ISSN 1070-3632, Russian Journal of General Chemistry, 2008, Vol. 78, No. 4, pp. 602–607. © Pleiades Publishing, Ltd., 2008.
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Thermodynamics of Sublimation of Calix[4]arene Complexes with Solvent Molecules

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Received July 6, 2007

Abstract—Some calix[4]arenes form complexes with solvent molecules, preserving the stoichiometric composition upon sublimation. The saturated vapor pressures of calix[4]arenes and their complexes with solvents were determined by the Knudsen effusion method in a wide temperature range. The changes in the standard thermodynamic functions of complexation in transfer from the condensed state to the gas phase were determined. It was found that the enthalpy term of the Gibbs energy of the complex formation increases with an increase in the conformational mobility of the ligand, and the entropy term increases as the ligand becomes less flexible and more rigid.

DOI: 10.1134/S1070363208040154

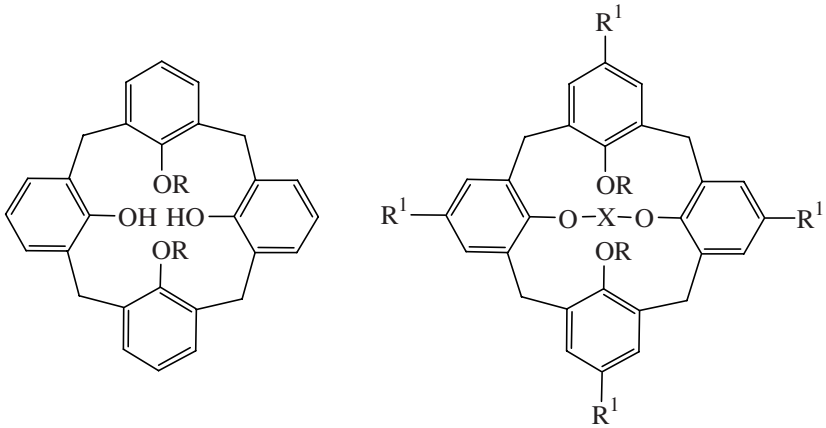
The term calixarenes refers to a class of macrocyclic receptors formed by condensation of phenols and aldehydes and having a structural cavity. Calixarenes are a promixing class of aromatic "hosts" exhibiting enhanced capability for cation–π interactions and for binding of small neutral "guests." As a result of active studies of this important class of molecular receptors in the past two decades, numerous compounds with diverse substituents arranged on the calixarene core have been synthesized [1]. Despite rapid progress of the calixarene chemistry, it is difficult to make unambiguous conclusions about the relationship between their structure and complexing properties, because of complicated character of the complexation [2]. Studies of the crystal structures of calix[4]arene hosts with included guests, mass-spectrometric studies of the host–guest interactions in the gas phase, and data obtained by methods of solution chemistry allow formulation of certain general relationships. Apparently, the decisive factor is the number of complexing centers in the host molecule [3], which is determined by steric and conformational factors. In some cases, the conformational mobility of the host should be restricted to enhance the stability of the complex, and bulky alkyl groups can prevent accommodation of the guest molecule because of steric hindrance.

There are publications demonstrating the correlation between the complexing properties of calixarenes toward gaseous guests and the complexation in solutions. Hirakata et al. [4] studied the binding of gaseous neutral guests with solid monodeoxycalix[4]arene host. They showed that the selectivity of the cavity of the solid host toward a guest is closely related to the free energy of complexation in solution. The degree of binding of gaseous guests with a solid host increases in the order acetone ≈ CH_2BrCl < CH_3CN < CH_3NO_2. This order is consistent with the free energies of complexation of these guests with monodeoxycalix[4]-arene, determined in CCl_4 solutions. Inokuchi et al. [5] studied complexes of organic cations with calix[*n*]-arenes of various configurations and ring sizes by mass spectrometry. The relative peak intensities showed that the complexes are stable in the gas phase, but the complexation selectivity in accordance with the sizes of the host and guest molecules considerably differs from that observed in solution, whereas the conformational selectivity obtained in the gas phase corresponds to the selectivity in solution. The use of mass spectrometry for studying interactions of calixarenes and resorcinolarenes with molecular guests in the gas phase is discussed in a review [6]. It is noted that studies of gas-phase interactions furnish unique information on the specificity of the supramolecular binding forces taking into account fine structural factors such as conformational dynamics and steric

hindrance. Appropriate implementation of the mass-spectrometric experiment allowed Vincenti and Irico [6] to ensure the host–guest complexation equilibrium directly in the gas phase. However, it furnished no data on the kinetics and mechanism of the reaction. Continuous evacuation of the system does not allow measurement of the current reactant concentrations and hence determination of the thermodynamic host–guest complexation constants.

Despite numerous studies dealing with the complexation of calixarenes with neutral guest molecules, determination of the constants and thermodynamic parameters of the complexation remains a complex experimental problem. Spectral methods commonly used for these purposes do not always allow estimation of the strength of supramolecular binding of a calixarene host with a neutral guest [7].

In this study, using the Knudsen effusion method, we determined for the first time the saturated vapor pressure of calix[4]arenes and their complexes with solvents in a wide temperature range. The installation and procedure of the effusion experiment are described in detail elsewhere [8]. We studied the following compounds: **I, II, III, IV, I** · CH_2Cl_2, C_6H_{14}**I** · CH_2Cl_2 · C_6H_{14}, **II** · C_6H_{14}, **III** · C_6H_{14}, and **IV** · CH_3OH.



I: R = H; **II**: R = CH_3; **III**: R = CH_3, R^1 = H, X = $CH_2CH_2(OCH_2CH_2)_4$; **IV**: R = CH_3, R^1 = *t*-Bu, X = $CH_2CH_2(OCH_2CH_2)_4$.

The thermodynamic parameters of sublimation of the compounds were calculated by well-known formulas:

$$\Delta H_{sub} = -R\mathrm{d}(\ln P)/d(1/T), \quad (1)$$

$$\Delta G_{sub} = -RT\ln (P/P_0), \quad (2)$$

$$\Delta S_{sub} = -d(\Delta G_{sub})/dT, \quad (3)$$

where P is the vapor pressure of the substance being sublimed, Pa; $P_0 = 1.013 \times 10^5$ Pa, atmospheric pressure; T, temperature, K; and $R = 8.314$ J mol^{-1} K^{-1}, gas constant.

Figure 1 shows the plots of ln P of the compounds vs. reciprocal temperature.

The temperature dependence of the vapor pressure in the ln P–T^{-1} coordinates is linear:

$$\ln P = a + b/T. \quad (4)$$

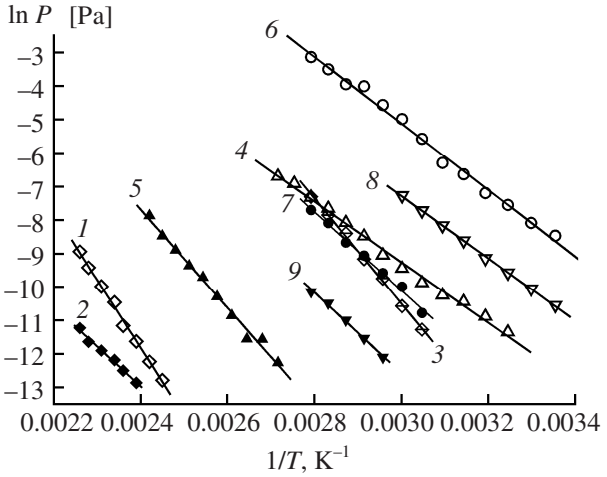


Fig. 1. Temperature dependence of the saturated vapor pressure: (*1*) **I**, (*2*) **I** · CH_2Cl_2, (*3*) **I** · CH_2Cl_2 · C_6H_{14}, (*4*) **II**, (*5*) **II** · C_6H_{14}, (*6*) **III**, (*7*) **III** · C_6H_{14}, (*8*) **IV**, and (*9*) **IV** · CH_3OH.

Table 1. Regression coefficients of the linear equation $\ln P = a + b/T$[a] and mean values of the enthalpy and entropy of sublimation of the compounds

Compound	a	b/1000	ΔH_{sub}, kJ mol^{-1}	ΔS_{sub}, J mol^{-1} K^{-1}
I	36.5±0.6	–20.1±0.3	167±2	207±5
I·CH_2Cl_2	15±1	–11.7±0.4	98±3	35±5
I·CH_2Cl_2·C_6H_{14}	36.6±0.9	–15.7±0.3	131±3	208±8
II	17.7±0.6	–9.0±0.2	75±2	71±5
II·C_6H_{14}	28±1	–14.7±0.5	122±4	134±10
III	24.6±0.7	–9.9±0.2	82±2	109±6
III·C_6H_{14}	25±1	–11.7±0.4	97±3	118±12
IV	20.8±0.5	–9.3±0.2	78±1	76±3
IV·CH_3OH	24±1.4	–12.1±0.5	100±4	100±12

[a] The correlation coefficient of the linear dependences is within 0.995–0.998. Vapor pressure P, Pa.

The parameters of linear equation (4) and the mean enthalpies and entropies of sublimation of the compounds studied are given in Table 1.

Although practical applications of the host–guest chemistry refer to the condensed phase, gas-phase studies give deeper insight into the nature of such interactions, taking into account specific features of the conformational and solvation effects. The higher flexibility of the calixarene structure becomes more important in the gas phase when free solvent molecules do not restrict free conformational changes of the calixarene molecule. The negative entropy term of the free energy of the host–guest complexation weakens the supramolecular interaction in the gas phase. Hence, the formation of complexes in the gas phase is favored by decreased flexibility of the calixarene core. This leads to a decrease in the negative entropy of complexation and makes the complex energetically stable [6]. A consequence of the decreased flexibility of a ligand is its increased selectivity, because rigid three-dimensional arrangement of its reactive sites should match the arrangement of the reactive sites of the guest, leading to stronger interaction. The rigidity of the calixarene core can be enhanced by different ways. One of them is introduction of bulky substituents into the upper or especially lower rim of the molecule, to block its structure in the cone conformation. However, this may make phenolic oxygen atoms of the calixarene inaccessible to potential guests, so that the complexing properties of the ligand will be determined exclusively by – electrons of the aromatic rings. Another procedure suggests the presence of rigid bridges at the upper or lower rim of the calixarene molecule [6].

It was shown previously that some calix[4]arenes form complexes with solvent molecules, preserving the stoichiometric composition upon sublimation [8]. A unique property of calixarene complexes to preserve the stoichiometric composition allows estimation of the energy characteristics of the complexation from the experimental data on the temperature dependence of the saturated vapor pressure. The thermodynamic cycle of transfer of calixarene, solvent, and calixarene–solvent complex from the condensed state to the gas phase can be represented as follows:

$$\begin{array}{ccc} n\mathrm{Host_g} + m\mathrm{Guest_g} & \rightarrow & n\mathrm{Host}\cdot m\mathrm{Guest_g} \\ \uparrow \qquad\qquad \uparrow & & \uparrow \\ n\mathrm{Host_s} + m\mathrm{Guest_l} & \rightarrow & n\mathrm{Host}\cdot m\mathrm{Guest_s} \end{array}$$

Separate steps of the cycle are characterized by the following enthalpies:

$$n\mathrm{Host_s} \rightarrow n\mathrm{Host_g} + \Delta H^0_1,$$

$$m\mathrm{Guest_l} \rightarrow m\mathrm{Guest_g} + \Delta H^0_2,$$

$$n\mathrm{Host}\cdot m\mathrm{Guest_s} \rightarrow n\mathrm{Host}\cdot m\mathrm{Guest_g} + \Delta H^0_3,$$

$$n\mathrm{Host_s} + m\mathrm{Guest_l} \rightarrow n\mathrm{Host}\cdot m\mathrm{Guest_s} + \Delta H^0_{\mathrm{complex1}},$$

$$n\mathrm{Host_g} + m\mathrm{Guest_g} \rightarrow n\mathrm{Host}\cdot m\mathrm{Guest_g} + \Delta H^0_{\mathrm{complex2}},$$

$$\Delta\Delta H^0_{\mathrm{complex}} = \Delta H^0_{\mathrm{complex2}} - \Delta H^0_{\mathrm{complex1}} = \Delta H^0_3 - (\Delta H^0_1 + \Delta H^0_2),$$

where Host is calixarene; Guest, solvent; nHost · mGuest, complex of calixarene with a solvent; n and m, stoichiometric coefficients; indices s and l refer to the corresponding condensed state, and g, to the gas phase; $\Delta H^0_{1,2,3}$ are the enthalpies of sublimation and vaporization of calixarene, solvent, and calixarene–solvent complex, respectively, under standard conditions; $\Delta H^0_{\mathrm{complex1}}$ and $\Delta H^0_{\mathrm{complex2}}$ are the standard enthalpies of complexation in the condensed state and in the gas phase, respectively.

Similarly, according to the Hess law, we obtain

$$\Delta\Delta G^0_{\mathrm{complex}} = \Delta G^0_{\mathrm{complex2}} - \Delta G^0_{\mathrm{complex1}} = \Delta G^0_3 - (\Delta G^0_1 + \Delta G^0_2).$$

Thus, the known quantities $\Delta H^0_{1,2,3}$ and $\Delta G^0_{1,2,3}$ allow calculation of the changes in the enthalpy $\Delta\Delta H^0_{\mathrm{complex}}$ and Gibbs energy $\Delta\Delta G^0_{\mathrm{complex}}$ of the

complexation in transfer from the condensed state to the gas phase, and also the corresponding change in the entropy: $T\Delta\Delta S^0_{complex} = \Delta\Delta H^0_{complex} - \Delta\Delta G^0_{complex}$.

The quantities $\Delta\Delta H^0_{complex}$, $\Delta\Delta G^0_{complex}$, and $T\Delta\Delta S^0_{complex}$ for the complexes **I** · CH_2Cl_2, **I** · CH_2Cl_2 · C_6H_{14}, **II** · C_6H_{14}, **III** · C_6H_{14}, and **IV** · CH_3OH are given in Table 2.

In the calculations, as the standard enthalpies of sublimation of calixarenes we took the mean values of the corresponding enthalpies (Table 1). The enthalpies of vaporization at 298.15 K of n-hexane, dichloromethane, and methanol are 7.4, 6.8, and 8.94 kcal mol^{-1}, respectively [9]. ΔG^0 of sublimation of calixarenes was calculated by Eq. (2) from the vapor pressures obtained by extrapolation of the temperature dependence to 298.15 K (Table 1). For the solvents, ΔG^0 of vaporization was calculated from the vapor pressures at 298.15 K [9].

Because the entropy of sublimation characterizes an increase in the conformational mobility of molecules in their transfer into the gas phase, it is possible to assess experimentally the relationship between the complexing properties of the calixarenes studied and their conformational mobility. It was shown by computer simulation [10] that the structure of ligand **I** allows it to take any conformation in the gas phase: *cone, partial cone*, *1,2-alternate*, or *1,3-alternate*, although in the solid state compound **I** exists esxlusively as a *cone* structure, owing to strong intermolecular hydrogen bonding. Hence, transfer of calixarene **I** from the solid state to the gas phase should be accompanied by a considerable increase in the entropy (Fig. 2).

The entropy of sublimation of the complex **I** · CH_2Cl_2 considered as a ligand for the process **I** · $CH_2Cl_2 + C_6H_{14} \rightarrow$ **I** · CH_2Cl_2 · C_6H_{14} is minimal in the series of the compounds in question, probably due to the formation of the stable complex **I** · CH_2Cl_2 and to considerably decreased mobility of the complex in the gas phase.

The conformational analysis of **II** was described in detail in [10]. From the calculation results, it was concluded that for dimethyl ether **II** none of the conformations is prevalent. The *cone* conformation is no longer the only conformation in which there can be hydrogen bonds (two in this case), and realization of other conformations with the more preferable bond energy or weaker electrostatic repulsion between the oxygen atoms becomes more probable. On the other hand, compound **II** can take in the gas phase any possible conformation because of its flexibility and absence of steric hindrance. Thus, in this case the entropy of sublimation should be low.

Table 2. Changes in the thermodynamic functions of complexation in transfer from the condensed state into the vapor phase

Compound	$\Delta\Delta G^0_{complex}$, kJ mol^{-1}	$\Delta\Delta H^0_{complex}$, kJ mol^{-1}	$T\Delta\Delta S^0_{complex}$, kJ mol^{-1}
I·CH_2Cl_2	–19	–98	–80
I·CH_2Cl_2·C_6H_{14} [a]	–43	–96	–54
II·C_6H_{14}	19	16	–3
III·C_6H_{14}	10	–16	–26
IV·CH_3OH	11	–15	–26
I·CH_2Cl_2·C_6H_{14} [b]	–24	2	26

[a] Formation by the scheme **I** + CH_2Cl_2 + $C_6H_{14} \rightarrow$ **I**·CH_2Cl_2·C_6H_{14}.
[b] Formation by the scheme **I**·CH_2Cl_2 + $C_6H_{14} \rightarrow$ **I**·CH_2Cl_2·C_6H_{14}.

The conformational mobility of compound **IV** is lower than that of **III**, apparently because of introduction of *tert*-butyl groups into the upper rim of the molecule. The presence of crown ether bridges also decreases the conformational mobility of **III** and **IV**.

Figure 2 shows how the changes in the thermodynamic functions of complexation in transfer from the

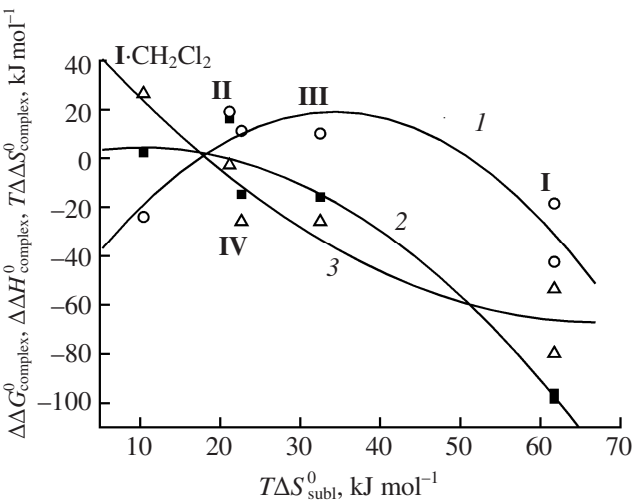


Fig. 2. Changes in the thermodynamic functions of complexation in transfer from the condensed state into the vapor phase. ($T\Delta S^0_{subl}$) entropy of sublimation of calixarene ligands **I**, **II**, **III**, **IV**, and **I** · CH_2Cl_2; (*1*) $\Delta\Delta G^0_{complex}$, (*2*) $\Delta\Delta H^0_{complex}$, and (*3*) $T\Delta\Delta S^0_{complex}$.

condensed state into the gas phase correlate with the entropy of sublimation of the corresponding ligand. It can be seen that, with a decrease in the conformational mobility of the ligand ($T\Delta S^0_{subl}$ decreases in the order **I** > **III** > **IV** > **II** > **I** · CH_2Cl_2), the negative change in the entropy of complexation in transfer from the condensed state to the gas phase $T\Delta\Delta S^0_{complex}$ decreases, and the quantity becomes positive for **I** · CH_2Cl_2. As already noted, higher flexibility of the calixarene structure determines the negative entropy contribution to the free energy of the host–guest complexation and weakens the supramolecular interaction in the gas phase. However, an increase in the entropy term $T\Delta\Delta S^0_{complex}$ in this series is accompanied by a decrease in the negative enthalpy $\Delta\Delta H^0_{complex}$, i.e., with a decrease in the conformational mobility of the ligand the enthalpy term of the Gibbs energy of formation of the complex decreases. As a result, the dependence of the free energy of complexation $\Delta\Delta G^0_{complex}$ on the conformational mobility of the ligand passes through a maximum and is negative for the two extreme cases of maximal and minimal conformational mobility. With an increase in the conformational mobility, the enthalpy term of the free energy of complex formation becomes prevalent, and at low mobility the entropy term prevails. The formation of the complex **I** · CH_2Cl_2 + C_6H_{14} → **I** · CH_2Cl_2 · C_6H_{14} is accompanied by almost zero thermal effect and is governed by the entropy term of the Gibbs energy. For ligands **II**, **III**, and **IV**, changes in the Gibbs energy of complexation $\Delta\Delta G^0_{complex}$ are small and positive, because the negative values of $T\Delta\Delta S^0_{complex}$ are not compensated by negative changes in the enthalpy $\Delta\Delta H^0_{complex}$. This fact suggests predominant complexation in the condensed state relative to the gas phase and is a consequence of insufficiently rigid structure of the ligand, which weakens the interaction in the gas phase.

Hence, in complexation in the gas phase it is necessary to take into account not only the negative entropy term of the free energy of the host–guest complexation, weakening the supramolecular interaction, but also the enthalpy term, which becomes prevalent with an increase in the conformational mobility of the ligand.

EXPERIMENTAL

Compounds **II**, **III**, and **IV** were prepared from commercially available 25,26,27,28-tetrahydroxycalix[4]arene **I** purchased from Aldrich, using the procedures of the classical calix[4]arene chemistry [3, 11–13]. The complexes **I** · CH_2Cl_2 · C_6H_{14}, **II** · C_6H_{14}, **III** · C_6H_{14}, and **IV** · CH_3OH were prepared by precipitation from methanol in solutions of the corresponding calixarenes in dichloromethane–hexane (1 : 1). Complex **I** · CH_2Cld2 was prepared by dissolution of **I** in CH_2Cl_2, followed by solvent evaporation. Prior to effusion experiments, all the compounds were additionally purified by fractional sublimation in a high vacuum. For the effusion experiment we took the middle fraction. The absence of degradation and the purity were checked by ^{1}H NMR spectroscopy.

The ^{1}H NMR spectra and analytical data for the complexes **I** · CH_2Cl_2 · C_6H_{14}, **II** · C_6H_{14}, **III** · C_6H_{14}, and **IV** · CH_3OH are given elsewhere [8].

I · CH_2Cl_2. ^{1}H NMR spectrum (200 MHz, $CDCl_3$), δ, ppm: 7.97 s (4H, OH), 7.39 d (8H, ArH_m, *J* 7.6 Hz), 6.73 t (4H, ArH_p, *J* 7.6 Hz), 5.65 s (2H, CH_2Cl_2), 4.33 s (4H, $ArCH_2Ar$), 3.42 s (4H, $ArCH_2Ar$). Found, %: C 68.32; H 5.07; Cl 13.94. $C_{28}H_{24}O_4$ · CH_2Cl_2. Calculated, %: C 68.38; H 5.14; Cl 13.97.

ACKNOWLEDGMENTS

The study was financially supported by the Russian Foundation for Basic Research (project no. 06-03-32 537-a).

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