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Bis-calix[4]arenes with imine linkages: synthesis and binding study of thiopheno bis-calix[4]arene with viologens

Gil Tae Hwang and Byeang Hyean Kim*

Department of Chemistry, Center for Biofunctional Molecules, Pohang University of Science and Technology, Pohang 790-784, South Korea

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Abstract

We have developed an efficient synthetic pathway for various bis-calix[4]arenes with imine linkages by using a simple condensation procedure and carried out the binding study of thiopheno bis-calix[4]arene with biologically interesting viologen guests.

Keywords: calixarenes; macrocycles; molecular recognition; imines.

Development of efficient synthetic routes for novel three-dimensional macrocycles is very important in host–guest supramolecular chemistry.[1] Many interesting receptor molecules with calix[4]arenes[2] as a key structural motif have been developed, including double or multiple calix[4]arenes,[3] which are covalently constructed through upper rim–upper rim linkage[4] and lower rim–lower rim fasion[5] or noncovalently generated through hydrogen bonding.[6] However, in most cases the yields of bis-calix[4]arenes are very low due to the preference of intramolecular cross-linking to the intermolecular dimerization. We report here very efficient syntheses of novel bis-calix[4]arenes **1**–**5** with imine linkages,[7,8] the X-ray crystal structures of bis-calix[4]arenes **1** and **2**, and molecular recognition studies with viologens and their analogues.

Synthetic routes for the bis-calix[4]arenes **1**–**5** are shown in Scheme 1. The condensation reactions of dialdehydes with 1.1 equiv. of diaminocalix[4]arene **6**[9] in refluxing CH_2Cl_2:MeOH (1:1 v/v) in the presence of $MgSO_4$ for 24 h provided the corresponding bis-calix[4]arenes **1**–**4** in excellent yields (95–98%; Scheme 1). However, in the case of bis-calix[4]arene **5**, the isolated yield was only 19%. This result suggests that the efficiency of macrocyclization via imine condensation depends strongly on the geometry of the aldehyde or amine. The structures of bis-calix[4]arenes **1**–**5** were fully characterized by elemental analysis, mass spectroscopy, IR, UV, ^{1}H NMR and ^{13}C NMR.[10]

* Corresponding author. Tel: +82-562-279-2115; fax: +82-562-279-3399; e-mail: bhkim@postech.ac.kr

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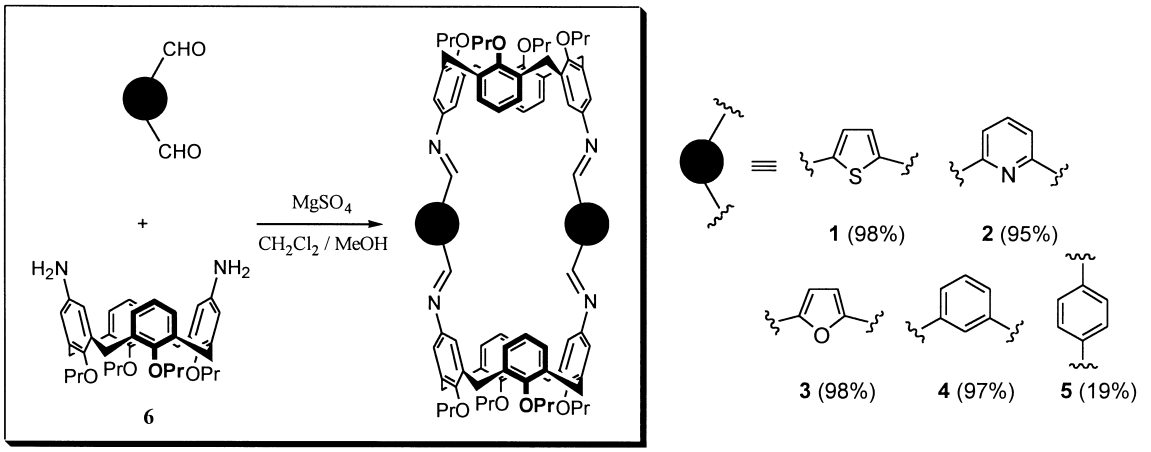

Scheme 1.

Fig. 1 shows the X-ray crystal structures of the bis-calix[4]arenes **1** and **2**.[11] These bis-calix[4]-arenes are all nanometer-sized macrocycles as seen in **1** (1.7 nm long) and **2** (1.8 nm long), and have good-sized cavities for host–guest complexation. The X-ray crystal structures clearly show that these calix[4]arenes adopt pinched cone conformations[8] in the solid state.

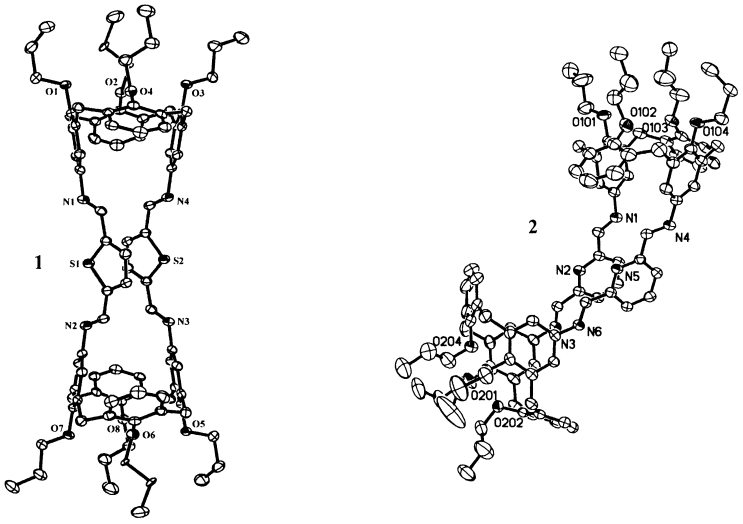

Figure 1. X-Ray crystal structures of bis-calix[4]arenes **1** and **2**. Two chloroform solvent molecules for **1**, and one methanol and a half of chloroform solvent molecules for **2**, are omitted for clarity

To show the utility of the bis-calix[4]arene hosts, we have carried out binding studies between the bis-calix[4]arenes and viologen-type guest molecules.[12] Viologens are well known as oxidation–reduction indicators and also have interesting biological activities. Diverse ranges of properties in the viologens are best understood and categorized in terms of their redox chemistry and the electron-poor nature of the viologen dication, and the viologens occupy a pivotal place in the field of electro-active organic molecules.[13] The structures of the guests for the molecular recognition

with the host **1** are shown in Fig. 2. The titration experiments were carried out by ^{1}H NMR spectroscopy in $CDCl_3$:CD_3OD (2:1 v/v, 300 K). The signals of imine and aromatic protons in the bis-calix[4]arene **1** shifted downfield when the viologens **7**–**11** were added to the host solution (the measured complexation-induced $\Delta\delta$ value of the imine proton of **1** was 0.30 ppm from δ 7.27 to δ 7.57 when 1.0 equiv. of viologen **7** was added), whereas no changes in the chemical shift values of **1** are detected when the compounds **12**–**14** were added. This indicates that suitable size of *N*-alkyl groups and the presence of the bipyridinium dication in viologens are essential to the inclusion process. The 1:1 complex was confirmed by a Job plot between bis-calix[4]arene **1** and the viologens (**9** and **11**). Nonlinear least-squares fitting analysis[14] of the complexation with **1** provided the association constant 727 M^{-1} for **7**, 515 M^{-1} for **8**, 320 M^{-1} for **9**, 154 M^{-1} for **10** and 124 M^{-1} for **11**. The signals of protons in the bis-calix[4]arene **2** did not shift upon addition of the viologens **7**, **9**, **10** and **11**, and other bis-calix[4]arenes **3–5** showed very weak affinities toward the viologen guests. These results indicate that the overall shape of host molecules and the electron density of aromatic linkers (thiophene, benzene, furan, pyridine) are the important factors in the binding affinity with the viologen guests.

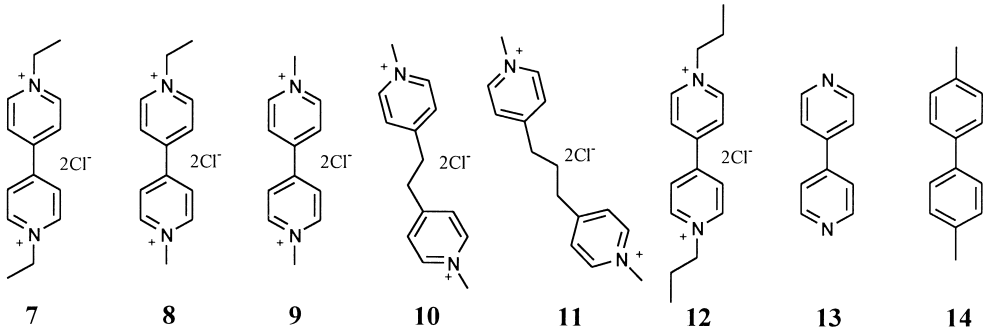

Figure 2. The structures of the guest molecules

In summary, we have developed an efficient synthetic pathway for making macrocyclic bis-calix[4]arenes with imine linkages and fully characterized the products, including the determination of the X-ray crystal structures. Thiopheno bis-calix[4]arene **1** shows good binding affinities toward biologically interesting viologen guests even in polar media. This one-step process to the bis-calix[4]arenes should widen our knowledge about these host systems and accelerate their supramolecular study in the future.

Acknowledgements

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References

1. (a) Lehn, J.-M. *Supramolecular Chemistry: Concepts and Perspectives*; VCH: Weinheim, 1995. (b) Cram, D. J.; Cram, J. M. *Container Molecules and Their Guests*; The Royal Society of Chemistry: Cambridge, 1994. (c) Kim, B. H.; Jeong, E. J.; Jung, W. H. *J. Am. Chem. Soc.* **1995**, *117*, 6390.

2. For reviews see: (a) Gutsche, C. D. *Top. Curr. Chem.* **1984**, *123*, 1. (b) Gutsche, C. D. *Calixarenes, Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, 1989; Vol. 1. (c) Gutsche, C. D. *Calixarenes Revisited*, *ibid*., 1998.
3. For reviews see: (a) Asfari, Z.; Weiss, J.; Vicens, J. *Synlett* **1993**, 719. (b) Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713.
4. (a) Böhmer, V.; Goldmann, H.; Vogt, W.; Vicens, J.; Asfari, Z. *Tetrahedron Lett.* **1989**, *30*, 1391. (b) Arduini, A.; Manfredi, G.; Pochini, A.; Sicuri, A. R.; Ungaro, R. L. *J. Chem. Soc., Chem. Commun.* **1991**, 936. (c) Araki, K.; Sisido, K.; Shinkai, S. *Tetrahedron Lett.* **1993**, *34*, 8297. (d) Asfari, Z.; Vicens, J.; Weiss, J. *Tetrahedron Lett.* **1993**, *34*, 627. (e) Pérez-Adelmar, J.-A.; Abraham, H.; Sánchez, C.; Rissanen, K.; Prados, P.; de Mendoza, J. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1009.
5. (a) Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1995**, *60*, 6070. (b) Ulrich, G.; Turek, P.; Ziessel, R. *Tetrahedron Lett.* **1996**, *37*, 8755. (c) McKervey, M. A.; Pitarch, M. *Chem. Commun.* **1996**, 1689. (d) Schmitt, P.; Beer, P. D.; Drew, M. G. B.; Sheen, P. D. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1840. (e) Stang, P. J.; Cao, D. H.; Chen, K.; Gray, G. M.; Muddiman, D. C.; Smith, R. D. *J. Am. Chem. Soc.* **1997**, *119*, 5163.
6. (a) Shimizu, K. D.; Rebek Jr., J. *Proc. Natl. Acad. Sci. USA* **1995**, *92*, 12403. (b) Castellano, R. K.; Kim, B. H.; Rebek Jr., J. *J. Am. Chem. Soc.* **1997**, *119*, 12671. (c) Klok, H.-A.; Jolliffe, K. A.; Schauer, C. L.; Prins, L. J.; Spatz, J. P.; Möller, M.; Timmerman, P.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1999**, *121*, 7154.
7. (a) Jazwinski, J.; Lehn, J.-M.; Lilienbaum, D.; Ziessel, R.; Guilhem, J.; Pascard, C. *J. Chem. Soc., Chem. Commun.* **1987**, 1691. (b) de Mendoza, J.; Mesa, E.; Rodríguez-Ubis, J.-C.; Vázquez, P.; Vögtle, F.; Windscheif, P.-M.; Rissanen, K.; Lehn, J.-M.; Lilienbaum, D.; Ziessel, R. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1331.
8. Struck, O.; Chrisstoffels, L. A. J.; Lugtenberg, R. J. W.; Verboom, W.; van Hummel, G. J.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1997**, *62*, 2487.
9. Rudkevich, D. M.; Verboom, W.; Reinhoudt, D. N. *J. Org. Chem.* **1994**, *59*, 3683.
10. Selected spectroscopic data of **1**–**5**. Compound **1**: mp $>330^{\circ}$C (dec.); ^{1}H NMR (300 MHz, $CDCl_3$) 7.40 (s, 4H, imine H), 7.17 (d, 8H, $J=7.3$ Hz, ArH), 6.97 (t, 4H, $J=7.4$ Hz, ArH), 6.91 (s, 4H, ArH), 6.03 (s, 8H, ArH), 4.44 (d, 8H, $J=13.1$ Hz, $ArCH_2Ar$), 4.05 (t, 8H, $J=8.1$ Hz, OCH_2), 3.64 (t, 8H, $J=6.6$ Hz, OCH_2), 3.16 (d, 8H, $J=13.3$ Hz, $ArCH_2Ar$), 2.00 (seq, 8H, $J=7.4$ Hz, CH_2CH_3), 1.89 (seq, 8H, $J=7.4$ Hz, CH_2CH_3), 1.10 (t, 12H, $J=7.4$ Hz, CH_3), 0.89 (t, 12H, $J=7.4$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 157.9, 154.0, 150.2, 145.9, 145.2, 137.0, 133.8, 130.4, 129.1, 122.1, 120.0, 77.1, 31.1, 23.5, 22.9, 10.8, 9.8; FAB-MS (*m*/*z*) 1453.7 (M^++1), 1452.7 (M^+). Anal. calcd for $C_{92}H_{100}N_4O_8S_2$: C, 76.00; H, 6.93; N, 3.75. Found: C, 75.88; H, 6.92; N, 3.69. Compound **2**: mp $>384^{\circ}$C (dec.); ^{1}H NMR (300 MHz, $CDCl_3$) 7.77 (s, 4H, imine H), 7.56 (d, 8H, $J=7.7$ Hz, ArH), 7.20–7.04 (m, 12H, ArH), 6.90 (t, 2H, $J=7.3$ Hz, ArH), 6.20 (s, 8H, ArH), 4.44 (d, 8H, $J=13.3$ Hz, $ArCH_2Ar$), 4.04 (t, 8H, $J=8.2$ Hz, OCH_2), 3.60 (t, 8H, $J=6.6$ Hz, OCH_2), 3.37 (d, 8H, $J=13.5$ Hz, $ArCH_2Ar$), 1.97–1.76 (m, 16H, CH_2CH_3), 1.05 (t, 12H, $J=7.4$ Hz, CH_3), 0.89 (t, 12H, $J=6.8$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 157.9, 157.6, 155.3, 155.0, 154.4, 143.4, 136.8, 136.6, 135.9, 134.1, 133.7, 129.3, 129.2, 126.5, 122.8, 122.3, 121.9, 115.4, 77.0, 76.5, 31.4, 31.0, 23.5, 22.9, 22.7, 10.8, 9.7, 9.7; FAB-MS (*m*/*z*) 1444.7 (M^++2), 1443.7 (M^++1). Anal. calcd for $C_{94}H_{102}N_6O_8{\cdot}H_2O$: C, 77.23; H, 7.17; N, 5.75. Found: C, 77.54; H, 7.09; N, 5.75. Compound **3**: mp $>246^{\circ}$C (dec.); ^{1}H NMR (300 MHz, $CDCl_3$) 7.42 (s, 4H, imine H), 7.18 (d, 8H, $J=7.2$ Hz, ArH), 7.02 (t, 4H, $J=7.0$ Hz, ArH), 6.56 (s, 4H, ArH), 6.12 (s, 8H, ArH), 4.46 (d, 8H, $J=13.2$ Hz, $ArCH_2Ar$), 4.08 (t, 8H, $J=8.2$ Hz, OCH_2), 3.66 (t, 8H, $J=6.5$ Hz, OCH_2), 3.17 (d, 8H, $J=13.3$ Hz, $ArCH_2Ar$), 2.05–1.85 (m, 16H, CH_2CH_3), 1.11 (t, 12H, $J=7.3$ Hz, CH_3), 0.90 (t, 12H, $J=7.4$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 157.6, 154.3, 153.9, 144.5, 144.3, 136.7, 133.9, 129.0, 122.5, 120.2, 114.8, 77.1, 76.4, 31.1, 23.4, 22.8, 10.8, 9.7; FAB-MS (*m*/*z*) 1422.6 (M^++2), 1421.6 (M^++1). Anal. calcd for $C_{92}H_{100}N_4O_{10}{\cdot}2.5H_2O$: C, 75.33; H, 7.21; N, 3.82. Found: C, 75.45; H, 7.27; N, 3.62. Compound **4**: mp $>220^{\circ}$C (dec.); ^{1}H NMR (300 MHz, $CDCl_3$) 7.49 (s, 2H, ArH), 7.31 (s, 4H, imine H), 7.27 (d, 4H, $J=7.7$ Hz, ArH), 7.21 (d, 8H, $J=7.2$ Hz, ArH), 7.07–6.98 (m, 4H, ArH), 6.86 (t, 2H, $J=7.6$ Hz, ArH), 6.11 (s, 8H, ArH), 4.50 (d, 8H, $J=13.1$ Hz, $ArCH_2Ar$), 4.10 (t, 8H, $J=8.1$ Hz, OCH_2), 3.68 (t, 8H, $J=6.7$ Hz, OCH_2), 3.21 (d, 8H, $J=13.3$ Hz, $ArCH_2Ar$), 2.04 (seq, 8H, $J=7.9$ Hz, CH_2CH_3), 1.91 (seq, 8H, $J=7.1$ Hz, CH_2CH_3), 1.13 (t, 12H, $J=7.4$ Hz, CH_3), 0.92 (t, 12H, $J=6.5$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 157.9, 157.6, 157.2, 153.8, 145.3, 137.0, 136.8, 136.1, 134.0, 133.7, 130.4, 129.0, 128.0, 122.7, 121.9, 120.4, 119.4, 77.2, 76.4, 31.2, 23.5, 22.9, 22.9, 10.8, 9.8; FAB-MS (*m*/*z*) 1441.8 (M^++1), 1440.8 (M^+). Anal. calcd for $C_{96}H_{104}N_4O_8$: C, 79.97; H, 7.27; N, 3.89. Found: C, 80.26; H, 7.33; N, 3.80. Compound **5**: mp $>205^{\circ}$C (dec.); ^{1}H NMR (300 MHz, $CDCl_3$) 7.38 (s, 4H, imine H), 7.19 and 7.16 (s, 16H, ArH), 6.98 (t, 4H, $J=7.4$ Hz, ArH), 6.09 (s, 8H, ArH), 4.47 (d, 8H, $J=13.1$ Hz, $ArCH_2Ar$), 4.07 (t, 8H, $J=8.2$ Hz, OCH_2), 3.65 (t, 8H, $J=6.6$ Hz, OCH_2), 3.18 (d, 8H, $J=13.2$ Hz, $ArCH_2Ar$), 2.06–1.84 (m, 16H, CH_2CH_3), 1.10 (t, 12H, $J=7.4$ Hz, CH_3), 0.89 (t, 12H, $J=7.4$ Hz, CH_3); ^{13}C

NMR (75 MHz, $CDCl_3$) 157.8, 156.7, 153.9, 145.4, 137.7, 136.9, 133.8, 129.1, 128.1, 122.1, 119.9, 77.2, 23.5, 22.9, 10.9, 9.8; FAB-MS (*m*/*z*) 1441.8 (M^++1), 1440.8 (M^+). Anal. calcd for $C_{96}H_{104}N_4O_8$: C, 79.97; H, 3.89; N, 7.27. Found: C, 80.13; H, 3.59; N, 7.52.

11. *Crystal data* for **1**: $C_{92}H_{100}N_4O_8S_2{\cdot}2CHCl_3$, $M = 1692.62$, crystal system: triclinic, space group: $P\bar{1}$, $a = 10.03980(10)$ Å, $b = 12.6750(2)$ Å, $c = 19.0134(4)$ Å, $\alpha = 71.5080(10)^\circ$, $\beta = 86.9880(10)^\circ$, $\gamma = 73.63^\circ$, $V = 2199.75(6)$ Å^3, $Z = 1$, $d_{calc} = 1.278$ g cm^{-3}, $T = 188(2)$ K, Siemens SMART diffractometer with CCD detector, Mo K_α ($\lambda = 0.71073$ Å), $\mu = 3.01$ cm^{-1}, of 8962 measured data, 6589 were independent ($R_{int} = 0.0337$), $R1$ [$I > 2s(I)$] = 0.0609, $wR2$ (all data) = 0.1341 and GOF = 1.174. *Crystal data* for **2**: $C_{94}H_{102}N_6O_8{\cdot}CH_3OH{\cdot}0.5CHCl_3$, $M = 1535.54$, crystal system: triclinic, space group: $P\bar{1}$, $a = 13.00690(10)$ Å, $b = 18.7630(2)$ Å, $c = 20.87830(10)$ Å, $\alpha = 112.2880(10)^\circ$, $\beta = 95.7700(10)^\circ$, $\gamma = 108.6870^\circ$, $V = 4320.41(6)$ Å^3, $Z = 2$, $d_{calc} = 1.180$ g cm^{-3}, $T = 188(2)$ K, Siemens SMART diffractometer with CCD detector, Mo K_α ($\lambda = 0.71073$ Å), $\mu = 1.20$ cm^{-1}, of 17 302 measured data, 12 742 were independent ($R_{int} = 0.0279$), $R1$ [$I > 2s(I)$] = 0.0801, $wR2$ (all data) = 0.2371 and GOF = 0.976.
12. Zhong, Z.; Ikeda, A.; Shinkai, S. *J. Am. Chem. Soc.* **1999**, *121*, 11906.
13. (a) Monk, P. M. S. *The Viologens*; John Wiley: Chichester, 1998. (b) Asakawa, M.; Brown, C. L.; Menzer, S.; Raymo, F. M.; Stoddart, J. F.; Williams, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 2614. (c) Amabilino, D. B.; Ashton, P. R.; Boyd, S. E.; Lee, J. Y.; Menzer, S.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2070.
14. Macomber, R. S. *J. Chem. Educ.* **1992**, *69*, 375.