1372 J. Org. Chem. **2002,** *67,* 1372−1375

Chromogenic Azo-Coupled Calix[4]arenes

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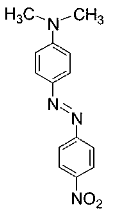
Received August 31, 2001

Abstract: Novel 1,3-alternate calix[4]azacrowns having an azo chromophoric pendent group were synthesized, and their 1,3-alternate conformations were confirmed by X-ray crystal structure. In view of the hypsochromical UV band shifting upon cation complexation, azo-coupled calix[4]azacrown-5 (**3**) showed the most selective shifting with alkali and alkaline metal ions. In addition, **3** revealed K$^+$ ion selectivity not only due to the size comparability between the K$^+$ ion and the azacrown-5 loop but also due to a significant K$^+$−π interaction between the two aromatic rings and the K$^+$ ion. The UV band shifting is also dependent on the lipophilicity of the species of counteranion used.

Calix[4]arenes have been shown to be useful 3-D molecular building blocks for the synthesis of receptors with specific properties.[1] Calix[4]crown ethers have attracted intense interest as certain metal ion-selective extractants due to the complexation of the metal ion not only with the crown ether but also with the two aromatic rings (cation/π-interaction) when fixed in the 1,3-alternate conformation.[2−5] Calixazacrown compounds were also studied for synthesis and selective metal ion binding.[6−8]

A combination of dyes and crown ethers was reported for the color change upon the specific metal ion complexation.[9] The amine nitrogen atoms simultaneously possess an electron-donor function to complexed cations as well as to the chromophore. The absorption bands of the chromoionophores **2** in the visible region are hypsochromically shifted by the complexation of alkali and alkaline earth metal ions.[10] The strongest λ_{max} shift is known to be affected by the cation which best fits into the ligand cavity.[11]



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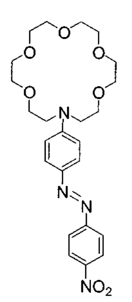

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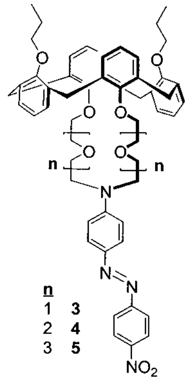

However, the color change of the azacrown compounds, i.e., the 1,3-alternate *N*-chromogenic calix[4]azacrown, in which an azo-coupled azacrown ether is cyclized with two 1,3-positioned hydroxyl group of calix[4]arene, has never been investigated. We now herewith report the synthesis of a series of chromogenic calixazacrowns **3**−**5** and their color change upon the metal ion complexation.

The synthesis began with 1,3-dipropyloxy-2,4-ethylene glycolic dichloride (**6**−**8**)[12] which has the 1,3-alternate conformation as described in Scheme 1. The cyclization reaction of **6**−**8** with *N*-phenyldiethanolamine in the presence of NaOH gave crystalline compounds **9**−**11** where $n = 1-3$, respectively. Subsequently, the diazonium salt obtained from the reaction of *p*-nitroaniline with NaNO$_2$ was in situ added to a solution of **9**−**11**, providing the desired products **3**−**5** as red crystals. The presence of a singlet peak at around 3.8 ppm in the ^{1}H NMR as well as the presence of a single peak at 38 ppm in the ^{13}C NMR spectra confirmed that **3**−**5** maintained 1,3-alternate conformations.

The crystals of **3** suitable for X-ray study were grown by slow evaporation of a methanol/CH$_2$Cl$_2$ (1:4) solution. It was crystallized in the triclinic space group *P*-1. It contains two crystallographically independent molecules (A and B in Figure 1). The structure is a saddle-shaped 1,3-alternate conformation; the aromatic rings are tilted up and down alternately related to the α-C$_4$ core. The α-C$_4$ core forms a square plane, and the average displacement of the core atoms from the mean plane is 0.04 (A) and 0.03 (B) Å, respectively. Two aromatic rings having a -O(CH$_2$)$_2$CH$_3$ pendant on the same side form dihedral angles of 46.2(2)° (A) and 43.0(2)° (B), while the two aromatic rings as a member of the azacrown in the opposite direction form dihedral angles of 45.2(2)° (A) and 55.0(2)° (B), respectively. The dihedral angles between two aromatic rings attached to the azo group are quite different [8.2(3)° for A and 25.2(3)° for B].

Compound **1** as a reference material gave no change in the UV spectra (CH$_3$CN) upon various metal ion complexations obviously because it does not have a cyclic

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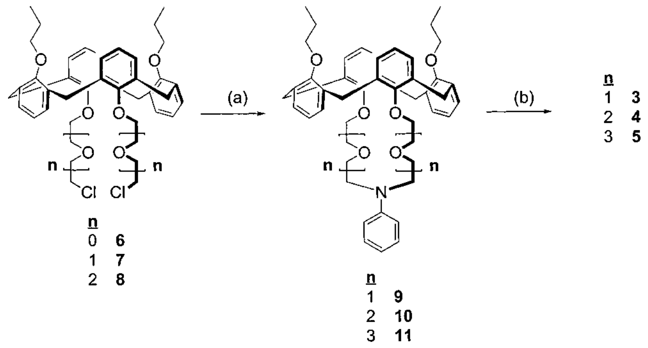
10.1021/jo0108921 CCC: $22.00

Scheme 1. Synthetic Route for 3−5[a]



[a] (a) PhN(CH$_2$CH$_2$OH), NaOH, 1,4-dioxane; (b) *p*-nitroaniline, AcOH, H$_2$SO$_4$/DMF.

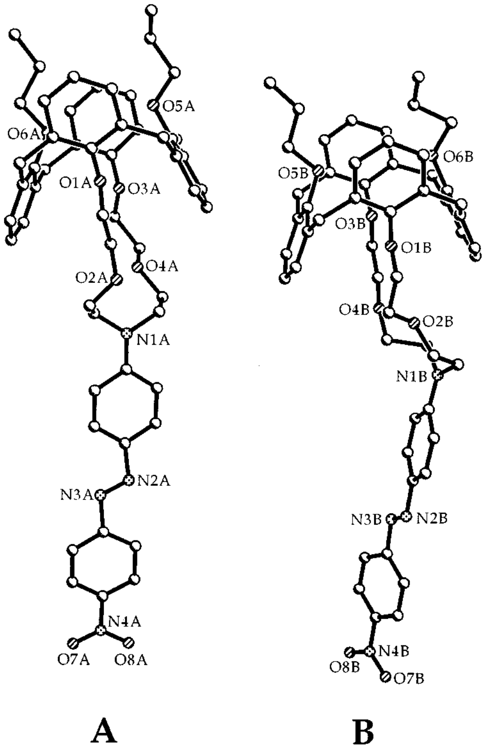


Figure 1. X-ray crystal structure of **3**. Disorder part and hydrogen atoms are omitted for clarity.

array to entrap the metal ion. With respect to the UV-band shifting, **2** was reported to show K$^+$ and Ba^{2+} ion selectivities due to size compatibility between the azacrown cavity and the metal cation.[10] In donor−acceptor chromophores, the electronic excitation is mostly accompanied by a charge density shift in the direction of the acceptor substituents of the chromoionophore, i.e., increases in the dipole moments take place.[12] Since it can be postulated that the amine nitrogen atoms of the chromoionophores (**2**−**5**) are positively polarized, the excited states are more strongly destabilized by cations than the ground states; therefore, hypsochromic shifts result.[13] Figure 2 shows the cation selectivity of **3**. In both cases of SCN$^-$ and ClO$_4$$^-$ as counteranions, the K$^+$ ion was mostly selective to give the largest hypsochromical UV band shifting, implying that the K$^+$ ion is the most suitable for **3**. For **4** and **5**, however, there was no change in the UV band upon the metal ion complexation because the cavities of the azacrowns-7 and -9 are too large to properly encapsulate any of the tested cations. Although the metal ion can be entrapped by the azacrown cavity, the metal ion would be located in the middle of two facing benzene rings to have a M$^+$−π interaction. This brought a far distance between the nitrogen atom and the metal ion and gave *non*-chromogenicity. The UV band shifting of **2** to compare with that of **3** under the same experimental conditions was carried out and the results are shown in Figure 3. When **2** and **3** were titrated with K$^+$ ion (0−100 equiv), **3** revealed a more remarkable hypsochromical band shifting than **2**. Although the azacrown cavity (ca. 3.6−4.1 Å) of **3** is relatively larger than the K$^+$ ion (2.76 Å), it strongly recognizes the K$^+$ ion not only because of an electrostatic interaction between the azacrown cavity and the K$^+$ ion but also because of a significant K$^+$−π interaction between the two aromatic rings (C10A and C22A) and the K$^+$ ion when the calix[4]arene is fixed in the 1,3-alternate conformation.[8]

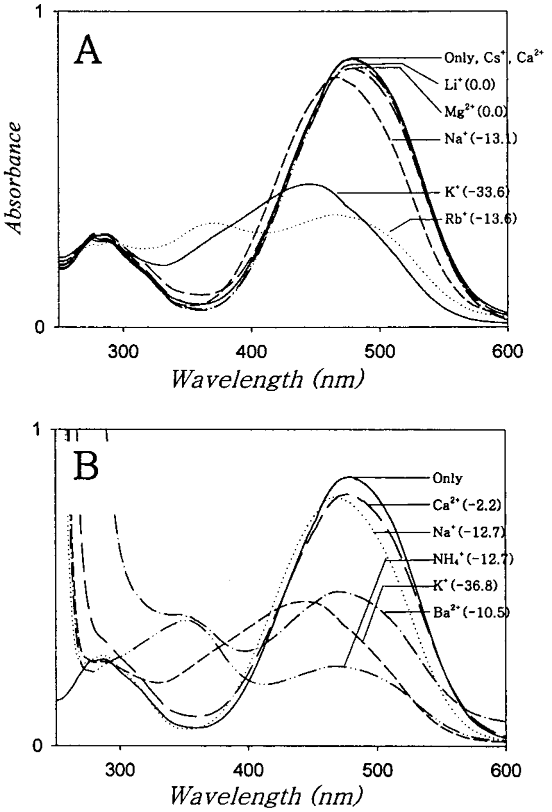


Figure 2. UV spectra of **3** in the presence of MClO$_4$ (A) and in the presence of MSCN (B). Initial ligand concentration: 0.025 mM/CH$_3$CN. Added metal ion: 10 equiv. Numbers in parentheses indicate the extent of band shifting compared with that of ligand only: λ_{max} (L·M$^+$) − λ_{max}(L).

During the course of elucidating the complexation behavior of **3** and metal cations, an anion effect was unexpectedly observed. To determine the anion selectivity, we examined the partitioning of a series of potassium salts of anions during cation complexation. The corresponding UV spectra are shown in Figure 4. An empirical lipophilicity series of anions, the so-called Hofmeister selectivity series, is useful to consider the anion effect. It is usually in the order of ClO$_4$$^-$ > NO$_3$ > Cl$^-$ > H$_2$PO$_4$ > SO$_4$$^{2-}$.[14] The results carried out in this UV experiment

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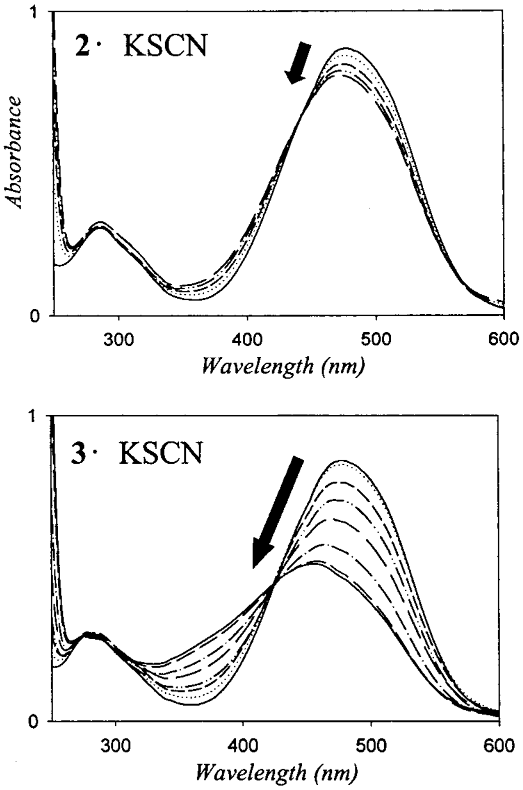

Figure 3. Hypsochromic band shifting of **2** and **3** upon the addition of KSCN (0−100 equiv). Initial concentration of both **2** and **3**: 0.025 mM/CH_3CN.

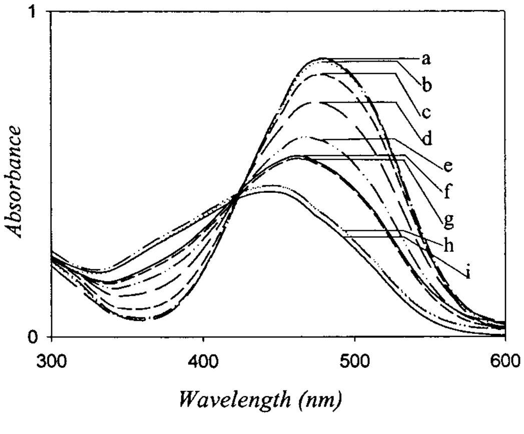

Figure 4. UV spectra of **3** in the presence of K^+X^-. Initial ligand concentration: 0.025 mM/CH_3CN. Added metal ion: 10 equiv a: SO_4^{2-} (0.0) . b: HPO_4^{2-} (0.0). c: Cl^- (−2.2). d: CH_3COO^- (−7.0). e: ClO_3^- (−10.5). f: Br^- (−18.9). g: NO_3^- (−16.2). h: ClO_4^- (−33.0). i: SCN^- (−36.8). (−) numbers indicate λ_{max} (L·M^+) − λ_{max}(L).

showed the same trend as follows: $SCN^- > ClO_4^- > NO_3^- > Br^- > ClO_3^- > CH_3CO_2^- > Cl^- > HPO_4^{2-} > SO_4^{2-}$. One can conclude about this anion effect that when the metal cation contains a lipophilic anion (softer), it would be more easily bound to the ligand.[15]

In conclusion, three novel chromogenic 1,3-alternate calix[4]azacrowns in which the azacrown ring size is varied using azacrowns-5, -7, and -9 were synthesized and the structures were confirmed by NMR and HRMS. An X-ray crystallographic determination was carried out for **3**. Among these compounds, the azo-coupled calix[4]-azacrown-5 (**3**) showed the most selective hypsochromical shift for the complexations with alkali and alkaline metal ions. In addition, **3** revealed K^+ ion selectivity not only due to the size comparability between the K^+ ion and the azacrown-5 loop but also due to a significant $K^+-\pi$ interaction between the two aromatic rings and the K^+ ion. The UV band shifting is also dependent on the lipophilicity of the species of counteranion used.

Experimental Section

Analytical Procedures. Starting materials **6**−**8** were prepared as described in the literature.[8] Acetonitrile was predried from molecular seives (3 Å) and distilled over diphosphorus pentaoxide. The ^1H NMR data are available in the Supporting Information.

Syntheses. *N*-[(4-Nitrophenyl)(azo)phenyl]-25,27-bis(1-propyloxy)calix[4]azacrown-5 (3), 1,3-Alternate. A diazonium salt of 4-nitroaniline was prepared by adding an aqueous solution of sodium nitrite (0.04 g, 0.51 mmol) dropwise into a homogeneous mixture of 0.03 mL of sulfuric acid and 1 mL of glacial acetic acid. The mixture was stirred at 0 °C for 5 min. The diazonium salt solution was added dropwise into a solution of *N*-phenyl-25,27-bis(5-chloro-3-oxapentyloxy)-26,28-bis-(1-propyloxy)calix[4]arene (**9**) (0.30 g, 0.40 mmol) in 50 mL of *N*,*N*-dimethylformamide at 0 °C. The solution was stirred for an additional 12 h at 0 °C. $CHCl_3$ (50 mL) and water (50 mL) were added, and the organic layer was separated and dried over $MgSO_4$. Removal of the organic solvent in vacuo afforded a reddish oil. Column chromatography on silica gel with EtOAc: hexane (1:3) as eluent (R_f = 0.42) provided **3** as a reddish crystalline solid in 28% yield. Mp 253−258 °C. IR (KBr pellet, cm^{-1}): 1513, 1336 (NO_2). FAB MS *m*/*z* (M^+) calcd 891.06, found 891.01. Calcd for $C_{54}H_{58}N_4O_8$: C, 72.72; H, 6.51. Found: C, 72.69; H, 6.54.

***N*-[(4-Nitrophenyl)(azo)phenyl]-25,27-bis(1-propyloxy)-calix[4]azacrown-7 (4)** was prepared by a method similar to that used for **3** in 60% yield. Mp 118−126 °C. IR (KBr pellet, cm^{-1}): 1513, 1336 (NO_2). The sample crystallized from H_2O gave the following microanalysis. Calcd for $C_{58}H_{66}N_4O_{10}\cdot 0.3H_2O$: C, 69.64; H, 6.62. Found: C, 69.63; H, 6.82.

***N*-[(4-Nitrophenyl)(azo)phenyl]-25,27-bis(1-propyloxy)-calix[4]azacrown-9 (5)** was prepared by a method similar to that used for **3** in 62% yield. Mp 80.0−80.5 °C. IR (KBr pellet, cm^{-1}): 1513, 1336 (NO_2). The sample crystallized from CH_2Cl_2 gave the following microanalysis. Calcd for $C_{62}H_{74}N_4O_{12}\cdot 0.2CH_2Cl_2$: C, 68.84; H, 6.86. Found: C, 68.75; H, 7.10.

***N*-Phenyl-25,27-bis(1-propyloxy)calix[4]azacrown-5 (9), 1,3-alternate.** A solution of 25,27-bis(1-propyloxy)-26,28-bis(5-chloro-3-oxapentyloxy)calix[4]arene (1.00 g, 1.50 mmol), *N*-phenyldiethanolamine (0.27 g, 1.49 mmol), and NaOH (0.18 g, 4.52 mmol) in 100 mL of 1,4-dioxane was refluxed for 72 h under nitrogen. After 1,4-dioxane was removed in vacuo, 50 mL of CH_2Cl_2 and 50 mL of water were added. The organic layer was separated and dried over $MgSO_4$. Removal of the organic solution in vacuo gave a pale yellow oil. Column chromatography on silica gel with ethyl acetate:hexane (1:8) afforded **9** as an white solid. Yield: 21.4%. Mp 148−149 °C. IR (KBr pellet, cm^{-1}): 1384 (Ar−N), 1243 (C−N). Calcd for $C_{48}H_{55}N_4O_6\cdot 0.1H_2O$: C, 77.44; H, 7.42. Found: C, 77.45; H, 7.39.

***N*-Phenyl-25,27-bis(1-propyloxy)calix[4]azacrown-7 (10)** was prepared by a method similar to that used for **9** in 23.3% yield. Mp 86.4−87.4 °C. IR (KBr pellet, cm^{-1}): 1359 (Ar−N), 1251 (C−N). FAB MS *m*/*z* (M^+) calcd 830.06, found 830.01.

***N*-Phenyl-25,27-bis(1-propyloxy)calix[4]azacrown-9 (11)** was prepared by a method similar to that used for **9** in 20.1% yield. Mp 87−88 °C. IR (KBr pellet, cm^{-1}): 1251 (C−N). Calcd for $C_{56}H_{71}NO_{10}\cdot 0.1C_6H_{14}$ (*n*-hexane): C, 73.28; H, 7.84. Found: C, 73.66; H, 7.56.

X-ray Crystal Structure. The crystal was mounted on a Siemens Smart diffractometer equipped with a graphite-monochromated Mo Kα (λ = 0.71073 Å) radiation source and a CCD detector. A total of 45 frames of two-dimensional diffraction images were collected and processed to obtain the cell param-

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eters and orientation matrix. Data collection was performed at room temperature. A total of 1271 frames of two-dimensional diffraction images were collected, each of which was measured for 10 s. The frame data were processed to give structure factors using the program SAINT.[16] Crystal data of **3**: $C_{54}H_{58}N_4O_8$, $M = 891.04$, triclinic, space group P-1(No. 2), $a = 13.887(1)$, $b = 16.337(1)$, and $c = 21.939(2)$ Å, $\alpha = 78.217(2)$, $\beta = 79.035(2)$, and $\gamma = 82.381(2)°$, $V = 4760.8(7)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.243$ g cm^{-3}, $F(000) = 1896$, $\mu = 0.84$ cm^{-1}, $T = 298$ K, $2\theta_{max} = 56.7°$. Crystallographic data and additional details of the data collection and refinement are summarized in Table S1−S5 and in Figure S1 of the Supporting Information. The structure was solved by direct methods and refined by full matrix least squares against F^2 for all data using SHELXTL software.[17] All non-H atoms were refined with anisotropic displacement parameters. In the refined structure, the propyloxy pendants show relatively large thermal vibration and three atoms in the ether linkage and propyloxy pendant (O4 and C34 for A; O51 for B) were disordered over two sites with occupancies of 0.5. The C−H atoms were added at their calculated positions [$U_{iso} = 1.2U_{eq}$-(C)] and refined using a riding model. Final full matrix least-squares refinement on F^2 with all 21945 reflections and 1218 variables converged to $R_1 = 0.0779$ ($I > 2\sigma(I)$), wR$_2$ (all data) = 0.2896.

Acknowledgment. This research was supported by a Grant from the Korea Research Foundation (KRF-2000-015-DP0246).

Supporting Information Available: Additional Tables (Table S1−S5), ^{1}H NMR data (Data S1−S6), and detailed crystal structure (Figure S1). This material is available free of charge via the Internet at http://pubs.acs.org.

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