Protonation and Energetical Investigations of Calix[4]-cyclen-benzo-crown-6 and Its Complexes with Zinc and Copper

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Protonation constants of calix[4]-cyclen-benzo-crown-6, **L** in 1×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH at 25 °C determined by potentiometric titration are log K_1 = 10.91, log K_2 = 10.30, log K_3 = 6.24 and log K_4 = 2.55. Stability constants for the receptor **L** complexes with Cu(II) and Zn(II) in 1×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH at 25 °C were determined by UV-VIS spectrometric titration. Stability constants of the CuL and ZnL complexes as logβ are 4.37 and 3.45, respectively. Stabilization energies for protonations of receptor **L**, derived from ab initio Hartree-Fock method with 6-31G basis set, are ΔE_1 = -290.1, ΔE_2 = -205.0, ΔE_3 = -124.9 and ΔE_4 = -26.9 kcal/mol and complexation energy of ZnL complex is -370.3 kcal/mol.

Key Words : Cyclen, Calixarene, Complexation, Protonation

Introduction

Since the last decade, calixarenes have received more attention from supramolecular chemists for their intriguing structures and versatile complexation ability.[1-4] Particularly, *p-tert*-butylcalix[4]arenes have widely attracted many researchers as very useful building blocks for preparing receptors for cations, anions and neutral molecules. Chemical modifications at the lower rim of *p-tert*-butylcalix[4]arene by alkylation of the phenolic groups with ester,[5] amide,[6] ketone,[7] carboxylic acid,[8] hydroxamic,[9] pyridine,[10] pyridyl and bipyridyl, alkyl thioether[11] and phosphinite[12] functioning pendant groups have been described and their metal complexing properties such as binding ability, ionophoric behaviors and complexation stability have been investigated. Arnaud-Neu *et al.* have reported the study of acid-base characteristics of calixarene carboxylates,[13] calixarene-crown-6[14] and alkyl calixaryl ester and ketones[15] and their complexation properties towards alkali, alkaline earth metal ions by potentiometric titrations. The calixarene carboxylates were also examined for their complexation with lanthanide metals.[16] The potentiometric titration technique was demonstrated to give accurate equilibrium constants for each metal complexes and can thus determine the selectivity of each calix[4]arene derivatives towards metal ions. Selective recognition of a receptor to metal ions depends on the ring size and number of donor atoms in the receptor, the cyclen (aza and oxo) derivative of calix[4]arene as receptor **L** (shown in Figure 1) is, therefore, of interest for investigation of its complexation with metal cations and protonation.

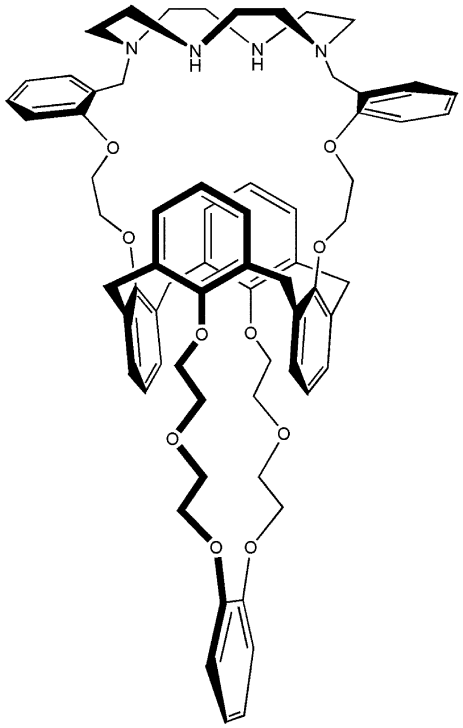

Figure 1. Structure of calix[4]-cyclen-benzo-crown-6.

Experimental Section

Potentiometric Measurements: The protonation constants of the receptor **L** were determined by means of potentiometric titrations. Concentrations of free hydrogen ion [H^+] in the solution were measured by a combined electrode (Mettler DG 113-SC) connected to an automatic titrator (Mettler DL 25) at 25 °C. The electrode was calibrated at pH = 2.0 with a standard solution of 1.00×10^{-2} M $HClO_4$ by adjusting the Nernstian slope based on the isopotential point of pH 8.30 = 0.0 mV. According to the junction potentials of the electrode, the pH of the solution can be corrected by using the following formula.[13]

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$$pH_{corrected} = pH_{observed} + a - b\,[H^-]_{observed}$$

The constants a and b were determined from the pH measurements of the solutions of 1.00×10^{-3} M $HClO_4$ and 1.00×10^{-2} M $Bu_4NCF_3SO_3$ prepared in 40% CH_2Cl_2/CH_3OH. All potentiometric titrations were carried out at 25 °C with deviation of ± 0.1 °C, regulated by an external Heto DT-2 thermostat. The titrations were performed under argon atmosphere. Typically, 10 mL of the ligand solution was titrated with the Bu_4NOH solution in a temperature-controlled beaker. The ligand concentration was varied from 9.00×10^{-4} M to 9.70×10^{-4} M. At least 40 points of each potentiometric titration were used in computations for the equilibrium constants. Protonation constants of the receptor **L** were refined using the SUPERQUAD[17] program.

The 1,3-alternate calix[4]-cyclen-benzo-crown-6, receptor **L** was synthesized according to the reported procedure.[18] The solution of the electrolyte was obtained by dissolution of a weighed quantity of $Bu_4NCF_3SO_3$ (Fluka) in 40% CH_2Cl_2/CH_3OH. The ionic strength was kept at 1.00×10^{-2} M for all experiments. The solution of receptors **L** (1.00×10^{-3} M) and their corresponding titrant base, Bu_4NOH (1.00×10^{-2} M) were prepared in 40% CH_2Cl_2/CH_3OH, 1.00×10^{-2} M $Bu_4NCF_3SO_3$. A standard solution of $HClO_4$ (*ca.* 1.00×10^{-2} M) in the background solution was used to adjust the pH of the working solution.

UV-VIS Spectrometric Measurements: The solutions of calix[4]-cyclen-benzo-crown-6 were prepared by dissolving the weighted quantities of receptor **L** in 1.00×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH. The solutions of transition metal ions Cu^{2+} and Zn^{2+} were prepared by dissolution of the weighted quantities of $Cu(CF_3SO_3)_2$ and $Zn(CF_3SO_3)_2$ in 1.00×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH, respectively. As working solution, 3.00 cm^3 of receptor **L** in 1.00×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH solution was placed in UV-VIS titrating cell (cuvet size *ca.* 4 cm^3). UV-VIS spectrometric titrations were recorded against the supporting electrolyte. The titrations were performed at 25 °C. Metal ion solution 0.05 cm^3 was added for each titration step using a micro syringe of size 2.00 cm^3, GS-1200, Gilmont (connected with capillary Teflon tube). At least ten titration steps were performed and UV-VIS absorbances of titrating solutions were recorded within the range of 200 to 400 nm. Absorbance data recollected from the whole range of UV-VIS spectra stepping by 10 to 20 nm were used in evaluation process for determination of stability constant of complex using the SIRKO program.[19]

Ab initio Calculations Section

Most stable structure of receptor **L** and its zinc complex were carried out by geometry optimization using semiempirical AM1 method.[20] The single-point energies of the optimized geometries of receptor **L** computed by *ab initio* calculations with HF/6-31G[21-23] methods were obtained. The complexation energy of ZnL were derived from the HF/6-31G energies of its related species. All calculations were performed with Gaussian 03 program.[24]

Table 1. Protonation constants of calix[4]-cyclen-benzo-crown-6, receptor **L** in 1.00×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH at 25 °C

	Protonation					Log K
K_1 :	**L**	+	H^-	⇌	LH^+	10.91 ± 0.13
K_2 :	LH^-	+	H^-	⇌	LH_2^{2+}	10.30 ± 0.25
K_3 :	LH_2^{2-}	+	H^-	⇌	LH_3^{3+}	6.24 ± 0.26
K_4 :	LH_3^{3-}	+	H^-	⇌	LH_4^{4+}	2.55 ± 0.28

Results and Discussion

Protonation constants of the calix[4]-cyclen-benzo-crown-6, receptor **L** in 1.00×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH at 25 °C are shown in Table 1. First and second protonation constants expressed as log K_1 and log K_2 are approximately same magnitude (10.91 and 10.30, respectively) but obviously different from third and fourth protonation constants (log K_3 and log K_4). The first two and second two protonation constants correspond to the protonations according to the two secondary-amine and two tertiary-amine nitrogen atoms of the receptor **L**, respectively. Distribution curves species of the receptor **L** in 40% CH_2Cl_2/CH_3OH at 25 °C, $C_L = 9.10 \times 10^{-3}$ M are shown in Figure 2. The species distribution curves show that the LH_4^{4+} species is steeply decreased from around 30% mol at pH 2.6 to less than 5% at pH higher than 4.0. Over 70% of the LH_3^{3-} species exists within the pH range of 3.1 to 5.8. The LH_2^{2-} species appears at pH 8.3 (~97%). The LH^+ species exists within the pH range of 8.3 to ~11. The maximum population of LH^- species appears at pH 10.6 (~50%). The free ligand species, **L** exists at pH higher than ~9.5 and its highest population is steeply increased at higher pH. The present species of **L** in 1.00×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH depend on pH of solution as shown in Table 2. Stability constants of the complex **L** with Cu(II) and Zn(II)

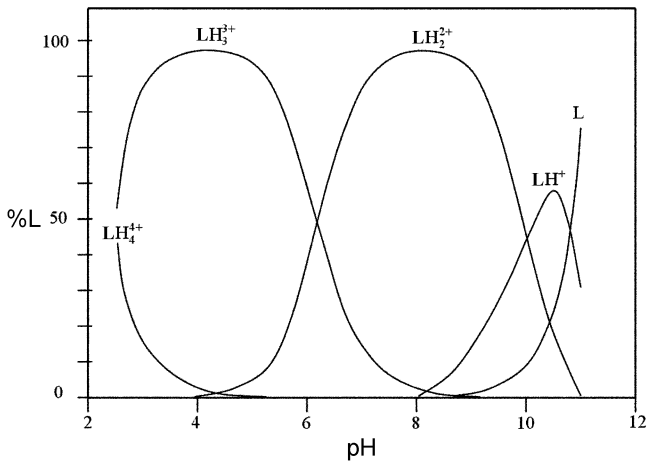

Figure 2. Distribution curves species of the receptor **L** in 40% CH_2Cl_2/CH_3OH at 25 °C, $C_L = 9.10 \times 10^{-3}$ M.

Table 2. Predominant species of calix[4]-cyclen-benzo-crown-6, **L** in 1.00×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH at 25 °C, depending on the pH of solution

Predominant species	pH ranges
L	> ~9
LH^+	8.3 to ~11
LH_2^{2-}	4 to ~11
LH_3^{3-}	~3 to ~8.3
LH_4^{4-}	< ~4.5

Table 3. Stability constants (log β) of CuL and ZnL complexes in 1.00×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH at 25 °C

Complexes	log β
CuL^{2+}	4.37 ± 0.005
ZnL^{2-}	3.45 ± 0.005

Table 4. Protonation energies of the calix[4]-cyclen-benzo-crown-6, **L** and stabilization energy of its zinc complex derived from the HF/6-31G method

	Reactions	Protonation energies (kcal/mol)
ΔE_1	$L + H^+ \rightleftharpoons LH^+$	-290.1
ΔE_2	$LH^+ + H^+ \rightleftharpoons LH_2^{2+}$	-205.0
ΔE_3	$LH_2^{2+} + H^+ \rightleftharpoons LH_3^{3+}$	-124.9
ΔE_4	$LH_3^{3+} + H^+ \rightleftharpoons LH_4^{4+}$	-26.9
$\Delta E_{complex}$	$L + Zn^{2+} \rightleftharpoons ZnL^{2+}$	-370.3

in 1.00×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH at 25 °C, in terms of log b are shown in Table 3. The receptor **L** seems to form strong complex with Cu^{2+} rather than Zn^{2+} ions.

Protonation energies of the calix[4]-cyclen-benzo-crown-6, **L** and stabilization energy of its zinc complex derived from the HF/6-31G method are listed in Table 4. The protonation energies of receptor **L** have been investigated with respect to their relation to the corresponding protonation constants as shown in Figure 3. The protonation energy,

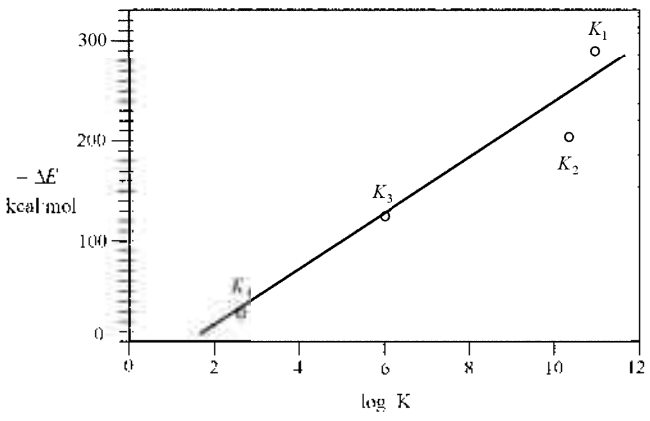

Figure 3. Correlation between protonation energies of the receptor **L** and their corresponding log K.

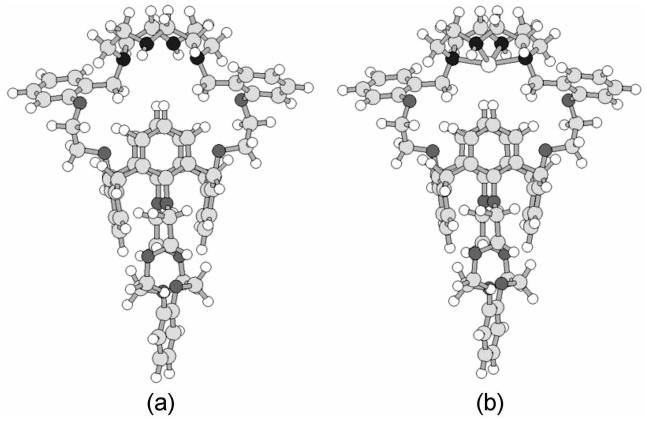

Figure 4. AM1 optimized structures of (a) calix[4]-cyclen-benzo-crown-6 and (b) its zinc complex.

ΔE is closely related to the reaction enthalpy ΔH ($\Delta E = \Delta H - P\Delta V$). As volume changes in the system can be expected to very small, the protonation energy of the system will nearly equal to the reaction enthalpy. The logarithm of the equilibrium constant is partly dependent on the enthalpy ($\Delta H = \Delta G + T\Delta S$ and $\Delta G = -2.302\ RT \log K$). The relation between the protonation energies and their corresponding log K could be linear, therefore, if ΔS and solvation contribution to ΔH were constant for all protonation processes. A tendency towards such a linear correlation between computed protonation energies and corresponding log K of this system cannot be recognized as shown in Figure 3. This result is probably caused by the differences in ΔS and also from the calculation without hydration model.

Structure of the calix[4]-cyclen-benzo-crown-6 and its zinc complex obtained with the AM1 optimization method are shown in Figure 4. As four donor nitrogen atoms of receptor **L** coordinate to a zinc ion, distorted tetrahedral geometry of the Zn**L** complex is presented as shown in Figure 4(b). This complex geometry agrees with tetrahedral geometry of $[Zn(NH_3)_4]^{2+}$.[25]

Conclusions

The protonation constants of calix[4]-cyclen-benzo-crown-6 in 1×10^{-2} M $Bu_4NCF_3SO_3$ in 40% CH_2Cl_2/CH_3OH at 25 °C determined by potentiometric method are log K_1 = 10.91, log K_2 = 10.30, log K_3 = 6.24 and log K_4 = 2.55. The stability constants of the Cu**L** and Zn**L** complexes, determined by UV-VIS spectrometric titration, as log β are 4.37 and 3.45, respectively. The stabilization energies for protonation of receptor **L**, derived from HF/6-31G energies, are ΔE_1 = -290.1, ΔE_2 = -205.0, ΔE_3 = -124.9 and ΔE_4 = -26.9 kcal/mol and complexation energy of Zn**L** complex is -370.3 kcal/mol.

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References

1. (a) Shinkai, S. *Tetrahedron* **1993**, *49*, 8933. (b) Böhmer, V. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713.
2. Lhoták, P. L.; Shinkai, S. *J. Synth. Org. Chem. Jpn.* **1995**, *53*, 963.
3. Pochini, A.; Ungaro, R. In *Comprehensive Supramolecular Chemistry*; Vögel, F., Ed.; Pergamon Press: 1996; p 103.
4. Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713.
5. McKervey, M. A.; Seward, E. M.; Ferguson, G.; Ruhl, B. L.; Harris, S. J. *J. Chem. Soc., Chem. Commun.* **1985**, 388.
6. Chang, S. K.; Kwon, S. K.; Cho, I. *Chem. Lett.* **1987**, 947.
7. Ferguson, G.; Kaitner, B.; McKervey, M. A.; Seward, E. M. *J. Chem. Soc., Chem. Commun.* **1987**, 584.
8. Ludwig, R.; Matsumoto, H.; Takeshita, M.; Ueda, K.; Shinkai, S. *Supramol. Chem.* **1995**, *4*, 319.
9. Nagasaki, T.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1063.
10. Bottino, F.; Giunta, L.; Pappalardo, S. *J. Org. Chem.* **1989**, *54*, 5407.
11. Beer, P. D.; Martin, J. P.; Drew, M. G. B. *Tetrahedron* **1992**, *48*, 9917.
12. Matt, D.; Loeber, C.; Vicens, J.; Asfari, Z. *J. Chem. Soc., Chem. Commun.* **1993**, 604.
13. Arnaud-Neu, F.; Barrett, G.; Harris, S. J.; Owens, M.; McKervey, M. A.; Schwing-Weill, M.-J.; Schwinté, P. *Inorg. Chem.* **1993**, *32*, 2644.
14. Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud-Neu, F.; Fanni, S.; Schwing, M.-J.; Egberink, R. J. M.; de Jong, F.; Reinhoudt, D. *J. Am. Chem. Soc.* **1995**, *117*, 2767.
15. Arnaud-Neu, F.; Collins, E. M.; Deasy, M.; Ferguson, G.; Harris, S. J.; Kaitner, B.; Lough, A. J.; McKervey, M. A.; Marques, E.; Ruhl, B. L.; Schwing-Weill, M.-J.; Seward, E. M. *J. Am. Chem. Soc.* **1989**, *111*, 8681.
16. Arnaud-Neu, F.; Cremin, S.; Harris, S.; McKervey, M. A.; Schwing-Weill, M.-J.; Schwinté, P.; Walker, A. *J. Chem. Soc., Dalton Trans.* **1997**, 329.
17. Gans, P.; Sabatini, A.; Vacca, A. *J. Chem. Soc., Dalton Trans.* **1985**, 1195.
18. Pulpoka, B.; Jamkratoke, M.; Tuntulani, T.; Ruangpornvisuti, V. *Tetrahedron Lett.* **2000**, *41*, 9167.
19. Vetrogen, V.; Lukyamenko, N. G.; Schwing-Weill, M. J.; Arnaud-Neu, F. *Talanta* **1994**, *41*, 2105.
20. (a) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4499. (b) Davis, L. P.; Guidry, R. M.; Williams, J. R.; Dewar, M. J. S.; Rzep, H. S. *J. Comput. Chem.* **1981**, *2*, 433. (c) Dewar, M. J. S.; McKee, M. L.; Rzepa, H. S. *J. Am. Chem. Soc.* **1978**, *100*, 3607. (d) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F. *J. Am. Chem. Soc.* **1985**, *107*, 3902. (e) Dewar, M. J. S.; Reynolds, C. H. *J. Comput. Chem.* **1986**, *2*, 140.
21. (a) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1971**, *54*, 724. (b) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257.
22. (a) Hariharan, P. C.; Pople, J. A. *Theo. Chim. Acta* **1973**, *28*, 213. (b) Hariharan, P. C.; Pople, J. A. *J. Mol. Phys.* **1974**, *27*, 209.
23. Gordon, M. S. *Chem. Phys. Lett.* **1980**, *76*, 163.
24. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, Jr. T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, Revision B.03*; Gaussian, Inc.: Pittsburgh, PA, 2003.
25. Brown, T. L.; LeMay, H. E., Jr.; Bursten, B. E. *Chemistry the Central Science*; Pentice-Hall: New Jersey, 1997; p 903.