Thermal gravimetry, mass spectrometry and solid-state ^{13}C NMR spectroscopy—simple and efficient methods to characterize the inclusion behaviour of *p-tert*-butylcalix[*n*]arenes

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The solid state inclusion of various organic solvent molecules in *p-tert*-butylcalix[4]arene and *p-tert*-butylcalix[6]arene has been studied by thermal gravimetry and electron impact mass spectrometry (EI-MS). The host–guest ratio varies from 1 : 2 to 4 : 1 and the nature of included guest has been determined by EI-MS. Thermal gravimetric analysis of solvent–*p-tert*-butylcalix[*n*]arene complexes gives a qualitative order of intramolecular forces involved. Structural information obtained by cross-polarization magic angle spinning (CP-MAS) ^{13}C NMR spectroscopy is in good agreement with known data from single-crystal X-ray diffraction analysis.

Introduction

Calixarenes are a well established class of compounds in today's supramolecular chemistry. *p-tert*-Butylcalix[*n*]arene ($n = 4$, 6, 8) can be easily obtained in good yields by base catalysed cyclisation of *p-tert*-butylphenol and formaldehyde,[1] so many derivatives of calixarenes are based upon these parent compounds. Introducing functional groups like ethers,[2] esters,[3] amides,[4] thioamides[5] and ketones[6] at the lower rim of the calixarene moiety leads to host molecules with remarkable cation selectivities. In recent years examples of anion selective receptors have also been explored.[7] These developments have made calixarenes very useful platforms for ion-selective electrodes,[8] chemically modified field effect transistors (CHEMFETS)[9] or transport molecules.[10] Calix[4]arenes can adopt four discrete conformers, *i.e.* cone, partial cone, 1,2-alternate and 1,3-alternate.[1] For applications in host–guest chemistry suitable preorientation of the conformers is important. The cone conformation is especially useful for the complexation of neutral organic guests. Many complexes of calixarenes with solvent molecules have been studied by X-ray diffraction methods in the solid state[11] and by solvent-induced chemical shift measurements by NMR spectroscopy in solution.[12] Since X-ray analysis of calixarene–solvent clathrates is sometimes difficult and suitable single crystals are often difficult to obtain, we were looking for alternative methods to determine key features of host–guest interactions between calixarenes and neutral molecules,[13] namely stoichiometry, binding strength and structure. In this paper we will describe a combination of thermogravimetric analysis (TGA),[14] mass spectrometry, and CP-MAS ^{13}C NMR spectroscopy[15] applicable for this purpose.

Results and discussion

Thermal gravimetric analysis

Thermal gravimetric analysis (TGA) is a simple and effective method for the investigation of inclusion phenomena. It is especially convenient for small, volatile organic guest molecules. A typical curve obtained by TGA of *p-tert*-butylcalix[4]arene–solvent complexes is shown in Fig. 1. From the loss of weight Δm (%), the corresponding host–guest ratio can be calculated easily. Furthermore ΔT_{bp}, the difference between T_1 and the boiling point of the solvent, represents a qualitative measure for the binding strength of the guest molecule in the crystal lattice. All thermogravimetric results are summarized in Table 1.

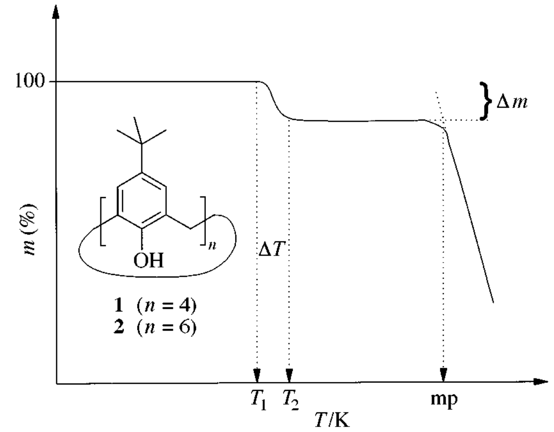

Fig. 1 Typical thermogravimetric analysis of a *p-tert*-butylcalix[*n*]-arene–solvent clathrate

Thermogravimetric methods were combined with information from electron impact mass spectrometry (EI-MS) to determine the nature of included solvent molecules. All intercalary guests were identified and impurities by other solvent molecules could be excluded by this method. In all cases only one type of guest molecule could be detected. *p-tert*-Butylcalix[4]arene **1** forms complexes with aromatic and CH-acidic guest molecules in the solid state. The sequence of ΔT_{bp} values implies a qualitative relationship of the binding strength with the shape and the CH-acidity of the included guest. Carbon disulfide is bound very tightly in the solid state, as indicated by a very high ΔT_{bp} of 219 °C, the highest ΔT_{bp} value observed. The interactions of CS_2 with **1** are much stronger than those of all other solvents examined. This is surprising since it is known that CH–π interactions are decisive for the complexation of non-polar guests in the hydrophobic calixarene cavity. The nature of the intramolecular forces involved in the strong binding of CS_2 are not yet known. The observed host–guest ratios (n : 1) can be rationalised by the existence of complexed and empty *p-tert*-butylcalix[4]arene. This is in good agreement with the observation that the host–guest ratio can be influenced by various conditions during crystallisation and drying, but usually n : 1 host–guest ratios like 1 : 1, 2 : 1, or 3 : 1 were obtained. THF as a guest gives a 3 : 1 ratio which does not fit into this

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Table 1 Results of the thermogravimetric analysis of solvent complexes of *p-tert*-butylcalix[4]arene **1** and *p-tert*-butylcalix[6]arene **2**

Host	Guest	Δm (%)	T_1/°C	ΔT^a/°C	$\Delta T_{bp}{}^b$/°C	Mp/°C	Host–guest ratio
1	toluene	10.0	139	12	28	347	1:1
	m-xylene	7.6	189	75	49	347	2:1
	o-xylene	7.6	231	38	91	349	2:1
	THF	25.1	188	29	121	337	1:3
	$CHCl_3$	16.0	186	29	124	341	1:1
	acetone	4.0	186	40	130	328	2:1
	CH_2Cl_2	12.6	255	28	215	346	1:1
	CS_2	3.0	265	12	219	351	4:1
2	toluene	6.0	117	28	6	405	3:2
	m-xylene	7.5	162	158	22	417	4:3
	THF	12.0	111	123	44	393	1:2
	CH_2Cl_2	13.5	373	20	333	393	1:2
	CS_2	2.0		continuous		391	4:1

[a] $\Delta T = T_2 - T_1$ (see Fig. 1). [b] $\Delta T_{bp} = T_1 - T_{bp}$ (T_{bp} is the boiling point of the solvent).

series but is in agreement with results from the solid-state NMR spectroscopy (*vide infra*).

p-tert-Butylcalix[6]arene **2** is not as suitable as **1** as a host molecule for small organic solvent molecules. The ΔT_{bp} values are usually lower than those obtained for *p-tert*-butylcalix[4]arene and the host–guest ratios cannot be explained by the sole existence of a combination of complexed and empty host **2**. This indicates a non-specific complexation behaviour of solvent molecules on interstitial positions in the crystal lattice. All these findings are in agreement with data from similar clathrates which have already been identified by X-ray diffraction analysis.[11]

^{13}C CP-MAS NMR spectroscopy

Thermal gravimetric analysis and mass spectrometry give only a rough idea of the inclusion of small guests in calixarene cavities and provide little information on the nature of binding in these ensembles. We felt that ^{13}C CP-MAS NMR spectrometry would be very useful for this purpose since it does not require single crystals.

Fig. 2 shows ^{13}C CP-MAS NMR spectra of empty *p-tert*-butylcalix[4]arene (*a*) and a chloroform complex of **1** (*b*) as a typical example of a clathrate. Surprisingly the number of signals decreases with solvent complexation. Empty *p-tert*-butylcalix[4]arene must have a lower symmetry than the complexed host. Structural information can be obtained from a comparison of chemical shifts of included solvent molecules in the solid state and in solution. Table 2 summarizes selected data for this approach.

The upfield shift (CIS = 6.2 ppm) relative to solution data[16] of the absorption assigned to the methyl carbon of included toluene is in good agreement with another CP-MAS study of this clathrate.[17] This shift is ascribed to the formation of a calixarene *endo*-complex with the methyl carbon pointing inside the cavity. In analogy, small upfield shifts can also be found for CS_2, chloroform, acetone and THF (Table 2, entries 2–5). In these cases a calixarene–solvent *endo*-complex seems likely and in fact this could be confirmed by X-ray diffraction analysis for the inclusion of carbon disulfide. The X-ray analysis indicates an inclusion of CS_2 deep in the cavity of the calixarene host. The complex formed exhibits a high symmetry (C_4) as well as a slight distortion of the enclosed guest. Therefore the CIS can be explained by ring current effects of adjacent phenyl rings of the host and the observed bond alternance of the guest upon complexation.[18]

The spectra of the THF–*p-tert*-butylcalix[4]arene clathrate show many other signals for the included solvent molecule in addition to those given in Table 2. The deviation of the latter peaks from those of pure THF is less than 0.2 ppm. Taking into account that the calix[4]arene cavity is not big enough to host three THF molecules this observation can be explained as follows. One THF sits inside the cavity with the oxygen atom pointing outside, as indicated by the larger upfield shift (Δ = 1.8 ppm) for C-3. Two solvent molecules must be located more or less undistorted between the *p-tert*-butylcalix[4]arenes on interstitial positions.

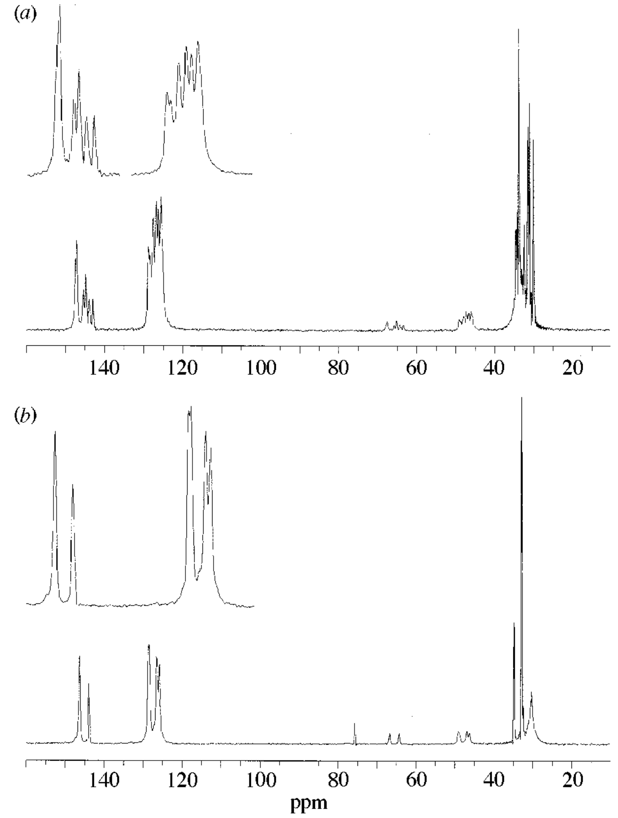

Fig. 2 ^{13}C CP-MAS NMR spectra of empty **1** (*a*) and its complex with chloroform (*b*)

Conclusion

The combination of TGA, MS and solid-state NMR spectroscopy is a powerful tool to gather qualitative and quantitative data for the inclusion phenomena of non-polar guests in calixarene hosts. In the solid state *p-tert*-butylcalix[4]arene forms stable complexes with small organic guests and the resulting host–guest ratios can be easily determined by TGA. The very strong binding of CS_2 inside the cavity is not fully understood yet. Structural ideas based on thermal gravimetric analysis were supported by solid-state NMR. In the case of CS_2, toluene, chloroform and acetone *endo* calixarene complexation is likely. The 3:1 THF–**1** complex seems to have two THF molecules located on interstitial positions and one inside the

Table 2 Selected CP-MAS ^{13}C NMR data of *p-tert*-butylcalix[4]arene **1**–solvent complexes

			δ_C		
Entry	Guest	Assignment	Solid	Solution	CIS[a]/ppm
1	toluene[b]	aromatic-*C*	138.8	137.7	1.1
		Ph–CH_3	15.2	21.4	−6.2
2	CS_2	CS_2	190.1	192.3	−2.2
3	$CHCl_3$	$CHCl_3$	75.7	77.0	−1.3
4	acetone	H_3C–*C*O	201.9	206.5	−4.6
		H_3C–CO	27.5	29.8	−2.3
5	THF	O–CH_2–CH_2	67.5	67.7	−0.2
		O–CH_2–CH_2	66.8	67.7	−0.9
		O–CH_2–CH_2	23.7	25.5	−1.8

[a] CIS = Complexation induced chemical shift = $\Delta\delta = \delta$ (solid state) − δ (solution). [b] Other signals were hidden under *p-tert*-butylcalix[4]arene absorptions.

cavity, the oxygen atom pointing outside. As expected, *p-tert*-butylcalix[6]arene does not form simple *endo* complexes.

The characterisation of clathrates of *p-tert*-butylcalix[6]arene and *p-tert*-butylcalix[8]arene with CP-MAS NMR, IR and raman spectroscopy, as well as molecular modeling methods, is currently under investigation. Furthermore, detailed studies of the CS_2–*p-tert*-butylcalix[4]arene complex with a focus on the nature of the strong binding are also further research goals.[18]

Experimental

Calixarenes were prepared by procedures known in the literature.[19] Complexes of calixarenes with solvents were prepared by dissolution of the host molecule in the solvent or solvent mixture. Crystals of the host–guest clathrates were obtained by slow evaporation of excess solvent and were air dried. Empty *p-tert*-butylcalix[*n*]arenes were prepared by heating a toluene complex prepared as described above at 180 °C and 10^{-3} mbar for four days. Thermogravimetric analysis was performed under nitrogen on a Perkin-Elmer 7 series thermal analysis system. The heating rate was 10 °C min^{-1} in every case. EI-MS were recorded with a Varian Mat 711 or SSQ 7000 (Finnigan Mat). CP-MAS ^{13}C NMR spectroscopy was performed on an Bruker DSX 400 (100.6 MHz) equipped with a 4 mm MAS probehead. The crystalline powder samples were loaded in boronitride rotors and spun at 8 000 Hz at 293 K. The spectra were referenced externally to a standard glycine sample.

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