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Short communication

Thermodynamics of interactions between organic ammonium ions and sulfonatocalixarenes

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Abstract

Calorimetric titration and NMR experiments in aqueous phosphate buffer (pH 7.2) at 298.15 K have been done to determine the binding mode, complex stability constants and thermodynamics (ΔG°, ΔH°, and $T\Delta S^\circ$) for 1:1 inclusion complexation of water-soluble calix[*n*]arenesulfonates (CnAS, $n = 4$ and 6) and thiacalix[4]arene tetrasulfonate (TCAS) with acethylcholine, carnitine, betaine and benzyltrimethylammonium ion. The results show the inclusion complexations are driven by enthalpy ($\Delta H^\circ < 0$), accompanied by negative entropic changes ($\Delta S^\circ < 0$). The binding affinities (C4AS > C6AS > TCAS) are discussed from the viewpoint of CH–π/π–π interactions, electrostatic interactions and size/shape-fit relationship between host and guest.

Keywords: Microcalorimetry; Complex stability constants; Thermodynamic parameters; Inclusion complexation; Calix[*n*]arenesulfonates

1. Introduction

Possessing hydrophobic cavities made of several phenolic units linked via methylene groups, calixarenes are able to selectively recognize various neutral and charged inorganic/organic guests [1]. Water-soluble calixarenes have become increasingly important in supramolecular chemistry [2] because they allow the study of basic forces involved in host–guest recognition processes in a solvent where most biological processes occur. Especially, complexation of tetraalkylammonium salts by synthetic receptors has received extensive attention in the last few years [3], and these studies led to the disclosure of the important role played by weak cation–π interactions [4] in the recognition process. Arena et al. [5] investigated the binding behaviors of some *p*-sulfonatocalix[4]arenes with trimethylammonium group or benzene ring of aromatic ammonium cations by NMR, calorimetry and molecular mechanics calculations. In addition, molecular dynamic simulations of the association between *p*-sulfonatocalix[4]arene and inorganic (rare-earth metal cations) or organic cations (quaternary ammonium cations) are also reported [6]. Herein, we report the molecular binding thermodynamics of calix[*n*]arenesulfonates (CnAS, $n = 4$ and 6) and thiacalix[4]arene tetrasulfonate (TCAS) with acethylcholine (Ach), carnitine (Carn), betaine (Beta), and benzyltrimethylammonium (BTMA) ion (Chart 1). The calorimetric titration and NMR results establish a correlation between the thermodynamic parameters and complex conformation, and reveal the factors controlling the correlation.

2. Experimental

Calix[*n*]arenesulfonates (CnAS, $n = 4$ and 6) and thiacalix[4]arenesulfonate (TCAS) were synthesized according to the reported method [7,8]. Ach (97%), BTMA (97%), Carn (>98%) and Beta (99%) were purchased from Tokyo Chemical Industry Co. Ltd. All calorimetric experiments were performed in an aqueous phosphate buffer (0.1 mol dm^{-3}, pH 7.2) at atmospheric pressure and 298.15 K with a Microcal VP-ITC calorimeter. The net reaction heat in each run was calculated by the "one set of binding sites" model [9] (Fig. 1).

3. Results

The stability constants (K_s) and thermodynamic parameters for host–guest inclusion complexation are listed in

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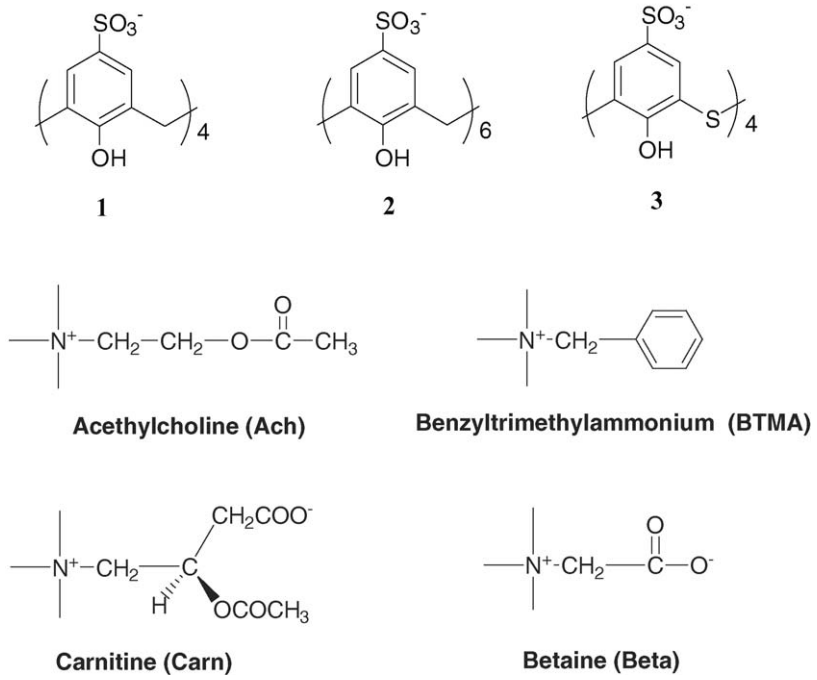

Chart 1. Structures of host calix[*n*]arenes and guest molecules.

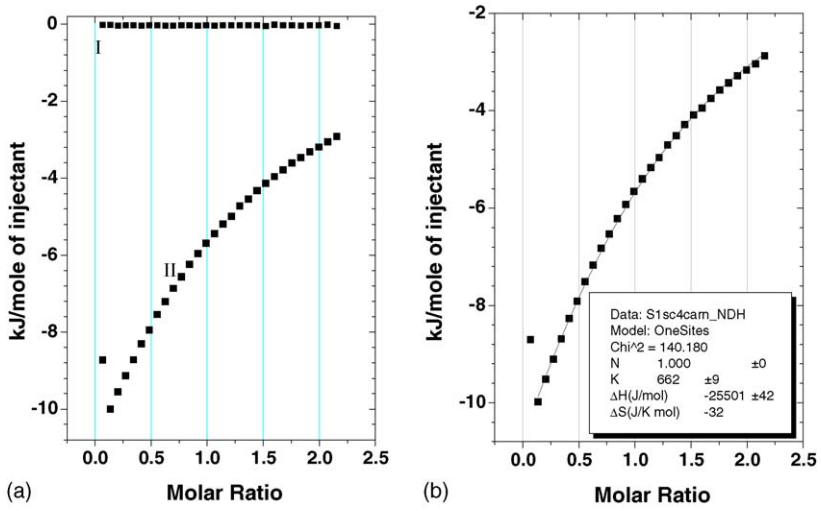

Fig. 1. (a) Heat effects of the dilution (I) and of the complexation reaction of Carn with C4AS (II) for each injection during a calorimetric titration. (b) Net heat effects obtained by subtracting the dilution heat from the reaction heat, fitted by the one set of binding sites model.

Table 1. All the titration data give 1:1 stoichiometry between host and guest, which is consistent with literatures [5,6].

^{1}H NMR spectra of complexes of C4AS or TCAS with organic ammonium guests were recorded and compared with those of free guests to explore the possible binding mode between hosts and guests. Some representative results are listed in Table 2.

In all cases, the guest protons were observed as a single resonance due to the fast exchange between a free guest and a complexed one on the NMR time scale. As can be seen in Table 2, the δ values of guest protons appreciably shift to high field after complexation with calixarenes.

4. Discussion

The conformation of C6AS in water is less rigid than C4AS, and the 1,3-alternate conformer seems to be the stable structure in neutral aqueous solution [10,11]. C6AS usually forms 1:1 complexes with guest molecules such as trimethylanilinium chloride [12], 1-Adamantyltrimethylammonium chloride [12] and some amino acids [11]. This is consistent with our present results showing the 1:1 stoichiometry of C6AS with all the four guests. Moreover, examinations with the Corey–Pauling–Koltun (CPK) molecular model clearly demonstrate that C4AS or TCAS can only accommodate one organic ammonium guest in its hydrophobic cavity.

Table 1
Complex stability constants (K_s) and thermodynamic parameters for the inclusion complexation of organic ammonium guests with CnAS and TCAS in phosphate buffer solution (pH 7.2) at 298.15 K

Host	Guest	K_s	$-\Delta G^\circ$ (kJ mol^{-1})	$-\Delta H^\circ$ (kJ mol^{-1})	$-T\Delta S^\circ$ (kJ mol^{-1})
C4AS	Ach	13803 ± 40	23.63 ± 0.01	30.12 ± 0.04	6.49 ± 0.08
	BTMA	12022 ± 165	23.29 ± 0.04	32.34 ± 0.02	9.00 ± 0.13
	Carn	648 ± 13	16.05 ± 0.05	25.76 ± 0.25	9.71 ± 0.04
	Beta	416 ± 3	14.95 ± 0.02	26.23 ± 0.17	11.25 ± 0.08
C6AS	Ach	5370 ± 4	21.29 ± 0.00	35.06 ± 0.13	13.81 ± 0.33
	BTMA	4365 ± 30	20.78 ± 0.02	34.98 ± 0.08	14.23 ± 0.21
	Carn	562 ± 17	15.70 ± 0.08	31.21 ± 0.54	15.48 ± 0.33
	Beta	263 ± 4	13.81 ± 0.04	31.71 ± 0.08	17.87 ± 0.25
TCAS	Ach	537 ± 27	15.58 ± 0.13	17.03 ± 0.42	1.46 ± 0.13
	BTMA	1862 ± 19	18.67 ± 0.03	31.17 ± 0.17	12.55 ± 0.25
	Carn	21 ± 1	7.55 ± 0.12	15.15 ± 0.67	7.53 ± 0.75
	Beta	12	6.28 ± 0.00	10.29 ± 0.13	4.02 ± 0.08

Table 2
$\Delta\delta$[a] of BTMA and Beta in the presence of 1 equiv. of C4AS or TCAS

Host	BTMA					Beta	
	$-CH_3$	$-CH_2-Ar$	*o*-H	*m*-H	*p*-H	$-CH_2-$	$-CH_3$
C4AS	−0.35	−0.31	−0.28	−0.34	−0.45	−0.13	−0.31
TCAS	0.13	0.06	−0.10	−0.19	−0.28	−0.08	−0.22

[a] $\Delta\delta = \delta$ (with 1 equiv. of host) − δ (free guest). Negative values indicate the upfield shift.

A close comparison of the $\Delta\delta$ values of BTMA protons after complexation with C4AS shows that BTMA is encapsulated from either the aromatic moiety or the methyl group without regioselectivity. The complexation mode of BTMA by C4AS may be due to CH–π interaction in addition to π–π interaction, in accord with earlier results [13]. In sharp contrast, TCAS regioselectively includes BTMA into its cavity from the aromatic side, indicating that the quaternary ammonium group does not fit comfortably into the enlarged cavity of TCAS compared to C4AS. However, complexation of C4AS/TCAS with Beta shows that both C4AS and TCAS include Beta from the ammonium side, but the $\Delta\delta$ values of Beta protons induced by complexation with C4AS are larger than those by TCAS. According to the NMR data, the possible binding modes for the complexation of ammonium guests with C4AS and TCAS are shown in Fig. 2.

The calixarenes form stable complexes with all ammonium guests, showing similar molecular selectivity, C4AS > C6AS > TCAS for each guest. Among the host calixarenes examined, possessing the smallest cavity with a relatively high π electron density, C4AS gives the largest K values for all ammonium guests. That is attributed to the good size-fit and strong CH–π/π–π interactions between host and guest. All of the calixarenes examined show much stronger binding abilities towards Ach and BTMA than towards Carn and Beta. Both Carn and Beta have electronegative carboxyl groups. According to the reported pK_a values [10,14], C4AS and TCAS have five negative charges at pH 7.2, i.e. four anionic sulfonate groups and one deprotonated phenolic hydroxy group, whereas C6AS has six anionic sulfonate groups and two deprotonated phenolic hydroxy groups. Therefore, the electrostatic repulsion from the sulfonate groups of calixarenes will weaken the host–guest binding. The K value of TCAS/BTMA complex is 3.5 times larger than that of TCAS/Ach complex, indicating that binding of the aromatic ring of the guest with TCAS is much stronger than binding of the ammonium group. However, the K value of C4AS with BTMA is similar to that of C4AS with Ach because

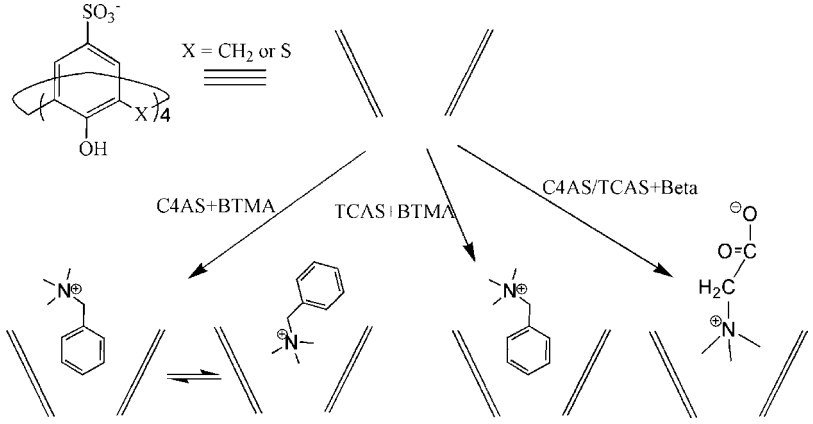

Fig. 2. Possible binding modes of guests with C4AS and TCAS.

C4AS can equally bind either the phenyl portion or the ammonium group efficiently.

The host–guest inclusion complexation is mainly driven by the favorable enthalpic changes, which indicates that π-stacking (including π–π or CH–π) and van der Waals interactions play a crucial role in the host–guest complexation. Because electrostatic interactions usually contribute to positive enthalpic changes [6a], we deduce that electrostatic interactions are not dominating forces in the association process. All of the host–guest complexations exhibit unfavorable entropic changes, because the association process leads to loss of conformational freedom. Likewise, the inclusion of neutral aromatic guests by cyclophanes in water is also enthalpically driven with a negative entropic contribution [15]. However, the entropic term herein is less unfavorable than that of neutral guests since the partial desolvation of quaternary ammonium and sulfonate groups upon interaction gives a positive contribution to entropic changes [5a].

C6AS shows more favorable enthalpic changes but weaker binding abilities than C4AS. Coleman and co-workers [16] reported that guest molecule can be totally immobilized within the double cone cavity of the 1,3-alternate conformer of C6AS. Therefore, we deduce that the large enthalpic gain of C6AS is partially cancelled by the high entropic loss arising from the loss of degrees of freedom upon complexation. Upon complexation with BTMA, both C4AS and TCAS give more negative enthalpic change than with the other guests owing to the π–π interactions between calix[4]arenes and the aromatic ring of BTMA. Surprisingly, the entropic loss of TCAS with BTMA is larger than that of C4AS. One possible explanation for the unexpected entropic change is that the regioselective complexation mode of TCAS with BTMA leads to a good size-fit between the aromatic group of BTMA and the TCAS cavity, which consequently results in the larger losses of the conformational freedoms of hosts and guests.

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References

[1] Danil de Namor, R.M. Cleverley, M.L. Zapata-Ormachea, Chem. Rev. 98 (1998) 2495.
[2] A. Pochini, R. Ungaro, in: F. Vogtle (Ed.), Comprehensive Supramolecular Chemistry, vol. 2, Pergamon, Oxford, 1996, pp. 103–149.
[3] (a) H.-J. Schneider, D. Güttes, U. Schneider, J. Am. Chem. Soc. 110 (1988) 6449;
(b) P.C. Kearny, L.S. Mizoue, R.A. Kumpf, J.E. Forman, A. McCurdy, D.A. Dougherty, J. Am. Chem. Soc. 115 (1993) 9907.
[4] J.C. Ma, D.A. Dougherty, Chem. Rev. 97 (1997) 1303.
[5] (a) G. Arena, A. Casnati, A. Contino, G.G. Lombardo, D. Sciotto, R. Ungaro, Chem. Eur. J. 5 (1999) 738;
(b) G. Arena, A. Casnati, A. Contino, F.G. Gulino, D. Sciotto, R. Ungaro, J. Chem. Soc., Perkin Trans. 2 (2000) 419.
[6] (a) C. Bonal, Y. Israëli, J.-P. Morel, N. Morel-Desrosiers, J. Chem. Soc., Perkin Trans. 2 (2001) 1075;
(b) A. Mendes, C. Bonal, N. Morel-Desrosiers, J.-P. Morel, P. Malfreyt, J. Phys. Chem. B. 106 (2002) 4516.
[7] (a) S. Shinkai, S. Mori, T. Tsubaki, T. Sone, O. Manabe, Tetrahedron Lett. 25 (1984) 5315;
(b) S. Shinkai, S. Mori, H. Koreishi, T. Tsubaki, O. Manabe, J. Am. Chem. Soc. 108 (1986) 2409.
[8] N. Iki, T. Horiuchi, H. Oka, K. Koyama, N. Morohashi, C. Kabuto, S. Miyano, J. Chem. Soc., Perkin Trans. 2 (2001) 2219.
[9] Y. Liu, E.-C. Yang, Y. Chen, Thermochim. Acta 429 (2005) 163.
[10] J.L. Atwood, D.L. Clark, R.K. Juneja, G.W. Orr, K.D. Robinson, R.L. VincentIa, J. Am. Chem. Soc. 114 (1992) 7559.
[11] N. Douteau-Guével, A.W. Coleman, J.P. Morel, N. Morel-Desrosiers, J. Chem. Soc., Perkin Trans. 2 (1999) 629.
[12] S. Shinkai, K. Araki, T. Matsuda, O. Manabe, Bull. Chem. Soc. Jpn. 62 (1989) 3856.
[13] S. Shinkai, K. Araki, T. Matsuda, N. Nishiyama, H. Ikeda, L. Takasu, M. Iwamoto, J. Am. Chem. Soc. 112 (1990) 9053.
[14] H. Matsumiya, Y. Terazono, N. Iki, S. Miyano, J. Chem. Soc., Perkin Trans. 2 (2002) 1166.
[15] (a) S.B. Ferguson, E.M. Seward, F. Diederich, E.M. Sanford, A. Chou, P. Inocencio-Szweda, C.B. Knobler, J. Org. Chem. 53 (1988) 5593;
(b) D.B. Smithrud, T.B. Wyman, F. Diederich, J. Am. Chem. Soc. 113 (1991) 5420.
[16] N. Douteau-Guével, A.W. Coleman, J.P. Morel, N. Morel-Desrosiers, J. Chem. Soc., Perkin Trans. 2 (1999) 629.