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# Influence of the guest molecular size on the thermodynamic parameters of host–guest complexes between solid *tert*-butylcalix[4]arene and vapours of organic compounds

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The shape of guest molecules has a significantly greater influence on the free energy of supramolecular effect in the formation of solid complexes of *tert*-butylcalix[4]arene than on their stoichiometry.

Molecular recognition of ion species and small neutral molecules by calix[4]arenes has been intensively studied.[1–4] Some information is currently available on the stoichiometry of calix[4]arene complexes with organic guests[5–8] and the free energy of formation of these complexes in solution[3,4] but a detailed structural understanding remains lacking. This provides an impetus to search for macroscopic structural parameters that may be used for describing and predicting the thermodynamic characteristics of host–guest complexes of calix[4]arene derivatives. In this paper we report the structural trends in the vapour guest binding by solid *tert*-butylcalix[4]arene **1**.

To examine the influence of the guest molecular structure on the molecular recognition thermodynamics the sorption isotherms of 12 organic compounds with solid **1** were determined. The sorption isotherms were obtained by the method of gas chromatographic headspace analysis described earlier.[9,10] The host **1**[11] was purified from volatile impurities by heating at 190–210 °C during 3–4 h in a vacuum (100 Pa). In the presence of guests no additional chromatographic peaks were observed in the headspace over purified **1**. Sorbate purity tested by GLC was > 99.5%. The isotherms were corrected referred to the sorbate loss on equilibration which was estimated in blank experiments without solid host. This loss is equal to 0.5–2% of the total sorbate amount in the vial for most guests studied at $P/P_0 > 0.3$ depending on their volatility. Maximum losses are 3% for cyclohexane and 8% for n-hexane. The accuracy of sorbate activity determination lies in the interval from 5% (for $P/P_0 > 0.5$) to 10% (for $P/P_0 < 0.1$). Examples of sorption isotherms obtained are presented in Figure 1. The sorption isotherms of benzene, toluene, acetonitrile and ethanol have been described earlier.[9] The limiting activity coefficients of the guests in toluene solution $\gamma^\infty$ were determined with a 10% precision by the same experimental method of headspace analysis[10] for infinitely dilute solutions (0.2 vol.% for alcohols and 1 vol.% for other solutes). The absence of a concentration dependence for the $\gamma^\infty$ values was checked in each case.

The isotherms obtained have a guest threshold activity $a_{thr}$ needed for incorporation of guest in solid cavitand. Up to this activity weak binding of the guests by solid **1** is observed. Above the guest threshold activity $a_{thr}$ the guest sorption significantly increases, which indicates the formation of a stable inclusion complex. Analogous threshold phenomena were observed previously for the formation of solid host–guest complexes.[12–15] At a guest activity $0.6 < P/P_0 < 0.8$ the saturation of the isotherms obtained takes place. The methanol isotherm with a very large threshold activity reaches saturation at the upper end of the activity interval studied. The values of the guest threshold activity $a_{thr}$ and the guest–host molar ratio $S_{sat}$ in the solid phase at the sorption saturation are summarized in Table 1. The value of $a_{thr}$ is given as the guest activity at solid phase composition $0.25S_{sat}$. It may be seen (Table 1) that the saturation is achieved at sorbate/cavitand molar ratio in the solid phase corresponding to 2:1, 1:1 or 1:2 complex formation. Comparison with the available X-ray data for solid calixarene **1** complexes (column 7) indicates a good agreement of complex stoichiometry and sorbate/cavitand saturation ratio $S_{sat}$. Thus, the last value ($S_{sat}$) can be used for the estimation of host–guest complex stoichiometry.

The sorption isotherms observed cannot be described by monolayer (Langmuir) or multilayer (BET) adsorption models. For a description of such sorption behaviour the Hill equation (1) was used.[17]

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

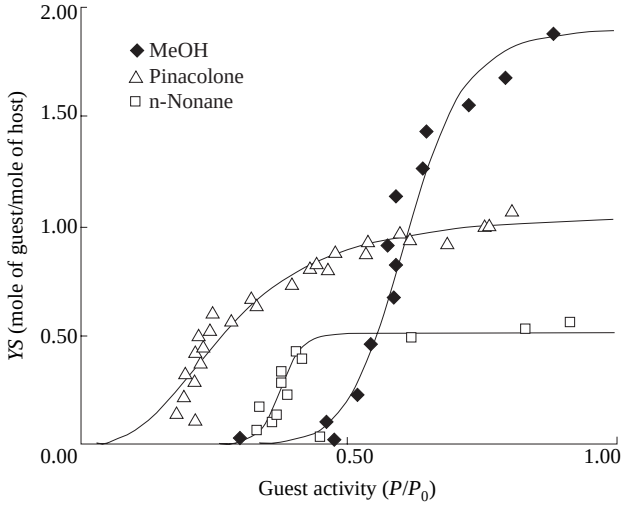


**Figure 1** Vapour sorption isotherms for various guests on solid *tert*-butylcalix[4]arene at 298 K. The lines correspond to the isotherms calculated by the Hill equation (1).

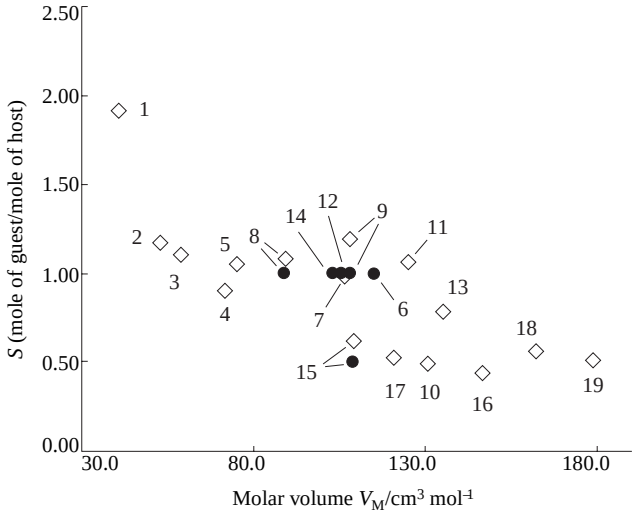


**Figure 2** Correlation between the stoichiometry $S$ of saturated solid host–guest complexes of *tert*-butylcalix[4]arene and the molar volume $V_M$ of the guests. Point numbers correspond to the number of guests in Table 1. Empty points are $S$ values obtained in this work. Filled points are X-ray data.[5–8]

**Table 1** Sorption isotherm parameters for vapour guests on solid *tert*-butylcalix[4]arene at 298 K.[a]

| Entry | Guest | $MR_D$/ cm$^3$ mol$^{-1}$ | $V_M$/ cm$^3$ mol$^{-1}$ | $a_{thr}$ | $S_{sat}$ | $S$ ($S_{lit}$) | (ln $C$)/$N$ | $\Delta(YS)$[b] | $\delta$[c] | $\Delta G_c$/ kJ mol$^{-1}$ | $\gamma$ | $\Delta G_{trans}$/ kJ mol$^{-1}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Methanol | 8.3 | 40.5 | 0.54 | 1.99 | 1.91 | 0.50 | 0.03–1. 89 | 0.03 | –1. 2 | 21.8 | –8.9 |
| 2 | Acetonitrile | 11.1 | 52.4 | 0.13 | 1.15 | 1.17 | 1.63 | 0.06–1. 20 | 0.03 | –4. 0 | 4.33 | –7.7 |
| 3 | Ethanol | 12.9 | 58.4 | 0.36 | 1.13 | 1.10 | 0.91 | 0.17–1. 15 | 0.02 | –2. 3 | 17.4; 15.4[d] | –9 .3 |
| 4 | Propionitrile | 16.0 | 71.3 | 0.09 | 0.95 | 0.91 | 2.08 | 0.07–0. 92 | 0.01 | –5. 2 | 2.92 | –7.8 |
| 5 | n-Propanol | 17.5 | 74.8 | 0.29 | 0.93 | 1.05 | 1.00 | 0.06–1. 11 | 0.04 | –2. 5 | 15.9 | –9.3 |
| 6 | n-Pentane | 25.3 | 115.3 | | | (1[e]) | | | | | | |
| 7 | Chlorobutane | 25.5 | 104.5 | | | (1[e]) | | | | | | |
| 8 | Benzene | 26.2 | 88.9 | 0.04 | 1.07 | 1.08 (1[f]) | 2.92 | 0.07–1. 09 | 0.01 | –7. 3 | 0.97 | –7.2 |
| 9 | Cyclohexane | 27.7 | 108.0 | 0.09 | 1.20 | 1.20 (1[e]) | 2.20 | 0.08–1. 24 | 0.02 | –5. 5 | 1.36 | –6.3 |
| 10 | n-Hexane | 29.9 | 130.8 | 0.13 | 0.50 | 0.50 | 1.88 | 0.00–0. 51 | 0.03 | –4. 7 | 1.50 | –5.7 |
| 11 | Pinacolone | 30.0 | 125.0 | 0.19 | 1.05 | 1.07 | 1.29 | 0.11–1. 01 | 0.04 | –3. 2 | 1.47 | –4.2 |
| 12 | Toluene | 31.1 | 106.3 | 0.08 | 0.99 | 0.99 (1[g]) | 2.24 | 0.03–1. 00 | 0.02 | –5. 6 | 1.00 | –5.6 |
| 13 | *tert*-Butyl acetate | 31.7 | 134.8 | 0.20 | 0.87 | 0.79 | 1.27 | 0.05–0. 82 | 0.03 | –3. 2 | 1.40 | –4.0 |
| 14 | Nitrobenzene | 32.8 | 102.9 | | | (1[e]) | | | | | | |
| 15 | Anisole | 32.9 | 108.7 | 0.06 | 0.63 | 0.62 (0.5[h]) | 2.58 | 0.06–0. 65 | 0.01 | –6. 4 | 1.31 | –7.1 |
| 16 | n-Heptane | 34.5 | 146.5 | 0.12 | 0.49 | 0.44 | 1.94 | 0.06–0. 45 | 0.01 | –4. 8 | 1.68 | –6.1 |
| 17 | *o*-Xylene | 35.9 | 120.5 | 0.3 | 0.55 | 0.60 | 1.10 | 0.05–0. 58 | 0.02 | –2. 7 | 1.09 | –2.9 |
| 18 | n-Octane | 39.2 | 162.5 | 0.14 | 0.61 | 0.56 | 1.72 | 0.07–0. 57 | 0.01 | –4. 3 | 1.69[d] | –5 .6 |
| 19 | n-Nonane | 43.8 | 178.6 | 0.35 | 0.52 | 0.52 | 0.98 | 0.07–0. 53 | 0.02 | –2. 4 | 1.90 | –4.0 |

[a]The estimated error of $a_{thr}$ is ±10%, the error of $S_{sat}$ and $S$ is ±5%; the error of $\Delta G_c$ is ±0.4 kJ mol$^{-1}$ . [b]$\Delta(YS)$ is the solid phase interval composition $YS$ for which $S$ and (ln $C$)/$N$ were calculated from equation (1). [c]$\delta$ is the standard deviation of the approximation in the interval $\Delta(YS)$ for the shortest distances between experimental points and calculated line: $\delta = (\sum\{[(P/P_0)_{calc} - (P/P_0)_{exp}]^2 + [(YS)_{calc} - (YS)_{exp}]^2\}/(n-2))^{1/2}$. [d]Data from ref. 16. [e]Data from ref. 8. [f]Data from ref. 6. [g]Data from ref. 5. [h]Data from ref. 7.

In equation (1), $Y$ is the complex saturation degree, $S$ is the stoichiometry, $C$ is the sorption constant, $N$ is the cooperativity constant and $YS$ is the experimentally determined solid phase composition (mole of guest per mole of host). Approximation of the sorption isotherms by the Hill equation gives two important characteristics of complex formation: the stoichiometry $S$ and the ratio (ln $C$)/$N$.

$RT$(ln $C$)/$N$ is the total binding free energy $\Delta G_c$ of the guest by solid host when ln ($P/P_0$) is given by equation (1) as a function of $Y$:

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

Term $\Delta G_c$ is equal to the transfer free energy of 1 mole of guest from the standard state of pure liquid to the saturated solid host–guest comple x at the guest activity $P/P_0 = 1$ and corresponds to a complex formation free energy calculated for one mole of the guest. The values $S$ (mole guest/mole host), ln $C/N$ and $\Delta G_c$ are listed in Table 1. Clearly there is agreement between the stoichiometry values obtained from the sorbate/ cavitand saturation ratio $S_{sat}$, the Hill equation and X-ray experiments.

Analysis of the obtained data shows the dependence of the complex stoichiometry on the guest molecular size. Small molecules (like methanol) form 2:1 complexes whereas larger molecules form 1:1 or 1:2 complexes. The molar volume $V_M$ and molar refraction $MR_D$ are often considered as molecular size parameters. We tried to correlate the complex stoichiometry with both of them. Molar refraction was calculated by the Lorenz–Lorentz equation. The correlation of $S$ values with the guest molar volume $V_M$ (Figure 2) is rather poor. In Figure 3 a plot of $S$ *vs.* $MR_D$ values of the guests is presented. Obviously the dependence is stepwise. There are three definite areas in which 2:1, 1:1 and 1:2 complexes are formed. The stoichiometry changes are observed at 9–1 1 cm$^3$ mol$^{-1}$ (from 2:1 to 1:1 complex) and at 30–32 cm$^3$ mol$^{-1}$ (from 1:1 to 1:2 complex). This correlation includes linear, branched, cyclic aliphatic and aromatic compounds. It means that the shape of the guest molecule has hardly any effect on the complex stoichiometry. So, the dependence presented in Figure 3 allows us to predict the stoichiometry of solid calixarene **1** complexes with different organic guests. The specific features of the guest molecular structure may be essential within the interval of $MR_D$ where the stoichiometry changes take place. For example, guests with a compact molecular structure such as *tert*-butyl acetate ($MR_D$ =

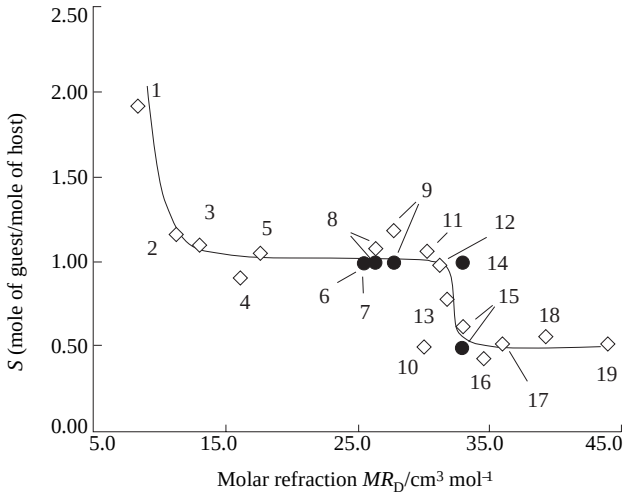


**Figure 3** Correlation between the stoichiometry $S$ of saturated solid host–guest complexes of *tert*-butylcalix[4]arene and the molar refraction $MR_D$ of the guests. Point numbers correspond to the numbers of guests in Table 1. Empty points are $S$ values obtained in this work. Filled points are X-ray data.[5–8]

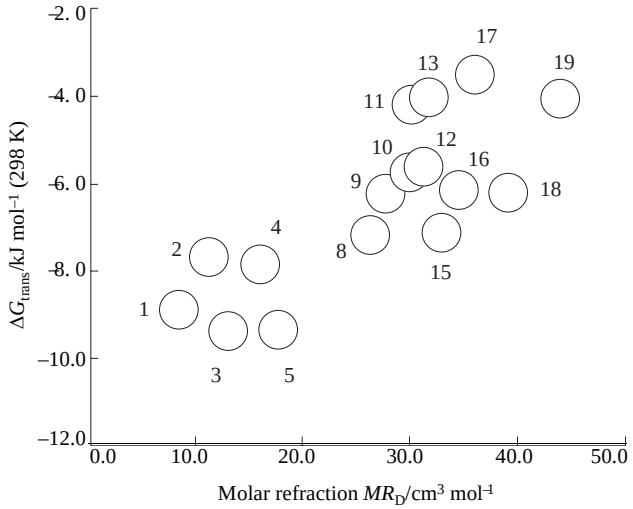


**Figure 4** Correlation between the free energy of guest transfer from toluene solution to a saturated solid complex with *tert*-butylcalix[4]arene $\Delta G_{trans}$ and molar refraction $MR_D$ of guests. Point numbers correspond to the numbers of guests in Table 1.

= 31.7 $cm^3\ mol^{-1}$) and pinacolone ($MR_D$ = 30.0 $cm^3\ mol^{-1}$) form a 1:1 complex, whereas linear n-hexane ($MR_D$ = 29.9 $cm^3\ mol^{-1}$) forms a 1:2 complex.

Encouraged by the results obtained for the complex stoichiometry, we tried to find an analogous dependence for $\Delta G_c$ values. Unfortunately there is no definite correlation between $\Delta G_c$ and the $MR_D$ or $V_M$ values of the guests studied. It may be due to the variation of the energy of molecular interactions in standard states of pure liquid guest that is unequal for the guests with different molecular composition. In order to estimate the difference between the energy of supramolecular host–guest interactions in the solid phase and molecular interactions in solution we determined the free energy of transfer $\Delta G_{trans}$ of the guest from the solution in toluene at infinite dilution to the saturated solid complex with **1**:

$$\Delta G_{trans} = \Delta G_c - RT \ln \gamma^{\infty}$$

where $\gamma^{\infty}$ is the guest limiting activity coefficient in toluene. The values of $\Delta G_{trans}$ and $\gamma^{\infty}$ are given in Table 1. Toluene was chosen as a solvent that can model the hydrophobic environment of the guest molecule in a host–guest complex. The value of $\Delta G_{trans}$ can therefore be assumed to be the estimated free energy of the supramolecular effect distinguishing the host–guest complex from an ordinary solution. This supramolecular effect probably arises from the reduced energy of cavity formation in solid cavitand **1** with bowl-like molecules and may also include the energy of simultaneous conformational changes in neighbouring host molecules, because formation of the studied solid host–guest complexes is a cooperative process.

In terms of this model the supramolecular effect for solid cavitand **1** must depend on the size of the guest molecules as well as on complex stoichiometry, since the studied host **1** has an internal molecular cavity of restricted size. The correlation between $\Delta G_{trans}$ and the guest molar refraction $MR_D$ (Figure 4) demonstrates the molecular recognition properties of solid *tert*-butylcalix[4]arene. There is a certain decrease in the observed supramolecular effect with the growth of the guest molecular size. The sharpest decrease in $-\Delta G_{trans}$ values of the studied guests is exhibited by branched molecules of pinacolone and *tert*-butylacetate and by alkyl substitution at the aromatic ring in the series benzene > toluene > *o*-xylene. For the series of studied n-alkanes only the largest, n-nonane, has a significantly lower $-\Delta G_{trans}$ value whereas for other alkanes it is approximately constant. Its value does not change within the studied sets of nitriles and alcohols. The reason for the slightly higher $-\Delta G_{trans}$ values for alcohols than for nitriles is probably due to the ability of alcohols to undergo weak hydrogen bonding with the host **1**, which is underestimated by their limiting activity coefficients in toluene solution. The shape and the size of the guest molecules therefore has a significantly greater influence on the free energy of the supramolecular effect in the formation of solid complexes of *tert*-butylcalix[4]arene than on their stoichiometry.

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