Estimation of the Free Energy of the Supramolecular Effect on Host–Guest Complex Formation between Solid *tert*-Butylcalix[4]arene and Vapors of Organic Compounds

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Abstract. The free energy of the supramolecular effect was estimated by the difference of the free energy of the solid host-guest complex formation between the vapor guest and the solid *tert*-butylcalix[4]arene (**1**) and the free energy of the guest solvation in toluene. These thermodynamic parameters were obtained from the vapor sorption isotherms of the guests with various molecular structure by solid **1** and limiting activity coefficients of the guests in toluene determined by headspace gas chromatographic analysis. The supramolecular effect was found to decrease slightly with the increase of the guest molecular size.

Key words: vapor sorption isotherms, headspace gas chromatographic analysis, solid macrocyclic calixarene, thermodynamics of molecular recognition

1. Introduction

The molecular recognition properties of macrocyclic cavitands are generally recognized to be due to the three-dimensional nature of their molecular cavity [1, 2]. Examination of the available experimental data on the selectivity of macrocyclic cavitands towards the neutral molecules of organic substances allows us to make two quite opposite conclusions about the observed supramolecular effects. The high selectivity of the host-guest binding was found for calixarene derivatives in solution [1, 3]. On the contrary, the data on the binding of vapor guests by the monolayers of resorcin[4]arene and α-cyclodextrin determined by the quartz microbalance method do not reveal significant molecular recognition as compared with the binding of the same vapor guests by thin layers of polymers and the guest partition coefficients between vapor phase and solution [4]. In our previous work [5] the solid *tert*-butylcalix[4]arene was shown to have the other shape of the guest sorption isotherm than observed for its thin layer (40 nm) [6]. These apparent

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contradictions demonstrate that even for calixarenes with a hydrophobic molecular cavity it is not known whether their molecular recognition properties have definite quantitative constraints, or their selectivity is practically unlimited.

The aim of the present work is the quantitative thermodynamic description of the supramolecular effects at vapor guest binding by solid *tert*-butylcalix[4]arene **1** and comparison of the observed supramolecular binding properties with solvation effects in the liquid phase.

2. Experimental

The synthesized [7] host **1** was purified from nonvolatile impurities by recrystallization from benzene + ethanol mixture. Purification of **1** from volatile impurities was performed by heating at 190-210 °C during 3–4 hours in vacuum (100 Pa). In the presence of the guests no additional chromatographic peaks were observed for the headspace over purified **1**. Sorbate purity tested by GLC was above 99.5%. Purified samples of calixarene **1** (200 mg) were placed in 15-mL vials. The liquid organic compound (sorbate) was carefully dosed with a microsyringe on the internal walls of the vials in order to avoid direct contact between liquid sorbate and the solid calixarene. The volume of the added liquid was in the range 1–40 μl depending on the guest molar volume. Immediately afterwards the vials were sealed with fluoroplaste (0.2 mm) and silicon linings. The sealed samples were equilibrated for 100 hours at 298 K.

Vapor sorption isotherms of organic guests were determined by gas chromatographic headspace analysis as a function of the guest uptake by solid host *vs*. the guest activity. An automated headspace sampler of original design [8] was used to dose the vapor phase from the sealed vial into a capillary chromatographic column. In this sampler a principle of electropneumatic dosing, described in [9], is applied. A fused silica chromatographic column (25 m × 0.2 mm, SE-54) and a flame ionization detector were used in the analysis. The guest thermodynamic activity ($a = P/P_0$) was determined for each sample at 298 K as the ratio of the height (area) of the guest chromatographic peaks for vapor phase samples of the studied system and of the pure liquid guest. The precision of the sorbate activity determination is in the interval from 5% (for $P/P_0 > 0.5$) to 10% (for $P/P_0 < 0.1$). The uptake of the guest was calculated as the difference between the quantity of added sorbate and its amount in the vapor phase. The obtained isotherms were corrected on the equilibration losses that were estimated in blank experiments without solid host. After each experiment the solid samples were treated as mentioned above to expel the guest molecules and determination of the sorption isotherm was performed once more. The sorption isotherms in these subsequent experiments did not differ within experimental errors.

The limiting activity coefficients of the guests in toluene solution γ^∞ were determined with precision $\pm10\%$ by the same headspace technique for infinitely

dilute solutions (0.2 vol.% for alcohols and 1 vol.% for other solutes). The absence of the concentration dependence of the γ^∞ values was tested in each case.

The saturated vapor pressures of *tert*-butylacetate and pinacolone were also determined with the help of headspace analysis by the quantity of doses necessary to eliminate the liquid phase from the vial. The value of one dose was determined by decreasing part of the substance peak height (area) depending on the dose number. The information obtained in this experiment allows us to calculate the vapor pressure of the studied substance with precision $\pm 10\%$.

3. Results and Discussion

The sorption isotherms of 12 organic substances with various molecular structure were determined by the static method of gas chromatographic headspace analysis (Figure 1). The sorption isotherms of benzene, toluene, acetonitrile and ethanol have been described earlier [5]. The isotherms obtained have a guest threshold activity $a_{\mathrm{thr}} = (P/P_0)_{\mathrm{thr}}$ needed for its incorporation in the solid calixarene. Up to this activity a weak binding of the guests by solid (**I**) is observed. Over the guest threshold activity a_{thr} the guest sorption significantly rises indicating the formation of the stable inclusion complex. At the guest activity $0.6 < P/P_0 < 0.8$ saturation of the isotherms obtained takes place. The observed sorption isotherms can not be described by monolayer (Langmur) or multilayer (BET) adsorption models. For a description of such sorption behavior the Hill equation (1) was used [10]:

$$YS = SC(P/P_0)^N/(1 + C(P/P_0)^N),\tag{1}$$

where Y is the complex saturation extent, S – stoichiometry, C – sorption constant, N – cooperativity constant, YS – experimentally determined solid phase composition (mol of guest per mol of host). The approximation of the sorption isotherms by the Hill equation gives two stable solutions: the stoichiometry S and the ratio $(\ln C)/N$. The values of the guest threshold activity a_{thr}, S and $(\ln C)/N$ are summarized in Table I. The value of a_{thr} is given as the guest activity at the solid phase composition $0.25S$ because at this YS value the minimal guest activity is observed for the most studied systems.

It may be seen (Table I) that the complex stoichiometry S values obtained correspond to 2:1, 1:1 or 1:2 host/guest ratio. Comparison with the available X-ray data [11–14] for solid calixarene **1** complexes demonstrates their good agreement with the complex stoichiometry S obtained in the present work. $-RT(\ln C)/N$ is the total transfer free energy of 1 mole of guest from the standard state of pure liquid to the saturated solid host-guest complex at the guest activity $P/P_0 = 1$ if the $\ln(P/P_0)$ value is given by Equation (1) as a function of Y:

$$\Delta G_c = RT \int_0^1 \ln(P/P_0)\mathrm{d}Y = -RT(\ln C)/N.\tag{2}$$

Table I. Parameters of sorption isotherms of vapor guests on solid *tert*-butylcalix[4]arene at 298 K.[a]

N	Guest	a_{thr}	S (S_{lit})	$(\ln C)/N$	$\Delta(YS)$[f]	δ[g]	ΔG_c kJ/mol	P_0 kPa	$\Delta G_c(v)$ kJ/mol	γ^∞	ΔG_{soln} kJ/mol	ΔG_{solv} kJ/mol	ΔG_{trans} kJ/mol
1.	Methanol	0.54	1.91	0.50	0.03–1.89	0.03	−1.2	17.0[h]	−5.7	21.8	7.6	3.2	−8.9
2.	Acetonitrile	0.13	1.17	1.63	0.06–1.20	0.03	−4.0	11.9[i]	−9.3	4.33	3.6	−1.7	−7.7
3.	Ethanol	0.36	1.10	0.91	0.17–1.15	0.02	−2.3	7.87[h]	−8.6	17.4; 15.4[j]	7.1	0.8	−9.3
4.	Propionitrile	0.09	0.91	2.08	0.07–0.92	0.01	−5.2	6.19[h]	−12.1	2.92	2.7	−4.3	−7.8
5.	*n*-Propanol	0.29	1.05	1.00	0.06–1.11	0.04	−2.5	2.73[h]	−11.4	15.9	6.9	−2.1	−9.3
6.	Benzene	0.04	1.08 (1[b])	2.92	0.07–1.09	0.01	−7.3	12.7[h]	−12.4	0.97	−0.1	−5.2	−7.2
7.	Cyclohexane	0.09	1.20 (1[c])	2.20	0.08–1.24	0.02	−5.5	13.0[h]	−10.6	1.36	0.8	−4.3	−6.3
8.	*n*-Hexane	0.13	0.50	1.88	0.00–0.51	0.03	−4.7	20.2[h]	−8.7	1.50	1.0	−3.0	−5.7
9.	Pinacolone	0.19	1.07	1.29	0.12–1.08	0.04	−3.2	6.28	−10.1	1.47	1.0	−5.9	−4.2
10.	Toluene	0.08	0.99 (1[d])	2.24	0.03–1.00	0.02	−5.6	3.79[h]	−13.7	1.00	0.0	−8.1	−5.6
11.	*tert*-Butylacetate	0.20	0.79	1.27	0.05–0.82	0.03	−3.2	5.00	−10.6	1.40	0.8	−6.6	−4.0
12.	Anisole	0.06	0.62 (0.5[e])	2.58	0.06–0.65	0.02	−6.4	0.456[h]	−19.8	1.31	0.7	−12.7	−7.1
13.	*n*-Heptane	0.12	0.44	1.94	0.06–0.45	0.01	−4.8	6.10[h]	−11.8	1.68	1.3	−5.7	−6.1
14.	*o*-Xylene	0.30	0.60	1.10	0.05–0.58	0.04	−2.7	0.885[h]	−14.4	1.09	0.2	−11.5	−2.9
15.	*n*-Octane	0.14	0.56	1.72	0.07–0.57	0.01	−4.3	1.86[h]	−14.2	1.69[j]	1.3	−8.6	−5.6
16.	*n*-Nonane	0.35	0.52	0.98	0.07–0.53	0.02	−2.4	0.570[h]	−15.2	1.90	1.6	−11.2	−4.0

[a] The estimated error of a_{thr} is 10%; the error of S is 5%; the error of ΔG_c is 0.4 kJ/mol; the error of γ^∞ is 10%.
[b] Data from ref. [11].
[c] Data from ref. [12].
[d] Data from ref. [13].
[e] Data from ref. [14].
[f] $\Delta(YS)$ is the interval of solid phase composition YS for which S and $(\ln C)/N$ were calculated by Equation (1).
[g] δ is standard deviation of the approximation in the interval $\Delta D(YS)$ for shortest distances between experimental points and calculated line:

$$\delta = \sqrt{\sum(((P/P_0)_{calc} - (P/P_0)_{exp})^2 + ((YS)_{calc} - (YS)_{exp})^2)/(n-2)}$$

[h] Data from ref. [15].
[i] Data from ref. [16].
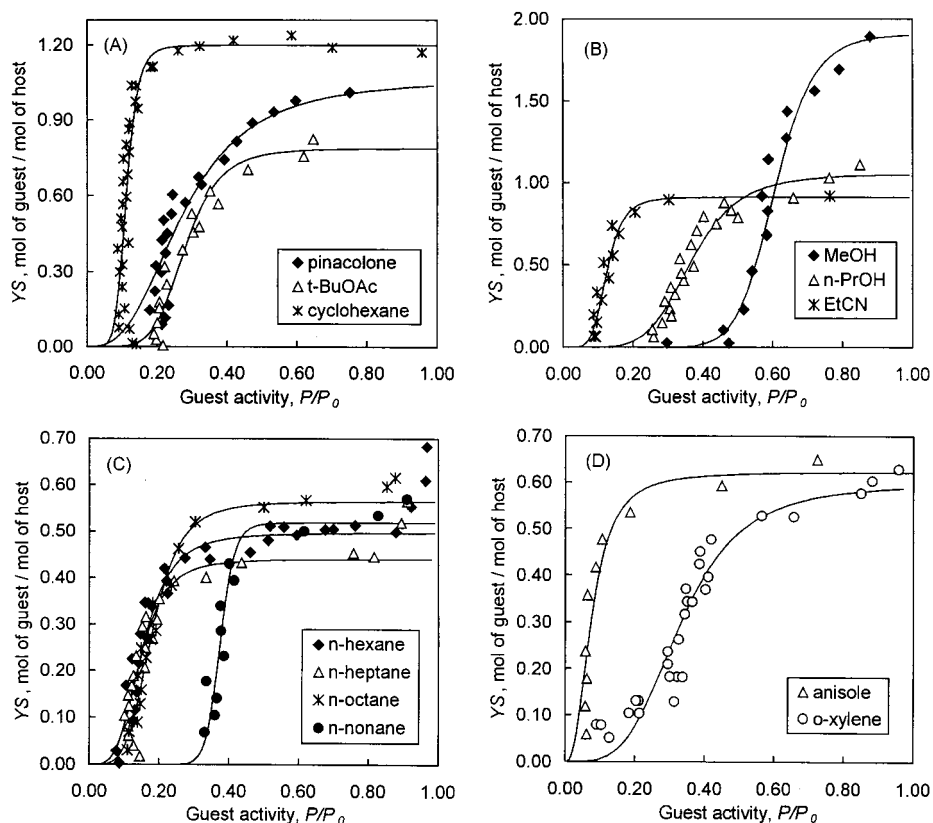[j] Data from ref. [17].

Figure 1. Vapor sorption isotherms of various guests on solid *tert*-butylcalix[4]arene at 298 K. The lines correspond to the isotherms calculated by the Hill Equation (1).

ΔG_c corresponds to a complex formation free energy calculated for one mole of the guest. The ΔG_c values are listed in Table I. Comparison of the ΔG_c values for the studied guests shows that they are in the range between -1.2 kJ/mol for methanol and -7.3 kJ/mol for benzene. Analysis of the relation between the complex formation free energy ΔG_c and the guest molecular structure is complicated by the different standard states for different guests. The energies of the molecular interactions in pure liquid generally do not coincide for the substances with unlike molecular composition. The simplest approach to this problem is the determination of the free energy of complex formation between solid host and vapor guest:

$$\Delta G_c(\mathrm{v}) = \Delta G_c + RT \ln(P_0/101325\,\mathrm{Pa}) \tag{3}$$

where P_0 is the saturated vapor pressure of pure liquid guest at 298 K.

To estimate the contribution of the supramolecular interactions in the ΔG_c and $\Delta G_c(\mathrm{v})$ values the limiting activity coefficients of the guest γ^∞, solution and solvation free energies of the guests in toluene were determined:

$$\Delta G_{\mathrm{soln}} = RT \ln \gamma^\infty \tag{4}$$

$$\Delta G_{\mathrm{solv}} = RT \ln \gamma^\infty + RT \ln(P_0/101325 Pa). \tag{5}$$

Toluene was chosen as a solvent that can model the hydrophobic environment of the guest molecule in calixarene **1**. Data on $\Delta G_c(\mathrm{v})$, ΔG_{solv}, ΔG_{soln}, γ^∞ and P_0 are given in Table I. On Figures 2 and 3 plots of $\Delta G_c(\mathrm{v})$ vs. ΔG_{solv} and ΔG_c vs. ΔG_{soln} respectively are presented. Correlation between the $\Delta G_c(\mathrm{v})$ and ΔG_{solv} values (Figure 2) shows that the selectivity pattern of solid host **1** towards the studied vapor guests follows closely the binding selectivity pattern of liquid toluene and does not indicate significant "molecular recognition" properties of solid calix[4]arene (**1**). This fact is in agreement with the data on selectivity obtained for cavitand monolayers [4]. Comparison of the ΔG_c and ΔG_{soln} values shows that calixarene **1** has a higher selectivity to liquid guests than liquid toluene especially for branched guests and alkanes. Still the selectivity is less than can be expected from the stability constants of the host-guest complexes of calixarene derivatives in dilute solutions in CCl_4 determined by the NMR method [1, 3]. So the selectivity of solid host **1** to vapor guests is mainly stipulated by the difference of the molecular interaction energy for different guests that is approximately the same for organic substances as the solutes in liquid solutions and as the guests in solid host-guest complexes. This statement is equivalent to the conclusion made earlier on analysis of resorcin[4]arene and α-cyclodextrin monolayer selectivity [4]. Nevertheless, this conclusion does not contradict the existence of supramolecular host-guest interactions themselves. The energy of these interactions may be estimated by the difference of the free energies of the vapor guest binding in the solid host–guest complex $\Delta G_c(\mathrm{v})$ and solvation of the same substance in toluene ΔG_{solv}. The plot in Figure 2 demonstrates essentially the higher binding affinity of the solid calixarene **1** to the studied vapor guests than that of liquid toluene. The difference between the $\Delta G_c(\mathrm{v})$ and ΔG_{solv} values:

$$\Delta G_{\mathrm{trans}} = \Delta G_c(\mathrm{v}) - \Delta G_{\mathrm{solv}} = \Delta G_c - RT \ln \gamma^\infty \tag{6}$$

for the studied guests is in the interval from -4 to -9 kJ/mol (Table I). This contribution may be stipulated by the reduced free energy of cavity formation in the solid host **1** because of its rigid bowl-like molecular structure. The guests with small molecules (methanol, acetonitrile) are bound with minimal cavity formation energy costs. The guests with large molecules cannot have a much higher cavity energy gain because the volume of the calixarene **1** internal cavity is restricted. Besides, the additional reorganization free energy of the host **1** crystal lattice may be necessary to fit large and especially branched guest molecules. These considerations
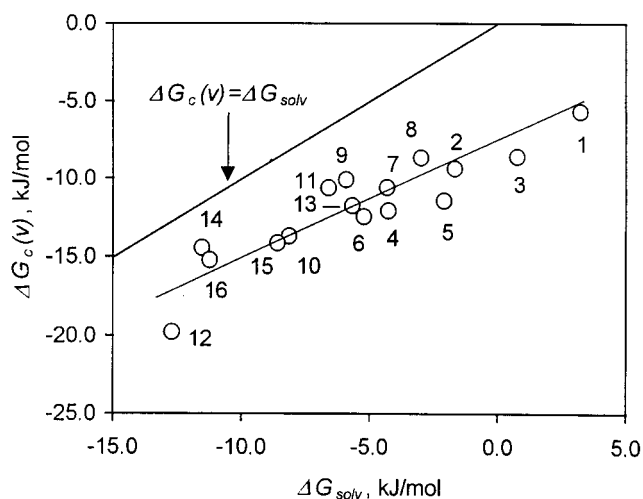
Figure 2. Correlation between the free energy of the solid host **1** + vapor guest complex formation $\Delta G_c(v)$ and the guest solvation free energy in toluene ΔG_{solv} at 298 K. Point numbers correspond to the numbers of the guests in Table I.
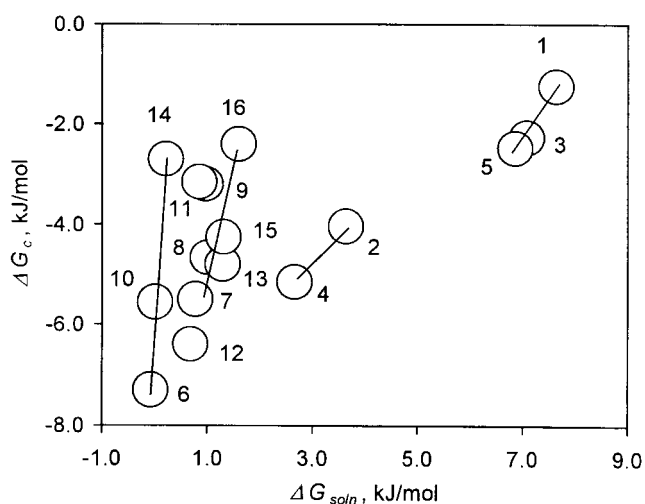

Figure 3. Correlation between the free energy of the solid host **1** + liquid guest complex formation ΔG_c and the guest solution free energy in toluene ΔG_{soln} at 298 K. Point numbers correspond to the numbers of the guests in Table I. The straight lines join the points of the guests with similar molecular composition.

allow us to explain a weak tendency of decreasing ΔG_{trans} values with the increase of the guest molecular size in the studied systems and the relatively strong effect of the guest molecular embranchment in the series: benzene–toluene–o-xylene.

Acknowledgements

References

1. A. Arduini, W. M. McGregor, D. Paganuzzi, A. Pochini, A. Secchi, F. Ugozzoli, and R. Ungaro: *J. Chem. Soc., Perkin Trans. 2* 839 (1996).
2. K. D. Schierbaum, T. Weiss, E. U. Thoden van Velzen, J. F. J. Engbersen, D. N. Reinhoudt, and W. Gopel: *Science* **265**, 1413 (1994).
3. S. Smirnov, V. Sidorov, E. Pinkhassik, J. Havlicek, and I. Stibor: *Supramol. Chem.* **8**, 187 (1997).
4. J. W. Grate, S. J. Patrash, M. H. Abraham, and C. M. Du: *Anal. Chem.* **68**, 913 (1996).
5. V. V. Gorbatchuk, I. S. Antipin, A. G. Tsifarkin, B. N. Solomonov, and A. I. Konovalov: *Mendeleev Commun.* 215 (1997).
6. F. L. Dickert and O. Schuster: *Mickrochim. Acta* **119**, 55 (1995).
7. C. D. Gutsche, M. Iqbal, and D. Stewart: *J. Org. Chem.* **51**, 742 (1986).
8. V. V. Gorbatchuk, S. A. Smirnov, B. N. Solomonov, and A. I. Konovalov: *Zh. Obsch. Khim.* **60**, 1200 (1990) [*J. Gen. Chem. USSR* (Engl. Transl.) **60**, 1069 (1990)].
9. B. Kolb, P. Pospisil, T. Borath, and M. Auer: *J. High Res. Chromatogr. Chromatogr. Commun.* **2**, 283 (1979).
10. J. T. Edsall, and H. Gutfreund: *Biothermodynamics* Wiley, New York (1983).
11. R. Ungaro, A. Pochini, G. D. Andreetti, and V. Sangermano: *J. Chem. Soc., Perkin Trans. 2* 1979 (1984).
12. E. B. Brouwer, J. A. Ripmeester, and G. D. Enright: *J. Inclusion Phenom. Mol. Recogn.* **24**, 1 (1996).
13. G. D. Andreetti, R. Ungaro, and A. Pochini: *J. Chem. Soc., Chem. Commun.* 1005 (1979).
14. R. Ungaro, A. Pochini, G. D. Andreetti, and P. Domiano: *J. Chem. Soc., Perkin Trans. 2* 197 (1985).
15. T. Boublik, E. Hala, and V. Fried: *The Vapour Pressures of Pure Substances*, Elsevier, Amsterdam (1973).
16. M. Lencka, A. Szafranski, and A. Maczynski: *Verified Vapor Pressure Data,* v. 1, PWN, Warszawa (1984).
17. J. H. Park, A. Hussam, P. Couasnon, D. Fritz, and P. W. Carr: *Anal. Chem.* **59**, 1970 (1987).