

Synthesis and Color Modulation of an Unsymmetrical Calix[4]-bis-crown Incorporating *p*-Nitro-azobenzene as a Chromoionophoric Mixed Receptor

Hwan Gyu Lee,^{†,§} Joobeom Seo,^{*,*} and Kyu Seong Choi^{§,*}

[†]Department of Material Science and Engineering, Yonsei University, Seoul 120-749, Korea

^{*}Korea Institute of Geoscience and Mineral Resources, Daejeon 305-350, Korea. *E-mail: joobeomi@gmail.net

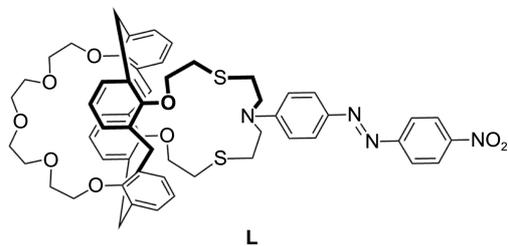
[§]Department of Science Education and Kyungnam Institute of the Gifted Education in Science, Kyungnam University, Changwon 631-701, Korea. *E-mail: kschoi@kyungnam.ac.kr

Received January 3, 2013, Accepted February 13, 2013

Key Words : Azo-attached calix[4]-bis-crown, Mercury(II), Mixed receptor

Calix[4]arenes have been shown to be versatile building blocks for the development of new types of receptors with specific properties.¹ For example, calix[4]crowns offer particular promise as the fusion of calix[4]arene and crown units by bridging through entities to accommodate the guests.² Calix[4]-bis-crown is the family of the macrotricycles derived from one calix[4]arene and two crown rings which can bind two guests in its two crown cavities.³ In particular, unsymmetrical calix[4]-bis-crowns which contain one crown ring on one side and other mixed-donor ring on the other side of the calix[4]arene unit also have been reported as mixed receptors.⁴

The chromogenic chemosensors based on the macrocyclic receptors are especially attractive because the selective guest determination can be carried out by the naked eye, without use of instrumentation.⁵ We previously have reported two chromogenic NS₂-macrocycles which showed mercury(II) selectivity.⁶ As an extension of this work to develop new types of chromogenic macrocyclic system, we report the synthesis and color modulation of an azo-attached unsymmetrical calix[4]-bis-crown **L** as a novel chromoionophoric mixed receptor which can bind the soft and hard metal ions in its two different crown cavities.



Experimental Section

General. All commercial reagents including solvents were of analytical reagent grade where available. FT-IR spectra were measured with a Thermo Scientific Nicolet iS10 spectrophotometer. NMR spectra were recorded on a Bruker DRX-300 spectrometer (300 MHz). UV-vis spectra were recorded on a Scinco S-3100 UV-vis spectrophotometer. The electro-

spray ionization (ESI) mass spectra were obtained on a Thermo Scientific LCQ Fleet spectrometer.

Synthesis of Ligand (L). As shown in Scheme 1, to a refluxed solution of K₂CO₃ (0.845 g, 6.11 mmol) and ditosyl derivative **2**⁷ (1.5 g, 1.53 mmol) in THF (100 mL), a solution of *N,N*-bis(2-mercaptoethyl)aniline^{5c} (0.392 g, 1.83 mmol) in THF (30 mL) was added under nitrogen. The reaction mixture was refluxed for 24 h. After removal of the solvent, the resulting solid was dissolved in CH₂Cl₂ and the organic layer was washed with water. The organic layer was dried over anhydrous Na₂SO₄ and evaporated to give the crude product. Flash column chromatography on silica-gel using 50% ethyl acetate/*n*-hexane led to isolation of *N*-phenylated precursor **3** as a white solid (0.36 g, 25%). mp 136-138 °C. ESI mass (*m/z*): 847 ([M]⁺). IR (KBr, cm⁻¹): 2996, 1596, 1504, 1458, 1355, 1213, 1143, 1093, 1008, 764. ¹H NMR (300 MHz, CDCl₃) δ 7.26 (d, 2H, *NAr*), 7.13 (d, 8H, *Ar*), 6.94 (m, 4H, *Ar*), 6.71 (m, 3H, *NAr*), 3.93 (ss, 8H, ArCH₂Ar), 3.56 (m, 12H, OCH₂CH₂OCH₂), 3.43 (m, 8H, ArOCH₂), 3.11 (t, 4H, OCH₂CH₂S), 2.67 (t, 4H, SCH₂CH₂N), 2.09 (t, 4H, SCH₂CH₂N).

L was synthesized by the reaction of the diazonium salt^{5c} of *p*-nitroaniline with **3**. The diazonium salt solution was added dropwise into a solution of **3** in DMF at 0 °C and then the solution mixture was further stirred for 12 h at 0 °C. After removal of the solvent, the resulting solid was dissolved in CH₂Cl₂ and the organic layer was washed with water. The organic layer was dried over anhydrous Na₂SO₄ and evaporated to give a reddish oil. Flash column chromatography on silica-gel using 50% ethyl acetate/*n*-hexane as the eluent led to the isolation of **L** as a red solid (80%). mp 242-245 °C. IR (KBr, cm⁻¹): 2923, 2854, 1598, 1514, 1458, 1390, 1336, 1217, 1135, 1097, 1004, 763. ESI mass (*m/z*): 996 ([M]⁺). ¹H NMR (300 MHz, CDCl₃, δ, each subscript proton number refers the corresponding proton shown in Figure S1): 8.35 (d, 2H, H₁₅), 7.96 (d, 4H, H_{13,14}), 7.14 (d, 8H, H₁₁), 6.92 (m, 4H, H₁₀), 6.77 (d, 2H, H₁₂), 3.92 (ss, 8H, H₅), 3.57 (m, 16H, H₁₋₄), 3.33 (t, 4H, H₆), 3.10 (t, 4H, H₇), 2.73 (t, 4H, H₉), 2.10 (t, 4H, H₈). ¹³C NMR (300 MHz, CDCl₃) δ 156.6, 155.8, 150.7, 147.5, 144.1, 134.2, 133.7, 133.7, 129.6, 129.0, 128.7, 126.4, 124.6, 123.1, 123.0, 122.7,

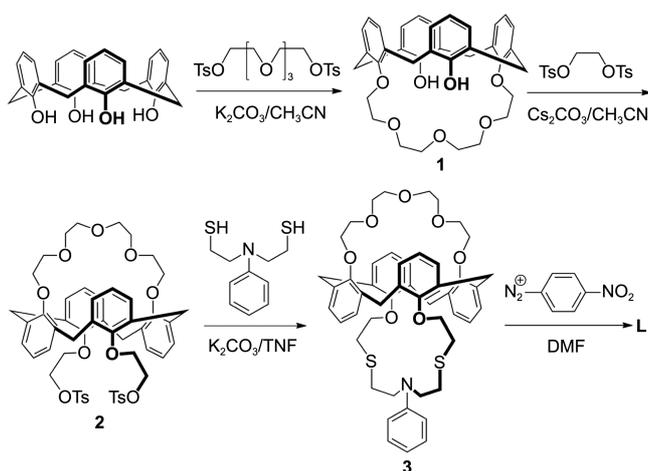
122.3, 111.0, 72.6, 70.6, 69.8, 68.2, 67.5, 50.1, 38.1, 30.1, 29.7.

Results and Discussion

Synthesis and Crystal Structure of L. The target **L** was synthesized by two-step cyclization reactions. First, the cyclization of calix[4]arene with tetraethylene glycol ditosylate, employing K_2CO_3 afforded calix[4]-mono-crown-5 (**1**).⁸ Ditosylation of **1** with ethyleneglycol ditosylate led to calix[4]-mono-crown-5 ditosyl derivative **2**.⁸ The cyclization of **2** with *N,N*-bis(2-mercaptoethyl)aniline^{5c} in the presence of K_2CO_3 afforded *N*-phenylated derivative **3** as a key precursor. Subsequently, the diazonium salt was *in situ* added to a solution of **3**, providing **L** as a red solid.

The structure of **L** was also characterized in the solid state by single crystal X-ray crystallography (Figure 1). Single crystals of **L** suitable for X-ray analysis were obtained by slow evaporation from the solution of methanol. The crystal structure gave an evidence of the 1,3-alternate conformation of the calix[4]arene unit. The conformation of two unsymmetrical bridging rings, which connect two opposite xylyl groups differ from the donor sets: the O_5 ring is unfolded and the S_2O_2N ring is bent.

Cation-Induced Color Changes. For investigating the metal-induced color changes of **L**, group I, II, transition, and heavy metal ions are adopted. In acetonitrile, **L** exhibited an intense absorption at 473 nm (red, $\epsilon_{max} = 21000 \text{ dm}^3 \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$) which can be assigned to charge-transfer band.⁵ Figure 1 shows the spectral changes of **L** after adding five equivalents of the metal perchlorates. When ClO_4^- was



Scheme 1. Synthesis of **L**.

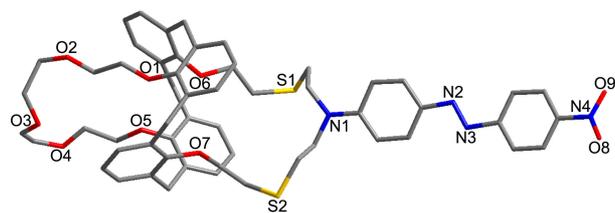


Figure 1. Crystal structure of **L**.

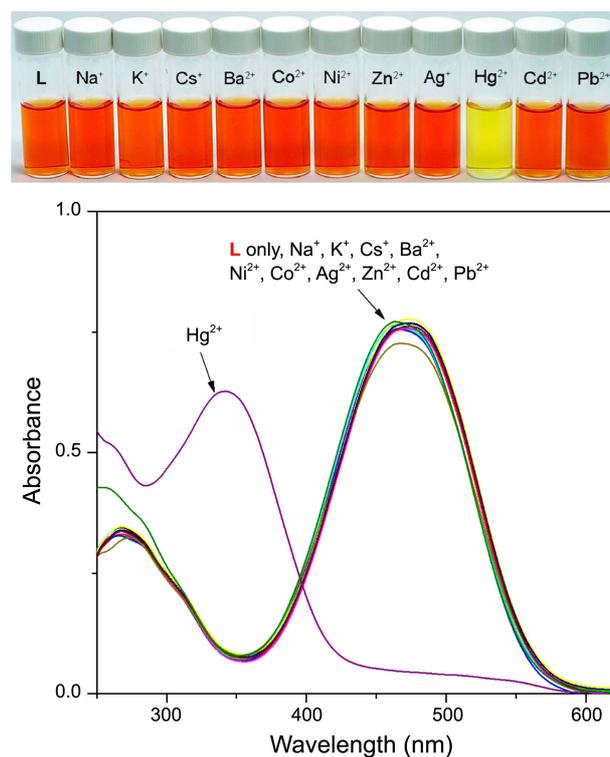


Figure 2. UV-vis spectral changes of **L** ($3.0 \times 10^{-5} \text{ M}$) in the presence of metal perchlorates (5.0 equiv) in acetonitrile.

adopted as a counter anion, the largest metal ion induced hypochromic shifts for Hg^{2+} (to 341 nm; $\Delta\lambda = 132 \text{ nm}$) resulted in color change from red to pale-yellow.

In order to probe the origins of the observed selectivity toward Hg^{2+} , the solution behaviors of mercury(II) perchlorate complex of **L** were investigated by UV-vis titration (Figure 3). The addition of mercury(II) perchlorate into the **L** solution in acetonitrile causes decrease of absorbance at 473 nm and increase of band at 341 nm up to 1.0 equivalent (metal-to-ligand) to give an isobestic point at 400 nm. Thus, a 1:1 complexation was evident from the titration curve (see the inset in Figure 3), suggesting the stable stoichiometric

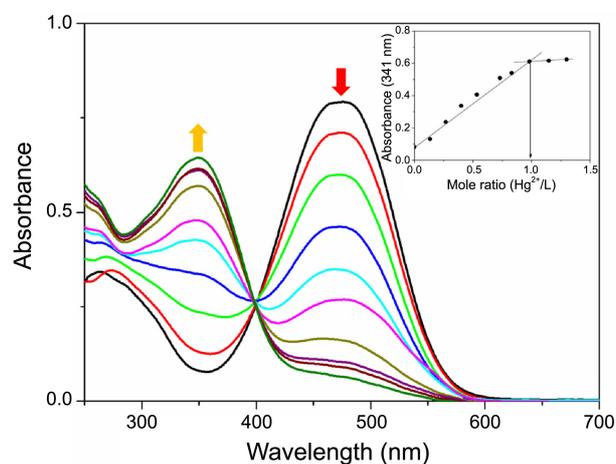


Figure 3. UV-vis titration of **L** ($3.0 \times 10^{-5} \text{ M}$) with $Hg(ClO_4)_2$ in acetonitrile. Inset: titration curve showing 1:1 stoichiometry.

complex formation in solution as the origin of the observed selectivity.

Anion-Effect on Color Changes. During the course of investigating the metal-ion complexation and related metal-induced color changes of **L**, an interesting anion effect on the color change for **L** was observed. As already mentioned showing Figure 2, the addition of $\text{Hg}(\text{ClO}_4)_2$ to the solution of **L** resulted in the largest hypochromic shift unlike other metal ions investigated. However, the same experimental works with metal nitrates instead of perchlorates gave, for instance, more or less no significant spectral shifts (color changes) upon addition of selected metal ions (Figure 4(a)). Notably, the mercury(II) nitrate induced no spectral shift but

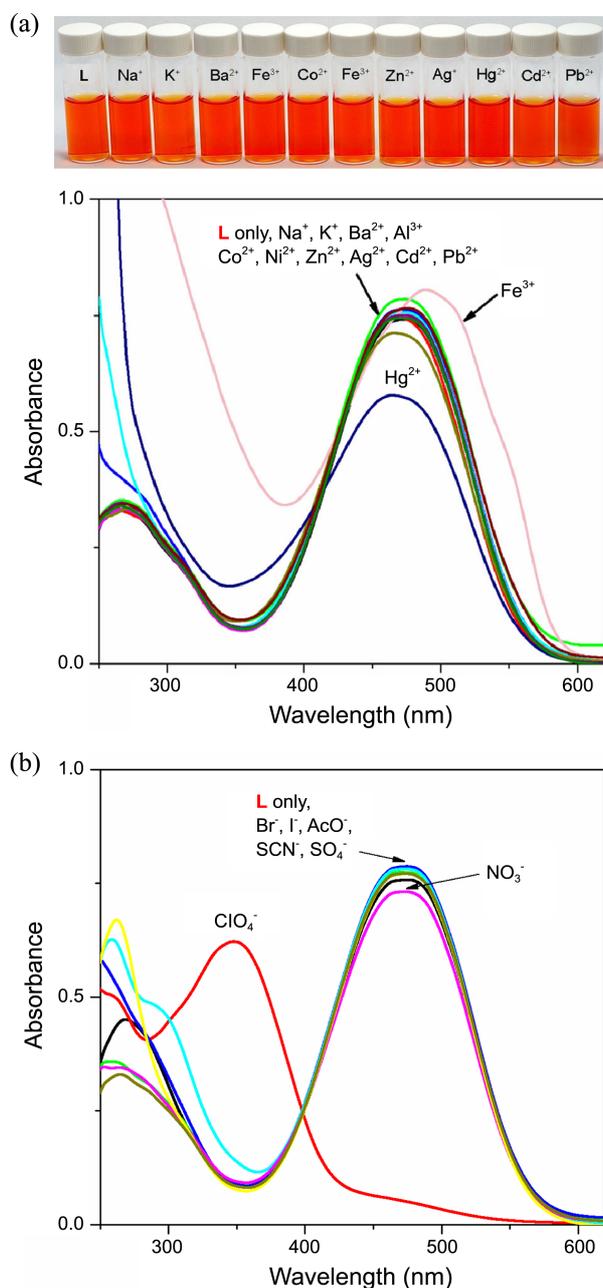


Figure 4. UV-vis spectral changes of **L** (3.0×10^{-5} M) in the presence of (a) metal nitrates (5.0 equiv) and (b) mercury(II) salts (5.0 equiv) in acetonitrile.

just ~20% decrease of the peak intensity.

Some more mercury(II) salts with different anions were also employed in the same experimental work. As can be seen in Figure 4(b), no color changes were observed upon addition of HgBr_2 , HgI_2 , $\text{Hg}(\text{NO}_3)_2$, $\text{Hg}(\text{CH}_3\text{COO})_2$, $\text{Hg}(\text{SCN})_2$, or HgSO_4 . Consequently, it is found that the color change for **L** with Hg^{2+} is controlled by anions. The behavior observed reflects the structure of the respective complex generated.

For further understanding of the anion effect on color changes, we have isolated the red crystalline complex from the reaction of **L** with $\text{Hg}(\text{NO}_3)_2$ in $\text{CH}_2\text{Cl}_2/\text{MeOH}$. Although this crystal is of poor quality and several crack can be seen, an approximate crystal structure with the formula being $[\text{Hg}(\text{L})(\text{NO}_3)_2]_n$ is obtained (Figure S2 in Supporting Information). Each exo-coordinated Hg^{2+} is in a distorted tetrahedral environment with its coordination sites occupied by two S atoms from two different ligands and two NO_3^- ions. It obviously shows that the N donor in the macrocycle is not bound to Hg^{2+} , and hence the Hg^{2+} is located outside the cavity. Thus, it is concluded that the observed anion effect of the mercury(II) salts on the color changes is due to the anion coordination ability. Similar behavior was reported previously.^{5c} Therefore, the observed no color change with mercury(II) nitrate can be explained in terms of the strong coordination of the NO_3^- acting to prevent Hg-N bond formation which induces color change from red to pale-yellow by ClO_4^- .

Bication System for the Mixed Receptor. Single crystals of the corresponding heteronuclear complexes of the mixed receptor **L** were not able to be obtained. Instead, the binding behaviors of **L** toward Hg^{2+} as well as $\text{Hg}^{2+}/\text{K}^+$ were further investigated by ESI-mass and UV-vis experiments. The ESI-mass spectra with mercury(II) perchlorate were dominated by mononuclear mercury(II) complex species such as $[\text{HgL}]^{2+}$ (m/z 599), $[\text{HgL}(\text{CH}_3\text{CN})]^{2+}$ (m/z 619) and $[\text{HgL}(\text{ClO}_4)]^+$

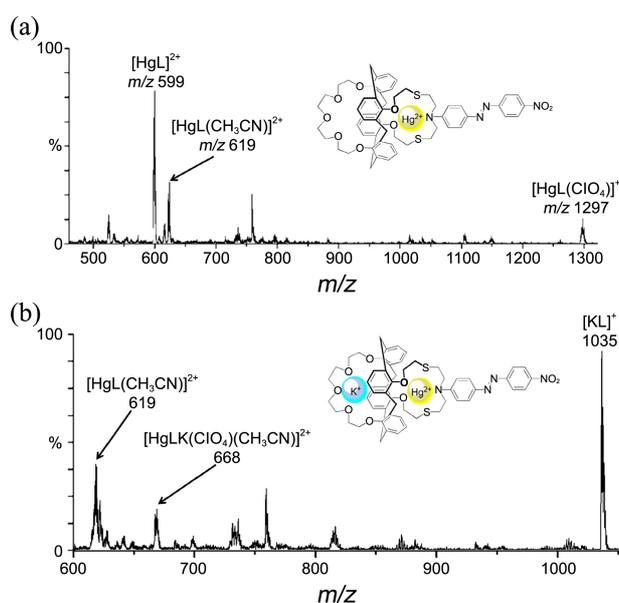


Figure 5. ESI-mass spectra of the complex solutions: the samples were prepared by dissolving (a) **L**+ $\text{Hg}(\text{ClO}_4)_2$ (1.0 equiv) and (b) **L**+ $\text{Hg}(\text{ClO}_4)_2$ (1.0 equiv)+ KClO_4 (1.0 equiv) in acetonitrile.

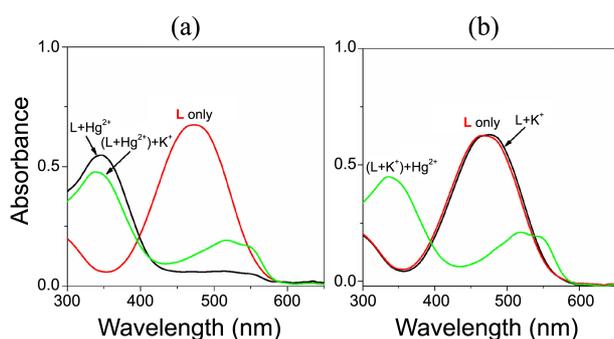


Figure 6. Spectral changes of **L** on stepwise addition of hard (K^+ , 1.0 equiv) and soft (Hg^{2+} , 1.0 equiv) metal perchlorates: (a) red: **L** only, black: **L**+ Hg^{2+} , and green: (**L**+ Hg^{2+})+ K^+ and (b) red: **L** only, black: **L**+ K^+ , and green: (**L**+ K^+)+ Hg^{2+} .

(m/z 1297) (Figure 5(a)). The heterobinuclear species corresponding to $[HgLK(ClO_4)(CH_3CN)]^{2+}$ (m/z 668) was also observed in mass spectra with a mixture of mercury(II) and potassium(I) perchlorates, suggesting the behavior of **L** as an unsymmetrical receptor (Figure 5(b)).

In a stepwise and comparative UV-vis study, the formation of the heterodinuclear complex was also monitored by observing the color probe (Figure 6). For example, the addition of one equivalent of mercury(II) perchlorate to the solution of **L** causes larger blue shift (from red to black lines in Figure 6(a)). On addition of one more equivalent of potassium(I) perchlorate, more or less no further shift was observed (green line in Figure 6(a)). This behavior confirms the different affinity of the donor sets - the Hg^{2+} is not bonded as strongly in the O_5 -cavity as it is in the O_2S_2N -cavity. However, addition of one equivalent of K^+ to the above solution of Hg^{2+} complex led to a minimum spectral change, in accord with the formation of the heterodinuclear species $[HgLK]^{2+}$. In another word, the second metal cation (hard metal ion) effect on the primary soft metal recognition was negligible in terms of the mixed receptor.

The UV-vis spectra of **L** were also obtained under conditions involving the reverse order of perchlorate salt addition (Figure 6(b)). According to the spectral changes on addition of one equivalent of potassium(I) perchlorate to the solution of **L** (red to black lines in Figure 6(b)), the potassium(I) ion is accommodated in the O_5 -ring cavity and then the added Ag^+ occupies the O_2S_2N ring cavity to form the heterodinuclear species $[HgLK]^{2+}$. Interestingly, the UV-vis spectrum for the sample containing both of Hg^{2+} and K^+ in Figure 6(a) (green line) shows the same pattern to those in Figure 6(b) (green line), suggesting that the respective structural conversions finally reach the same heterodinuclear complexation equilibrium position.

In summary, an *azo*-attached unsymmetrical calix[4]-bis-crown **L** was synthesized and its solid structure was characterized by single crystal X-ray analysis. The chromoionophoric property of **L** was investigated by monitoring changes

in the UV-vis spectra of **L** on addition of the metal perchlorates. The largest cation-induced hypochromic shift for Hg^{2+} resulted in color change from red to pale-yellow, where as no significant color change was observed upon addition of other metal ions. From the spectroscopic titration data, the origin of the observed selectivity toward Hg^{2+} was revealed as a result of the stoichiometric (1:1) stable complexation of **L** with Hg^{2+} . In the Hg^{2+} sensing by **L**, the anion controlled color changes was observed and this can be explained by endo- or exocyclic complexation due to the difference of anion coordinating ability. The formation of heterodinuclear (Hg^{2+}/K^+) complexation of **L** as a mixed receptor was confirmed by ESI mass study. In a stepwise and comparative UV-vis spectroscopy study, the formation of the heterodinuclear complex was also monitored by observing the color probe.

Crystallographic data have been deposited with CCDC (Deposition No. CCDC-917230 for **L**). These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html> or from CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, E-mail: deposit@ccdc.cam.ac.uk

Acknowledgments. This research was supported by Kyungnam University Research Fund, 2012.

Supporting Information. The NMR spectrum of **L**, X-ray data for **L**, and the approximate crystal structure of mercury(II) nitrate complex of **L** can be found here.

References

- (a) Gutsche, C. D. *Acc. Chem. Res.* **1983**, *16*, 161. (b) Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.* **1985**, *107*, 6052. (c) Gutsche, C. D. *Calixarenes*; Royal Society of Chemistry: Cambridge, 1989.
- (a) Ma, J. C.; Dougherty, D. A. *Chem. Rev.* **1997**, *97*, 1303. (b) Lhotak, P.; Shinkai, S. *J. Phys. Org. Chem.* **1997**, *10*, 273. (c) Casanti, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767.
- (a) Abidi, R.; Asfari, Z.; Harrowfield, J. M.; Sobolev, A. N.; Vicens, J. *Aust. J. Chem.* **1996**, *49*, 183. (b) Pulpoka, B.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **1996**, *35*, 6315. (c) Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713.
- (a) Asfari, Z.; Lamare, V.; Dozol, J. F.; Vicens, J. *Tetrahedron Lett.* **1999**, *40*, 691. (b) Asfari, Z.; Thuéry, P.; Nierlich, M.; Vicens, J. *Tetrahedron Lett.* **1999**, *40*, 499. (c) Lee, J. Y.; Kim, H. J.; Park, C. S.; Sim, W.; Lee, S. S. *Chem. Eur. J.* **2009**, *15*, 8989.
- (a) Gerd, H.; Vögtle, F. *Acc. Chem. Res.* **1985**, *18*, 65. (b) Quang, D. T.; Kim, J. S. *Chem. Rev.* **2010**, *110*, 6280. (c) Sancenón, F.; Martínez-Mañez, R.; Soto, J. *Angew. Chem. Int. Ed.* **2002**, *41*, 1416. (d) Lee, S. J.; Jung, J. H.; Seo, J.; Yoon, I.; Park, K.-M.; Lindoy, L. F.; Lee, S. S. *Org. Lett.* **2006**, *8*, 1641.
- Lee, H. G.; Lee, J.-E.; Choi, K. S. *Inorg. Chem. Comm.* **2006**, *9*, 582.
- Sim, W.; Lee, J. Y.; Kwon, J.; Kim, M. J.; Kim, J. S. *Bull. Korean Chem. Soc.* **2002**, *23*, 879.
- Kim, J. S.; Shon, O. J.; Ko, J. W.; Cho, M. H.; Yu, I. Y.; Vicens, J. *J. Org. Chem.* **2000**, *65*, 2386.