ORIGINAL ARTICLE

Thermodynamics of sublimation of calix[4]arene complexes with solvent molecules

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Abstract The inclusion of small neutral organic guests (C_6H_{14}, CH_2Cl_2, CH_3OH) by calix[4]arene receptors was found by ^1H NMR spectroscopy and microanalysis. The studied calix[4]arenes can form stable intramolecular complexes with solvent molecules which keep the stoichiometric composition without changing under conditions of the sublimation experiment. The saturated vapour pressures of calix[4]arenes and complexes of calix[4]arenes with solvent molecules were determinated for the first time by the Knudsen's effusion method in the wide temperature range. The changing of standard thermodynamic parameters of complexation by transfer process from condensed state to vapour phase was estimated. It was shown that the large flexibility of the calixarene ligand structure corresponds to a strongly negative entropic contribution as well as negative enthalpy term to the Gibbs energy of formation of host–guest complexes in the gas phase.

Keywords Calixarenes · Host–guest · Molecular recognition · Sublimation enthalpy

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Introduction

Calix[4]arenes represent an interesting class of pre-organized aromatic hosts exhibiting an enhanced ability for cation-π interaction and inclusion of small neutral organic guests. In many biological systems, metal cation-π interactions play an important role in molecular recognition, and atmospheric detection of odorant vapours of organic compounds is one of the most important problems of environment monitoring. Moreover the recognition of neutral organic molecules and cations by synthetic receptors is a topic of current interest in supramolecular and analytical chemistry. It was shown that some compounds such crown ethers and calixarenes forming inclusion complexes with some organic guest molecules and cations can be used for the development of sensors and components of microelectronic systems [1]. The growing interest in these materials is due to the simplicity of their synthesis, thermal stability and the extreme ease of deposition under thin film form [2–5]. From the study of crystal structures of calixarene hosts including organic molecules and research of host–guest calixarene chemistry in the gas phase by mass spectroscopy as well as results obtained by solution chemistry, several conclusions of general validity were drawn [6]. Probably, the strength of the host–guest interaction depends on the potential guest molecule nature, the cavity size and the conformation of the macrocycles, substituents on the upper and lower rim of the calixarenes which influence the cavity size, the conformation and the flexibility of the host molecule, the number of the ligating sites of the host (e.g., the number of the oxygen atoms in the polyether ring). In spite of available facts, conclusions

regarding the relationship between the structure and the binding properties of a particular host are rather difficult because of the complex relations between the complex formation constants and the structure of both the host and the guest molecules.

There are evidences that the small neutral guest selectivity in the cavity of solid calixarene host is closely related to the free energy of complexation in solution [7]. In the last 10 years, host–guest chemistry in the gas phase has been studied by mass spectroscopy [8], and it turns out that the ionization mode determines whether the results obtained by mass spectroscopy reflect those of solution chemistry. Shinkai et al. [9] have studied organic cation complexes with several calix[*n*]arenes of differing conformation and ring size by the use of positive secondary ion mass spectrometry. Relative peak intensities have been shown to reflect the complex stability in the gas phase but selectivity of the complexation with respect to the size of both the host and the guest differs greatly from that observed in solution. Whereas the conformation selectivity found in the gas phase paralleled that of the solution, the hole-size selectivity of guests was found to be different for the gas and the condensed phases. Despite the enormous work developed to characterize calixarene receptors and investigate their chemistry in solution, very few studies have been undertaken to date to investigate the interaction between them and organic guest molecules in the gas phase [10]. However gas-phase studies provide interesting perspective for host–guest interactions. As the solvent is absent, no solvation effects can modify the electronic and thermodynamic properties nor the geometrical constraints of supramolecular binding, so that pure intrinsic interaction between the two counterparts is uncovered, free from any third-body influence.

Experimental

In this study, the temperature dependences of the saturated vapour pressures of calix[4]arenes and complexes of calix[4]arenes with solvent molecules were determined with the aim to estimate the changing of relative standard thermodynamic parameters of complexation by transfer process from condensed state to vapour phase. 25,27-dimethoxy-26,28-dihydroxycalix[4]arene (**II**), 25,27-dimethoxy-calix[4]arene crown-6 (**III**), 25,27-dimethoxy-5,11,17,23-tetra-*p-tert*-butylcalix[4]arene crown-5 (**IV**), 25,27-diethoxy-5,11,17,23-tetra-*p-tert*-butylcalix[4]arene crown-5 (**V**), 25,27-bis(benzyloxy)-5,11,17,23-tetra-*p-tert*-butylcalix[4]arene crown-5 (**VI**), 25,27-dimethoxy-5,11,17,23-tetra-*p-tert*-
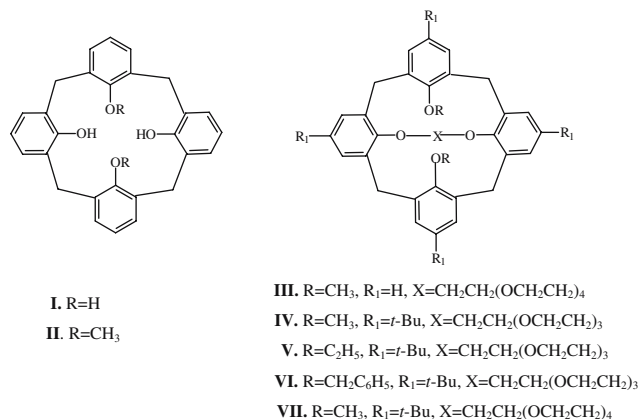
butylcalix[4]arene crown-6 (**VII**) were synthesized used available from Aldrich 25,26,27,28-tetra-hydroxycalix[4]arene (I) (Fig. 1) according to methods described by the authors [11–14]. Calix[4]arenes (**I–IV, VII**) are present as a cone structure, compounds (**V, VI**) are in the partial-cone conformation. The complexes (**I**)·C_6H_{14}·CH_2Cl_2, (**II**)·C_6H_{14}, (**III**)·C_6H_{14} and (**VII**)·CH_3OH were obtained by crystallization from mixture $CH_3OH/C_6H_{14}/CH_2Cl_2$. The complex (**I**)·$CH_2Cl_2$ was obtained by solution of (**I**) in CH_2Cl_2 and then by evaporation of the solvent. ^1H NMR spectra were recorded with Bruker VC-300 (300 MHz) spectrometer in $CDCl_3$.

Compound (**I**)·CH_2Cl_2. Found: C, 68.32; H, 5.07; Cl, 13.94. Anal. Calcd for $C_{28}H_{24}O_4$·CH_2Cl_2: C, 68.38; H, 5.14; Cl, 13.97. ^1H NMR δ 7.97 (s, 4H, OH), 7.39 (d, $J = 7.6$ Hz, 8H, ArH_{meta}), 6.73 (t, $J = 7.6$ Hz, 4H, ArH_{para}), 5.65 (s, 2H, CH_2Cl_2), 4.33 (s, 4H, ArCH$_2$Ar), 3.42 (s, 4H, ArCH$_2$Ar).

Compound (**I**)·C_6H_{14}·$CH_2 Cl_2$Found: C, 70.59; H, 6.72; Cl, 11.93 Anal. Calcd for $C_{28}H_{24}O_4 \cdot C_6H_{14} \cdot CH_2Cl_2$: C, 70.56; H, 6.70; Cl, 11.91. ^1H NMR δ 7.95 (s, 4H, OH), 7.41 (d, $J = 7.6$ Hz, 8H, ArH_{meta}), 6.71 (t, $J = 7.6$ Hz, 4H, ArH_{para}), 5.68 (s, 2H, CH_2Cl_2), 4.31 (s, 4H, ArCH$_2$Ar), 3.40 (s, 4H, ArCH$_2$Ar), 0.98 (m, 8H, C_6H_{14}), 0.58 (t, 6H, C_6H_{14}).

Compound (**II**)·C_6H_{14}. Found: C, 80.30; H, 7.80. Anal. Calcd for $C_{30}H_{28}O_4 \cdot C_6H_{14}$: C, 80.27; H, 7.78. ^1H NMR δ: 7.71 (s, 2H, OH), 7.82 (d, $J = 7.5$ Hz, 4H, ArH_{meta}), 6.87 (d, $J = 7.6$ Hz, 4H, ArH_{meta}), 6.74–6.66 (m, $J = 7.2$ Hz, 4H, ArH_{para}),4.31 (d, $J = 13.1$ Hz, 4H, ArCH$_2$Ar), 3.82 (s, 6H, OCH$_3$), 3.41 (d, $J = 13.2$ Hz, 4H, ArCH$_2$Ar), 0.97 (m, 8H, C_6H_{14}), 0.55 (t, 6H, C_6H_{14}).

Compound (**III**) ·C_6H_{14}. Found: C, 74.59; H, 8.11. Anal. Calcd for $C_{40}H_{46}O_8 \cdot C_6H_{14}$: C, 74.56; H, 8.08. ^1H NMR δ: 7.80 (d, $J = 7.6$ Hz, 4H, ArH_{meta}),

Fig. 1 The structural formulas of the calix[4]arenes

I. R=H

II. R=CH$_3$

III. R=CH$_3$, R$_1$=H, X=CH$_2$CH$_2$(OCH$_2$CH$_2$)$_4$
IV. R=CH$_3$, R$_1$=*t*-Bu, X=CH$_2$CH$_2$(OCH$_2$CH$_2$)$_3$
V. R=C$_2$H$_5$, R$_1$=*t*-Bu, X=CH$_2$CH$_2$(OCH$_2$CH$_2$)$_3$
VI. R=CH$_2$C$_6$H$_5$, R$_1$=*t*-Bu, X=CH$_2$CH$_2$(OCH$_2$CH$_2$)$_3$
VII. R=CH$_3$, R$_1$=*t*-Bu, X=CH$_2$CH$_2$(OCH$_2$CH$_2$)$_4$

7.41 (d, J = 7.6 Hz, 4H, ArH$_{meta}$), 6.71–6.63 (m, J = 7.1 Hz, 4H, ArH$_{para}$), 4.41 (d, J = 13.2 Hz, 4H, ArCH$_2$Ar), [4.10, 4.02, 3.92, 3.85 (m, 16H, –OCH$_2$CH$_2$O–)], 3.71 (s, 4H, –OCH$_2$CH$_2$O–), 3.12 (s, 6H, OCH$_3$), 3.38 (d, J = 13.2 Hz, 4H, ArCH$_2$Ar), 0.95 (m, 8H, C$_6$H$_{14}$), 0.52 (t, 6H, C$_6$H$_{14}$).

Compound **(VII)** ·**CH$_3$OH**. Found: C, 75.16; H, 9.01. Anal. Calcd for C$_{56}$H$_{78}$O$_8$·CH$_3$OH: C, 75.13; H, 8.97. ^{1}H NMR δ: 7.78 (s, 4H, ArH$_{meta}$), 7.39 (s, 4H, ArH$_{meta}$), 4.44 (d, J = 13.1 Hz, 4H, ArCH$_2$Ar), [4.15, 4.06, 3.93, 3.81 (m, 16H, –OCH$_2$CH$_2$O–)], 3.64 (s, 4H, –OCH$_2$CH$_2$O–), 3.25 (s, 3H, *CH$_3$*OH), 3.10 (s, 6H, OCH$_3$), 3.40 (d, J = 13.2 Hz, 4H, ArCH$_2$Ar), 1.30 (s, 18H, –C(CH$_3$)$_3$), 1.26 (s, 18H, –C(CH$_3$)$_3$), 1.10 (s, 1H, CH$_3$*OH*).

Sublimation enthalpies are an important property of the condensed phase as far as this quantity is a macroscopic measure of the magnitude of intermolecular interactions. A variety of experimental techniques have been developed to measure the sublimation enthalpies of solids. In the present paper the sublimation experiments were carried out by the Knudsen's effusion method. A weighed in a glass container (±0.05 mg) sample is placed into the effusion cell. The experimental cell was made of stainless steel with internal volume of about 4 cm^3. The internal diameter of the glass container is about 10 mm, the ratio of sample surface area to effusion orifice area is about from 80 to 300. The design of the experimental cell provides a device for vapourproof effusion orifice closing during establishing the steady regime of measurements. The temperature of the effusion cell is maintained by means of thermocouples battery with accuracy ±0.1°C. The vapour pressure in the effusion cell is determined by Knudsen's equation (1):

$$P = (\Delta m/\alpha \cdot \beta \cdot S_{\text{eff}} \cdot \tau) \cdot (2\pi \cdot R \cdot T/M)^{1/2} \qquad (1)$$

where Δm is a weight loss through an orifice of area S_{eff}, β is the Klausing's factor which takes into account the finite length of the orifice, α is a condensation coefficient, τ is the effusion time, M is the molecular weight, T is a temperature and R is the ideal gas constant.

The effusion equipment was calibrated using naphthalene (m.p.353.43 K) and benzoic acid (m.p.395.5 K). The obtained values of sublimation enthalpies of naphthalene 72.4 ± 0.6 kJ mol^{-1} and benzoic acid 89.8 ± 0.7 kJ mol^{-1} are in good agreement with recommended values [15]. In addition calix[4]arenes **(I–VII)** and their complexes with solvent molecules were purified by sublimation in a high vacuum of 10^{-5} Torr using a temperature gradient furnace. The

absence of decomposition and impurities was controlled by ^{1}H NMR spectra. To estimate a condensation coefficient α the sublimation measurements were carried out using two orifices of different effective areas $\beta \cdot S_{\text{eff}}$ (2.21·10^{-7} m^2 and 8.48·10^{-7} m^2) as well as Langmuir method (sublimation from surface of the effusion material). It was found that the measured vapour pressure was independent of both the orifice area and the measurement method (Knudsen or Langmuir). Thus for all compounds under investigation α was equal 1.

The experimentally determined vapour pressure data were described in coordinates ln P versus 1/T by Eq. (2):

$$\ln P = A + B/T \qquad (2)$$

The value of the sublimation enthalpy is calculated by the Clausius–Clapeyron Eq. (3):

$$\Delta H^T_{\text{sub}} = -R \cdot \partial \ln P / \partial (1/T) \qquad (3)$$
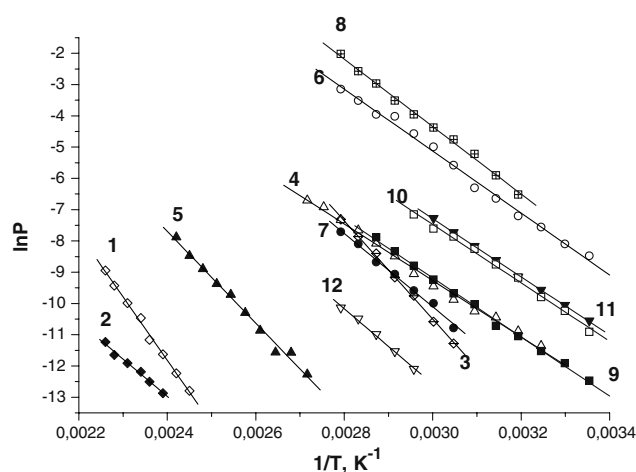
The value of sublimation entropy is calculated as

$$\Delta S^T_{\text{sub}} = -\partial (\Delta G^T_{\text{sub}})/\partial T \qquad (4)$$

where $\Delta G^T_{\text{sub}} = -RT \cdot \ln(P/P_0)$ and $P_0 = 1.013 \cdot 10^5$ Pa.
$$(5)$$

Results and discussion

The results of vapour pressure measurements are plotted in Fig. 2. The least squares constants A and B

Fig. 2 The temperature dependence of the vapour pressures of the studied compounds: 1, **(I)**; 2, **(I)**·CH$_2$Cl$_2$; 3, **(I)**·CH$_2$Cl$_2$·C$_6$H$_{14}$; 4, **(II)**; 5, **(II)**·C$_6$H$_{14}$; 6, **(III)**; 7, **(III)**·C$_6$H$_{14}$; 8, **(IV)**; 9, **(V)**; 10, **(VI)**; 11, **(VII)**; 12, **(VII)**·CH$_3$OH

Table 1 The least squares constants A and B corresponding to Eq. (2), sublimation enthalpies and entropies of studied compounds

Compound	A	$B/1000$	ΔH_{sub}^{T}, kJ mol^{-1}	ΔS_{sub}^{T}, J mol^{-1}K^{-1}
(**I**)	36.5 ± 0.6	-20.1 ± 0.3	167 ± 2	207 ± 5
(**I**)·CH$_2$Cl$_2$	15 ± 1	-11.7 ± 10.4	98 ± 13	35 ± 15
(**I**)·C$_6$H$_{14}$·CH$_2$Cl$_2$	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$_6$H$_{14}$	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$_6$H$_{14}$	25 ± 1	-11.7 ± 0.4	97 ± 3	118 ± 12
(**IV**)	28.0 ± 0.6	-10.8 ± 0.2	90 ± 2	137 ± 5
(**V**)	19.2 ± 0.5	-9.5 ± 0.2	79 ± 2	65 ± 4
(**VI**)	20.5 ± 0.8	-9.3 ± 0.3	78 ± 3	74 ± 7
(**VII**)	20.8 ± 0.5	-9.3 ± 0.2	78 ± 1	76 ± 3
(**VII**)·CH$_3$OH	24 ± 1.4	-12.1 ± 0.5	100 ± 4	100 ± 12

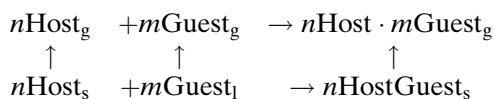corresponding to (2) as well as enthalpies and entropies of sublimation are presented in Table 1.

It has been shown by us earlier [16] that the studied compounds can be classified into roughly two groups. The compounds (**I**), (**II**), (**III**) and (**VII**) can form stable intramolecular aggregates (**I**)·**CH$_2$Cl$_2$**, (**I**)·**C$_6$H$_{14}$·CH$_2$Cl$_2$**, (**II**)·**C$_6$H$_{14}$**, (**III**)·**C$_6$H$_{14}$** and (**VII**)·**CH$_3$OH** which keep the stoichiometric composition without changing under conditions of the sublimation experiment. The calix[4]arenes (**IV**), (**V**) and (**VI**) do not form stable host–guest complexes with the solvent molecules. The calix[4]arenes (**V**) and (**VI**) are in the partial-cone conformation and their potential cavities are full with their own groups (''endo-positioned'' ethoxy and benzyloxy groups, respectively) [11]. The structure difference of the calix[4]arenes (**IV**) and (**VII**) is the additional group OCH$_2$CH$_2$ in the crown polyether ring of (**VII**). Calix[4]arene (**VII**) forms the stable intramolecular aggregate with the solvent molecule as a result of the increase of length of the polyether ring of (**VII**). The inclusions of organic molecules to the cavities of calixarenes (**II**), (**III**) and (**VII**) stabilize the crystal lattice energies increasing the values of the sublimation enthalpies. The sublimation enthalpy of ligand (**I**) is higher than enthalpies of (**I**)·**CH$_2$Cl$_2$** and (**I**)·**C$_6$H$_{14}$·CH$_2$Cl$_2$**. The complex (**I**)·**C$_6$H$_{14}$** is unstable and decomposed under sublimation. The capability of calixarene structures to form under vacuum stable complexes obviously depends on features of their crystal lattices. Atwood et al. recently reported that the well-known host compound *p-tert*-butylcalix[4]arene can undergo dramatic single-crystal to single-crystal phase transitions. They obtained diffraction-quality single crystals by sublimation of the compound at 280°C under reduced pressure [17]. The authors showed that the pure sublimed host material adopts a bilayer type of structure, featuring pairs of calixarenes facing one another in a slightly offset

fashion. This motif results in the formation of isolated pockets of about 235 Å^3 per dimeric unit. Although there are no channels leading to these voids, the crystal is able to absorb guest molecules into its lattice with concomitant translation of adjacent bilayers relative to one another [18, 19].
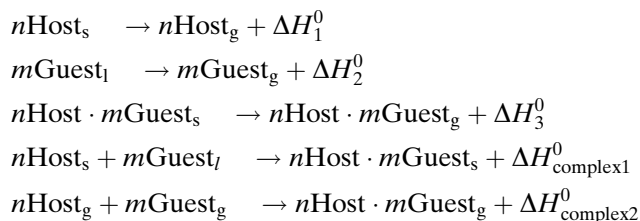
The large flexibility of the calixarene structure is emphasized in the gas phase, where no solvent molecule limits the free conformational changes of the molecule. Consequently, the constraints associated with the formation of host–guest complexes correspond to a strongly negative entropic contribution, resulting in the weakening of the supramolecular interaction. The formation of host–guest complexes in the gas phase is favored by any form of derivatization that reduces the flexibility of the calixarene backbone. This decreases the entropic loss associated to the formation of the host–guest complex, making it energetically feasible. A secondary effect of the reduced flexibility of the ligand is its increased selectivity, as the rigid three-dimensional arrangement of its binding sites should complement those of the guest to produce strong interaction. The stiffening of the calixarene structure has been achieved in several ways. One way is to introduce bulky substituents, especially in the lower rim of the molecule, in order to block its structure in the cone conformation. In such a case, it may happen that the calixarene oxygen become quite inaccessible to the candidate guests, restricting the binding properties of the ligand to the π-electrons of its aromatic rings. Thus, other substituents with target binding properties are frequently introduced at the upper rim of the calixarene structure. Another way is the presence of one or more bridges at the upper rim of the cavity, provided that these bridges are rather rigid [10].

The unique property of complexes of calixarenes with solvent molecules to keep the stoichiometric

composition without changing under conditions of the sublimation experiment efforts an opportunity to estimate the thermodynamic functions of complexation using data on temperature dependence of saturated vapour pressures. The thermodynamic cycle for the transfer process of calixarene, solvent and the complex of calixarene with solvent from the condensed state to the gas phase is considered to be:

$$n\text{Host}_g + m\text{Guest}_g \rightarrow n\text{Host} \cdot m\text{Guest}_g$$
$$\uparrow \qquad\qquad \uparrow \qquad\qquad\qquad \uparrow$$
$$n\text{Host}_s + m\text{Guest}_l \rightarrow n\text{HostGuest}_s$$

The appropriate enthalpies correspond to the stages:

$$n\text{Host}_s \rightarrow n\text{Host}_g + \Delta H_1^0$$

$$m\text{Guest}_l \rightarrow m\text{Guest}_g + \Delta H_2^0$$

$$n\text{Host} \cdot m\text{Guest}_s \rightarrow n\text{Host} \cdot m\text{Guest}_g + \Delta H_3^0$$

$$n\text{Host}_s + m\text{Guest}_l \rightarrow n\text{Host} \cdot m\text{Guest}_s + \Delta H_{\text{complex1}}^0$$

$$n\text{Host}_g + m\text{Guest}_g \rightarrow n\text{Host} \cdot m\text{Guest}_g + \Delta H_{\text{complex2}}^0$$

The relative binding enthalpy is computed by the difference:

$$\Delta(\Delta H_{\text{complex}}^0) = \Delta H_{\text{complex2}}^0 - \Delta H_{\text{complex1}}^0$$
$$= \Delta H_3^0 - (\Delta H_1^0 + \Delta H_2^0)$$

Similarly, assuming that the system is reversible:

$$\Delta(\Delta G_{\text{complex}}^0) = \Delta G_{\text{complex2}}^0 - \Delta G_{\text{complex1}}^0$$
$$= \Delta G_3^0 - (\Delta G_1^0 + \Delta G_2^0)$$

where, Host is a calixarene; Guest is a solvent; nHost$\cdot$$m$Guest is a complex of the calixarene with solvent; n and m characterize the stoichiometry of the complex; the subscript signs s, l correspond to the condensed state, g corresponds to the gas phase, respectively; $\Delta H_{1,2,3}^0$ and $\Delta G_{1,2,3}^0$ are the standard enthalpies and Gibbs energies of

vapour formation of calixarene, solvent and the complex of the calixarene with the solvent, respectively; $\Delta H_{\text{complex1}}^0$, $\Delta H_{\text{complex2}}^0$ and $\Delta G_{\text{complex1}}^0$, $\Delta G_{\text{complex2}}^0$ are the standard enthalpies and Gibbs energies of complexation in the condensed state and in the gas phase, respectively.

Thus the certain values of $\Delta H_{1,2,3}^0$ and $\Delta G_{1,2,3}^0$ allow us to calculate the relative binding enthalpies $\Delta(\Delta H_{\text{complex}}^0)$ and Gibbs energies $\Delta(\Delta G_{\text{complex}}^0)$ of complexation by transfer process from the condensed state to the gas phase and the corresponding changing of entropy $T\Delta(\Delta S_{\text{complex}}^0) = \Delta(\Delta H_{\text{complex}}^0) - \Delta(\Delta G_{\text{complex}}^0)$. The relative standard thermodynamic functions of complexation $\Delta(\Delta H_{\text{complex}}^0)$, $\Delta(\Delta G_{\text{complex}}^0)$, $T\Delta(\Delta S_{\text{complex}}^0)$ for the complexes $(I)\cdot CH_2Cl_2$, $(I)\cdot CH_2Cl_2\cdot C_6H_{14}$, $(II)\cdot C_6H_{14}$, $(III)\cdot C_6H_{14}$ and $(VII)\cdot CH_3OH$ are presented in Table 2. The sublimation enthalpies at the mean temperatures of measurements were assumed as the standard sublimation enthalpies of calixarenes and complexes of calixarenes with solvents (Table 1). The evaporation enthalpies of C_6H_{14}, CH_2Cl_2 and CH_3OH at 298.15 K are 7.4; 6.8 and 8.94 kcal mol^{-1} [20], respectively. The standard sublimation Gibbs energies ΔG^0 of calixarenes and their complexes were calculated by Eq. (5) using vapour pressures values obtained by extrapolation of the temperature dependence of vapour pressures to 298.15 K (Table 1). The standard evaporation Gibbs energies ΔG^0 of solvents were calculated using vapour pressures values at 298.15 K [20].

As the sublimation entropy characterizes the free conformational changes of the molecule by the transfer process to the gas phase, it is possible to estimate the correlation between flexibility of the calixarene structure and the complexation properties.

Grootenhuis et al. [21] assessed some of the structural and energetical properties of calix[4]arenes by various computational methods. They found that the preferred conformation of calix[4]arene depends on the number and the positions of the substituents on the oxygen atoms and is mainly determined by electrostatic interactions. In a number of cases the

Table 2 The relative standard thermodynamic functions of complexation by transfer process from the condensed state to the gas phase

Compound	$\Delta(\Delta G_{\text{complex}}^0)$, kJ mol^{-1}	$\Delta(\Delta H_{\text{complex}}^0)$, kJ mol^{-1}	$T\Delta(\Delta S_{\text{complex}}^0)$, kJ mol^{-1}
$(I)\cdot CH_2Cl_2$	−19	−98	−80
$(I)\cdot CH_2Cl_2\cdot C_6H_{14}$[a]	−43	−96	−54
$(II)\cdot C_6H_{14}$	19	16	−3
$(III)\cdot C_6H_{14}$	10	−16	−26
$(VII)\cdot CH_3OH$	11	−15	−26
$(I)\cdot CH_2Cl_2\cdot C_6H_{14}$[b]	−24	2	26

[a] complexation process: $(I) + CH_2Cl_2 + C_6H_{14} \rightarrow (I)\cdot CH_2Cl_2\cdot C_6H_{14}$

[b] complexation process: $(I)\cdot CH_2Cl_2 + C_6H_{14} \rightarrow (I)\cdot CH_2Cl_2\cdot C_6H_{14}$

conformation with the lowest calculated energy is different from the conformation found in solution and in the solid state. In order to study conformational interconversions the authors [21] carried out molecular dynamics simulations on one isolated molecule of 25,26,27,28-tetrahydroxy-5,11,17,23-tetra-p-methylcalix[4]arene at temperatures of 300, 600, and 800 K for 50 ps. Inspection of MD movies suggested that at 300 K the motions of the two phenol moieties opposite to each other were initially strongly coupled when the calixarene was in its *cone* conformation. After 35 ps one of the phenol moieties did break its hydrogen bonds with the other phenols and flipped through the cavity, resulting in the *partial cone* conformation. After adopting the *partial cone* conformation for a few picoseconds the molecule started interconverting between the 1,2- and *1,3- alternate* conformations and the *partial cone*. At 600 K only one conformational interconversion was observed in the 50-ps trajectory. However, the amplitude of the coupled movements of the phenolic moieties was much larger at this temperature. At 800 K an almost continuous interconversion of the calixarene was observed. It is quite clear from the MD movies that the strongly coupled movement of the two pairs of opposite phenol moieties favors the conformational transitions. So compound (I) is conformationally mobile in the gas phase and can interconvert between the *cone*, *partial cone*, *1,2-alternate*, *1,3-alternate* conformations, although in the solid state it is present exclusively as a *cone* structure due to strong intramolecular hydrogen bonding [11, 18]. Consequently, the transfer of calixarene (I) from the solid state to the gas phase must be accompanied by high value of sublimation entropy.

The conformational analysis of calixarene (II) is described in [21]. For the dimethyl ether (II) none of the conformations is clearly preferred in the calculations. The *cone* conformation is not anymore the only conformation in which all possible (in this case two) H bonds can be accommodated, and therefore, other conformations that have a more favorable VDW or bonded energy or have a lower electrostatic repulsion between the oxygen atoms become important. On the other hand, the dimethyl ether (II) can in principle assume every possible conformation due to its flexibility in the gas phase. Thus the sublimation process should be characterized in this case by low value of sublimation entropy.

The flexibility of (I)·CH_2Cl_2 (which is considered as the ligand in the complexation process (I)·CH_2Cl_2 + C_6H_{14} → (I)·CH_2Cl_2·C_6H_{14}) is constrained greatly as a result of the formation of host–guest complex. The presence of the crown polyether
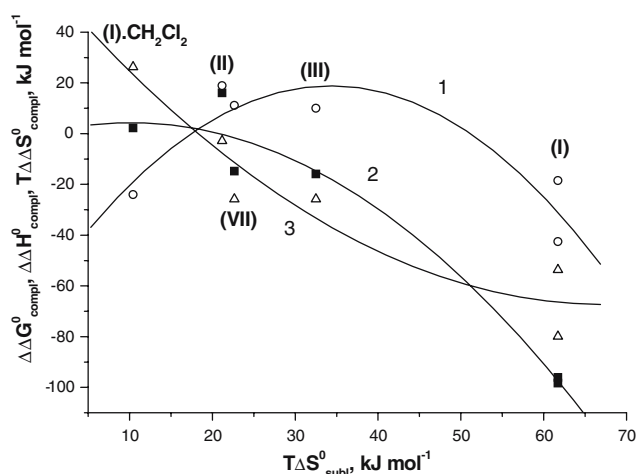
Fig. 3 The relative standard thermodynamic functions of complexation by transfer process from the condensed state to the gas phase. $T\Delta S_{subl}^0$ is sublimation entropy of calixarene ligands (I), (II), (III), (VII) and (I)· CH_2Cl_2; 1, $\Delta(\Delta G_{compl}^0)$; 2, $\Delta(\Delta H_{compl}^0)$; 3, $T\Delta(\Delta S_{compl}^0)$

ring at the lower rim of the cavity reduces the flexibility of the calixarene structures (III) and (VII) in comparison with (I) and (II). *tert*-Butyl groups introduced at the upper rim of the calixarene structure (VII) reduce the flexibility of the calixarene backbone as compared to (III).

The relative standard thermodynamic functions of complexation by transfer process from the condensed state to the gas phase versus sublimation entropy of calixarene ligands, $T\Delta S_{subl}^0$, are shown in Fig. 3. It is obvious that the smaller value of sublimation entropy ($T\Delta S_{subl}^0$ values decrease in order (I) > (III) > (VII) > (II) > (I)·CH_2Cl_2) corresponds to the more positive entropic term $T\Delta(\Delta S_{complex}^0)$ to the relative standard Gibbs energy of complexation $\Delta(\Delta G_{complex}^0)$. On the other hand, the negative enthalpy contribution $\Delta(\Delta H_{complex}^0)$ to the Gibbs energy of complex formation $\Delta(\Delta G_{complex}^0)$ increases with increasing of $T\Delta S_{subl}^0$. As a result the flexibility dependence of the relative standard Gibbs energy of complexation ($\Delta(\Delta G_{complex}^0)$ versus $T\Delta S_{subl}^0$) is an extremal function. The negative values of $\Delta(\Delta G_{complex}^0)$ correspond to the maximal and minimal conformational changes of the calixarene ligand structures by transfer process from the solid state to the gas phase. The entropic contribution to the relative free energy of complexation dominates when the flexibility of calixarene is reduced whereas the enthalpy term prevails when the flexibility is large. The complex formation (I)·CH_2Cl_2 + C_6H_{14} → (I)·CH_2Cl_2·C_6H_{14} is accompanied by negligible enthalpy effect and is governed by the entropic contribution to the relative Gibbs energy of the complexation process.

The values of the relative Gibbs energy of complexation of (II), (III) and (VII) are positive since negative values of $T\Delta$ ($\Delta S^0_{complex}$) are not balanced by negative values of Δ (ΔH^0_{compl}). Hence the preferred complexation occurs in the condensed state coming out of insufficient rigid structures of calixarene ligands (II), (III) and (VII). Thus it must be taken into consideration that the large flexibility of the calixarene ligand structure corresponds to a strongly negative entropic contribution as well as negative enthalpy term to the Gibbs energy of formation of host–guest complexes in the gas phase.

Conclusions

The studied calix[4]arenes can form stable intramolecular complexes with solvent molecules which keep the stoichiometric composition without changing under conditions of the sublimation experiment. Small organic molecules can stabilize the crystal lattice energies increasing the values of the sublimation enthalpies. The complexation properties of the studied compounds depend on the conformation flexibility of the host molecule.

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