Nonregular structure–property relationships for inclusion parameters of *tert*-butylcalix[5]arene†

Marat A. Ziganshin,[a] Alexey V. Yakimov,[a] Goulnaz D. Safina,[a] Svetlana E. Solovieva,[b] Igor S. Antipin[a,b] and Valery V. Gorbatchuk*[a]

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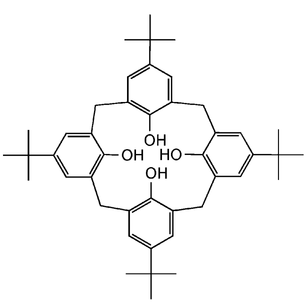
The effect of macrocycle size on the structure–property relationships was studied for inclusion compounds of *tert*-butylcalix[*n*]arenes ($n = 4,5$) with volatile organic guests having various molecular size and group composition. Vapor-sorption isotherms, guest-inclusion stoichiometry and Gibbs energy, thermostability parameters and decomposition enthalpies were determined for host–guest compounds (clathrates) obtained using saturation of solid calixarene powder with guest vapor. The increase of the host macrocycle in the studied calixarene pair changes the observed structure–property relationship from the guest-binding selectivity mostly seen in inclusion Gibbs energy to the high sensitivity for guest structure in inclusion stoichiometry. The host with the larger macrocycle has more clathrates with stepwise formation and decomposition. Specific types of guest binding with solid hosts are discussed.

Introduction

The ideal supramolecular receptor is a "lock" fitted for a "key" substrate. This can be reached for multifunctional substrates in liquid solutions using multiple H-bonding per guest molecule.[1] For volatile compounds having no more than one functional group, one option is a solid receptor having packing restrictions on the guest size and shape.[2,3] The receptors of choice for volatile substrates are the solid calixarenes, forming stable inclusion compounds with complicated structure–property relationships. In such compounds, the major factor for host–guest interaction and binding selectivity is the size of the preorganized cavity in the receptor lattice, which depends on the size of the host macrocycle.[4,5]

For sensor applications, the highest host–guest affinity is desirable for better sensitivity together with the lowest stability of binding product for the sensor reversibility. The ratio of these parameters also depends on the size of the calixarene macrocycle. For example, *tert*-butylcalix[4]arene, forming rather stable clathrates with toluene,[6,7] remains practically insensitive to toluene vapors in quartz crystal microbalance (QCM) sensors[2,8] despite its high binding affinity for toluene.[9] *tert*-Butylcalix[6]arene, having less stable clathrates and lower binding affinity for this guest,[5] shows much higher sensitivity for toluene vapors in QCM sensors.[2,8] One cannot extrapolate rather simple structure–property relationships found for clathrates of *tert*-butylcalix[4]arene[10] and *tert*-butylthiacalix[4]arene[4] to those of larger calixarene macrocycles, because even these two hosts with very close structures have very different selectivity patterns.[4]

The structure–property relationships for calixarene inclusion compounds are not easy to reveal because of a number of cooperative effects such as guest-binding threshold,[11–14] enhanced stability (even of gas clathrates),[15,16] memory effects after the low-temperature decomposition of host–guest inclusion compounds,[13] the dependence of inclusion stoichiometry on temperature[17,18] and small impurities.[10,19] Hence, the choice of the standard conditions for the initial host preparation and host–guest binding is important.



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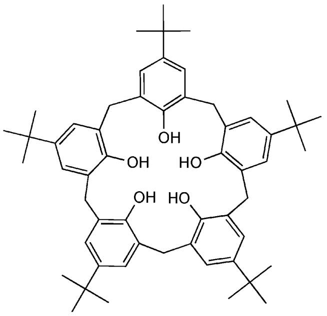

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In this paper, the effect of the host macrocycle size on the guest-inclusion parameters, thermal stability and structure–property relationships was studied for clathrates of *tert*-butylcalix[4]arene (**1**) and *tert*-butylcalix[5]arene (**2**) prepared under comparable conditions in solid host–guest vapor systems. These systems model the guest binding–release by calixarenes in sensors.

Experimental

tert-Butylcalix[4]arene (**1**)[20] was purified as described elsewhere[4]. *tert*-Butylcalix[5]arene (**2**)[21] was purified from nonvolatile impurities using multiple recrystallizations from hexane, and from volatile impurities by heating for 8 hours at 200 °C in a vacuum (100 Pa). This high temperature treatment, also conducted on **1**, was used to remove possible host memory of previous clathrate packing. The calixarene powder did not change its white color during this procedure, which was used as a criterion of host purity. The absence of volatile impurities was checked by a headspace GC method: 3–5 w/w% of methanol was added to the host sample in

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[a] *Institute of Chemistry, Kazan State University, Kremlevskaya 18, Kazan, 420008, Russia. E-mail: Valery.Gorbatchuk@ksu.ru; Fax: +7 843 2927418; Tel: +7 843 2315309*

[b] *A. E. Arbuzov Institute of Organic and Physical Chemistry, KSC RAS, ul. Akad. Arbuzova 8, 420088, Kazan, Russia*

† Electronic Supplementary Information (ESI) available: Additional TG–DSC data for pure *tert*-butylcalix[4]arene and *tert*-butylcalix[5]arene and their clathrates. See http://dx.doi.org/10.1039/b701082f/

a hermetically closed vial, and its headspace was analyzed after 24 hours of equilibration. The purified calixarenes had no less than 99% purity, estimated using thin-layer chromatography.

Calixarene **2**, prepared as written above, was characterized by X-ray powder diffraction (XRPD) studies, see the Electronic Supplementary Information (ESI)†. According to the diffractogram obtained, the guest-free form of host **2** used in vapor-sorption studies in the present work has the same packing as the dense form of this guest-free host prepared elsewhere by prolonged heating of its toluene clathrate at 160 °C.[22] The diffractogram for host **1**, prepared as for the present studies, was published earlier.[23] This diffractogram coincides with that calculated from monocrystal X-ray data for self-included dense form of host **1**, crystallized from tetradecane solution at 70 °C.[24] In the same paper,[23] the product of host **1** saturation with toluene vapor at 298 K was shown to have the same packing as 1 : 1 clathrate crystallized from toluene solution.[25] Purified guests [26] had at least 99.5% purity.

The vapor-sorption isotherms were determined using the static method of headspace GC analysis.[5,12] For this, the equal portions of purified host (80 mg) were equilibrated with different amounts (1–49 μl) of guest for 72 h at 298 K (24 h for dichloromethane) in hermetically closed 15 ml vials, and then their headspace was analyzed. Using this method, the relative vapor pressure (≈thermodynamic activity) of guest P/P_0 and the guest uptake A, in moles of guest per mole of host, were determined, where P and P_0 are the partial vapor pressures of guest in the studied system and of pure liquid guest, respectively. The error in P/P_0 determination varied from 5% (for $P/P_0 > 0.5$) to 10% (for $P/P_0 < 0.1$). Nearly half of this error is systematic and corresponds to the error of headspace analysis for a sample of pure liquid guest. The error of the guest uptake determination was 5%. The sorption isotherms for the most studied host–guest systems were determined 2–4 times for the same host samples purified from the bound guest as described above.

The composition of clathrates, prepared from the equilibration of host powder with saturated vapor of guest at 298°, as mentioned above, was determined using thermogravimetry (TG) with microthermoanalyzer MGDTD-17S (Setaram) For this, the clathrate samples of 10–15 mg were studied at static atmospheric pressure in 280 μl aluminium crucibles with holes of 4 mm in diameter. The registration of their weight began in less than 2 minutes after the vial with the host–guest system was opened. The rate of temperature increase in this experiment was 4 K min^{-1}. For each clathrate, its stability was checked in a TG experiment for at least 1 h at 20 °C without heating. For clathrates unstable under these conditions, the temperatures scanning was performed only after the stable weight had been reached.

Simultaneous thermogravimetry and differential scanning calorimetry (DSC) was performed using an STA 449 C Jupiter thermoanalyzer (Netzsch) with a temperature rate of 4 K min^{-1} in an argon atmosphere with a total flow rate of 20 ml min^{-1}. For this, 5 mg samples of host–guest clathrates were prepared through vapor saturation, as written above, in aluminium crucibles (40 μl) with lids having 3 holes, each of 0.5 mm in diameter. Combined TG–DSC analysis began 15–20 minutes after the clathrates were removed from the system with saturated guest vapor, giving the composition value of clathrates stable at room temperature.

The error in the TG experiments with both methods is 2–5% depending on the clathrate stability. Initial hosts are stable in the air up to 230 °C (**1**) and 220 °C (**2**). Under an argon flow, both pure hosts practically do not lose mass up to 260 °C, but above 230 °C host **2** changes its color, and at 260 °C becomes brown. TG curves for pure hosts, determined under static air conditions, are given in Electronic Supplementary Information (ESI)†.

Results and discussion

Vapor-sorption isotherms

The sorption isotherms obtained for the guest partition between vapor and solid *tert*-butylcalix[5]arene (**2**) at 298 K are shown in Fig. 1. The isotherms for *tert*-butylcalix[4]arene (**1**) determined earlier under the same conditions[4,9,12] are also given for comparison.

In most cases, the observed sorption isotherms have a one-step shape with a steep increase of binding from zero level near the threshold guest activity P/P_0 (Fig. 1). They have a saturation part at higher guest activities. This isotherm shape corresponds to the phase transition from the initial host without guest to the host–guest inclusion compound (clathrate).[4,10,11] Such isotherms were fitted using the following equation:[27]

$$A = SC(P/P_0)^N/(1 + C(P/P_0)^N) \quad (1)$$

where S = inclusion stoichiometry (mole of guest per mole of host), C = sorption constant, and N = cooperativity parameter.

The sorption isotherms of cyclohexane and propionitrile on host **2** have two steps, and the chloroform isotherm for this host has three steps (Fig. 1a,c,d). These isotherms were fitted by generating a version of eqn (1) for each step and summing them. Only points with $P/P_0 < 0.85$ were included in the calculation for all isotherms obtained because above this activity level, the capillary condensation of the guest between the host powder particles may be significant. The fitting procedure was described elsewhere.[9]

The fitting parameters of the isotherms obtained are given in Table 1. The inclusion threshold values $a_{0.5S}$, corresponding to the guest activity at the 50% saturation of host for each inclusion step, are given instead of sorption constants C:

$$a_{0.5S} = \exp(-(\ln C)/N) \quad (2)$$

Host **2** powder does not sorb methanol vapors. The guest uptake in this system is below the level of experimental error at $P/P_0 < 0.85$. The sorption isotherm of ethanol on this host has no pronounced saturation part. For its approximation, the arbitrary chosen stoichiometry value $S = 1$ was used.

For one-step isotherms or separate inclusion steps described by eqn (1), the threshold activity value $a_{0.5S}$ relates to inclusion Gibbs energy, or Gibbs energy of guest transfer from a standard state of pure liquid to the saturated clathrate:

$$\Delta G_c = RT\int_0^1 \ln(P/P_0)dY = RT\ \ln\ a_{0.5S} \quad (3)$$

where $Y = A/S$ is the host-saturation extent. For multi-step sorption isotherms, the total inclusion Gibbs energy ΔG_c is the weighted average of $\Delta G_c^{(i)}$ values for separate inclusion steps:

$$\Delta G_c = \frac{\sum S_i \Delta G_c^{(i)}}{\sum S_i} \quad (4)$$

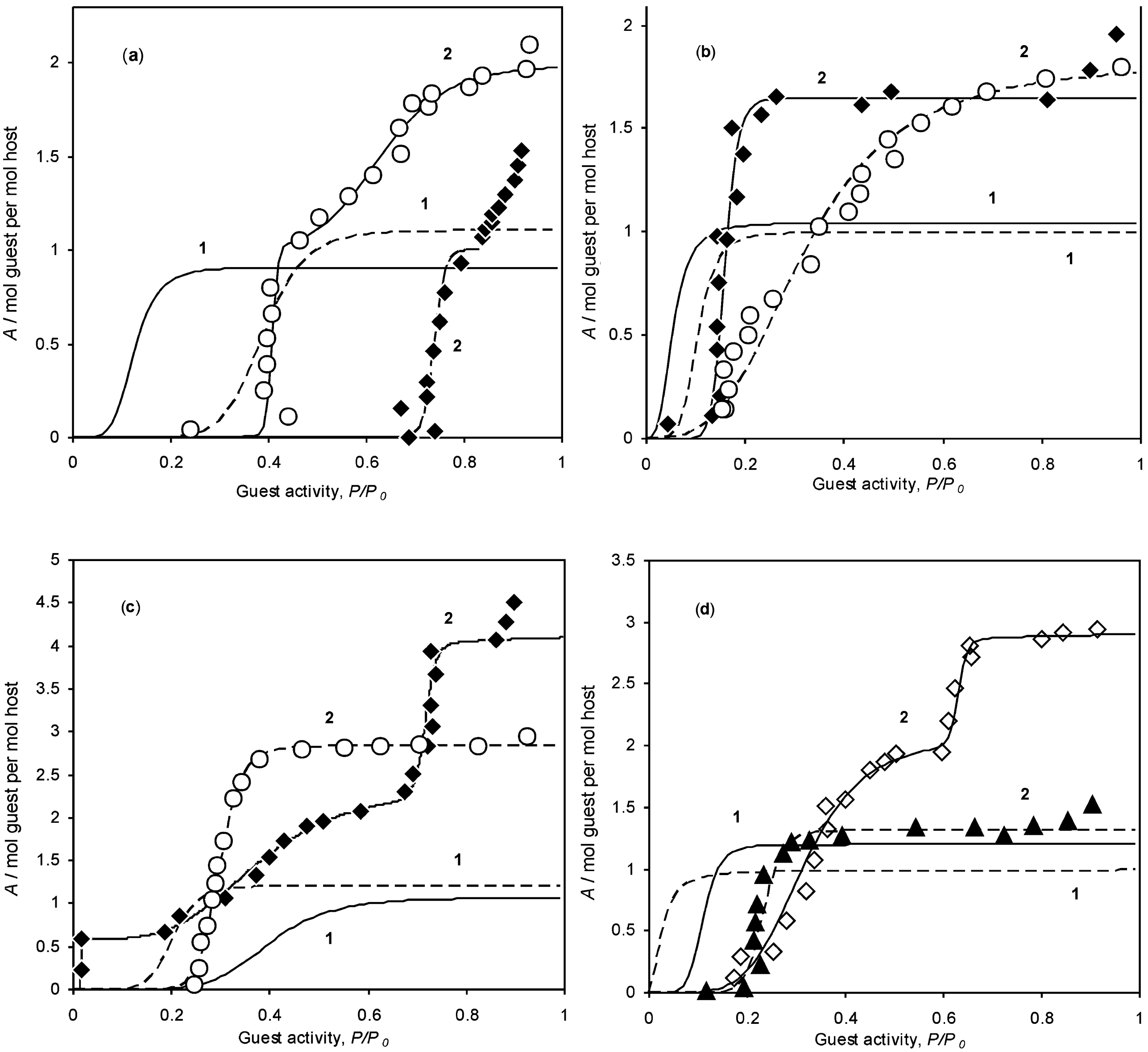

Fig. 1 Vapor sorption isotherms of (a) propionitrile (—) and ethanol (—), (b) benzene (—) and toluene (—), (c) chloroform (—) and tetrachloromethane (—), (d) cyclohexane (—) and dichloromethane (—) on *tert*-butylcalix[4]arene (**1**) and *tert*-butylcalix[5]arene (**2**). The data for host **1** are from ref. 4,9,12.

Table 1 Parameters of sorption isotherms on solid *tert*-butylcalix[4]arene (**1**) and *tert*-butylcalix[5]arene (**2**) in binary systems with guest vapors at Δ = 298°[a]

		N		ΔG_c/kJ mol^{-1}		*S*	
Guest	$a_{0.5S}$	**2**	*d*	**1**[b]	**2**[c]	**1**[b]	**2**[d]
EtOH	0.74	69	0.06	−2.3	−0.7	1.10	—[f]
EtCN	0.41; 0.63[e]	70; 9[e]	0.02	−5.2	−1.7 (−2.23; −1.15)	0.91	1.99 (1.01)
CH_2Cl_2	0.23	12	0.04	−8.9	−3.6	0.99	1.31
$CHCl_3$	0.015; 0.38; 0.72[e]	80; 4.0; 66[e]	0.02	−2.3	−2.9(−10.4; −2.4; −0.83)	1.07	4.13 (0.59; 1.77)
C_6H_6	0.16	12	0.04	−7.3	−4.6	1.08	1.65
CCl_4	0.30	13	0.02	−3.9	−3.0	1.2	2.83
c-C_6H_{12}	0.32; 0.63[e]	5.1; 72[e]	0.04	−5.5	−2.4 (−2.86; −1.14)	1.20	2.91 (2.06)
$C_6H_5CH_3$	0.32	3.2	0.20	−5.6	−2.8	0.99	1.81

[a] Parameters of methanol sorption isotherm on solid host **1** are $\Delta G_c = -1.2$ kJ mol^{-1} and $S = 1.91$[12]; host **2** does not bind methanol vapors; δ is standard deviation. [b] Data from Ref. 4,9,12. [c] In brackets, the ΔG_c values of separate inclusion steps are given. [d] In brackets, the guest mole numbers added in the first or first and second inclusion step are given. [e] Parameters of separate inclusion steps for isotherms fitted using a sum of 2 or 3 versions of eqn (1). [f] Stoichiometry was not determined.

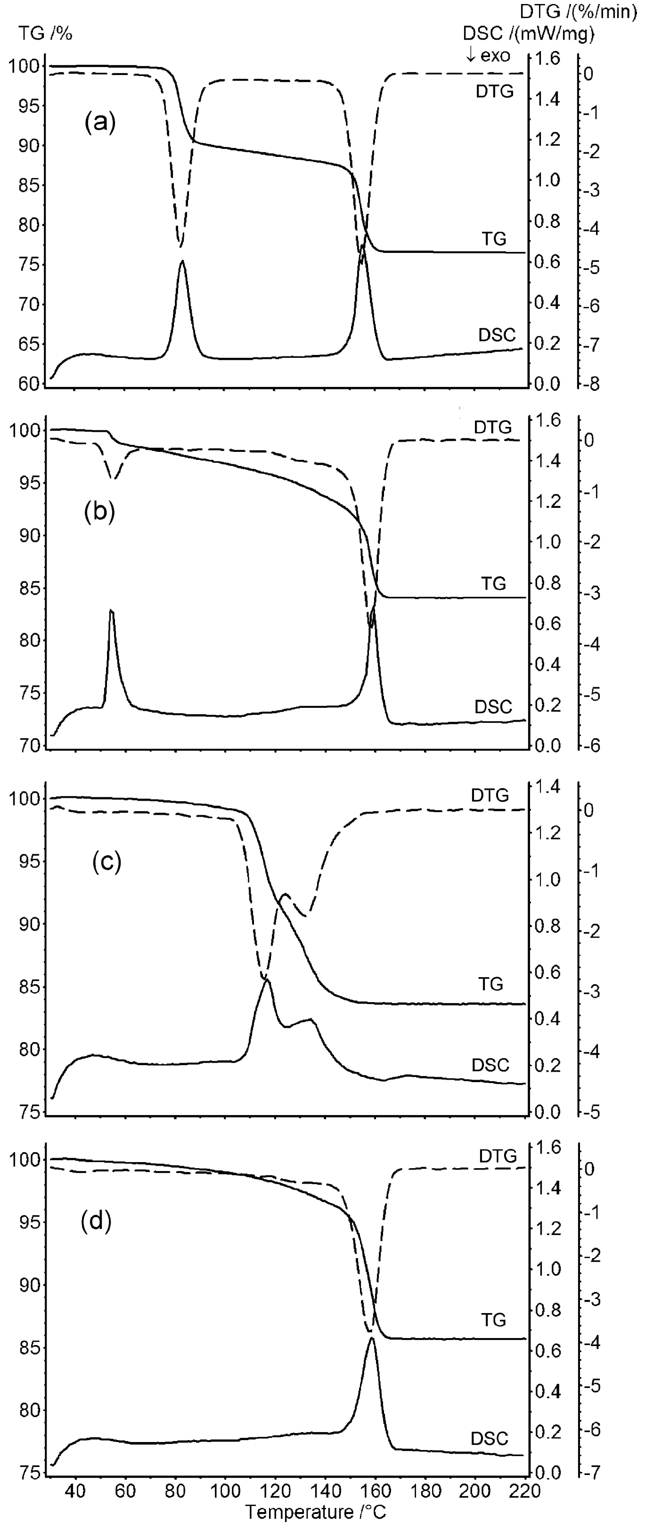

Fig. 2 The data of simultaneous TG–DSC experiment for saturated clathrates of *tert*-butylcalix[5]arene (**2**) with cyclohexane (a), pyridine (b), toluene (c) and benzene (d).

where S_i is the guest mole number included in the i-th step of clathrate formation. The calculated ΔG_c and $\Delta G_c^{(i)}$ values are given in Table 1.

Host **2** has higher inclusion threshold values $a_{0.5S}$, and higher inclusion Gibbs energies ΔG_c than host **1** for all studied guests except for chloroform, Table 1. The higher $a_{0.5S}$ and ΔG_c values may be caused by smaller pre-organized cavities per bound guest molecule in the initial guest-free state of calixarene **2**. Being an H-donor, chloroform probably overcomes this barrier in host **2**, which can bind guests interstitially.[22,28–31]

Thermostability and stoichiometry of host–guest inclusion compounds

The results of TG experiments for the studied clathrates for inclusion compounds prepared through saturation of host powder with guest vapor are given in Table 2. For inclusion compounds with a one-step TG curve, the mass loss Δm (%) for the complete decomposition of clathrate, and corresponding stoichiometry values S_{TG} were calculated, Table 2.

While all clathrates of host **1** are stable at room temperature, clathrates of host **2** with pyridine, CH_2Cl_2, $CHCl_3$, 1,2-$C_2H_4Cl_2$, C_2HCl_3, and C_2Cl_4 lose guest partially at room temperature, 20 °C, Table 2. Also, clathrates of **1** with toluene and of **2** with pyridine and cyclohexane have TG curves with two steps above 30 °C. The mass loss Δm, inclusion stoichiometry S_{TG}, and temperature of DTG peaks, T_{max}, for each decomposition step are given in Table 2. The other characteristic temperatures are given in ESI†.

The number of decomposition steps for clathrates studied do not generally coincide with the number of formation steps for the same clathrates at 298 K (Fig. 1, 2). An exception is **2**·3*c*-C_6H_{12} clathrate, which has 2 steps for both formation and decomposition.

The clathrates having TG curves with more than one guest-elimination step and several other clathrates were also studied using simultaneous TG–DSC analysis (Fig. 2), Table 2. For each guest-elimination step, the molar enthalpies ΔH_i were calculated, Table 3. These data help to find out whether any thermally induced transitions without mass loss take place in clathrate decomposition. Such a phenomenon was observed for **1**·$C_6H_5CH_3$ clathrate at 230 °C (Fig. 3). The data for this clathrate generally reproduce the separately determined TG[6] and DSC[7] curves for the same host–guest system. The observed DSC endothermic peak at 230 °C is a result of phase transition to the less tight head-to-head packing of host **1**.[7] The studied clathrates of **2** do not have such transitions below 230 °C. At higher temperatures, host **2** becomes chemically unstable.

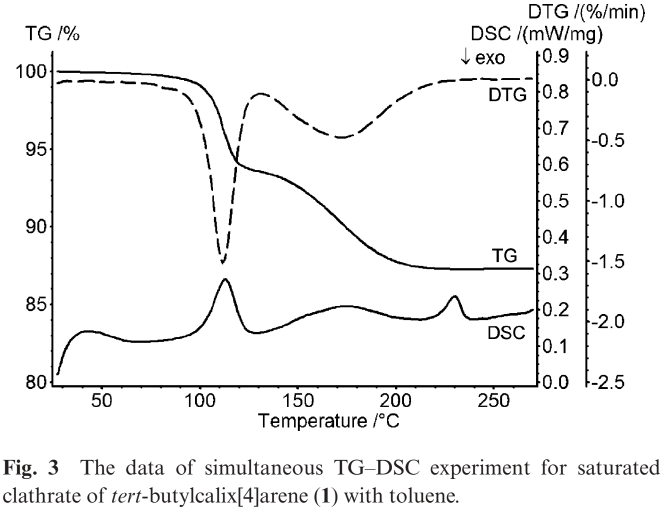

Fig. 3 The data of simultaneous TG–DSC experiment for saturated clathrate of *tert*-butylcalix[4]arene (**1**) with toluene.

Table 2 Data from TG analysis for clathrates of *tert*-butylcalix[4]arene (**1**) and *tert*-butylcalix[4]arene (**2**) prepared using saturation of host powders with guest vapors

			$T_{\max}$/°C		Δm (%)		S_{TG}	
Number	Guest	$\mathrm{MR_D}$/mol cm^{-3}	**1**	**2**	**1**	**2**	**1**	**2**
1	MeOH[a]	8.3	71	—	6.72	—	1.42	—
2	MeCN	11.1	147	75	6.24	6.56	1.05; 1[b]; 1.25[c]	1.39
3	EtOH	12.9	147	74	6.71	6.0	1.01	1.13
4	EtCN	16.0	169	127	8.20	11.46	1.05	1.91
5	Acetone	16.1	156	101	8.79	7.31	1.08; 1[d]	1.10
6	CH_2Cl_2	16.2	154	99	11.66	11.32 (6.33[e])	1.01	1.22 (0.54[f])
7	*n*-PrOH	17.5	160	99	8.92	6.98	1.06	1.01
8	*i*-PrOH	17.5	154	90	9.04	7.28	1.07	1.06
9	DMF[g]	19.7	185	154	11.23	14.99	1.13	1.96; 2[h]
10	1,2-$C_2H_4Cl_2$	20.6	161	118	13.82	18.95 (8.65[e])	1.05	1.92 (1.04[f])
11	$CHCl_3$	21.3	157	131	16.47	35.13 (16.75[e])	1.07	3.68 (1.93[f])
12	1,4-Dioxane	21.7	176	108	12.38	23.32	1.04	2.80
13	*n*-BuOH	22.1	147	118	10.72	8.06	1.05	0.96
14	Pyridine[g]	24.1	178	55; 158	10.99	18.93 (3.7[e]; 3.1[i])	1.01; 1[j]	2.39 (1.93[f]; 1.70[k])
15	C_2HCl_3	25.3	150	94	17.12	28.33 (6.83[e])	1.02	2.44 (1.85[f])
16	C_6H_6[g]	26.2	160	158	11.39	14.33	1.07; 1[j]	1.74
17	CCl_4	26.6	151	120	20.22	35.97	1.09	2.96
18	*c*-C_6H_{12}[g]	27.9	153	83; 155	12.61	23.53 (10.47[i])	1.11; 1[l]	2.97; 1.64[k]
19	*n*-Hexane	29.9	166	130	6.80	6.74	0.55; 0.5[m]	0.68; 0.3[n]
20	C_2Cl_4	30.3	121	136	20.30	30.80 (5.68[e])	1.00	2.18 (1.78[f])
21	Toluene[o]	31.1	111; 173[q]	116	12.74 (6.51[i])	16.48	1.03 (0.5[k]); 1[p]	1.74; 2[q]
22	*n*-Heptane	34.5	167	134	7.89	7.34	0.55	0.64
23	*n*-Octane	39.2	160	162	8.30	9.44	0.53	0.74
24	Isooctane	39.3	145	118	8.54	17.28	0.53	1.48
25	*n*-Decane	48.4	96	161	7.68	8.46	0.38	0.53

[a] Host **2** does not bind methanol. [b] Data from Ref. 32. [c] Data from Ref. 33. [d] Data from Ref. 34. [e] Mass loss at room temperature. [f] Stoichiometry of clathrate stable at room temperature, 20 °C. [g] TG data for clathrate of this guest with **2** are from simultaneous TG–DSC analysis. [h] Data from Ref. 30. [i] Mass loss in the first decomposition step above room temperature. [j] Data from Ref. 35. [k] Stoichiometry of clathrate formed after the first decomposition step above room temperature. [l] Data from Ref. 36. [m] Data from Ref. 37. [n] Data from Ref. 28. [o] TG data of this guest with **1** are from simultaneous TG–DSC analysis. [p] Data from Ref. 25. [q] Data from Ref. 22.

Combined TG–DSC data for host–guest clathrates help to give a better insight into the nature of thermal transitions in these systems. In the majority of cases, the enthalpy of guest elimination ΔH_{i} is a little higher than the enthalpy of guest sublimation ΔH_{s}. This is possible, if the host cavity almost completely collapses when the guest is removed, while the enthalpy of guest molecular interactions is approximately the same in the clathrate and in the liquid guest. Such a collapse probably does not occur in the first decomposition step of **2**·1.93 pyridine clathrate, which has $\Delta H = 90$ kJ mol^{-1} $\approx 2.3\ \Delta H_{\mathrm{s}}$. Nearly half of this value may be the excessive enthalpy of cavities created in solid phase after the partial guest removal at relatively low temperature, $T_{\max} = 55$ °C. The same phenomenon may also take place when calixarenes are used as receptor materials in quartz microbalance sensors, where the inclusion threshold is usually not observed on sorption isotherms.[2,38] The enthalpy of the endothermic transition of host **1** at 230 °C, $\Delta H_3 = 10$ kJ mol^{-1}, is only 26% of the value for toluene-sublimation enthalpy. The size ratio of created host cavity to the toluene molecule may also be 26%.

The total stoichiometry values, S and S_{TG}, calculated from vapor-sorption isotherms and TG curves, respectively, coincide with the experimental errors for all inclusion compounds having a host-saturation part on sorption isotherms at guest activity $P/P_0 = 0.6$–0.85, Tables 1 and 2. For clathrates of **1** with methanol, of **2** with ethanol, and of **3** with cyclohexane, having no such saturation part, headspace analysis may overestimate the

Table 3 Enthalpies of clathrate decomposition from simultaneous TG–DSC data

Clathrate	ΔH_{s}[a]/kJ mol^{-1}	ΔH_1[b]/kJ mol^{-1}	ΔH_2[b]/kJ mol^{-1}	ΔH_3[c]/kJ mol^{-1}
1·1.03 $C_6H_5CH_3$	38.0	50 ± 4	49 ± 3	10 ± 1
2·2.97 *c*-C_6H_{12}	33.0	41 ± 2	44 ± 2	
2·2.39 Pyridine	40.2	90 ± 15	41 ± 4	
2·1.74 $C_6H_5CH_3$	38.0	71 ± 3		
2·1.74 C_6H_6	33.8	46 ± 2		
2·1.96 DMF	46.9	[d]	37 ± 4	

[a] Enthalpy of sublimation ΔH_{s} from Ref. 39. [b] ΔH_1 and ΔH_2 are the enthalpies of the heat flow peaks corresponding to the first and second steps of clathrate decomposition, respectively, per mole of guest. [c] Enthalpy per mole of host corresponding to the phase transition at 230 °C without mass loss. [d] ΔH_1 is not determined, TG–DSC curves for this clathrate are given in ESI.

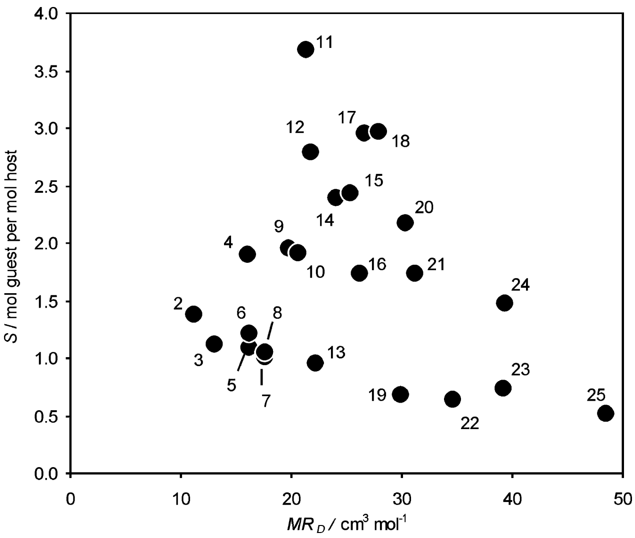

Fig. 4 Correlation between the inclusion stoichiometry S and guest molar refraction MR_D for saturated clathrates of host **2**. Point numbers correspond to the numbers of guests in Table 2.

guest-inclusion capacity because of the multilayer sorption on host powder at $P/P_0 > 0.85$. Hence, for these clathrates, thermogravimetry data may be preferred because in the used experimental technique the excessive non-bound guest is eliminated.

The observed temperatures of DTG peaks, T_{max}, indicate the relative thermal stability of clathrates, Table 2. In most cases, the clathrates of host **2** have lower T_{max} values for the last guest-elimination step than clathrates of host **1**. The exclusions are clathrates of benzene, C_2Cl_4, cyclohexane, *n*-octane and *n*-decane with **2**, which have the same or higher stability by this parameter than those of **1**. But clathrates of **2** with all of these guests, except for *n*-decane, have a lower decomposition onset temperature (see ESI†). This stability difference is in line with the lower guest-binding affinity of host **2**, Table 1.

Within the series of clathrates of one host, the order of thermal stability does not have a simple correlation with the order of guest-binding affinity derived from the values of inclusion Gibbs energy, ΔG_c, at 298 K, Tables 1 and 2. Probably, a temperature increase to 100–150 °C changes the cooperative molecular interactions in the solid phase of the clathrates studied.

Molecular recognition

Molecular recognition in the studied systems is linked to the two types of guest-binding selectivity: (1) by the inclusion threshold and (2) by the inclusion stoichiometry. The first one is related to the cooperativity of clathrate formation. Once the guest structural change increases the threshold activity $a_{0.5S}$ up to 1, the guest condensation takes place instead of the host–guest binding. This situation can be seen for the methanol–ethanol pair. For calixarene **1**, these guests have $a_{0.5S}$ values of 0.61 and 0.40, respectively. For host **2**, ethanol has $a_{0.5S} = 0.68$, while the threshold activity of methanol is too large for this guest to be bound. Hence, host **2** is more selective for this pair of guests. The observed inclusion affinity order for these two guests may be explained by the stronger average molecular interactions in liquid methanol than in ethanol, which can be seen from limiting activity coefficients of methanol, $\gamma^{\infty} = 21.8$, and ethanol, $\gamma^{\infty} = 17.4$ in, the non-hydrogen-bonding solvent, toluene at 298 K.[9]

Inclusion Gibbs energies having values a little lower than zero create the possibility for molecular recognition of guest homologues in clathrate formation. In this respect, host **2** is more selective than host **1**. However, the variation of ΔG_c values for studied clathrates of host **1** is higher than for host **2**, Table 1. In this ordinary way, host **1** is more selective. So, the selectivity of clathrate formation is more variable than that of host–guest binding in liquid solutions having no concentration threshold for complexation.

The second specific type of clathrate-formation selectivity can be seen in the comparison of structure–property relationships for guest-inclusion stoichiometries S of two studied hosts. The stoichiometry data obtained for host **1**, Table 2, confirm a rather simple stepwise relationship between S values and guest-size parameter MR_D earlier found for clathrates of this calixarene prepared in comparable conditions.[10] Selectivity is observed only in the zones of stoichiometry transition with $MR_D = 8.3$–11 and 30–31.7 $cm^3\ mol^{-1}$. Outside these MR_D ranges, host **1** is unselective despite a large variation of inclusion Gibbs energy ΔG_c, Table 1.[12] Host **2** is much more selective in this respect. Its relationship between inclusion stoichiometry S and guest-size parameter MR_D (Fig. 3) cannot be rationalized with any simple and general line or curve. So, a relatively small variation of host structure gives a strong change in guest-binding selectivity.

The structural causes of the observed selectivity differences for **1** and **2** can be seen when comparing their clathrate packing from available X-ray data. Host **1** has *endo*-calyx guest-binding with 1:1 and 1:2 guest-host stoichiometries for clathrates formed near 298 K.[15,35,36,40] Such an inclusion type prevents the conversion of higher guest–host affinity into the higher inclusion capacity S. The known clathrates breaking the observed stepwise relationship are formed only at relatively high temperature, 70 °C, and have a quite different binding motif: interstitial guest inclusion.[18,24,41]

The interstitial inclusion is probably intrinsic for host **2** at 298 K. This host tends to bind guest molecules, at least partially, outside the interior space of the host bowls.[22,28–31] Two structural types of guest inclusion may be the cause of the observed multi-step guest binding and clathrate decomposition for host **2** (Fig. 1, 2).

Such packing should create much less restrictions on the size of bound guest than the inclusion inside the macrocycle calyx. Hence, the S *vs.* MR_D plot for host **2** has two groups of guests (Fig. 4). One group includes acetonitrile, acetone, dichloromethane, alcohols and linear alkanes that follow the stepwise descending relationship with 1 : 1 and 1 : 2 stoichiometries observed for host **1**, Table 2. The second group includes mostly cyclic and branched guests along with propionitrile, DMF and polychlorinated hydrocarbons. These guests have inclusion stoichiometry $S \geq 1.5$, and for them the packing both inside and outside the host **2** bowls can be expected, like for toluene[22] and DMF.[30] These guests with compact molecules are able to compete with self-inclusion of host **2**,[22] while linear guests from the first group, are probably included only interstitially, like hexane,[28] with relatively low stoichiometry, $S = 0.51$. For example, contrary to host **1**, host **2** appears to be selective for an *n*-octane–isooctane pair.

The observed less negative inclusion Gibbs energies for host **2** than for host **1** may be a result of such conversion of higher guest–host affinity into the higher inclusion capacity S. For example, the vapor-sorption isotherm of chloroform has 3 steps, where the second and the last two $CHCl_3$ molecules are bound with larger and larger activity thresholds (Fig. 1), Table 1. Hence, ΔG_c, which is the average value per bound guest molecule, for chloroform may be less negative than for the guests, *e.g.* benzene and dichloromethane, that are less complementary with host **2** in terms of inclusion stoichiometry, *S*. This effect should have a smoothing influence on the host selectivity by inclusion Gibbs energy, which one can see from comparison of the ΔG_c data for the hosts studied.

Conclusions

A specific feature of the host–guest clathrate formation process for two *tert*-butylcalix[*n*]arenes is the rather independent performance of two selectivity types: (1) by activity (relative vapor pressure) threshold of guest binding, and (2) by inclusion stoichiometry. Only one of them may be observed for a given set of guests depending on the host molecular structure and clathrate packing. This observation helps to understand the low predictability of structure–property relationships for host–guest binding in solid phase, and to foresee the situations where such relationships may be more predictable. Hence, more directed molecular design may be done to obtain hosts for selective sensors or guest storage.

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