Nonlinear Structure−Affinity Relationships for Vapor Guest Inclusion by Solid Calixarenes

**Valery V. Gorbatchuk,*,† Alexej G. Tsifarkin,† Igor S. Antipin,† Boris N. Solomonov,†
Alexander I. Konovalov,† Pavel Lhotak,‡ and Ivan Stibor‡**

*Contribution from the Department of Chemistry, Kazan State University, Kremlevskaya 18,
Kazan, 420008, Russia, and the Department of Organic Chemistry, Institute of Chemical Technology,
Technická 5, 166 28 Prague 6, Czech Republic*

*Received: November 29, 2001; In Final Form: March 14, 2002*

The structure−affinity relationships were studied for the guest inclusion parameters of solid *tert*-butylthiacalix-[4]arene (**1**) and *tert*-butylcalix[4]arene (**2**). The inclusion stoichiometry and inclusion free energy were calculated by the sorption isotherms obtained for guest vapor−solid host systems by the static method of headspace gas chromatographic analysis at 298 K. The obtained sorption isotherms have an inclusion threshold for guest thermodynamic activity corresponding to the phase transition between the initial host phase and the phase of inclusion compound. Unlike *tert*-butylcalix[4]arene, its thia analogue having a larger molecular bowl is able to bind only initial members of each studied homological series. All inclusion compounds of **1** formed upon host saturation by guest vapors have the same 1:1 stoichiometry, while for **2** the inclusion stoichiometry depends on the guest molecular size. A linear correlation between the inclusion free energy (standard state: infinitely dilute guest solution in toluene) and the guest size parameter (molar refraction) was observed for **1**: ΔG_{trans} (kJ mol^{-1}) = −12.24 + 0.568MR_D ($n = 7$, $r = 0.972$, RSD = 0.6). This correlation is regarded as a part of the V-like structure−affinity relationship with a minimum for a guest that is complementary to the host cavity.

Introduction

Molecular recognition in solid-phase host−guest binding is generally a more complex phenomenon than solvation selectivity in liquids. For liquid solutions the linear structure−energy relationship is usually observed in the absence of specific solute−solvent coordination or for simple solvent−solute interaction with the single donor−acceptor or H-bond.[1] Molecular recognition in the supramolecular systems is based on host−guest structural complementarity,[2] which is essentially a nonlinear property. This nonlinearity can be found in the discrete changes of the stoichiometry of host−guest inclusion compounds with variation of the guest molecular structure.[3−7] More guest and host structural features are relevant for the guest inclusion than for solvation of organic compounds. For liquid solutions the knowledge of the solute and solvent molecular group composition is often enough for the prediction of solvation parameters.[8] The guest inclusion parameters depend, besides, on the host shape and symmetry, conformational flexibility/ rigidity, and configuration of the H-bonding network.[3,9] The knowledge of parameters of guest molecular recognition by solid hosts can help to improve the host molecular design, especially when the full structural picture of the guest inclusion is not available.

An effective strategy for the study of the host structural influence on guest inclusion can be the examination of the structure−affinity relationships for hosts with a few different structural features. This approach was realized consistently only for the stoichiometry of the inclusion compounds.[3,4,10−12] The ability of the inclusion compound to crystallize from the host solution in liquid guest is often used as a qualitative host−guest affinity parameter.[3,4,10−12] Another related parameter is the difference between the guest boiling temperature and the decomposition temperature of the inclusion compounds.[13] Estimation of the guest binding energy is not a simple problem for the inclusion process due to its high cooperativity,[14−17] sensitivity to temperature,[18−20] and the presence of other components.[15,21−25] These effects, if not controlled, can considerably distort the relationship between the obtained inclusion parameters and the host and guest molecular structure.
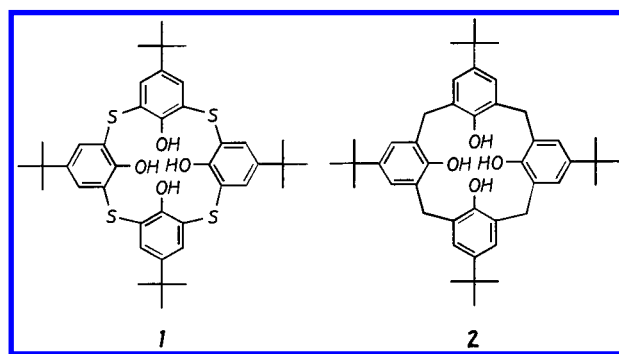

In this study we examined the structure−affinity relationships of two solid receptors: *tert*-butylthiacalix[4]arene (**1**) and *tert*-butylcalix[4]arene (**2**). Both hosts are known to form a number of crystalline stoichiometrical inclusion compounds with the guest inside the host molecular cavity.[7,26−33] Host **1** has a larger bowl diameter of 7.8 Å (the distance between the 1,3-bridge atoms) than host **2** (7.2 Å).[32] Comparison of the host coalescence temperatures estimated by ^{1}H NMR data in CDCl$_3$ solutions shows that thiacalixarene **1** is more flexible than calixarene **2**.[34] Despite their similar molecular structures, these hosts have

* Corresponding author: e-mail valery.gorbatchuk@ksu.ru; phone 7 8432 315509; fax 7 8432 380994.
† Kazan State University.
‡ Institute of Chemical Technology.
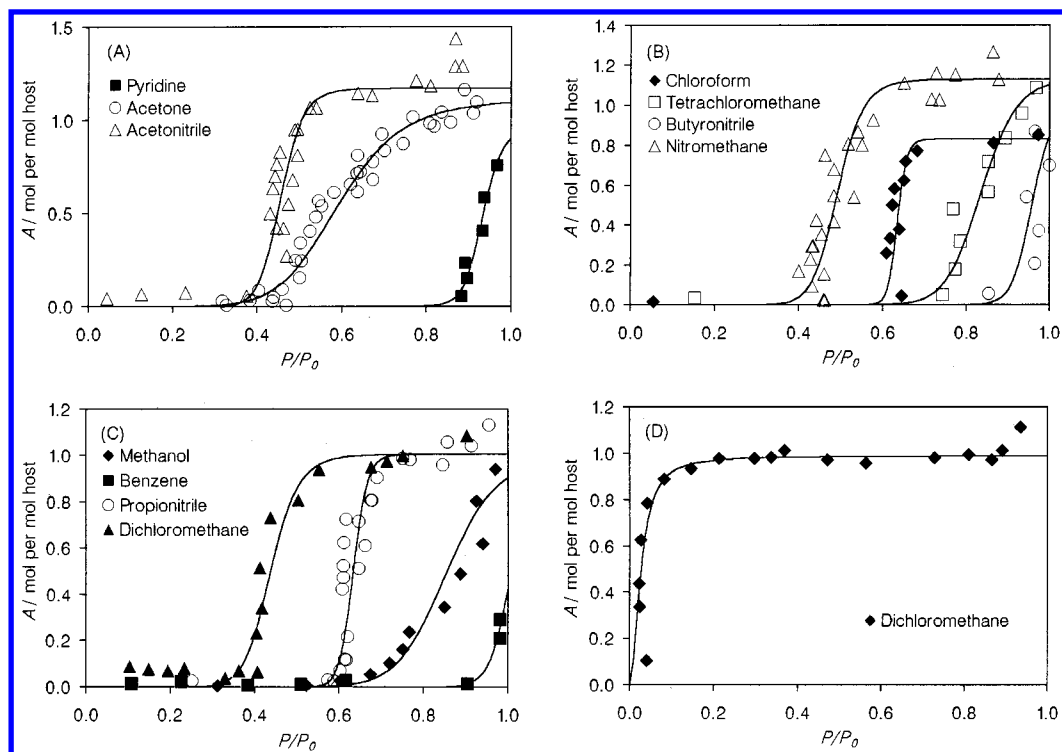
Figure 1. Vapor sorption isotherms at 298 K for solid hosts: (A−C) for solid *tert*-butylthiacalix[4]arene (**1**) and (D) for solid *tert*-butylcalix[4]-arene (**2**). The lines are the sorption isotherms calculated from the Hill equation (eq 1).

different packing of their inclusion compounds. The host−guest compounds of calixarene **1** have channel-type packing with a head-to-tail host orientation.[32] Host **2** has brick-type packing of its inclusion compounds, where the host has a head-to-head orientation.[29,30,33] For both hosts the inclusion compounds with other packing patterns are not stable or were not prepared at room temperature.[20,35] In the present work the solid inclusion compounds of hosts **1** and **2** were obtained by vapor saturation of solid host under strictly comparable conditions, and simple structure−property relationships of host−guest binding in the solid phase were revealed.

Results and Discussion

Vapor Sorption Isotherms. The inclusion properties of solid hosts **1** and **2** were studied for the same set of guests with various molecular sizes and group compositions. The obtained vapor sorption isotherms are shown in Figure 1. Host **1** does not bind the vapors of aliphatic alcohols larger than methanol or of aliphatic nitriles and ketones larger than propionitrile and acetone, respectively. It does not bind also the vapors of dioxane, pyridine, or any hydrocarbons. For host **2** the vapor sorption isotherm of dichloromethane was determined in addition to those reported earlier.[5,6,36,37] The attempt to determine the vapor sorption isotherm of nitromethane on host **2** did not show significant binding in the guest activity range of 0−0.9.

As well as most isotherms obtained earlier for calixarene **2**[5,6,36,37] the sorption isotherms obtained in this work have a significant binding threshold for guest activity $a_{thr} = (P/P_0)_{thr}$. Up to this activity a weak host−guest affinity is observed. Above the threshold activity a_{thr}, the guest uptake A 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. The sharp increase of the guest uptake A at $(P/P_0) > 0.88$ observed on some isotherms corresponds to the formation of liquid phase in the system. The absence of

significant guest binding below the inclusion threshold a_{thr} means that the studied host does not have significant porosity.[17] Hence, no capillary condensation in the micropores can be expected for studied systems at low guest activities $P/P_0 < 0.88$, where host saturation by guest vapor is observed.

The existence of the guest inclusion threshold is usually interpreted as a result of the phase transition of the solid host phase upon guest inclusion.[15−17,37,38] The powder X-ray diffractograms of the initial host and of the host saturated by guest vapors are often used for justification of this assumption.[15,17] The specific shape of the sorption isotherm, with zero slope above the guest activity threshold, is also sufficient experimental evidence of the solid-phase transition.[17] A decrease of the isotherm slope to a zero value above the guest threshold activity a_{thr} means that there is no liquid phase in the system with nonporous sorbent at the guest activity below this saturation part. Such a conclusion was made even for the analogous "knee" of water adsorption isotherms on the essentially microporous activated carbons.[39] According to the Gibbs phase rule for a system with two components (host and guest, $c = 2$) and a fixed temperature, we have $f = c − p + 1 = 2 − p + 1 = 0$ at the guest activity threshold. It gives the existence of three phases at the threshold point, $p = 3$. One of them is the gas phase. The other two phases are solid, if there is no liquid phase in the system. Above and below the guest threshold activity a_{thr} there is only one solid phase in the system according to the same rule.

For a description of such sorption (inclusion) behavior, the Hill equation can be used:[5,6,15]

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

where S = inclusion stoichiometry, C = sorption constant, N = cooperativity constant, and A = experimentally determined solid-phase composition (moles of guest per mole of host). The points of sorption isotherms on the second cooperative increase

Vapor Guest Inclusion by Solid Calixarenes

J. Phys. Chem. B, Vol. 106, No. 23, 2002 **5847**

TABLE 1: Approximation Parameters of Vapor Sorption Isotherms for Solid *tert*-butylthiacalix[4]arene (1) and *tert*-butylcalix[4]arene (2) at 298 K[a]

		host **1**				host **2**
entry	guest	$a_{0.5S}$	S	N	δ^b	$a_{0.5S}$
1	MeOH	0.86	-; 1[c]	14[d]	0.03[d]	0.61[e]
2	MeCN	0.46	1.17	17	0.03	0.20[e]
3	MeNO$_2$	0.49	1.13	16	0.05	f
4	EtCN	0.63	1.01	39	0.03	0.124[e]
5	Me$_2$CO	0.59	1.11	8	0.04	0.47[e]
6	CH$_2$Cl$_2$[g]	0.44	1.00, 1[c]	14	0.05	0.027
7	CHCl$_3$	0.63	0.83; 1[c]	58	0.02	0.40[e]
8	CCl$_4$	0.84	1.13	20	0.03	0.204[e]

[a] The estimated error of $a_{0.5S}$ is 10%; the error of *S* is 5%; parameters *S* and *N* of the sorption isotherms of host **2** are available in ref 6. [b] δ is standard deviation of the approximation for the shortest distances between experimental points and the line calculated by eqs 1 and 2. [c] Reference 32. [d] Calculated at the fixed stoichiometry value *S* = 1 mol of guest/mol of host. [e] $a_{0.5S}$ values were calculated from (ln *C*)/*N* values in ref 6. [f] Nitromethane vapor is not included by host **2** in the guest activity range of 0−0.9. [g] For the system **2** + CH$_2$Cl$_2$ the next parameters were obtained in the present work: *S* = 0.99, *N* = 2.0, δ = 0.02.

of the guest uptake above (P/P_0) > 0.88 were not included in the approximation, because they do not correspond to the guest inclusion as mentioned above. The approximation of the obtained sorption isotherms by the Hill equation gives two stable solutions: the stoichiometry *S* and the ratio (ln *C*)/*N*. The cooperativity constant *N* and the sorption constant *C* are determined with relatively large errors, especially for isotherms with practically vertical parts at the inclusion threshold. These errors are compensated in the ratio (ln *C*)/*N*. The last value directly relates to the threshold activity of the guest at the extent of host saturation *A* = 0.5*S*:

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

The values of the approximation parameters *S*, *N*, and $a_{0.5S}$ calculated by eqs 1 and 2 are summarized in Table 1. In addition, the values of threshold activity $a_{0.5S}$ calculated from (ln *C*)/*N* values for host **2**[6] are given in Table 1.

For all studied systems the cooperativity constant *N* has a much larger value than the inclusion stoichiometry *S* (Table 1). It means that more host molecules participate in the guest inclusion below saturation than are required for the formation of the stoichiometrical compound. The same situation was observed also in earlier studies of vapor guest−solid host inclusion.[5,6,15,36,37] This property may be regarded as intrinsic to the formation of lattice inclusion hosts, where the host packing changes upon guest binding are more important than direct host−guest coordination.

Comparison of the binding threshold activity $a_{0.5S}$ for the studied hosts reveals the difference in their binding properties. Some guests have very high binding affinity for host **2** and no affinity for host **1**. For example, the vapor sorption isotherms of benzene and pyridine on host **2** have (ln *C*)/*N* values corresponding to the binding thresholds $a_{0.5S}$ of 0.032 and 0.019, respectively.[6,37] Solid host **1**, having relatively small structural distinctions from host **2**, does not bind these guests from the vapor phase. The isotherms of pyridine and benzene sorption by host **1** have threshold values $a_{0.5S}$ > 0.90, where guest inclusion cannot be distinguished from the formation of liquid phase in the studied systems (Figure 1). Host **1** has higher inclusion thresholds for guest activity than host **2** in all cases except nitromethane (Table 1).
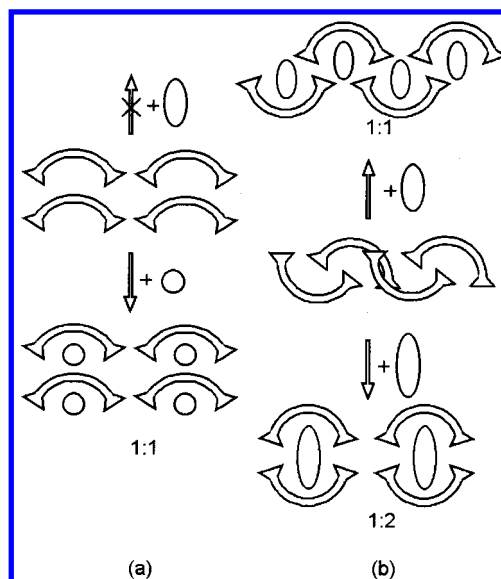
Figure 2. Schematic presentation of the stoichiometry−guest size relationship for the guest binding by host **1** (a) and by host **2** (b) at 298 K. Schemes of the inclusion compounds correspond to X-ray data from ref 32 for host **1**, and from ref 7, 26−31 for host **2**. Self-included structure of the empty host **2** is described in ref 7. The supposed packing of the empty host **1** is the extrapolation from the packing of its inclusion compounds.[32]

Inclusion Stoichiometry−Guest Size Relationship. The inclusion stoichiometries *S* determined in the vapor sorption experiment correspond to 1:1 composition for inclusion compounds of host **1** and for compound **2·**CH$_2$Cl$_2$ (Table 1). Available X-ray data[32] on the stoichiometry of the studied inclusion compounds crystallized from host **1** solutions in liquid guests are also given in Table 1. There is agreement between the stoichiometry obtained in the present work and the results of the X-ray method. Inclusion compounds of host **2** with the same guests also have 1:1 inclusion stoichiometry with the exception of methanol (*S* = 2)[6] and nitromethane (no significant binding). However, the general dependence of the stoichiometry *S* on the guest molecular size for host **2** is essentially more complicated than for host **1**. Solid host **1** binds a limited number of guests and cannot form 2:1 and 1:2 inclusion compounds upon saturation by guest vapors. Guest binding ability of solid host **2** is much wider under the same conditions. It binds at least 23 organic compounds (including 22 guests studied earlier[5,6,37]) with different molecular sizes (C$_1$−C$_9$) and group composition. The inclusion stoichiometry for host **2** fits the stepwise descending dependence (from 2:1 to 1:2 guest/host molar ratio) on the guest molar refraction MR_D.[5,6] Molar refraction MR_D is an effective molecular size parameter for the correlation with thermodynamic parameters of the "gas → infinitely dilute solution" transition of nonelectrolytes according to our studies of solvation thermodynamics.[40,41]

The different stoichiometry−guest size relationships for inclusion compounds of hosts **1** and **2** may be stipulated by the different packing patterns, both in their free-of-guest forms and in the inclusion compounds. The scheme of this structural effect is given in Figure 2. Self-included empty host **2** endures only slight rotation (28°) and translation movements at 1:1 guest inclusion.[7] Host **2** does not make much larger movements to include the larger guests with 1:2 (guest/host) stoichiometry (Figure 2). On the contrary, the transformation of 1:1 inclusion compounds of host **1** to 1:2 compounds requires the complete interconversion of the host molecules (Figure 2). The higher

TABLE 2: Free Energies of Guest Transfer to Saturated Inclusion Compounds 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	MR_D (cm³ mol⁻¹)	$\gamma_t{}^\infty$	$\Delta G_c{}^1$ (kJ mol⁻¹) exp	$\Delta G_c{}^1$ (kJ mol⁻¹) calc[b]	$\Delta G_c{}^2$ (kJ mol⁻¹) exp	$\Delta G_{trans}{}^1$ (kJ mol⁻¹) exp	$\Delta G_{trans}{}^1$ (kJ mol⁻¹) calc[c]	$\Delta G_{trans}{}^2$ (kJ mol⁻¹) exp
1	MeOH	8.3	21.8[d]	−0.4	0.1	−1.2[d]	−8.0	−7.5	−8.9[d]
2	MeCN	11.1	4.33[d]	−1.9	−2.3	−4.0[d]	−5.6	−5.9	−7.7[d]
3	MeNO₂	12.6	3.81[e]	−1.8	−1.8	*f*	−5.1	−5.1	*f*
4	EtCN	16.0	2.92[d]	−1.1	−0.5	−5.2[d]	−3.8	−3.2	−7.8[d]
5	Me₂CO	16.1	1.82[e]	−1.3	−1.6	−1.9[e]	−2.8	−3.1	−3.4[e]
6	CH₂Cl₂	16.3	0.98	−2.0	−3.1	−8.9	−1.9	−3.0	−8.8
7	CHCl₃	21.3	0.80[e]	−1.1	−0.7	−2.3[e]	−0.6	−0.1	−1.7[e]
8	CCl₄	26.4	1.15[e]	−0.4	3.1	−3.9[e]	−0.8	2.8	−4.2[e]
9	EtOH	12.9	17.4[d], 15.4[g]	*f*	2.2	−2.3[d]	*f*	−4.9	−9.3[d]
10	PrCN	20.4	1.87[e]	*f*	0.9	−2.9[e]	*f*	−0.7	−4.5[e]
11	pyridine	24.1	1.28[e]	*f*	2.0	−8.1[e]	*f*	1.4	−8.7[e]
12	benzene	26.2	0.97[d]	*f*	2.5	−7.3[d]	*f*	2.6	−7.2[d]

[a] The error of ΔG_c is 0.2 kJ mol⁻¹; the error in $\gamma_t{}^\infty$ is 10%. [b] Calculated by eqs 5 and 10. [c] Calculated by eq 10. [d] Reference 37. [e] Reference 6. [f] No guest vapor inclusion by solid host below guest activity 0.88; for these guests $a_{0.5S} > 0.92$, $\Delta G_c > -0.20$ kJ mol⁻¹, and ΔG_{trans} (kJ mol⁻¹) $> -0.20 - RT \ln \gamma_t{}^\infty$ according to eqs 2, 3 and 5, respectively. [g] Reference 44.

flexibility of host **1** macrocycle[34] in solution obviously does not matter in its solid state at 298 K.

The observed simple guest size−inclusion stoichiometry relationships are not valid if the inclusion compounds obtained under different conditions are taken into consideration. Inclusion compound **2·**1,4-butanediamine crystallized at 70 °C has a higher stoichiometry value $S = 1.75$[20] than many inclusion compounds of this host with smaller guest molecules except methanol.[5,6,26,28,30,31,37] The crystals with essentially different stoichiometry values for the same host−guest pairs were obtained by cooling the hot saturated solutions of host **1** in liquid guests.[34,35] Their stoichiometries generally do not coincide with the data obtained at 298 K by the vapor saturation method in the present work. The effect of the crystallization temperature on the stoichiometry of the inclusion compounds was observed in several works.[18−20] For example, 1:1 stoichiometry of the 2,2′-bis(9-hydroxyfluoren-9-yl)biphenyl·CH₃CN inclusion compound obtained by vapor saturation of the solid host at 25 °C[6] coincides with the stoichiometry of the inclusion compound crystallized at room temperature from the acetonitrile solution.[42] Crystallization from a hot solution of the same host in acetonitrile gave 2:1 (guest/host) inclusion stoichiometry.[10] Extremely slow decomposition kinetics observed for inclusion compounds[17] implies that the crystals obtained near the guest boiling point may be kinetically trapped upon cooling to the ambient temperature. Hence, the correct comparison of the structure−property relationships generally can be made for inclusion compounds prepared at the same temperature. The traces of the other compounds available in the solvent may also have a strong effect on the inclusion stoichiometry even if they are not included in the crystals.[21] Host saturation by guest vapor provides a much better opportunity to obtain inclusion compounds under strictly comparable conditions.

The other possible factor complicating the structure−property relationship for inclusion compounds is direct host−guest coordination by H-bonding or donor−acceptor interaction, which can change the overall configuration of the H-bonding network in the solid phase. No simple stoichiometry−guest size relationship of this kind was observed for 2,2′-bis(9-hydroxyfluoren-9-yl)biphenyl,[6,10] which is able to form H-bonds with proton-acceptor guests.[3,42] The cyclic array of intramolecular H-bonds of the hosts **1** and **2** does not favor the formation of H-bonds with the proton-acceptor guests. No host−guest H-bonds were observed in the host **1** + methanol inclusion compound[32] or in the inclusion compounds of host **2** with such

typical proton acceptors as pyridine,[26] anisole,[27] and nitrobenzene,[28,29] according to the X-ray data. It may be supposed that the host−guest H-bonding has no significant effect on the stoichiometry−guest size relationship for hosts **1** and **2** at 298 K.

Analysis of the stoichiometry−guest size relationship for inclusion compounds of host **1** reveals the difference in the properties of solid hosts and zeolites. These materials are often compared by their selectivity to the sorbate molecular size.[17] For zeolites the specific sorption capacity (sorbate monolayer volume in milliliters per gram) decreases with increasing sorbate molecular size.[43] The inclusion stoichiometry S of host **1** is not changed with a large variation of the guest size (Table 1). Respectively, the binding capacity of this host in milliliters per gram even increases with increasing guest molecular size. The induced fitting of the guest molecules into the flexible host lattice may be the cause of this behavior.
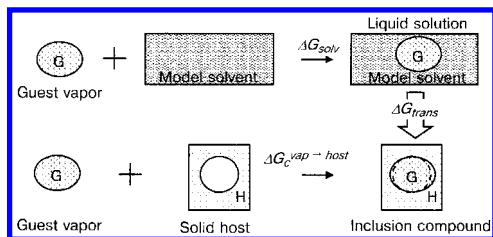
Inclusion Free Energy. The inclusion free energy for the studied systems can be calculated by the integration of the sorption isotherms having a saturation part:

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

where $Y = A/S$ is the host saturation extent. The inclusion free energy ΔG_c is the free energy of transfer of 1 mol of guest from the standard state of pure liquid to the saturated solid phase (inclusion compound). The right part of eq 3 is valid if the ln (P/P_0) value is given by eq 1 as a function of Y. The inclusion free energies ΔG_c obtained for studied systems are summarized in Table 2 together with the earlier obtained ΔG_c data for host **2**[6,37] given for comparison. The inclusion compounds of host **1** have ΔG_c values in the range from −0.4 to −2.0 kJ mol⁻¹. The values of ΔG_c for compounds of host **2** with the same guests are in the range of −1.2 to −8.9 kJ mol⁻¹. According to the ΔG_c values, guest inclusion by calixarene **2** is more favorable than by host **1** for all studied guest compounds with the exception of nitromethane.

The inclusion free energies ΔG_c calculated directly by sorption isotherms as well as the inclusion thresholds $a_{0.5S}$ are not suitable for analysis of the guest structure−binding property relationships because of the nonequivalence of the standard state of pure liquid for different guests. The best approach to this problem is use of the standard state of the guest solution in a model solvent with the same molecular interactions with a guest as in the inclusion compound (Figure 3). The excessive inclusion

Vapor Guest Inclusion by Solid Calixarenes

J. Phys. Chem. B, Vol. 106, No. 23, 2002 **5849**

Figure 3. Inclusion free energy ΔG_{trans} from the standard state of infinitely dilute solution in a model solvent with the same guest−shell molecular interactions as in the inclusion compound.

free energy for this standard state is given by

$$\Delta G_{\text{trans}} = \Delta G_c^{\text{vap}\rightarrow\text{host}} - \Delta G_{\text{solv}}^{\text{(model)}} = \Delta G_c - RT \ln \gamma_m^{\infty} \quad (4)$$

where $\Delta G_c^{\text{vap}\rightarrow\text{host}}$ and $\Delta G_{\text{solv}}^{\text{(model)}}$ are the free energies of the guest transfer from the ideal gas at $P = 101\,325$ Pa to the saturated inclusion compound and to the infinitely dilute solution in a model solvent, respectively, and γ_m^{∞} is a limiting activity coefficient of the guest in a model solvent. Toluene, having an aromatic π-system like the cavities of both studied hosts, is a suitable choice of standard solvent. The free energy of the guest transfer from toluene solution to the saturated inclusion compound ΔG_{trans} was used for analysis of supramolecular host−guest interactions:[6,37]

$$\Delta G_{\text{trans}} = \Delta G_c - RT \ln \gamma_t^{\infty} \quad (5)$$

where γ_t^{∞} is the limiting activity coefficient of the guest in toluene. The limiting activity coefficients of the studied guests γ_t^{∞} in toluene determined by the headspace method are given in Table 2.

If an adequate model solvent exists for a host, the maximal host−guest binding affinity by the inclusion free energy ΔG_{trans} and by the inclusion threshold activity $a_{0.5S}$ can be calculated for a given guest. For this calculation the value of ΔG_{trans} can be presented as a difference between free energies of guest−medium interactions ΔG_{int} and cavity formation ΔG_{cav} in solid host and in model solvent:

$$\Delta G_{\text{trans}} = \Delta G_c^{\text{vap}\rightarrow\text{host}} - \Delta G_{\text{solv}}^{\text{(model)}} =$$
$$[\Delta G_{\text{int}}^{\text{(host)}} + \Delta G_{\text{cav}}^{\text{(host)}}] - [\Delta G_{\text{int}}^{\text{(model)}} + \Delta G_{\text{cav}}^{\text{(model)}}]$$

The free energies of pairwise molecular interactions with a guest in inclusion compound and in standard solution are equal, $\Delta G_{\text{int}}^{\text{(host)}} = \Delta G_{\text{int}}^{\text{(model)}}$, according to the definition of the model solvent. So these contributions cancel out, leaving only the difference of free energies of cavity formation in solid host $\Delta G_{\text{cav}}^{\text{(host)}}$ and in model solvent $\Delta G_{\text{cav}}^{\text{(model)}}$:

$$\Delta G_{\text{trans}} = \Delta G_{\text{cav}}^{\text{(host)}} - \Delta G_{\text{cav}}^{\text{(model)}} \quad (6)$$

The free energy of cavity formation for solution or inclusion in any medium is an essentially positive value, $\Delta G_{\text{cav}} > 0$. So eq 6 can be written as

$$\Delta G_{\text{trans}} \geq -\Delta G_{\text{cav}}^{\text{(model)}} \quad (7)$$

This relationship (eq 7) means that the lower limit of the ΔG_{trans} values does not depend on the specific host structure but is defined by the guest size and by the solvent−solvent interactions in the model liquid medium. This limit can be reached if the host cavity is not changed upon guest inclusion. Besides, eq 7
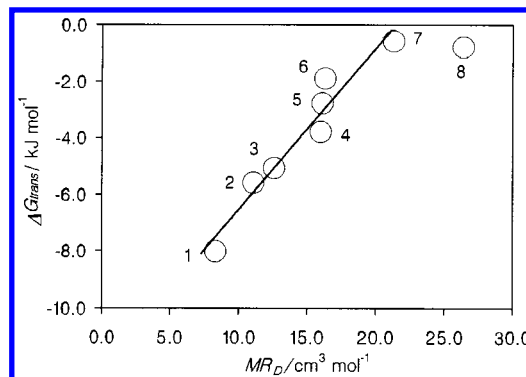
Figure 4. Correlation between the inclusion free energies ΔG_{trans} of *tert*-butylthiacalix[4]arene (**1**) and the guest molar refraction MR_D. Standard state is infinitely dilute solution of guest in toluene, $T = 298$ K. Point numbers correspond to the entry numbers of the guests in Table 2.

in combination with eqs 3 and 4 defines the lower limit of the guest inclusion threshold in any host for which the model solvent could be found:

$$a_{0.5S} \geq \exp[\ln \gamma_m^{\infty} - \Delta G_{\text{cav}}^{\text{(model)}}/RT] \quad (8)$$

The simplest evaluation of the cavity formation energy for solutions of nonelectrolytes can be made by the solvent vaporization energy.[45] For this evaluation the vaporization free energy of the model solvent toluene [$\Delta G_{\text{vap}} = -RT \ln (P_0/101325 \text{ Pa}) = 8.1 \text{ kJ mol}^{-1}$] should be corrected on the term of ideal gas expansion $RT \ln (RT/V_0)$, where $P_0 = 3.79$ kPa is the toluene-saturated vapor pressure at 298 K[46] and $V_0 = 106.3$ mL mol^{-1} is the toluene molar volume. So for toluene guest in toluene solvent, the value of $\Delta G_{\text{cav}}^{\text{(toluene)}}$ is equal to

$$\Delta G_{\text{cav}}^{\text{(toluene)}} \approx \Delta G_{\text{vap}} + RT \ln (RT/V_0) = 22 \text{ kJ mol}^{-1} \quad (9)$$

The estimates obtained by eqs 7−9 are more interesting for small guests such as methanol and acetonitrile, which have inclusion free energies ΔG_{trans} near 30−40% of $\Delta G_{\text{cav}}^{\text{(toluene)}}$ value in eq 9 (Table 2). Molar volume and molar refraction of methanol are equal to 39.2% and 27% of toluene molar volume and molar refraction, respectively. Hence, if the cavity formation free energy for a guest in toluene $\Delta G_{\text{cav}}^{\text{(toluene)}}$ is proportional to these molecular size parameters, the inclusion free energy ΔG_{trans} and threshold activity $a_{0.5S}$ of methanol for both hosts **1** and **2** (Tables 1 and 2) are quite near the limits imposed by eqs 7 and 8. In this case one cannot expect the inclusion threshold value $a_{0.5S}$ to be essentially lower than 0.6 for inclusion of methanol in any host effectively modeled by toluene. The same calculation for acetonitrile gives $a_{0.5S} > 0.05$. The observed experimental values of $a_{0.5S}$ for these guests (Table 1) do not exceed these limits. Larger guests do not come so close to the limits imposed by eqs 7 and 8 because their inclusion free energy ΔG_{trans} has less negative or the same value, and the value of $\Delta G_{\text{cav}}^{\text{(toluene)}}$ is higher. The limits (eqs 7 and 8) correspond to the maximal contribution of general molecular interactions in standard solution that can remain uncompensated upon guest transfer to the host preorganized cavity.

Guest Structure−Inclusion Free Energy Relationship. For the analysis of structure−affinity relationships, the inclusion free energies ΔG_{trans} of host **1** are plotted vs guest molar refraction MR_D in Figure 4. For host **2** and 22 guests these two parameters were correlated earlier.[6] Despite the similar molecular structure of hosts **1** and **2**, the correlations between ΔG_{trans} and MR_D are quite different. Host **2** does not have even a weak general

tendency in correlation between these two parameters.[6] No multiparameter linear relationship like LSER[1] (linear structure–energy relationship) was found for this host.[6] The value of ΔG_{trans} obtained in the present work for solid host **2** + CH_2Cl_2 vapor (Table 2) and the observed absence of nitromethane vapor binding by this host do not make this relationship simpler. On the contrary, practically linear correlation is observed in the case of host **1** for all studied guests with significant binding except tetrachloromethane, which was not included in the regression:

$$\Delta G_{\text{trans}} \ (\text{kJ mol}^{-1}) = -12.24 + 0.568 MR_D \qquad (10)$$

where $n = 7$, $r = 0.972$, and RSD = 0.6. The general linear relationship (eq 10) for both proton-donor and proton-acceptor guests proves the absence of significant H-bonding between the studied guests and host 1.

The intercept of eq 10 formally corresponds to the maximal supramolecular or crystal packing energy gain for a hypothetical guest with zero molecular volume. However, the value of ΔG_{trans} for such a guest is equal to zero because it cannot interact both with host and with standard solvent. So the dependence of the inclusion free energy ΔG_{trans} on molar refraction MR_D must be V-like: nonlinear with a minimum at $MR_D \leq 8.3 \ \text{cm}^3 \ \text{mol}^{-1}$ (below the molar refraction of methanol). This minimum point on the correlation of ΔG_{trans} vs MR_D corresponds to the maximal supramolecular effect at the guest inclusion.

The positive slope 0.568 of the ΔG_{trans} vs MR_D plot (Figure 4, eq 10) describes the loss of the guest inclusion free energy compared with the value of ΔG_{trans} for a guest corresponding to the minimum of this relationship. Hence, the addition of one CH_2 group to the guest molecule results in a decrease in the supramolecular effect (ΔG_{trans} becomes less negative) of $\sim$2.5 kJ mol^{-1}. This coefficient may be considered as a parameter of the host packing flexibility. Indeed, it should be equal to 0 if the inclusion flexibility of host is equal to the solvation flexibility of the model solvent. For solid host **2** a zero slope of the dependence of inclusion free energy ΔG_{trans} on the guest molar refraction MR_D was observed for homological series of the studied alcohols (methanol ≈ ethanol ≈ 1-propanol) and for the first two aliphatic nitrile homologues[6] (Table 2). But butyronitrile has a much more positive value of the inclusion free energy ($\Delta G_{\text{trans}} = -4.5$ kJ mol^{-1})[6] than the other two studied nitriles (Table 2): acetonitrile ≈ propionitrile < butyronitrile. Hence, the minimum with zero slope of the structure–affinity relationship ΔG_{trans} vs MR_D probably takes place for host **2** in the studied range of guest molecular sizes, and the preorganized cavities of this host are larger than the cavities of solid host **1**. It explains the ability of solid host **2** to bind a larger variety of guests both by size and by shape.

The guest shape is another molecular recognition factor, which can break a general guest size–inclusion free energy relationship into several separate trends. The shape effect can be seen for host **2**. For example, the inclusion affinity of rodlike acetonitrile to this host is rather high, $\Delta G_{\text{trans}} = -7.7$ kJ mol^{-1} (Table 2), while nitromethane, with nearly equal molecular size but a nonlinear structure, cannot be incorporated in solid host **2** in the same conditions. Host **2** also has much less negative ΔG_{trans} values for nonlinear acetone molecules than for linear EtCN or CH_2Cl_2 with almost the same molar refraction (Table 2). On the contrary, this solid host is not selective for the pair of linear homologues MeCN/EtCN.

The observed selectivity of host **2** for the guest shape and size is in agreement with the structural scheme given in Figure 2. According to this scheme the guests occupy longer cavities in host **2** than in host **1**, while the cavity width defined by the

calixarene bowl diameter is approximately equal in these hosts. Therefore, host **2** should have lower selectivity and higher inclusion affinity for the linear molecules than host **1**. For small nonlinear guests the width of the host cavity limits the inclusion affinity, so in this case the exchange of host **2** for host **1** should have less effect. Among the guests with molar refractions in the range of 11.1–21.3 cm^3 mol^{-1}, the linear guests (MeCN, EtOH, EtCN, CH_2Cl_2, and PrCN) have much higher affinity (more negative ΔG_{trans} values) for host **2** than for host **1**. The variation of ΔG_{trans} values of nonlinear guests (Me$_2$CO, MeNO$_2$, and CHCl$_3$) at the exchange of host **2** for host **1** is much less or has the opposite sign, as in the case of nitromethane (Table 2).

The combination of eqs 5 and 10 can be used for prediction of the ability of solid host **1** to include various vaporous guests, if the guest limiting activity coefficient in toluene γ_t^{∞} is known. For example, the predicted ΔG_c values for the inclusion compounds of ethanol, pyridine, butyronitrile, and benzene with host **1** are positive (Table 2). So the guest vapor inclusion in these systems should not take place. It is in agreement with the results of our sorption experiment.

Conclusions. Obtained results show that the small differences of the host molecular structure may have a drastic effect on the structure–binding property relationships for guest inclusion by solid host. These relationships can be masked by nonequivalence of the inclusion conditions and of the guest standard states. Such effects were diminished in the present work by the approach based on the method of host saturation by guest vapors and on the use of infinitely dilute guest solution in toluene as a guest standard state. A very simple linear relationship between the guest size parameter and the free energy of guest transfer from infinitely dilute toluene solution to the saturated inclusion compound is observed for host **1**. It is a part of the essentially nonlinear V-like dependence and has a predictive ability. Its minimum corresponds to the maximal supramolecular effect of the guest inclusion and depends on the host–guest structural complementarity. The observed maximal supramolecular effect for both studied calixarenes does not exceed the estimated free energy of the cavity formation in the standard solvent (toluene).

Experimental Section

The synthesized host **1**[34] and host **2**[47] were purified from involatile impurities by multiple crystallizations from chloroform and toluene, respectively. Purification of hosts **1** and **2** from volatile impurities was performed by heating at 200 °C during 5 h in a vacuum (100 Pa). No change of the hosts' white color 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,[48] was tested by GC to be better than 99.5% (99% for nitromethane). Purified host samples (100 mg each) were equilibrated for 72 h at 298 K with initially liquid guest in hermetically closed 15-mL vials without direct contact between liquid sorbate and the solid host. The vapor sorption isotherms were determined at 298 K as the dependencies of the guest uptake on its thermodynamic activity by the static method of gas chromatographic headspace analysis. The experimental procedure and equipment used were described earlier.[6] The error of the guest activity determination is in the interval from 5% (for $P/P_0 > 0.5$) to 10% (for $P/P_0 < 0.1$). The error of the guest uptake is 5% for the host saturation level above 50%. 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 error.

Vapor Guest Inclusion by Solid Calixarenes

J. Phys. Chem. B, Vol. 106, No. 23, 2002 **5851**

The limiting activity coefficient γ_t^{∞} of dichloromethane in toluene solution was determined with a precision $\pm 10\%$ for infinitely dilute solutions (1 vol %) by the same headspace technique described earlier.[6]

References and Notes

(1) Abraham, M. H.; Platts, J. A. *J. Org. Chem.* **2001**, *66*, 3484.

(2) Lehn, J.-M. *Supramolecular Chemistry: Concepts and Perspectives*; VCH: Weinheim, Germany, 1995.

(3) Weber, E. In *Comprehensive Supramolecular Chemistry*; Atwood, J. L., Davies, J. E., MacNicol, D. D., Vogtle, F., Eds.; Elsevier Science: Oxford, U.K., 1996; Vol. 6, Chapt. 17, pp 535−592.

(4) Weber, E.; Hens, T.; Brehmer, T.; Csöregh, I. *J. Chem. Soc., Perkin Trans. 2* **2000**, 235.

(5) Gorbatchuk, V. V.; Tsifarkin, A. G.; Antipin, I. S.; Solomonov, B. N.; Konovalov, A. I. *Mendeleev Commun*. **1999**, 11.

(6) Gorbatchuk, V. V.; Tsifarkin, A. G.; Antipin, I. S.; Solomonov, B. N.; Konovalov, A. I.; Seidel, J.; Baitalov, F. *J. Chem. Soc., Perkin Trans. 2* **2000**, 2287.

(7) Brouwer, E. B.; Udachin, K. A.; Enright, G. D.; Ripmeester, J. A.; Ooms, K. J.; Halchuk, P. A. *Chem. Commun.* **2001**, 565.

(8) Fredeslund, A.; Jones, R. L.; Prausnitz, J. M. *AIChE J.* **1975**, *21*, 1086.

(9) Bishop, R. *Chem. Soc. Rev.* **1996**, *25*, 311.

(10) Weber, E.; Wierig, A.; Scobridis, K. *J. Prakt. Chem.* **1996**, *338*, 553.

(11) Weber, E.; Hens, T.; Gallardo, O.; Csöregh, I. *J. Chem. Soc., Perkin Trans. 2* **1996**, 737.

(12) Weber, E.; Hens, T.; Li, Q.; Mak, T. C. W. *Eur. J. Org. Chem.* **1999**, 1115.

(13) Schatz, J.; Schildbach, F.; Lentz, A.; Rastätter, S. *J. Chem. Soc., Perkin Trans. 2* **1998**, 75.

(14) Dickert, F. L.; Keppler, M.; Zwissler, G. K.; Obermeier, E. *Ber. Bunsen-Ges. Phys. Chem.* **1996**, *100*, 1312.

(15) Furusho, Y.; Aida, T. *Chem. Commun.* **1997**, 2205.

(16) Coetzee, A.; Nassimbeni, L. R.; Achleitner, K. *Thermochim. Acta* **1997**, *298*, 81.

(17) Dewa, T.; Endo, K.; Aoyama, Y. *J. Am. Chem. Soc.* **1998**, *120*, 8933.

(18) Beketov, K.; Weber, E.; Seidel, J.; Köhnke, K.; Makhkamov, K.; Ibragimov, B. *Chem. Commun.* **1999**, 91.

(19) Nassimbeni, L. R. In *Molecular Recognition and Inclusion*; Coleman, A. W., Ed.; Kluwer: Dordrecht, The Netherlands, 1998; pp 135−152.

(20) Brouwer, E. B.; Udachin, K. A.; Enright, G. D.; Ripmeester, J. A. *Chem. Commun*. **2000**, 1905.

(21) Ungaro, R.; Pochini, A.; Andreetti, G. D.; Sangermano, V. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1979.

(22) Toda, F.; Tanaka, K.; Miyahara, I.; Akutsu, S.; Hirotsu, K. *Chem. Commun.* **1994**, 1795.

(23) Lee, S.-O.; Harris, K. D. M. *Chem. Phys. Lett.* **1999**, *307*, 327.

(24) Kuruma, K.; Nakagawa, H.; Imakubo, T.; Kobayashi, K. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1395.

(25) Brehmer, T. H.; Weber, E.; Cano, F. H. *J. Phys. Org. Chem.* **2000**, *13*, 63.

(26) Brouwer, E. B.; Enright, G. D.; Ratcliffe, C. I.; Facey, G. A.; Ripmeester, J. A. *J. Phys. Chem. B* **1999**, *103*, 10604.

(27) Ungaro, R.; Pochini, A.; Andreetti, G. D.; Domiano, P. *J. Chem. Soc., Perkin Trans. 2* **1985**, 197.

(28) Brouwer, E. B.; Ripmeester, J. A.; Enright, G. D. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1996**, *24*, 1.

(29) Brouwer, E. B.; Enright, G. D.; Ripmeester, J. A. *J. Am. Chem. Soc.* **1997**, *119*, 5404.

(30) Brouwer, E. B.; Gougeon, R. D. M.; Hirschinger, J.; Udachin, K. A.; Harris, R. K.; Ripmeester, J. A. *Phys. Chem. Chem. Phys.* **1999**, *1*, 4043.

(31) Brouwer, E. B.; Udachin, K. A.; Enright, G. D.; Ratcliffe, C. I.; Ripmeester, J. A. *Chem. Commun.* **1998**, 587.

(32) Akdas, H.; Bringel, L.; Graf, E.; Hosseini, M. W.; Mislin, G.; Pansanel, J.; de Cian, A.; Fischer, J. *Tetrahedron Lett.* **1998**, *39*, 2311.

(33) Arduini, A.; Caciuffo, R.; Geremia, S.; Ferrero, C.; Ugozzoli, F.; Zontone, F. *Supramol. Chem.* **1998**, *10*, 125.

(34) Sone, T.; Ohba, Y.; Moriya, K.; Kumada, H.; Ito, K. *Tetrahedron* **1997**, *53*, 10689.

(35) Iki, N.; Kabuto, C.; Fukushima, T.; Kumagai, H.; Takeya, H.; Miyanari, S.; Miyashi, T.; Miyano, S. *Tetrahedron* **2000**, *56*, 1437.

(36) Gorbatchuk, V. V.; Antipin, I. S.; Tsifarkin, A. G.; Solomonov, B. N.; Konovalov, A. I. *Mendeleev Commun*. **1997**, 215.

(37) Gorbatchuk, V. V.; Tsifarkin, A. G.; Antipin, I. S.; Solomonov, B. N.; Konovalov, A. I. *J. Inclusion Phenom. Macrocyclic Chem.* **1999**, *35*, 389.

(38) Barbour, L. J.; Caira, M. R.; Nassimbeni, L. R. *J. Chem. Soc., Perkin Trans. 2* **1993**, 2321.

(39) Alcañiz-Monge, J.; Linares-Solano, A.; Rand, B. *J. Phys. Chem. B* **2001**, *105*, 7998.

(40) Solomonov, B. N.; Konovalov, A. I.; Novikov, V. B.; Vedernikov, A. N.; Borisover, M. D.; Gorbatchuk, V. V.; Antipin, I. S. *Zh. Obsch. Khim*. **1984**, *54*, 1622.

(41) Solomonov, B. N.; Konovalov, A. I. *Uspekhi Khim*. **1991**, *60*, 45.

(42) Barbour, L. J.; Bourne, S. A.; Caira, M. R.; Nassimbeni, L. R.; Weber, E.; Skobridis, K.; Wierig, A. *Supramol. Chem.* **1993**, *1*, 331.

(43) Avnir, D.; Farin, D.; Pfeifer, P. *J. Chem. Phys.* **1983**, *79*, 3566.

(44) Park, J. H.; Hussam, A.; Couasnon, P.; Fritz, D.; Carr, P. W. *Anal. Chem.* **1987**, *59*, 1970.

(45) Hildebrand, J. H.; Scott, R L. *Regular solutions*; Prentice-Hall: Englewood Cliffs, NJ, 1962.

(46) Boublik, T.; Fried, V.; Hala, E. *The Vapour Pressures of Pure Substances*; Elsevier: Amsterdam, 1973.

(47) Gutsche, C. D.; Iqbal, M.; Stewart, D. *J. Org. Chem*. **1986**, *51*, 742.

(48) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*; Pergamon Press: Oxford, U.K., 1980.