Thermodynamic comparison of molecular recognition of vaporous guests by solid calixarene and diol hosts

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Molecular recognition of vaporous guests by the solid hosts 2,2′-bis(9-hydroxyfluoren-9-yl)biphenyl (**1**) and *tert*-butylcalix[4]arene (**2**) was studied. For this purpose the vapour sorption isotherms of 15 organic compounds with various molecular size and group composition with the solid hosts **1** and **2** were determined by static gas chromatographic headspace analysis. Most of the isotherms obtained show a definite inclusion threshold at a specific guest activity and a saturation part corresponding to the formation of stoichiometric supramolecular compounds. The stoichiometry of the host–guest compounds and free energies of their formation based on different standard states were determined. The free energy of guest transfer from the standard state of an infinitely dilute guest solution in toluene to the solid inclusion compound was assumed to be a molecular recognition parameter in the systems studied. For host **1** this transfer free energy exhibits a reasonably good 2-parameter correlation with guest molar refraction and free energy of H-bonding between guest and alcohols. Bad correlation was obtained for solid host **2**. The effect of the guest structural parameters on molecular recognition by hosts **1** and **2** is discussed in terms of the different size of potential cavities in the host crystals and different ability of the hosts to H-bond with guests.

Introduction

The nature of the "structure–binding affinity" relationship for solid host–guest compounds is one of the basic questions in supramolecular chemistry. In contrast to molecular interactions in solutions, where the molecular group composition of solute and solvent is of major importance,[1] the symmetry of the host molecules and the complementarity of the guest molecules to the host crystal lattice are relevant in clathrate formation.[2,3] Two essentially different types of solid phase guest binding can be distinguished for the numerous supramolecular hosts: (1) inclusion exclusively due to the low-density molecular packing of the solid host and (2) the formation of so-called coordinato-clathrates, where the guest incorporation into the loose host lattice is assisted by host–guest H-bonds[2] or other types of specific interaction. Bowl-like calixarenes[4] and diol compounds with bridged triarylmethanol double units[2,5] are good examples of hosts being capable of the guest inclusion by two mechanisms (1) and (2), respectively.

A quantitative comparison of the inclusion ability of different solid hosts requires the correct choice of the guest standard state. Most investigations have been made by means of quartz microbalances with thin layers of solid cavitands, and using a vaporous guest with a fixed concentration as the reference state.[6–8] However, molecular recognition by solid hosts expressed in terms of the absolute guest concentration in the vapour phase is often not essentially different from the selectivity of liquid solvents or amorphous polymers.[7,9] On the contrary, a high selectivity to the guest molecular shape was observed by the crystallization of clathrates from a solution of the host in liquid mixtures of isomers.[10,11]

A study of the "structure–binding affinity" relationships for host–guest inclusion compounds is complicated by the cooperativity of their formation in the solid phase. For solid *tert*-butylcalix[4]arene the vapour sorption isotherms of the guests studied show a sigmoidal shape characterized by an inclusion threshold at a definite guest activity.[12] The same shape of the sorption isotherms was observed for the binding of vaporous guests by a solid bisresorcinol derivative of anthracene[13] and by layers (500 nm) of pyridone derivatives on interdigital electric capacity sensors.[14] Cooperative threshold effects were also reported for the kinetics of vapour guest inclusion by solid hosts[15] and for the formation of liquid-crystalline host–guest compounds.[16] The existence of the guest inclusion threshold was regarded as evidence of a phase transition between 2 phases: free solid host and the host–guest inclusion compound.[13,15b,17] The corresponding change of the crystal structure in the solid phase during guest inclusion was proved using the powder X-ray method.[13,17] The value of the guest-inclusion threshold of solid *tert*-butylcalix[4]arene depends on the presence of relatively small concentrations of a third component in the system.[12a] The cooperative influence of a third component on the formation and the stoichiometry of solid host–guest clathrates was observed earlier for some other systems.[18] The guest molecular size and/or shape have significant influence on the inclusion threshold.[12b,13]

In the present work we have examined and compared the vapour inclusion properties of two solid hosts belonging to essentially different classes of synthetic supramolecular receptors: coordinato-clathrand 2,2′-bis(9-hydroxyfluoren-9-yl)biphenyl (**1**) and cavitand *tert*-butylcalix[4]arene (**2**). Both hosts are known to form a number of stoichiometric inclusion compounds with neutral molecules already described by X-ray methods.[4,5,11,19]

Results and discussion

Vapor sorption isotherms

The inclusion properties of solid hosts **1** and **2** were studied for

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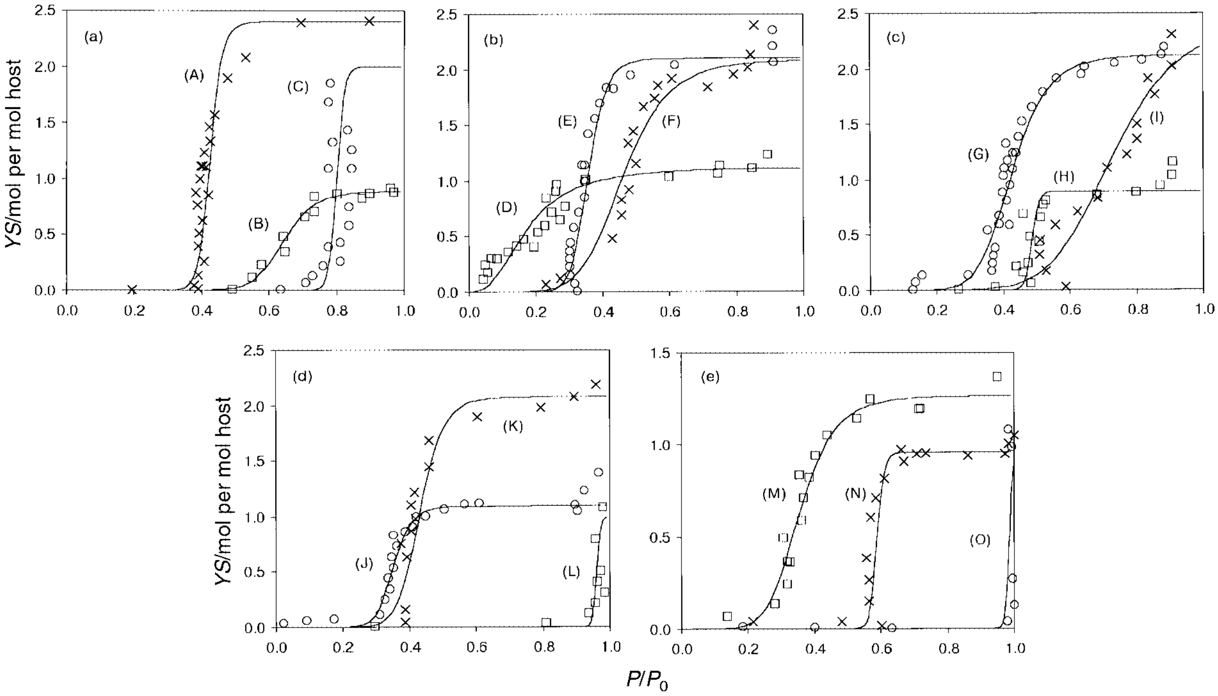
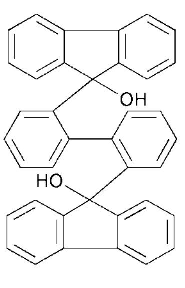


Fig. 1 Vapour sorption isotherms for solid 2,2′-bis(9-hydroxyfluoren-9-yl)biphenyl (**1**) at 298 K. Experimental points correspond to the following guests: (a): (A) MeOH, (B) CCl_4, (C) EtOH; (b): (D) pyridine, (E) EtCN, (F) acetone; (c): (G) Et_3N, (H) $CHCl_3$, (I) PrOH; (d): (J) MeCN, (K) PrCN, (L) toluene; (e): (M) 1,4-dioxane, (N) benzene, (O) cyclohexane. The lines are sorption isotherms calculated using the Hill equation [eqn. (1)].



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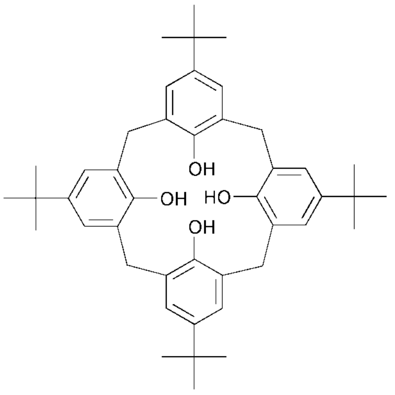

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the same set of guests with various molecular size and group composition. The sorption isotherms obtained are shown in the Figs. 1 and 2. Some of the sorption isotherms for host **2** were determined earlier.[12] Most of the isotherms obtained exhibit the threshold of the guest activity $a_{thr} = (P/P_0)_{thr}$ necessary for guest inclusion. Up to this activity a weak sorption affinity of the host is observed. Above the threshold activity a_{thr} the guest sorption sharply rises. At guest activities of $0.6 < (P/P_0) < 0.8$ saturation takes place in most cases indicating the formation of a stable inclusion compound. Sorption isotherms with a guest inclusion threshold cannot be described by monolayer (Langmuir) or multilayer (BET) adsorption models. For the description of such sorption (inclusion) behaviour the Hill equation [eqn. (1)][20] can be used, where Y is the inclusion

$$YS = SC(P/P_0)^N/[1 + C(P/P_0)^N] \qquad (1)$$

saturation extent, S is the stoichiometry, C is the sorption constant, N is the cooperativity constant and YS is the experimentally determined solid phase composition (mol of guest per mol of host). Approximation of the obtained sorption isotherms using the Hill equation gives two stable solutions: the stoichiometry S and the ratio $(\ln C)/N$. The second increase in the guest uptake at a guest activity $(P/P_0) > 0.85$, which is observed in some isotherms, corresponds to the formation of a liquid phase. So, the points of sorption isotherms corresponding to this second increase were not included in the approximation. The values of the guest threshold activity a_{thr}, and parameters S, N and $(\ln C)/N$ are summarized in Table 1. The value of a_{thr} is given as the guest activity at a solid phase composition $0.25S$ on the calculated Hill isotherm.

Inclusion stoichiometry

The calculated stoichiometries S (Table 1) correspond to 2 : 1, 1 : 1 or 1 : 2 (guest : host molar ratio) for calixarene **2** and 2 : 1 or 1 : 1 for host **1**. Available X-ray data[5,19d] on the stoichiometry of studied inclusion compounds are also given in Table 1. Agreement is found between the results from the two methods. However, a different stoichiometric composition of 2 : 1 was observed[21] for the clathrate of host **1** and acetonitrile from an NMR method for crystals obtained at slightly different crystallization conditions from those described in ref. 5. This type of host is known to form clathrates with different stoichiometries depending on the crystallization conditions.[22] This difference is probably caused by the cooperative nature of the inclusion process in the formation of crystalline clathrates. Inclusion compounds obtained by the vapour saturation method used in the present work are more suitable for the investigation of "structure–property" relationships because the inclusion conditions are strictly comparable for all hosts and guests.

The dependence of the stoichiometry S on the guest molecular size is different for the hosts studied. The stoichiometry values S obtained in the present work for calixarene **2** are in line with the earlier established stepwise dependence of inclusion stoichiometry on the guest molar refraction R_D for vaporous guest–solid host **2** systems.[23] There are three definite areas, where 2 : 1, 1 : 1 and 1 : 2 (mol of guest per mol of host) inclusion compounds are formed. The stoichiometry changes are observed at 9–11 $cm^3\ mol^{-1}$ (from 2 : 1 to 1 : 1) and at 30–32 $cm^3\ mol^{-1}$ (from 1 : 1 to 1 : 2). Molar refraction R_D appeared to be the effective molecular size parameter for these organic substances according to our studies of solvation thermodynamics.[24] The dependence of the inclusion stoichiometry S on the guest molar refraction for host **1** is not as simple as for

Table 1 Parameters of vapour sorption isotherms for solid 2,2′-bis(9-hydroxyfluoren-9-yl)biphenyl (**1**) and *tert*-butylcalix[4]arene (**2**) at 298 K[a]

		2,2′-Bis(9-hydroxyfluoren-9-yl)biphenyl (**1**)						*tert*-Butylcalix[4]arene (**2**)[c]				
Entry	Guest	R_D/cm^3 mol^{-1}	a_{thr}	S	(ln C)/N	N	δ[b]	a_{thr}	S	(ln C)/N	N	δ[b]
1	MeOH	8.3	0.41	2.40	0.85	24	0.02	0.55	1.91	0.50	11	0.03
2	MeCN	11.1	0.32	1.09; 1[d]	1.04	13	0.03	0.14	1.17	1.63	3.5	0.03
3	EtOH	12.9	0.79	—	0.22[e]	71[e]	0.04	0.36	1.10	0.91	9	0.02
4	EtCN	16.0	0.33	2.10	1.03	13	0.04	0.1	0.91	2.08	5.3	0.01
5	Me_2CO	16.1	0.39	2.09	0.77	7	0.05	0.44	0.95	0.76	15	0.03
6	PrOH	17.5	0.63	2.42	0.32	7	0.06	0.3	1.05	1.00	5.4	0.04
7	PrCN	20.4	0.39	2.08	0.84	12	0.06	0.3	1.06	1.17	33	0.04
8	$CHCl_3$	21.3	0.48	0.90	0.72	48	0.03	0.34	1.07	0.92	6.5	0.02
9	1,4-Dioxane	21.7	0.3	1.27	1.03	7	0.04	—	—	—	—	—
10	Pyridine	24.1	0.11	1.13	1.75	2.6	0.04	0.02	1.07; 1[f]	3.27	1.6	0.02
11	Benzene	26.2	0.58	0.96	0.53	54	0.03	0.03	1.08; 1[f]	2.92	2.1	0.01
12	CCl_4	26.4	0.6	0.89	0.44	14	0.03	0.18	1.2	1.59	8	0.04
13	Et_3N	33.8	0.37	2.12	0.85	8	0.05	0.08	0.53	2.45	20	0.02

[a] The estimated error of a_{thr} is 10%; the error of S is 5%. [b] δ is standard deviation of the approximation for the shortest distances between experimental points and the calculated line. [c] Sorption isotherms of MeOH, MeCN, EtOH, EtCN, PrOH and benzene on host **2** have already been determined[12] and these data are given. [d] Ref. 5. [e] Calculated at a stoichiometry value $S = 2$ from ref. 21. [f] Ref. 19*d*.

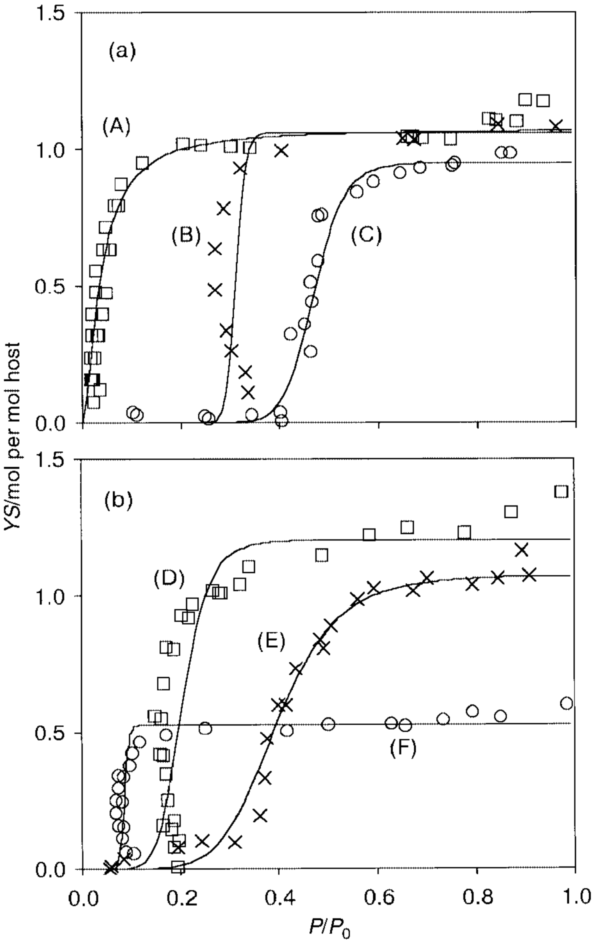

Fig. 2 Vapour sorption isotherms for solid *tert*-butylcalix[4]arene (**2**) at 298 K. Experimental points correspond to the following guests: (a): (A) pyridine, (B) PrCN, (C) acetone; (b): (D) CCl_4, (E) $CHCl_3$, (F) Et_3N. The lines are the sorption isotherms calculated using the Hill equation [eqn. (1)].

calixarene **2**. All studied guests with molar refraction $R_D < 21$ cm^3 mol^{-1} show stoichiometries near 2 : 1 (mol guest per mol of host **1**) except for acetonitrile (1 : 1). The guests with molar refraction $R_D > 21$ cm^3 mol^{-1} usually form 1 : 1 clathrates except for the triethylamine clathrate (2 : 1). It is interesting that the studied guests give higher or equal clathrate stoichiometries S with host **1** compared to the S values of the respective clathrates with host **2** despite the larger molecular cavity of the latter host. In host **1** only one of the active protons of the two OH-groups is able to participate in H-bonding with the guest according to X-ray data.[5] The strong host–guest hydrogen bonds may cause additional conformational constraints in the solid phase, which are analogous to those imposed by intramolecular H-bonds in the studied hosts. This effect probably enables the inclusion of the second guest molecule per molecule of host **1**. The H-bonds between host **1** and the guest molecules in their solid clathrates are considered to be an important factor of guest inclusion by this host.[21]

The *cone* conformation of host **2** does not favour H-bonding with the guest. All four OH-groups in the molecule of calixarene **2** participate in a cyclic system of intramolecular H-bonds.[18b] This intramolecular H-bonding reduces the free energy of possible H-bonds between host **2** and proton-acceptor guests, because disruption of the H-bonds is required for the formation of a new H-bond with a proton-acceptor. Besides, according to the X-ray data[4,19b–e] the guest incorporates inside the host **2** cavity at solid phase inclusion. The packing of calixarene **2** molecules in crystals of inclusion compounds does not allow the guest located within the host bowls to form H-bonds with the host molecules.[19b,d,e] No host–guest O–H···N or O–H···O hydrogen bonds were observed for crystals of host **2** inclusion compounds with such typical proton-acceptors as pyridine,[19d] anisole[19b] and nitrobenzene.[19c,e]. So H-bonding with proton-acceptor guests cannot be expected to have a significant influence on the structure–stoichiometry relationship for solid inclusion compounds of host **2**.

Inclusion free energies

The analysis of the contributions of different molecular interactions to host–guest binding requires the determination of the total energy of the solid phase inclusion process in systems with sigmoidal sorption isotherms. The ordinary stoichiometric equilibrium schemes generally cannot be applied for this purpose,[13] because the binding threshold is a result of the phase transition in the solid host.[13,17] The integration of the sorption isotherm having a saturation part gives the inclusion free energy as shown in eqn. (2), where ΔG_c is the transfer free energy of 1

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

mole of guest from the standard state of pure liquid to the saturated solid phase (inclusion compound). The right part of eqn. (2) is valid if the ln (P/P_0) value is given by eqn. (1) as a function of Y. The inclusion free energies ΔG_c determined from the sorption isotherms obtained are summarized in Table 2. The ΔG_c values for the systems host **1**–toluene and host

Table 2 Free energies of guest transfer to saturated solid clathrates of hosts **1** and **2** from the standard states of pure liquid guest ($\Delta G_c^{(1)}$ and $\Delta G_c^{(2)}$) and infinitely dilute solution in toluene ($\Delta G_{trans}^{(1)}$ and $\Delta G_{trans}^{(2)}$) at 298 K[a]

Entry	Guest	$\Delta G_c^{(1)}$/ kJ mol^{-1}	$\Delta G_c^{(2)}$/ kJ mol^{-1}	γ_t^∞	$\gamma^\infty_{EtOH/G}$	ΔG_H^{MeOH}/ kJ mol^{-1}	ΔG_H^{PhOH}/ kJ mol^{-1}	$\Delta G^{EtOH}_{CCl_4\to G}$/ kJ mol^{-1}	Exp. $\Delta G_{trans}^{(1)}$/ kJ mol^{-1}	Exp. $\Delta G_{trans}^{(2)}$/ kJ mol^{-1}	Eqn. (5) $\Delta G_{trans}^{(1)}$/ kJ mol^{-1}	Eqn. (6) $\Delta G_{trans}^{(1)}$/ kJ mol^{-1}	Eqn. (7) $\Delta G_{trans}^{(1)}$/ kJ mol^{-1}
1	MeOH	−2.1	−1.2[b]	21.8[b]	1.08[d]	−6.4[h]	−10.2[h]	−8.3	−9.7	−8.9	−8.9[n]	−8.9[n]	−9.0[n]
2	MeCN	−2.6	−4.0[b]	4.33[b]	3.90[c]	−6.2	−9.7	−5.1	−6.2	−7.7	−5.8	−5.8	−5.1
3	EtOH	−0.6	−2.3[b]	17.4;[b] 15.4[c]	1	−6.4[h]	−10.2[h]	−8.5	−7.6	−9.3	−8.0[n]	−7.9[n]	−8.3[n]
4	EtCN	−2.5	−5.2[b]	2.92[b]	3.7[e]	−6.2[i]	−9.7	−5.3	−5.2	−7.8	−4.8	−4.8	−4.3
5	Me_2CO	−1.9	−1.9	1.82	1.34	−7.2	−12.3	−7.8	−3.4	−3.4	−5.2	−5.4	−5.1
6	PrOH	−0.8	−2.5[b]	15.9[b]	0.92[c]	−6.4[h]	−10.2[h]	−8.7	−7.6	−9.3	−7.1[n]	−7.0[n]	−7.7[n]
7	PrCN	−2.1	−2.9	1.87	3.50[c]	−6.2[i]	−9.9	−5.4	−3.7	−4.5	−3.9	−3.9	−3.6
8	$CHCl_3$	−1.8	−2.3	0.8	0.73[f]	−0.9[j]	−0.9[j]	−1.6[m]	−1.2	−1.7	−1.7	−1.6	−2.3
9	1,4-Dioxane	−2.6	—	1.15[c]	2.15;[g] 2.49[c]	−6.8	−10.9	−6.6	−2.9	—	−3.9	−3.9	−3.8
10	Pyridine	−4.3	−8.1	1.28	0.96;[g] 0.80[c]	−8.4	−15.5	−8.6	−4.9	−8.7	−4.0	−4.5	−4.0
11	Benzene	−1.3	−7.3[b]	0.97[b]	18.3;[g] 15.2[c]	−2.4;[k] −5.2	−3.0	−1.3	−1.2	−7.2	−1.3	−1.1	−1.5
12	CCl_4	−1.1	−3.9	1.15	31.0;[g] 27.8[c]	0	0	0	−1.4	−4.2	−0.3	−0.4	−1.3
13	Et_3N	−2.1	−6.1	1.25	1.38;[g] 1.96[c]	−10.4	−16.5	−7.7	−2.7	−6.7	−2.9	−2.7	−2.1
14	Cyclohexane	≥0	−5.5[b]	1.36[b]	63.7[c]	0	0	1.8	≥−0.8	−6.3	0.0	−0.1	−0.3
15	Toluene	≥0	−5.6[b]	1	17.4;[b] 15.4[c]	−2.3;[l] −3.8	−3.5	−1.4	≥0	−5.6	−0.3	−0.2	−0.7

[a] The error in ΔG_c is 0.2 kJ mol^{-1}; the error in γ_t^∞ and $\gamma^\infty_{EtOH/G}$ is 10%; all data on free energies of hydrogen bonding ΔG_H^{MeOH} and ΔG_H^{PhOH} unless mentioned otherwise were calculated from stability constants of H-complexes[25] in the molar fraction scale and were determined in CCl_4 by the IR method, except for complexes of $CHCl_3$ with Et_2O (NMR method) and for complexes of PhOH with Me_2CO and dioxane (NIR method); the ΔG_H^{MeOH} values from ref. 25 are at 28 °C for benzene, toluene and MeCN, and at 22 °C for Et_2O, and at 20 °C for Et_3N; the ΔG_H^{PhOH} values are at 29 °C for Et_2O, benzene and toluene. [b] Ref. 12*b*. [c] Ref. 26. [d] Estimated by extrapolation of $\gamma^\infty_{EtOH/G}$ values in EtOH and PrOH. [e] Estimated as the average of $\gamma^\infty_{EtOH/G}$ values in MeCN and PrCN. [f] The limiting activity coefficient of $CHCl_3$ in Et_2O. [g] Ref. 27. [h] Et_2O was taken as proton-acceptor instead of the guest. [i] Taken to be equal to the ΔG_H^{MeOH} value of acetonitrile. [j] Free energy of H-bond between $CHCl_3$ and Et_2O in CCl_4 from ref. 25. [k] Calculated from the ratio of methanol limiting activity coefficients in benzene ($\gamma^\infty = 20.7$) and CCl_4 ($\gamma^\infty = 54.5$) from ref. 27. [l] Calculated from the ratio of methanol limiting activity coefficients in toluene ($\gamma_t^\infty = 21.8$)[12b] and CCl_4 ($\gamma^\infty = 54.5$).[27] [m] Calculated from the ratio of $CHCl_3$ activity coefficients in Et_2O ($\gamma^\infty = 0.73$) and CCl_4 ($\gamma^\infty = 1.37$). [n] Calculated from the doubled ΔG_H or $\Delta G^{EtOH}_{CCl_4\to G}$ value.

1–cyclohexane are practically equal to zero at any stoichiometry value S used in the approximation of the sorption isotherms. The ΔG_c values for the systems with significant guest inclusion are in the range from -0.6 to -4.3 kJ mol^{-1} for host **1** and from -1.2 to -8.1 kJ mol^{-1} for calixarene **2**. Guest inclusion by calixarene **2** is more favourable than by host **1** for most of the guests studied.

The obtained inclusion free energy ΔG_c values cannot be directly used in an analysis of "structure–binding energy" relationships because of the non-equivalence of the standard state of pure liquid for different guests. This problem can be resolved by the determination of the inclusion free energy using vaporous guest as the standard state [eqn. (3)].

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

The vaporous guest is implied to be the standard state when molecular recognition of cavitand-based sensors is described in terms of sensitivity to the absolute concentration (pressure) of the guest in the vapour phase.[6–9] In the case of relatively small ΔG_c contributions, the inclusion free energy $\Delta G_c(\mathrm{v})$ will be approximately proportional to the guest condensation free energy $-\Delta G_{vap}$. Therefore, any special molecular recognition by solid hosts may be masked.[9] An appropriate solution to this problem is the use as the standard state of an infinitely dilute solution of the guest in a solvent with the same molecular group composition as the group composition of the host cavity. Hexadecane was used as a reference solvent in the correlation[7a] of host–guest binding parameters with the Ostwald solubility parameter log L^{16}. But in this case the media polarizability difference between host cavity and solution is significant.[7a] For this reason, toluene having an aromatic π-system like the cavities of both the studied hosts is a better choice of reference solvent. The free energy of guest transfer from toluene solution to a saturated solid clathrate ΔG_{trans} was used for the analysis of supramolecular host–guest interactions [eqn. (4)],[12b,23] where

$$\Delta G_{trans} = \Delta G_c(\mathrm{v}) - \Delta G_{solv} = \Delta G_c - RT\ln\gamma_t^{\infty} \qquad (4)$$

$\Delta G_{solv} = RT\ln\gamma_t^{\infty} + RT\ln\,(P_0/101325\ \mathrm{Pa})$ and γ_t^{∞} is the limiting activity coefficient of the guest in toluene. In order to obtain the ΔG_{trans} values the limiting activity coefficients of studied guests γ_t^{∞} in toluene were determined by the headspace method (Table 2). The values of ΔG_{trans} for diol host **1** and calixarene **2** are plotted *vs.* guest molar refraction R_D in Figs. 3 and 4. In both cases there is no good correlation between the free energy of guest transfer from toluene to the saturated clathrate ΔG_{trans} and the guest molecular size parameter R_D. For host **2** even a weak general tendency is hard to find. But for host **1** some effect of the guest molecular size could be observed, if one takes into account the possibility of the stronger hydrogen bonding of host **1** with pyridine, triethylamine and alcohols. Pyridine and triethylamine are stronger proton-acceptors than the other guests studied according to the free energies of their H-complexes with methanol and phenol in tetrachloromethane solution[25] (Table 2). Alcohols are able to form two H-bonds with host **1** per one alcohol molecule. For inclusion compounds of calixarene **2** with alcohols a small contribution of host–guest hydrogen bonding also cannot be excluded, because ΔG_{trans} values of studied alcohols are more negative than the corresponding values for nitriles with approximately the same molecular size (Fig. 4, Table 2). The quotient $\Delta G_{trans}^{(1)}/\Delta G_{trans}^{(2)}$ of the free energies of the guest transfer from toluene to the inclusion compounds with host **1** and host **2**, respectively, is 0.7–1 for guests with $R_D < 22$ cm^3 mol^{-1}. This ratio is much lower for the larger guests. The difference between the free energies of supramolecular effect (the host packing energy gain due to the guest inclusion) may be higher for the studied hosts than the difference between the $\Delta G_{trans}^{(1)}$ and $\Delta G_{trans}^{(2)}$ values, because the value of $\Delta G_{trans}^{(1)}$ may contain a significant contribution from host–guest hydrogen bonding.

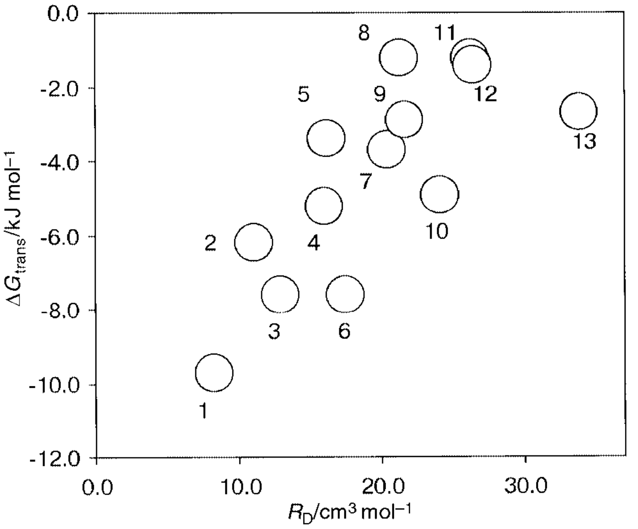

Fig. 3 Correlation between the free energy of the guest transfer from toluene solution to saturated solid clathrate with 2,2′-bis(9-hydroxyfluoren-9-yl)biphenyl (**1**) ΔG_{trans} and the guest molar refraction R_D. Point numbers correspond to the entry numbers of the guests in Table 2.

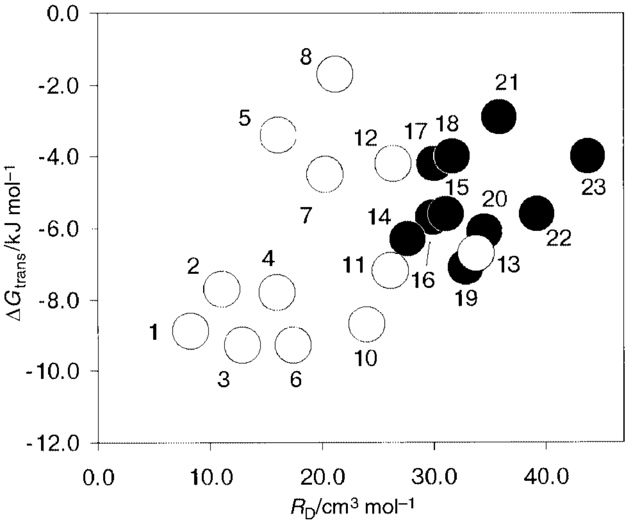

Fig. 4 Correlation between the free energy of the guest transfer from toluene solution to saturated solid clathrate with *tert*-butylcalix[4]arene (**2**) ΔG_{trans} and the guest molar refraction R_D. Point numbers from 1 to 15 correspond to the entry numbers in Table 2. Higher numbered points correspond to the guests: 16 hexane, 17 pinacolone, 18 *tert*-butyl acetate, 19 anisole, 20 *n*-heptane, 21 *o*-xylene, 22 *n*-octane and 23 *n*-nonane. The points for guests, for which significant guest inclusion by host **1** is observed, are marked by empty circles.

Structure–property relationships

In order to estimate the contributions of the hydrogen bonding and the packing effect, the transfer free energy ΔG_{trans} was correlated with the guest molar refraction R_D and the data on the free energy of H-bond formation ΔG_H in CCl$_4$ solution between the guest and the proton-donor compound taken as a model of host **1**. The largest number of ΔG_H values can be calculated from the H-bond stability constants for methanol and phenol.[25] So ΔG_H values of these alcohols obtained by the IR method[25] (Table 2) were used in the correlations given in eqns. (5) and (6).

$$\Delta G_{trans}/\mathrm{kJ\ mol^{-1}} = -5.58 + 0.200R_D + 0.391\Delta G_H^{\mathrm{MeOH}} \qquad (5)$$
$$(r = 0.955,\ \mathrm{RSD} = 0.8)$$

$$\Delta G_{\mathrm{trans}}/\mathrm{kJ\ mol^{-1}} = -5.76 + 0.204R_{\mathrm{D}} + 0.236\Delta G_{\mathrm{H}}^{\mathrm{PhOH}} \quad (6)$$
$$(r = 0.954,\ \mathrm{RSD} = 0.8)$$

The $\Delta G_{\mathrm{trans}}$ values for the studied alcohols were calculated using a doubled coefficient for ΔG_{H}, because one alcohol molecule is able to form two hydrogen bonds as proton-acceptor and proton-donor with host **1**. Since direct IR data for single H-bonds between alcohol molecules are not available, the ΔG_{H} values for H-complexes of methanol and phenol with diethyl ether[25] were used instead. For chloroform the free energy of its H-bond with diethyl ether[25] was taken for both correlations because chloroform can be a proton-donor but not a proton-acceptor. For very weak OH–π complexes between methanol and the aromatic hydrocarbons studied (benzene and toluene) the ΔG_{H} values determined by the IR method[25] seem to be overestimated. They are higher than the corresponding values for phenol (Table 2), which is assumed to be a stronger proton-donor than aliphatic alcohols. For this reason, the $\Delta G_{\mathrm{H}}^{\mathrm{MeOH}}$ values for benzene and toluene were evaluated using the free energy of methanol transfer from CCl_4 to a solution in liquid guest (Table 2). The last value was determined from the ratio of limiting activity coefficients of methanol in liquid guest and CCl_4. The values of $\Delta G_{\mathrm{trans}}$ predicted by eqns. (5) and (6) are given in Table 2. Both correlations for host **1** give practically the same rather good predictions of the $\Delta G_{\mathrm{trans}}$ values.

The intercepts of eqns. (5) and (6) formally correspond to the maximal supramolecular or crystal packing energy gain for a hypothetic guest with zero molecular volume and without host–guest H-bonds. However, the value of $\Delta G_{\mathrm{trans}}$ for such a guest is equal to zero from general considerations. So the dependence of transfer free energy $\Delta G_{\mathrm{trans}}$ on molar refraction R_{D} at a fixed ΔG_{H} value may have a minimum somewhere below the studied range of the guest molar refraction.

The positive value of the second term $0.20R_{\mathrm{D}}$ of eqns. (5) and (6) describes the loss of free energy due to the inclusion into the host crystal lattice of a guest molecule that is larger than the optimal one. Consequently, the addition of one CH_2-group to the guest molecule results in a transfer free energy $\Delta G_{\mathrm{trans}}$ reduction of ~0.9 kJ $\mathrm{mol^{-1}}$. Therefore, for the guests with 6 or more CH_2-groups the additional host–guest H-bonding is necessary to enable the formation of a solid inclusion compound.

The relatively small value 0.39 of the coefficient at $\Delta G_{\mathrm{H}}^{\mathrm{MeOH}}$ in eqn. (5) may be stipulated by two factors: (1) hindrances for optimal H-bonding due to requirements of a tight crystal packing of the solid inclusion compound and (2) the different embranchment at the C-atom bearing the OH-group in host **1** and the model compound methanol. The embranchment effect may be estimated. For example, the free energy of a H-bond between *tert*-butyl alcohol and pyridine in CCl_4 solution (−6.4 kJ $\mathrm{mol^{-1}}$) is equal to ~75% of the free energy of methanol–pyridine hydrogen bonding ($\Delta G_{\mathrm{H}}^{\mathrm{MeOH}} = -8.5$ kJ $\mathrm{mol^{-1}}$) under the same conditions.[25] Eqn. (6) has a lower value of the ΔG_{H} coefficient than eqn. (5) because phenol is a stronger proton-donor than methanol.

Instead of IR data, the free energy of ethanol transfer from tetrachloromethane to infinitely dilute solution in liquid guest $\Delta G^{\mathrm{EtOH}}_{\mathrm{CCl_4 \to G}}$ may be used as a descriptor of the guest hydrogen bonding affinity [eqn. (7)], where $\Delta G^{\mathrm{EtOH}}_{\mathrm{CCl_4 \to G}}$ values are calculated from the ratio of limiting activity coefficients of ethanol in liquid guest and tetrachloromethane. Limiting activity coefficients of ethanol $\gamma^{\infty}_{\mathrm{EtOH/G}}$ were determined earlier[26,27] and partially in the present work. The advantage of eqn. (7) is the

$$\Delta G_{\mathrm{trans}}/\mathrm{kJ\ mol^{-1}} = -5.35 + 0.164R_{\mathrm{D}} + 0.300\Delta G^{\mathrm{EtOH}}_{\mathrm{CCl_4 \to G}} \quad (7)$$
$$(r = 0.946,\ \mathrm{RSD} = 0.9)$$

absence of the problems existing in the investigation of the weak H-bonding by the IR-method. The values of $\Delta G^{\mathrm{EtOH}}_{\mathrm{CCl_4 \to G}}$ can be calculated for a great number of liquid substances for which limiting activity coefficients of ethanol $\gamma^{\infty}_{\mathrm{EtOH/G}}$ are available. Eqn. (7) allows the prediction of the $\Delta G_{\mathrm{trans}}$ values for host **1** as well as eqns. (5) and (6) (Table 2). Interpretation of the coefficients in eqn. (7) is more complicated, because the value $\Delta G^{\mathrm{EtOH}}_{\mathrm{CCl_4 \to G}}$ generally is not the pure free energy of hydrogen bonding.

No good correlations of $\Delta G_{\mathrm{trans}}$ values with the guest molar refraction and the same H-bonding parameters were obtained for the inclusion compounds between host **2** and the same set of guests [correlation coefficient $r \sim 0.67$–0.72 and standard deviation RSD ~2.0–2.1 for eqns. (5)–(7)]. For host **2** with a rigid intramolecular cavity the complementarity of the guest molecule by shape is probably no less an important factor for the inclusion free energy than the guest molecular size.

The combination of eqn. (4) and eqns. (5)–(7) can be used for the prediction of host **1**'s ability to include various vaporous guests in the solid phase, if the guest limiting activity coefficient in toluene $\gamma_{\mathrm{t}}^{\infty}$ and values of ΔG_{H} or $\Delta G^{\mathrm{EtOH}}_{\mathrm{CCl_4 \to G}}$ are known. For example, the predicted ΔG_{c} values for the inclusion compound of cyclohexane with host **1** are +0.8 [eqn. (5)], +0.7 [eqn. (6)] and +0.5 kJ $\mathrm{mol^{-1}}$ [eqn. (7)]. So the inclusion of vaporous cyclohexane by solid host **1** should not take place. Toluene as a guest has small negative predicted values of ΔG_{c} that are equal to the $\Delta G_{\mathrm{trans}}^{(1)}$ values given in Table 2. The experiment shows the absence of significant vapour inclusion for both guests (Fig. 1d, e). Since the ΔG_{H} values do not significantly change in homological rows of proton-acceptors,[25] the size of the largest compound in a homological row, which can be effectively included by solid host **1** from the vapour phase, depends on the type of the guest functional group.

Experimental

Host **1**,[11] supplied by Professor E. Weber (Institute of Organic Chemistry, Freiberg University of Mining and Technology, Freiberg, Germany), and the synthesized[28] host **2** were purified from involatile impurities by multiple crystallizations. Purification of hosts **1** and **2** from volatile impurities was performed by heating at 200 °C during 5 hours in a vacuum (100 Pa). No change of the host's white colour was observed after heating. In the presence of the guests no additional chromatographic peaks were observed in the headspace over the purified hosts. The purity of the studied guests, dried by standard techniques,[29] was tested by GC to be better than 99.5%. Purified samples of each host (100 mg) were placed in 15 ml vials. The liquid organic guest (sorbate) was dosed by means of a microsyringe into the open little glass containers placed inside the vials in order to avoid direct contact between liquid sorbate and the solid host. Immediately afterwards the vials were sealed with polytetrafluoroethylene (0.2 mm) and silicone linings. The sealed samples were equilibrated for 72 hours at 298 K. The equilibration process of host **1** with vapours of acetone and methanol is practically finished after 30 and 60 min, respectively.[30]

Vapour sorption isotherms of organic guests were determined by gas chromatographic headspace analysis as a dependence of the guest uptake by solid host on the guest activity. An automated headspace sampler of original design[31] was used to dose the vapour phase from the sealed vial into a capillary chromatographic column (Fig. 5). In the sampler the principle of electropneumatic dosing[32] is applied. The headspace sampling is performed by switching off and on the supply of carrier (He) to the inlet of chromatographic column and splitter by a computer-controlled electropneumatic valve. The dosing system does not contain any metal and non-heated elements in contact with vapour samples on the way from the vial to the chromatographic column. The total volume and surface of all connecting lines on this pathway are less than 30 μl and 60 $\mathrm{mm^2}$, respectively. The temperature of this pathway including the injection needle is kept near 100 °C by permanent heating. This permits the avoidance of the distortions caused by the sorption on internal parts of the dosing system for compounds with

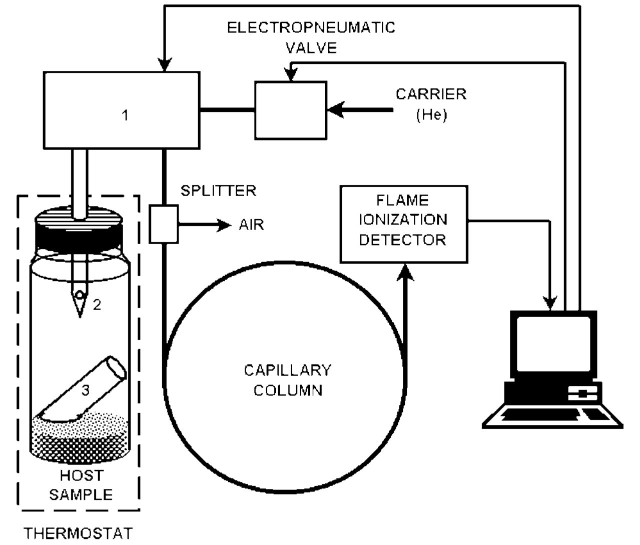

Fig. 5 Schematic representation of the headspace sampler for GC capillary column. 1, external part of the sampler thermostated at the column temperature (usually 100 °C); 2, heated injection needle; 3, glass container with liquid guest.

much lower volatility than those studied in the present work according to the results of the studies of sorption effect in GC headspace analysis.[33] A fused silica chromatographic column (25 m × 0.2 mm, SE-54) and a flame ionisation detector were used. The excessive carrier (He) pressure was 2.4 bar; the dosing time was 0.5 s and the volume of headspace sample was 0.5% of the total headspace volume in the vial.

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 vapour 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 guest uptake was calculated as the difference between the quantity of added guest and its amount in the vapour phase at equilibrium. The obtained isotherms were corrected for the equilibration losses that were estimated in blank experiments without solid host. After each experiment the solid samples were treated as mentioned above to remove the guest molecules and the determination of the sorption isotherm was repeated. 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 a precision ±10% 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 γ^∞ values was tested in each case. In contrast to the samples with solid hosts the equilibrium in hermetically closed 15 ml vials with 1 ml of liquid solution is reached in several minutes. The equilibration process was controlled by the chromatographic peak height or area of the solute in subsequent cycles of headspace GC analysis for the same vial with solution. Correction for the redistribution of some part of the solute to the vapour phase of the vial was made in each case. The theory of determination of limiting activity coefficients by GC headspace analysis was described earlier.[34]

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References

1 A. Fredeslund, R. L. Jones and J. M. Prausnitz, *AIChE J.*, 1975, **21**, 1086.

2 E. Weber, in *Comprehensive Supramolecular Chemistry*, eds. J. L. Atwood, J. E. Davies, D. D. MacNicol and F. Vogtle, Elsevier Science, Oxford, 1996, vol. 6, ch. 17, p. 535.

3 R. Bishop, *Chem. Soc. Rev.*, 1996, **25**, 311.

4 G. D. Andreetti, R. Ungaro and A. Pochini, *J. Chem. Soc., Chem. Commun.*, 1979, 1005.

5 L. J. Barbour, S. A. Bourne, M. R. Caira, L. R. Nassimbeni, E. Weber, K. Skobridis and A. Wierig, *Supramol. Chem.*, 1993, **1**, 331.

6 F. L. Dickert, U. P. A. Bäumler and H. Stathopulos, *Anal. Chem.*, 1997, **69**, 1000; K. D. Schierbaum, T. Weiss, E. U. Thoden van Velzen, J. F. J. Engbersen, D. N. Reinhoudt and W. Göpel, *Science*, 1994, **265**, 1413; F. L. Dickert and A. Haunschild, *Adv. Mater.*, 1993, **5**, 887; F. L. Dickert, A. Haunschild, V. Kuschow, M. Reif and H. Stathopulos, *Anal. Chem.*, 1996, **68**, 1058; P. Nelli, E. Dalcanale, G. Faglia, G. Sberveglieri and P. Soncini, *Sens. Actuators, B*, 1993, **13–14**, 302.

7 (*a*) M. R. Jarrett and H. O. Finklea, *Anal. Chem.*, 1999, **71**, 353; (*b*) J. Reinbold, K. Cammann, E. Weber, T. Hens and C. Reutel, *J. Prakt. Chem.*, 1999, **341**, 252.

8 F. L. Dickert and O. Schuster, *Adv. Mater.*, 1993, **5**, 826; F. L. Dickert and O. Schuster, *Mikrochim. Acta*, 1995, **119**, 55.

9 J. W. Grate, S. J. Patrash, M. H. Abraham and C. M. Du, *Anal. Chem.*, 1996, **68**, 913.

10 L. R. Nassimbeni, in *Molecular Recognition and Inclusion*, ed. A. W. Coleman, Kluwer, Dordrecht, 1998, p. 135; K. Kubono, N. Asaka, T. Taga, S. Isoda and T. Kobayashi, *J. Mater. Chem.*, 1994, **4**, 291; M. R. Caira, A. Horne, L. R. Nassimbeni and F. Toda, *Supramol. Chem.*, 1998, **9**, 231; M. R. Caira, A. Horne, L. R. Nassimbeni and F. Toda, *J. Chem. Soc., Perkin Trans. 2*, 1997, 1717; M. R. Caira, A. Horne, L. R. Nassimbeni and F. Toda, *J. Mater. Chem.*, 1997, **7**, 2145.

11 E. Weber, K. Skobridis, A. Wierig, S. Stathi, L. R. Nassimbeni and M. L. Niven, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 606.

12 (*a*) V. V. Gorbatchuk, I. S. Antipin, A. G. Tsifarkin, B. N. Solomonov and A. I. Konovalov, *Mendeleev Commun.*, 1997, 215; (*b*) V. V. Gorbatchuk, A. G. Tsifarkin, I. S. Antipin, B. N. Solomonov and A. I. Konovalov, *J. Inclusion Phenom. Macrocyclic Chem.*, 1999, **35**, 389.

13 T. Dewa, K. Endo and Y. Aoyama, *J. Am. Chem. Soc.*, 1998, **120**, 8933.

14 F. L. Dickert, M. Keppler and G. K. Zwissler, *Ber. Bunsenges. Phys. Chem.*, 1996, **100**, 1312; F. L Dickert and M. Keppler, *Adv. Mater.*, 1995, **7**, 1020.

15 (*a*) A. Coetzee, L. R. Nassimbeni and K. Achleitner, *Thermochim. Acta*, 1997, **298**, 81; (*b*) L. J. Barbour, M. R. Caira and L. G. Nassimbeni, *J. Chem. Soc., Perkin Trans. 2*, 1993, 2321.

16 B. Xu and T. M. Swager, *J. Am. Chem. Soc.*, 1995, **117**, 5011.

17 M. C. Caira, A. Coetzee, L. R. Nassimbeni, E. Weber and A. Wierig, *J. Chem. Soc., Perkin Trans. 2*, 1995, 281; M. C. Caira, A. Coetzee, L. R. Nassimbeni and F. Toda, *J. Chem. Res.* (*S*), 1996, 280; L. J. Barbour, M. R. Caira, L. R. Nassimbeni, A. Wierig and E. Weber, *Supramol. Chem.*, 1995, **5**, 153.

18 (*a*) N. Hayashi, Y. Mazaki and K. Kobayashi, *Adv. Mater.*, 1994, **6**, 654; (*b*) R. Ungaro, A. Pochini, G. D. Andreetti and V. Sangermano, *J. Chem. Soc., Perkin Trans. 2*, 1984, 1979.

19 (*a*) M. R. Caira, L. R. Nassimbeni, N. Winder, E. Weber and A. Wierig, *Supramol. Chem.*, 1994, **4**, 135; (*b*) R. Ungaro, A. Pochini, G. D. Andreetti and P. Domiano, *J. Chem. Soc., Perkin Trans. 2*, 1985, 197; (*c*) E. B. Brouwer, J. A. Ripmeester and G. D. Enright, *J. Inclusion Phenom. Mol. Recognit.*, 1996, **24**, 1; (*d*) E. B. Brouwer, G. D. Enright, C. I. Ratcliffe, G. A. Facey and J. A. Ripmeester, *J. Phys. Chem. B*, 1999, **103**, 10604; (*e*) E. B. Brouwer, G. D. Enright and J. A. Ripmeester, *J. Am. Chem. Soc.*, 1997, **119**, 5404.

20 J. T. Edsall and H. Gutfreund, *Biothermodynamics*, Wiley, New York, 1983.

21 E. Weber, A. Wierig and K. Scobridis, *J. Prakt. Chem.*, 1996, **338**, 553.

22 (*a*) K. Beketov, E. Weber, B. T. Ibragimov, J. Seidel and K. Köhnke, *Adv. Mater.*, 2000, **12**, 664; (*b*) M. R. Caira, *Des. Org. Solids*, 1998, **198**, 163.

23 V. V. Gorbatchuk, A. G. Tsifarkin, I. S. Antipin, B. N. Solomonov and A. I. Konovalov, *Mendeleev Commun.*, 1999, 11.

24 B. N. Solomonov, A. I. Konovalov, V. B. Novikov, A. N. Vedernikov, M. D. Borisover, V. V. Gorbatchuk and I. S. Antipin, *Zh. Obshch. Khim.*, 1984, **54**, 1622; B. N. Solomonov and A. I. Konovalov, *Usp. Khim.*, 1991, **60**, 45.

25 M. D. Joesten and L. J. Schaad, *Hydrogen Bonding*, Marcel Dekker, Inc., New York, 1974.

26 J. H. Park, A. Hussam, P. Couasnon, D. Fritz and P. W. Carr, *Anal. Chem.*, 1987, **59**, 1970.

27 V. V. Gorbatchuk, S. A. Smirnov, B. N. Solomonov and A. I. Konovalov, *Zh. Obshch. Khim.*, 1990, **60**, 1441.

28 C. D. Gutsche, M. Iqbal and D. Stewart, *J. Org. Chem.*, 1986, **51**, 742.

29 D. D. Perrin, W. L. F. Armarego and D. R. Perrin, *Purification of Laboratory Chemicals*, Pergamon Press, Oxford, 1980.

30 J. Seidel, G. Wolf and E. Weber, *Thermochim. Acta*, 1996, **271**, 141.

31 V. V. Gorbatchuk, S. A. Smirnov, B. N. Solomonov and A. I. Konovalov, *Zh. Obshch. Khim.*, 1990, **60**, 1200.

32 B. Kolb, P. Pospisil, T. Borath and M. Auer, *J. High Resolut. Chromatogr. Chromatogr. Commun.*, 1979, **2**, 283.

33 K. Schoene, W. Böhmer and J. Steinhanses, *Fresenius' Z. Anal. Chem.*, 1984, **319**, 903.

34 A. Hussam and P. W. Carr, *Anal. Chem.*, 1985, **57**, 793.