil dispersion) in 300 mL of THF, 2.92 mL of (CH₃O)₂SO₂ was added. After stirring for 2 days at room temperature, 6 mL of ammonia solution was added and stirred for 30 min, then acidified with 2 N HCl solution. The mixture was extracted with ether (2×100 mL). The

solvents were removed and the residue was triturated with MeOH to give 4.0 g (95%) of **2b**. ¹H NMR (CD₂Cl₂) δ 7.12 (d, 4H, ArH, $J=2.4$ Hz), 7.03 (s, 4H, ArH), 6.97 (d, 4H, ArH, $J=2.4$ Hz), 4.25 (s, 4H, -OCH₂-), 3.95 and 3.89 (two s, 12H, ArCH₂Ar), 2.96 (s, 12H, -OCH₃), 1.19 and 1.11 (two s, 54H, -C(CH₃)₃). ¹³C NMR (CD₂Cl₂) δ 154.47, 151.30, 147.93, 146.47, 134.05, 133.69, 133.29, 126.69, 126.41 and 116.34, (Ar and -CN), 60.33 (-OCH₂-), 57.77 (-OCH₃), 34.47, 31.71, 31.58, 31.41, 30.29 and 30.09 (ArCH₂Ar and -C(CH₃)₃). MAS-FAB m/z 1130 [M+Na]⁺. Anal. Calcd for C₇₄H₉₄N₂O₆: C, 80.29; H, 8.50; N, 2.53. Found: C, 80.84; H, 9.43; N, 2.51.

37,40-Bis(2-aminoethoxy)-5,11,17,23,29,35-hexa-tert-butyl-38,39,41,42-tetrahydroxycalix[6]arene (3a). A 20 mL of 1 M BH₃ solution was added to 3.0 g of **2a** under nitrogen atmosphere and refluxed for 1.5h. The solvents were removed and the residue treated with 25 mL of 2 N HCl and refluxed for 1h. After cooling down to room temperature, the white precipitate was collected and dried. The crude product was purified by column chromatography to yield 2.2 g (70%) of **3a** as hydrochloric salts. ¹H NMR (CDCl₃:CD₃OD=4:1) δ 7.11, 6.87, and 6.61 (three s, 12H, ArH), 3.96 (broad s, 12H, ArCH₂Ar), 3.34 and 2.48 (two broad s, 8H, -OCH₂CH₂-), 1.13 and 0.88 (two s, 54H, -C(CH₃)₃). ¹³C NMR (CDCl₃:CD₃OD=4:1) δ 152.60, 149.03, 147.23, 144.80, 133.66, 129.14, 127.69, 126.77, 126.30, 126.18 (Ar), 68.53 (-OCH₂-), 40.61 (-CH₂N-), 34.66, 32.84, 31.88, 31.79, and 30.57 (ArCH₂Ar and -C(CH₃)₃).

37,40-Bis(2-aminoethoxy)-5,11,17,23,29,35-tert-butyl-38,39,41,42-tetramethoxycalix[6]arene (3b). A 6 mL of 1 M BH₃ solution was added to 1.0 g of **2b** under nitrogen atmosphere and refluxed for 2h. The solvents were removed and the residue treated with 10 mL of 2 N HCl and refluxed for 1h. After cooling down to room temperature, 10% KOH solution was added until the solution became basic and extracted with CHCl₃ (2×40 mL). The solvents were removed and the residue triturated with MeOH to give 9.8 g (98%) of **3b**. ¹H NMR (CDCl₃) δ 7.07 (d, 4H, ArH, $J=2.4$ Hz), 6.97 (s, 4H, ArH), 6.92 (d, 4H, ArH, $J=2.4$ Hz), 3.93 and 3.87 (two broad s, 12H, ArCH₂Ar), 3.64 and 2.81 (two broad t, 8H, -OCH₂CH₂-), 2.92 (s, 12H, -OCH₃), 1.14 and 1.12 (two s, 54H, -C(CH₃)₃). ¹³C NMR (CDCl₃) δ 153.92, 152.26, 145.69, 133.35, 133.24, 126.03, 125.92 and 125.73 (Ar), 74.57 (-OCH₂-), 59.93 (-OCH₃), 42.53 (-CH₂N-), 31.41, 31.36, 30.78, 30.38 and 29.71 (ArCH₂Ar and -C(CH₃)₃). MAS-FAB m/z 1115 [M+2]⁺. Anal. Calcd for C₇₄H₁₀₂N₂O₆: C, 79.71; H, 9.16; N, 2.13. Found: C, 78.78; H, 9.55.

5,11,17,23,29,35-Hexa-tert-butyl-37,40-bis[(N'-phenylureido)ethyl]oxy-38,39,41,42-tetrahydroxycalix[6]arene (4a). To a 0.4 g (0.38 mmol) of **3a** in 15 mL of CH₂Cl₂ and 5 mL MeOH, 0.15 mL of phenylisocyanate and 0.6 mL of (Et)₃N was added and the mixture stirred for overnight under the nitrogen atmosphere. After removing the solvent, the residue was triturated with MeOH, filtered and dried to give 0.22 g (50%) of **4a**. ¹H NMR (CD₂Cl₂) δ 8.09 (s, 2H, -NH), 6.8-7.2 (m, 22H, ArH), 6.40 (br s, 2H, -NH), 4.28, 3.94, 3.53, and 3.48 (two pair of d, 12H, ArCH₂Ar), 4.07 (br s, 4H, -OCH₂-), 3.73 (m, 4H, -CH₂N-), 1.26 and 1.12 (two s, 54H, -C(CH₃)₃). ¹³C NMR

(CDCl₃) δ 148.56 (-NHCONH-), 143.58, 132.17, 128.63, 126.98, 126.61, 126.07 and 119.17 (Ar), 67.96 (-OCH₂-), 34.20, 33.95, 31.54, 31.15, and 25.60 (ArCH₂Ar and -C(CH₃)₃).

5,11,17,23,29,35-Hexa-tert-butyl-37,40-bis[(N'-phenylureido)ethyl]oxy-38,39,41,42-tetramethyloxycalix[6]arene (4b). To a 0.4 g (0.36 mmol) of **3b** in 20 mL of CHCl₃, 0.09 mL of phenylisocyanate was added and the mixture stirred for overnight under the nitrogen atmosphere. At the end of reaction, 20 mL of 1 N HCl solution was added, and stirred vigorously for 20 min, separated organic layer, and removed the solvent. The crude product was further purified by column chromatography (eluent hexane:THF=4:1) to give 0.42 g (88%) of **4b**. ¹H NMR (CD₂Cl₂) δ 7.74 (br s, 2H, -NH), 6.8-7.4 (m, 22H, ArH), 5.84 (br s, 2H, -NH), 4.46, 4.43, 3.54, and 3.46 (two pair of d, 12H, ArCH₂Ar), 3.18 (br s, 12H, -OCH₃), 3.3-3.6 (br s, 8H, -OCH₂CH₂N-), 1.15 and 1.09 (two s, 54H, -C(CH₃)₃). ¹³C NMR (CD₂Cl₂) δ 156.62 (-NHCONH-), 154.06, 152.48, 146.57, 146.44, 140.03, 133.83, 133.38, 133.13, 129.18, 128.99, 126.19, 122.27, 119.87 and 119.34 (Ar), 72.30 (-OCH₂-), 60.84 (-OCH₃), 40.93 (-CH₂N-), 34.45, 34.38, 31.73, 31.49, 30.45 and 30.10 (ArCH₂Ar and -C(CH₃)₃).

5,11,17,23,29,35-Hexa-tert-butyl-37,40-bis[(N'-phenylthioureido)ethyl]oxy-38,39,41,42-tetrahydroxycalix[6]arene (5a). To a 0.4 g (0.38 mmol) of **3a** in 15 mL of CH₂Cl₂ and 5 mL of MeOH, 0.15 mL of phenylisothiocyanate and 0.6 mL of (Et)₃N was added and the mixture stirred for overnight under the nitrogen atmosphere. As soon as triethylamine was added, the white precipitate was formed and then slowly disappeared. At the end of reaction 20 mL of 1 N HCl solution was added, and stirred vigorously for 20 min, separated organic layer, and removed the solvent. The crude product was further purified by column chromatography (eluent hexane:THF=4:1) to give 0.30 g (60%) of **5a**. ¹H NMR (CD₂Cl₂) δ 8.04, 7.72 and 7.35 (three br s, 8H, -NH and OH), 6.8-7.2 (m, 22H, ArH), 3.4-4.3 (m, 20H, ArCH₂Ar and -OCH₂CH₂N-), 1.25 and 1.09 (two s, 54H, -C(CH₃)₃). ¹³C NMR (CDCl₃) δ 181.72 (-NHCSNH-), 149.31, 149.02, 148.81, 148.04, 143.35, 143.17, 132.21, 132.10, 129.33, 129.17, 126.69, 126.55, 126.32, 125.90, 125.82, 125.45, 125.19 and 124.82 (Ar), 73.66 (-OCH₂-), 45.18 (-CH₂NH-), 34.28, 34.17, 33.93, 31.81, 31.55, and 31.13 (ArCH₂Ar and -C(CH₃)₃).

¹H NMR Titration. A 0.5 mL of 4 × 10⁻³ M solution

of the host in CD₂Cl₂ was prepared. To this solution 0, 0.3, 0.5, 0.8, 1.0, 1.2, 1.5, 2.0, 3.0, 5.0, and 10 equivalents of the tetrabutylammonium salts were added in the NMR tube and the spectra were recorded. The chemical shifts of the NH protons and ortho protons of phenyl group near urea unit were followed and plotted against the equivalents of guest added. ¹H NMR spectra and titration were recorded on a 300 MHz spectrometer.

Acknowledgment. The authors wish to acknowledge the financial support of the Korea Research Foundation by NON DIRECTED RESEARCH FUND, in the program year of 1997.

References

- Atwood, J. A.; Davies, J. E.; MacNicol, D. D.; Vögtle, F. In *Comprehensive Supramolecular Chemistry*; Gokel, G. W., Ed. Elsevier Science Ltd.: Oxford, UK, 1996; Vol. 1.
- Lehn, J.-M. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 89.
- Arnaud-Neu, F.; Collins, E. M.; Deasy, M.; Ferguson, G.; Harris, S. F.; Kaitner, B.; Lough, A. J.; Mckerverey, M. A. *J. Am. Chem. Soc.* **1989**, *111*, 8681.
- Dietrich, B. *Pure Appl. Chem.* **1993**, *65*, 1457.
- Atwood, J. L.; Holman, K. T.; Steed, J. W. *Chem. Comm.* **1996**, 1401.
- Rason, L. *Aust. J. Chem.* **1976**, *29*, 1635.
- Scheerder, J.; Fochi, M.; Engbersen, J. F. L.; Reinhoudt, D. N. *J. Org. Chem.* **1994**, *59*, 7815.
- Scheerder, J.; Engbersen, J. F. L.; Casnati, A.; Ungaro, R.; Reinhoudt, D. N. *J. Org. Chem.* **1995**, *60*, 6448.
- Fan, E.; Van Arman, S. A.; Kincaid, S.; Hamilton, A. D. *J. Am. Chem. Soc.* **1993**, *115*, 369.
- Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1992**, *57*, 3160.
- Nam, K. C.; Park, K. S. *Bull. Korean Chem. Soc.* **1995**, *16*, 153.
- Nam, K. C.; Choi, Y. J.; Kim, D. S.; Kim, J. M.; Chun, J. C. *J. Org. Chem.* **1997**, *62*, 6441.
- Hynes, M. J. *J. Chem. Soc., Dalton Trans.* **1993**, 311.
- Stability constants of I⁻ and ClO₄⁻ were omitted because virtually no binding was observed.
- Bordwell, E.; Algrim, D. J.; Harrelson, Jr. J. A. *J. Am. Chem. Soc.* **1988**, *110*, 5903.