Tetrahedron Letters 51 (2010) 3719–3723

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Novel 2,2′-bipyridine-modified calix[4]arenes: ratiometric fluorescent chemosensors for Zn^{2+} ion

Jun Feng Zhang [a], Sankarprasad Bhuniya [a], Young Hoon Lee [a], Changwan Bae [a], Joung Hae Lee [b,*], Jong Seung Kim [a,*]

[a] Department of Chemistry, Korea University, Seoul 130-701, Republic of Korea
[b] Korea Research Institute of Standards and Science, Daejon 305-600, Republic of Korea

ARTICLE INFO

Article history:
Received 5 April 2010
Revised 23 April 2010
Accepted 30 April 2010
Available online 9 May 2010

Keywords:
Chemosensor
Zinc
Bipyridine
Calixarenes
Ratiometric

ABSTRACT

Two calix[4]arene derivatives with modified bipyridine as binding sites have been designed and synthesized. Compounds **1** and **2** are the first 2,2′-bipyridine-modified calix[4]arene-based sensors that can detect Zn^{2+} selectively with respect to ratiometric fluorescent changes and red shift. A binuclear complex structure has been demonstrated in the binding modes of **1**-Zn^{2+} and **2**-Zn^{2+} complexes.

Recently, chemosensors based on the ion-induced fluorescence changes are becoming increasingly popular due to their simplicity, high sensitivity, and selectivity.[1] In particular, the development of a high selective fluorescent probe for zinc ion in the presence of a variety of other metal ions has received great attention.[2] Zinc ion is one of the most abundant transition-metal ions in mammals and plays crucial roles in many important biological processes such as protein synthesis, neural signal transduction, enzyme regulation, and gene expression.[3] The zinc deficiency could cause unbalanced metabolism, which is responsible for many severe diseases such as low blood sugar, Alzheimer's disease, epilepsy, ischemic stroke, and infantile diarrhea.[4] On the other hand, pancreatic islets containing relatively high concentrations of zinc ion could play critical roles in insulin biosynthesis, storage, and secretion.[5] Moreover, zinc is an agricultural and food waste product in the environment, excessive concentration of zinc may reduce the soil microbial activity, resulting in phytotoxic effect and other problems.[6] Therefore, the exploration of simple, quick, and efficient Zn^{2+}-selective fluorescent chemosensor is necessary not only for the fundamental research but also for biological application in living systems.

Calixarenes are well known for basic molecular scaffolds with structural rigidity, special molecular appearance, and facile introduction of fluorophore. Modifications of calixarenes have given rise to a great number of derivatives with tunable binding properties and a variety of fluorescent properties.[7] Some of them have been reported in our previous works and proved to be effective fluorescent sensors for Cu^{2+}, Ca^{2+}, Ag^{+}, In^{3+}, and some other metal ions.[8] In the present work, the calix[4]arenes in conjunction with binding groups would facilitate the recognition of metal ions.

Bipyridine ligand is well known and has been extensively used as a metal-chelating ligand due to its robust redox stability and ease of functionalization.[9,10] A distinguishing feature of this ligand working as a sensor is the sensitive response toward zinc ions with a significant red shift in emission,[11] which provides the potential to form a ratiometric fluorescent sensor that exhibits a spectral shift upon binding to the analytes of interest. Compared to multitudinous of zinc sensors functioning as cation-responsive optical switches that translate the binding event into either an increase or decrease of the emission intensity, only a few ratiometric fluorescent sensors for zinc have been reported.[11–13] Therefore, to develop a high selective and ratiometric fluorescent Zn^{2+} sensor by rationally modifying the calix[4]arenes structure and introducing of modified bipyridine as binding ligand attracts our attention. As the crown ether can act as a fluorescent ionophore and amide group could increase the solubility, for comparison, crown ether and amide group were introduced in **2**.

Herein, we report two novel fluorescent chemosensors, 25,27-di[methoxy(4-phenyl)-(6′-phenyl-2′,2″-bipyridine)]-26,28-dihydroxy-calix[4]arene (**1**) and 25,27-bis[*N*-(4-phenylmethyl-(6′-phenyl-

---

* Corresponding authors.
E-mail addresses: ecljh@kriss.re.kr (J.H. Lee), jongskim@korea.ac.kr (J.S. Kim).

doi:10.1016/j.tetlet.2010.04.135

2′,2″-bipyridine))aminocarbonyl-methoxy]calix[4]-crown-5 (**2**), which displayed a selective fluorescent change with Zn^{2+} in comparison with various metal ions examined in CH_3CN. Results showed that upon addition of Zn^{2+} to the solution of **1** and **2**, the fluorescence bands at 363 nm and 356 nm are decreased gradually and concomitantly the bands centered at 408 nm (for **1**) and 414 nm (for **2**) are increased, respectively. A red shift of approximately 45 nm and 58 nm was observed in **1** and **2**, respectively. To the best of our knowledge, **1** and **2** are the first example of 2,2′-bipyridine-modified calix[4]arene-based compounds used as Zn^{2+} fluorescent chemosensors with ratiometric fluorescent changes and red shift.

Fluorescent sensors **1** and **2** were prepared as outlined in Scheme 1. Compound **1** was synthesized by a typical Williamson ether synthesis. When compound **8** was reacted with 2 equiv of **6** in the presence of K_2CO_3 in CH_3CN, **1** was obtained in a moderate yield of 56%. Reaction of **3** and **4** with DMAP and EDCI in DMF at room temperature afforded fluorescent chemosensors **2** in 52% yields.[14]

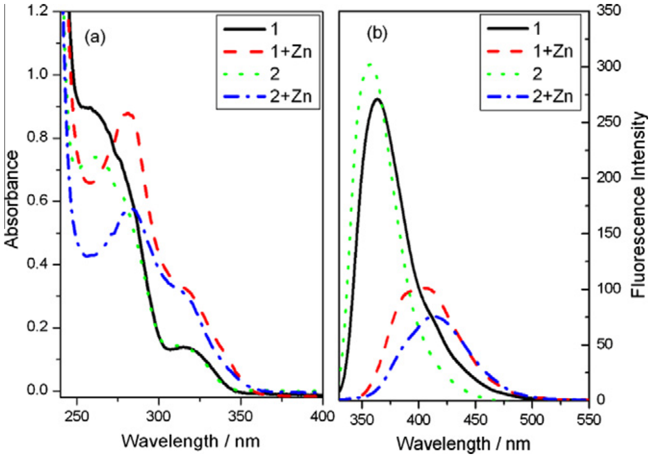
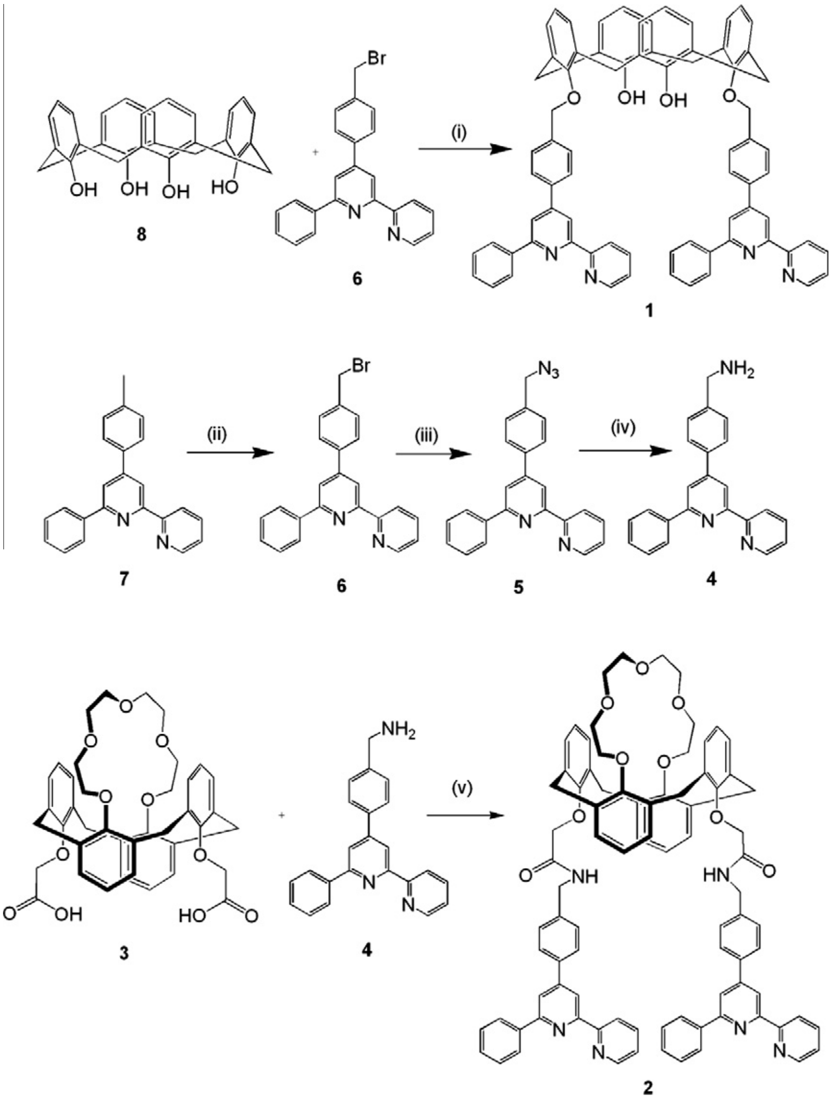


Figure 1. UV–vis spectra (a) and fluorescence spectra (b) of **1** (solid and dash lines) and **2** (dot and dash dot line) in the absence and in the presence of 5 equiv of $Zn(ClO_4)_2$ in dry CH_3CN.

Studies on the UV–vis absorption and fluorescent emission processes revealed that **1** and **2** showed sensitivity toward Zn^{2+} in CH_3CN. As shown in Figure 1a, in the absence of Zn^{2+}, **1** and **2** showed similar absorption band at 260 nm with small shoulder band at 314 nm. Upon addition of Zn^{2+} up to 5 equiv to the solution, a major absorption band at 282 nm with shoulder band at 320 nm and a major absorption band at 281 nm with shoulder



Scheme 1. Synthetic route of **1** and **2**. (i) K_2CO_3, CH_3CN reflux. (56%); (ii) NBS and small amount of BPO, CCl_4 reflux, (72%); (iii) NaN_3, DMF, 90 °C (83%); (iv) PPh_3 and ammonia water, pyridine rt (67%); (v) DMAP, EDCI, DMF rt (52%).

band at 319 nm were observed for **1** and **2**, respectively. In the fluorescent spectra, coordination of Zn^{2+} caused red shift from 363 nm to 408 nm for **1** and red shift from 356 nm to 414 nm for **2** (Fig. 1b).

To understand the binding mode of **1** and Zn^{2+}, UV–vis titration experiments were performed (Fig. 2). With gradual addition of Zn^{2+} to the solution of **1**, the UV–vis absorption band at 257 nm decreased sharply, whereas at 281 nm and 320 nm increased significantly, with an isosbestic point at 257 nm observed. Upon addition of 2 equiv of Zn^{2+} (Fig. 2 inset), the peaks at 257 nm and 281 nm reached their maxima, which could be assumed to the bipyridine-bounded zinc complex formation in **1.** Similar changes were observed upon addition of Zn^{2+} solution to the solution of **2** (Fig. 3) as well, indicating that **2** follows the same binding mode with Zn^{2+} as that of **1**, and the crown ethers and amides groups of **2** were not involved in the coordination.

To further investigate the sensing properties of **1**, we performed fluorescence titration of **1** (10 μM) with Zn^{2+} ion in CH_3CN solution. Figure 4 shows the gradual changes of the fluorescence spectra of **1** upon addition of Zn^{2+}. When the concentration of Zn^{2+} ion was increased, the fluorescence intensity at 363 nm was decreased with a new red shifted emission band centered at 408 nm. The red shift of emission band can be explained by stabilization of the intramolecular charge transfer (ICT) excited state of **1** and the formation of **1**-Zn^{2+} complexes.[13] After addition of 2 equiv of Zn^{2+}, the peak at 363 nm was evanesced (Fig. 4 inset) and the red shift reached its maximum. Similar fluorescent changes were noticed in aqueous solution upon successive addition of Zn^{2+} ion to **1** as shown in Figure S1. In another observation, we noticed that by changing of perchlorate counter ions with sulfate, acetate, or chloride there was no considerable change on optical properties of **1**, which implied that the optical properties of **1** were independent of counter anions (Fig. S2).

To know the insight of binding mode of ligand with zinc ion, we performed the Job plot experiment (Fig. S3). A maximum fluorescence change was observed when the molar fraction of the Zn^{2+} perchlorate versus ligand **1** was about 0.67, which implied a 1:2 complex (**1**-$2Zn^{2+}$) formation. Similarly, upon addition of Zn^{2+} to the solution of **2**, the fluorescence intensity at 356 nm decreased with the concomitant formation of a new red shifted emission band centered at 414 nm (Fig. 5), suggesting a binuclear complex (**2**-$2Zn^{2+}$) formation. From the fluorescence titration profiles, the dissociation constants (K_d) of **1**-Zn^{2+} and **2**-Zn^{2+} in CH_3CN solution

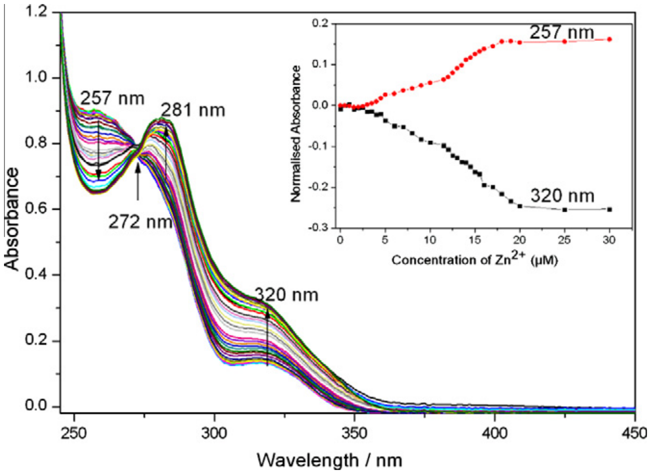


Figure 2. UV titrations of **1** (10 μM) upon addition of Zn^{2+} (0–30 μM) in acetonitrile. Inset: titration of the change in the absorption of **1** measured at 257 and 320 nm versus the concentration of added Zn^{2+} ions.

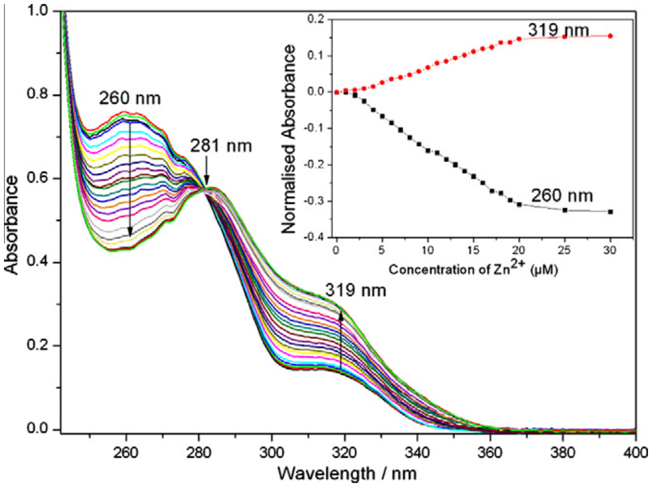


Figure 3. UV titrations of **2** (10 μM) upon addition of Zn^{2+} (0–30 μM) in acetonitrile. Inset: titration of the change in the absorption of **2** measured at 260 and 319 nm versus the concentration of added Zn^{2+} ions.

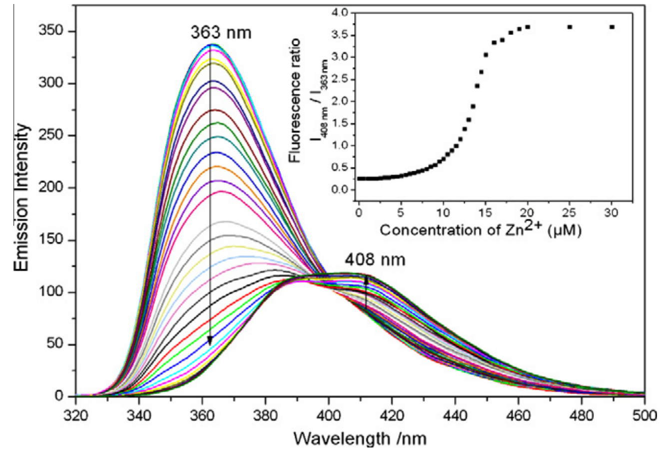


Figure 4. Changes in fluorescence spectra of **1** (10 μM) upon addition of $Zn(ClO_4)_2$ (0–30 μM) in acetonitrile (λ_{ex} = 320 nm). Inset: ratiometric calibration curve I_{408}/I_{363} as a function of Zn^{2+} concentration.

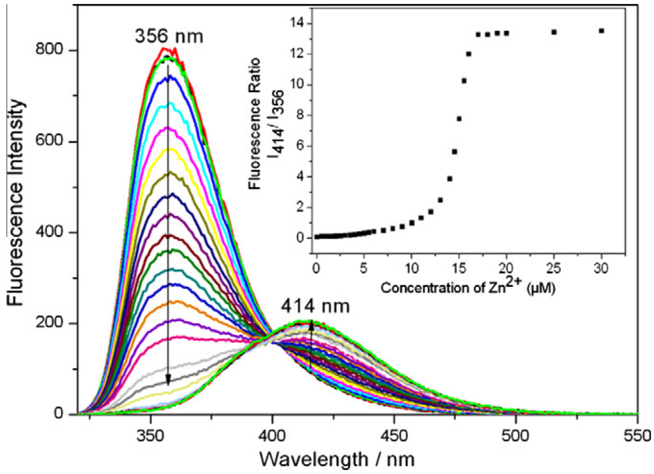


Figure 5. Changes in fluorescence spectra of **2** (10 μM) upon addition of $Zn(ClO_4)_2$ (0–30 μM) in acetonitrile (λ_{ex} = 320 nm). Inset: ratiometric calibration curve I_{414}/I_{356} as a function of Zn^{2+} concentration.

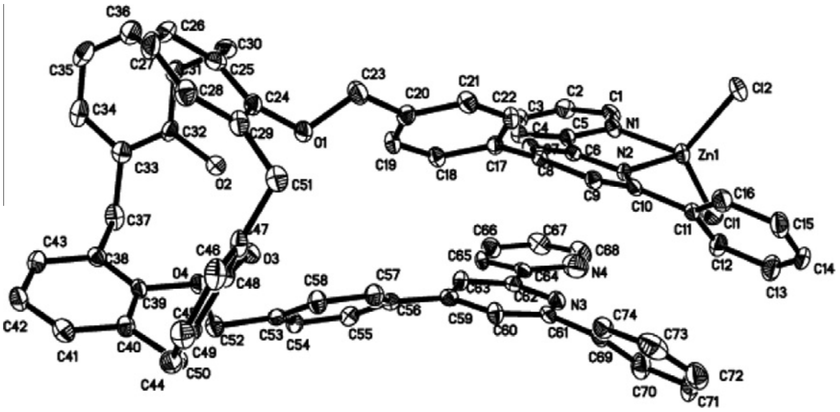


Figure 6. Perspective drawing (30% thermal ellipsoids) of the complex **1**-$ZnCl_2$ with the hydrogen atoms removed for clarity. Selected bonds length, (Å): Zn(1)–N(1) 2.072, Zn(1)–N(2) 2.084, Zn(1)–Cl(1) 2.192, Zn(1)–Cl(2) 2.201.

were calculated to be $K_d = 4.58 \times 10^{-3}$ and $K_d = 2.03 \times 10^{-3}$ for **1** and **2**, respectively.

As shown in Figure 6, further evidence for the binding mode was provided by **1**-$ZnCl_2$ single crystals structure. When **1** reacted with $ZnCl_2$ in a 1:1 molar ratio in acetonitrile solution at room temperature, the mononuclear **1**-$ZnCl_2$ complex with one bipyridine N,N-chelation coordinated to the Zn center was obtained. Unfortunately, attempts to prepare a crystal of the binuclear **1**-$2Zn^{2+}$ complex through the reaction of **1** and $ZnCl_2$ in a 1:2 molar ratio in organic solution were unsuccessful. However, depending on the **1**-$ZnCl_2$ crystal structure, it could be deduced that the coordination process of the two bipyridine groups in **1** with zinc ion was independent, that is, one bipyridine group in **1** could coordinate to one zinc ion independently, while the other bipyridine group did not involve in the coordination. We assumed that in the presence of more zinc ions, the free bipyridine group could coordinate to another zinc ion with the same coordination mode as that of the first bipyridine group. As a consequence, one molecular **1** can bind two molecular zinc ions, that well corresponds to the results of Job's plot. To get further insight on the characteristic of zinc complexation, the cation recognition was evaluated by ^1H NMR titration in DMSO-d^6. A partial ^1H NMR spectrum of **1**, upon addition of zinc cation, is shown in Figure S4. Notably, when 2 equiv of zinc cation was added, the proton signals of bipyridiyl moieties were considerably changed and broadened due to coordination of the zinc ion.

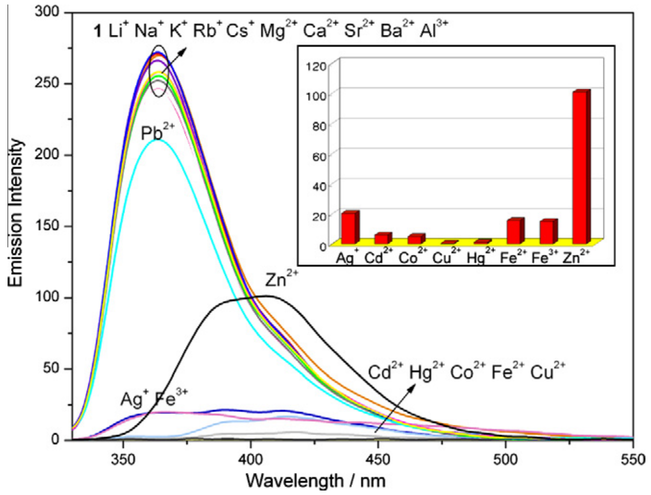


Figure 7. Fluorescence spectra of **1** (10 μM) in CH_3CN upon addition of various metal cation perchlorates (each concentration was 50 μM) with an excitation wavelength of 320 nm. Inset: plot of fluorescence intensity of **1** (10 μM) monitored at 408 nm with different metal ions.

The selectivity of the fluorescence response of **1** to zinc ions over other competitive metal ions was then examined. Figure 7 showed the fluorescence response of **1** to various metal ions in CH_3CN solution. Pb^{2+}, Al^{3+}, alkali (Li^+, Na^+, K^+, Rb^+, Cs^+), and alkaline earth (Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}) metal perchlorates did not show much change to the emission properties of **1**. However, some heavy and transition-metals, such as Ag^+, Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Cd^{2+}, and Hg^{2+}, showed significant quenching in the emission band at 363 nm. Most importantly, only the titration of Zn^{2+} showed a strong red shift to 408 nm which inferred that Zn^{2+} could be easily distinguished from other various metal ions (Fig. 6 inset) as tested. Similarly, **2** also showed high selective fluorescence response to zinc among various metal ions in CH_3CN solution. Titration of alkali and alkaline earth metal perchlorates did not show much change to the optical properties of **2** (Fig. S5).

Acknowledgment

This work was supported by the Creative Research Initiative program (No. 2010-0000728) of Korea Research Foundation.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.04.135.

References and notes

1. (a) de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515; (b) Valeur, B.; Leray, I. *Coord. Chem. Rev.* **2000**, *205*, 3; (c) Prodi, L.; Bolletta, F.; Montalti, M.; Zaccheroni, N. *Coord. Chem. Rev.* **2000**, *205*, 59; (d) Fabbrizzi, L.; Poggi, A. *Chem. Soc. Rev.* **1995**, *24*, 197.
2. (a) Que, E. L.; Domaille, D. W.; Chang, C. J. *Chem. Rev.* **2008**, *108*, 1517; (b) Kim, H. M.; Seo, M. S.; An, M. J.; Hong, J. H.; Tian, Y. S.; Choi, J. H.; Kwon, O.; Lee, K. J.; Cho, B. R. *Angew. Chem., Int. Ed.* **2008**, *47*, 5167; (c) Zhang, Y.; Guo, X.; Si, W.; Jia, L.; Qian, X. *Org. Lett.* **2008**, *10*, 473; (d) Wong, B. A.; Friedle, S.; Lippard, S. J. *J. Am. Chem. Soc.* **2009**, *131*, 7142; (e) Xu, Z.; Kim, G.-H.; Han, S. J.; Jou, M. J.; Lee, C.; Shin, I.; Yoon, J. *Tetrahedron* **2009**, *65*, 2307; (f) Zhou, Y.; Kim, H. N.; Yoon, J. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 125; (g) Xu, Z.; Baek, K.-H.; Kim, H. N.; Cui, J.; Qian, X.; Spring, D. R.; Shin, I.; Yoon, J. *J. Am. Chem. Soc.* **2010**, *132*, 601.
3. (a) Frederickson, C. J.; Koh, J.-Y.; Bush, A. I. *Nat. Rev. Neurosci.* **2005**, *6*, 449; (b) Fraker, P. J.; King, L. E. *Annu. Rev. Nutr.* **2004**, *24*, 277; (c) Bush, A. I.; Pettingell, W. H.; Multhaup, G.; Paradis, M.; Vonsattel, J.-P.; Gusella, J. F.; Beyreuther, K.; Masters, C. L.; Tanzi, R. E. *Science* **1994**, *265*, 1464.
4. (a) Koh, J. Y.; Suh, S. W.; Gwag, B. J.; He, Y. Y.; Hsu, C. Y.; Choi, D. W. *Science* **1996**, *272*, 1013; (b) Walker, C. F.; Black, R. E. *Annu. Rev. Nutr.* **2004**, *24*, 255.
5. Chausmer, A. B. *J. Am. Coll. Nutr.* **1998**, *17*, 109.
6. (a) Voegelin, A.; Pfister, S.; Scheinost, A. C.; Marcus, M. A.; Kretzschmar, R. *Environ. Sci. Technol.* **2005**, *39*, 6616; (b) Callender, E.; Rice, K. C. *Environ. Sci.*

Technol. **2000**, *34*, 232; (c) Li, L.; Dang, Y.-Q.; Li, H.-W.; Wang, B.; Wu, Y.-Q. *Tetrahedron Lett.* **2010**, *51*, 618.

7. Kim, J. S.; Quang, D. T. *Chem. Rev.* **2007**, *107*, 3780.
8. (a) Kim, S. K.; Lee, S. H.; Lee, J. Y.; Lee, J. Y.; Bartsch, R. A.; Kim, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 16499; (b) Kim, S. K.; Kim, S. H.; Kim, H. J.; Lee, S. H.; Lee, S. W.; Ko, J.; Bartsch, R. A.; Kim, J. S. *Inorg. Chem.* **2005**, *44*, 7866; (c) Kim, J.-M.; Min, S. J.; Lee, S. W.; Bok, J. H.; Kim, J. S. *Chem. Commun.* **2005**, 3427; (d) Choi, J. K.; Lee, A.; Kim, S.; Ham, S.; No, K.; Kim, J. S. *Org. Lett.* **2006**, *8*, 1601; (e) Kim, H. J.; Kim, S. K.; Lee, J. Y.; Kim, J. S. *J. Org. Chem.* **2006**, *71*, 6611; (f) Choi, J. K.; Kim, S. H.; Yoon, J.; Lee, K.-H.; Bartsch, R. A.; Kim, J. S. *J. Org. Chem.* **2006**, *71*, 8011; (g) Kim, J. S.; Kim, H. J.; Kim, H. M.; Kim, S. H.; Lee, J. W.; Kim, S. K.; Cho, B. R. *J. Org. Chem.* **2006**, *71*, 8016; (h) Lee, M. H.; Quang, D. T.; Jung, H. S.; Yoon, J.; Lee, C.-H.; Kim, J. S. *J. Org. Chem.* **2007**, *72*, 4242; (i) Park, S. Y.; Yoon, J. H.; Hong, C. S.; Souane, R.; Kim, J. S.; Matthews, S. E.; Vicens, J. *J. Org. Chem.* **2008**, *73*, 8212; (j) Han, D. Y.; Kim, J. M.; Kim, J.; Jung, H. S.; Lee, Y. H.; Zhang, J. F.; Kim, J. S. *Tetrahedron Lett.* **2010**, *51*, 1947.
9. Kaes, C.; Katz, A.; Hosseini, M. W. *Chem. Rev.* **2000**, *100*, 3553.
10. Goodall, W.; Williams, J. A. G. *Chem. Commun.* **2001**, 2514.
11. (a) Ajayaghosh, A.; Carol, P.; Sreejith, S. *J. Am. Chem. Soc.* **2005**, *127*, 14962; (b) Sreejith, S.; Divya, K. P.; Ajayaghosh, A. *Chem. Commun.* **2008**, 2903.
12. Carol, P.; Sreejith, S.; Ajayaghosh, A. *Chem. Asian J.* **2007**, *2*, 338.
13. Kozhevnikov, D. N.; Shabunina, O. V.; Kopchuk, D. S.; Slepukhina, P. A.; Kozhevnikova, V. N. *Tetrahedron Lett.* **2006**, *47*, 7025.
14. *General*: compounds 4-(tolyl)-6-phenyl-2,2′-bipyridine (**7**),[15] 4-(bromomethylphenyl)-6-phenyl-2,2′-bipyridine (**6**),[15] calix[4]arene (**8**),[8a] and 25,27-bis-(hydroxycarbonylmethoxy) calix[4]crown-5 (**3**)[8a] were synthesized according to the literature process. All reagents and solvents for synthesis were commercial and used without further purification. All the reactions have been performed under high pure nitrogen or argon atmosphere. Synthesized products have been purified by column chromatography on silica gel (100–200 mesh). All fluorescence and UV–vis absorption spectra were recorded in RF-5301PC and S-3100 spectrophotometer, respectively. NMR and mass spectra were recorded at Varian instrument (300 MHz) and FAB-MS mass spectra. X-ray crystal structure determination was performed with a Bruker SMART APEX CCD X-ray diffractometer, using graphite monochromated MoKα radiation (λ = 0.71073 Å, φ and ω scans). The data were reduced using SAINTPLUS and a multiscan absorption correction using SADABS was performed. The structure was solved using SHELXS-97, and full matrix least squares refinement against F^2 was carried out using SHELXL-97 in anisotropic approximation for non-hydrogen atoms. All hydrogen atoms were assigned on the basis of geometrical considerations and were allowed to ride upon the respective carbon atoms.

    Preparation of 4-azidemethylphenyl-6′-phenyl-2′,2′′-bipyridine (**5**): Under nitrogen, **6** (2.00 g, 5.0 mmol) and NaN_3 (0.4 g, 6.0 mmol) in 10 mL of DMF were stirred at 90 °C for 4 h and cooled to room temperature. EtOAc (100 mL) and H_2O (100 mL) were added and the water layer was extracted three times with EtOAc, the organic layers were dried over $MgSO_4$ and evaporated under vacuo. Column chromatography of the crude product by silica gel with hexane/EtOAc = 6:1 as eluent gave 1.51 g (83%) of **5** as a white solid. ^{1}H NMR (300 MHz): δ 4.38 (s, 2H, $-CH_2$), 7.30–7.35 (m, 1H), 7.42–7.57 (m, 5H), 7.79–7.88 (m, 3H), 7.95 (s, 1H), 8.21 (d, 2H, J = 6.9 Hz), 8.64–8.74 (m, 3H).

    Preparation of 4-aminomethylphenyl-6′-phenyl-2′,2′′-bipyridine (**4**): Under nitrogen, **5** (1.00 g, 2.75 mmol) and PPh_3 (2.20 g, 8.40 mmol) in 20 mL of pyridine were stirred at room temperature for 5 h, then 5 mL ammonia water (30%) was added. The reaction mixture was stirred for another 12 h at room temperature. The solvent was removed in vacuo. MC (100 mL) and H_2O (100 mL) were added and the water layer was extracted three times with MC, the organic layers were dried over $MgSO_4$ and evaporated under vacuo. Column chromatography of the crude product by silica gel with MC/MeOH = 95:5 as eluent gave 0.62 g (67%) of **4** as a white solid. ^{1}H NMR (300 MHz): δ 2.34 (s, 2H, $-NH_2$), 3.40 (s, 2H, $-CH_2$), 7.32–7.36 (m, 1H), 7.46–7.57 (m, 5H), 7.78–7.89 (m, 3H), 7.98 (s, 1H), 8.21 (d, 2H, J = 6.9 Hz), 8.63–8.73 (m, 3H).

    Preparation of 25,27-di[methoxy(4-phenyl)-(6′-phenyl-2′,2′′-bipyridine)]-26,28-dihydroxycalix[4]arene (**1**): To a solution of **5** (0.5 g, 1.2 mmol) in 100 mL acetonitrile and toluene (V/V = 1:1) were added **6** (1 g, 2.5 mmol) and K_2CO_3 (350 mg, 2.5 mmol) as a base. The reaction mixture was refluxed for 48 h and cooled down to room temperature. The solvent was removed in vacuo. CH_2Cl_2 (100 mL) and H_2O (100 mL) were added and the organic layer was washed three times with water, dried over $MgSO_4$, and evaporated under vacuo. Column chromatography of the crude product by silica gel with hexane/EtOAc = 4:1 as eluent gave 0.7 g (56%) of **1** as a white solid. ^{1}H NMR (300 MHz): δ 3.44 (d, 4H, J = 13 Hz), 4.43 (d, 4H, J = 13 Hz), 5.22 (s, 4H), 6.69 (t, 2H, J = 7.4 Hz), 6.82 (t, 2H, J = 7.1 Hz), 6.98 (d, 4H, J = 7.6 Hz), 7.10 (d, 4H, J = 7.5 Hz), 7.20–7.24 (m, 2H), 7.35–7.37 (m, 6H), 7.59–7.67 (m, 4H), 7.72 (d, 4H, J = 8.3 Hz), 7.86–7.93 (m, 8H), 8.29 (s, 2H), 8.11 (s, 2H), 8.33 (d, 2H, J = 7.9 Hz), 8.58 (d, 2H, J = 4.8 Hz). ^{13}C NMR (100 MHz): 31.54, 77.84, 117.04, 117.75, 119.11, 121.65, 123.56, 125.71, 126.87, 127.43, 127.71, 127.87, 128.40, 128.58, 128.79, 129.20, 133.29, 137.77, 137.92, 138.91, 148.06, 148.69, 151.78, 153.37, 156.46 ppm. FAB-MS (1064.43): 1065.12 [M+H$^+$].

    Preparation of 25,27-Bis[N-(4-phenylmethyl-(6′-phenyl-2′,2′′-bipyridine))amino-carbonyl-methoxy]calix[4]-crown-5 (**2**). To a solution of **3** (100 mg, 0.14 mmol) in DMF (10 ml) were added **4** (100 mg, 0.3 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (60 mg, 0.3 mmol), and 4-dimethylaminopyridine (DMAP) (40 mg, 0.3 mmol). The reaction mixture was stirred at room temperature for 24 h. H_2O (100 mL) was added and extracted with ethyl acetate (100 mL × 3), dried over $MgSO_4$, and evaporated under vacuo. Column chromatography of the crude product by silica gel with MC/MeOH = 30:1 as eluent gave 99 mg (52%) of **1** as a white solid. ^{1}H NMR (300 MHz): δ 3.37 (t, 4H, J = 5.9 Hz), 3.54 (s, 4H), 3.60–3.67 (m, 12H), 3.78 (d, 4H, J = 15.9 Hz), 3.86 (d, 4H, J = 15.8 Hz), 4.37 (d, 4H, J = 6.1 Hz), 6.61 (t, 2H, J = 7.5 Hz), 6.94 (t, 8H, J = 7.3 Hz), 7.19 (d, 4H, J = 7.5 Hz), 7.27–7.30 (m, 2H), 7.42–7.51 (m, 10H), 7.78–7.84 (m, 6H), 7.91 (s, 2H), 8.14 (d, 4H, J = 6.8 Hz), 8.64–8.66 (m, 6H). ^{13}C NMR (100 MHz): 37.27, 42.41, 57.64, 59.70, 68.79, 69.68, 69.99, 70.31, 72.30, 116.71, 118.22, 121.25, 123.22, 124.70, 127.22, 127.36, 128.68, 129.11, 129.54, 129.97, 134.09, 134.40, 136.41, 137.70, 138.97, 141.10, 149.62, 155.48, 155.61, 156.03, 156.34, 156.77, 168.98 ppm. ESI-MS (1336.56): 1337.5 [M+H$^+$].

    Single crystal data for **1**-$ZnCl_2$: $C_{74}H_{56}Cl_2N_4O_4Zn\cdot CH_3CN$, M_w = 1239.32, colorless crystal, size: 0.15 × 0.10 × 0.08 mm^3, triclinic, space group P − 1, a = 11.151(2) Å, b = 15.235(3) Å, c = 20.065(4) Å, α = 96.35(3) °, β = 102.95(3) °, γ = 95.27(3) °, V = 3277.6(1) Å^3, T = 170(2) K, Z = 2, D = 1.283 mg/m^3, ρ = 0.190 mm^{-1}, F(000) = 1316; 11795 reflections measured, of which 7869 were unique (R_{int} = 0.0322). 806 refined parameters, final R_1 = 0.0640 for reflections with $I > 2\sigma(I)$, wR_2 = 0.1780 (all data), GOF = 0.778. Final largest diffraction peak and hole: 1.356 and −0.467 e Å^{-3}.
15. Ding, J.; Pan, D.; Tung, C.-H.; Wu, L.-Z. *Inorg. Chem.* **2008**, *47*, 5099.